Sugar-sweetened beverages provide little nutritional value and have also been linked to increased coronary heart disease [de Koning L et al. *Circulation* 2012], gout [Choi HK, Curhan G. *BMJ* 2008], gallstone disease, kidney disease, fatty liver, decreased bone mineral density, and dental caries.

Visceral Adipose Tissue and Cardiometabolic Risk

Written by Rita Buckley

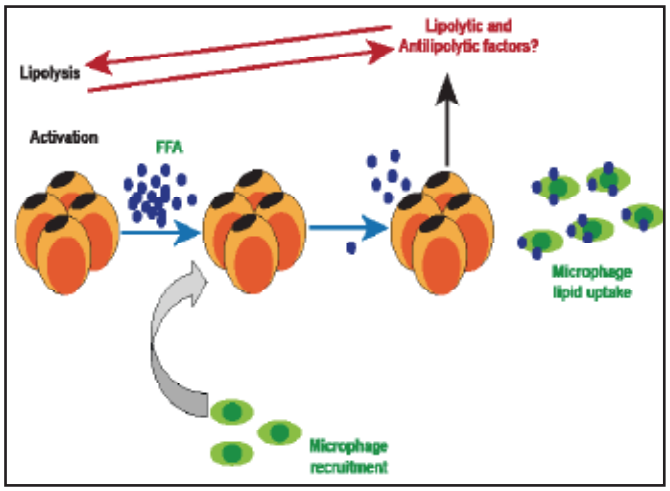
Abdominal obesity is a marker of dysfunctional adipose tissue [Després JP, Lemieux I. *Nature* 2006]. André Tchernof, PhD, Université Laval, Québec City, Québec, Canada, provided an overview of alterations in visceral and subcutaneous adipose tissue function in individuals with visceral obesity, with an emphasis on adipose tissue metabolism. He also discussed fat cell size, adipocyte hypertrophy and storage capacity; adipose tissue lipolysis; excess substrate and inflammation; mesenteric adipose tissue; and abdominal fat in severe obesity.

In a study of regional differences in adipocyte metabolism and visceral versus subcutaneous parameters across adiposity values in women, Tchernof et al. [*Diabetes* 2006] found that compared with omental adipocytes, subcutaneous adipocytes are larger, have higher lipoprotein lipase activity, and are more lipolytic on an absolute basis—factors that may reflect higher fat storage capacity. They also demonstrated that overall and visceral obesity had only minor effects on regional differences in adipose tissue metabolism.

Veilleux et al. [*Diabetes* 2011] reported that women characterized by omental adipocyte hypertrophy presented a deleterious lipid profile compared with those characterized by omental hyperplasia. Findings indicate that a 10% enlargement of omental adipocytes increased the risk of hypertriglyceridemia more than 4-fold, whereas enlarged subcutaneous adipocytes failed to significantly alter the risk of hypertriglyceridemia.

Obesity engenders a complex immune response in which macrophage accumulation in adipose tissue is a characteristic feature [Kosteli A et al. *J Clin Invest* 2010]. In women, visceral fat accumulation is an indicator of adipose tissue macrophage infiltration, and it is the best correlate of macrophage infiltration in both subcutaneous and fat compartments of lean to obese women [Michaud A et al. *Metabolism* 2012]. According to Kosteli et al. [*J Clin Inves* 2010] excess lipolysis could be one of the causal factors for adipose tissue macrophage infiltration (Figure 1).

Figure 1. Lipolysis, Macrophage Infiltration, and Inflammation.



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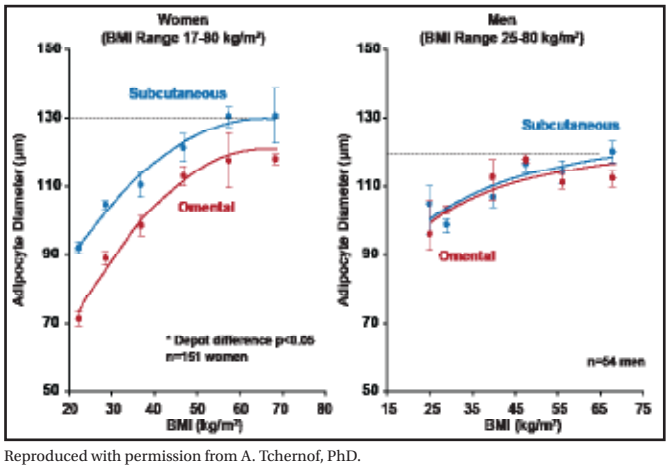
Regarding the correlations of fat cell size with obesity and fat distribution, all adiposity measures, including body mass index (BMI) and total body fat mass, as well as adipose tissue areas measured by computed tomography, are strongly and positively correlated with subcutaneous and omental adipocyte diameter (Figure 2) [Tchernof A et al. *Diabetes* 2006].

Figure 2. Adipocyte Diameter as a Function of BMI in Men and Women.



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Prof. Tchernof noted that in the lean to moderately obese range, visceral adipocyte hypertrophy is clearly related to dyslipidemia, independent of total adiposity and body fat

distribution. However, the fact that fat cell size reaches a plateau in individuals with severe obesity suggests it may not predict metabolic complications in this population. This conclusion coincides with reports from Lemieux et al. [*Diabetes Care* 2006] and Drapeau et al. [*Obes Surg* 2007] that cast doubt on the utility of waist circumference to predict metabolic abnormalities and complications in severely obese men and women.

Prof. Tchernof concluded the following:

- Visceral adipose tissue expands mostly through adipocyte hypertrophy and quickly becomes inefficient in storing excess lipids.
- Limited adipose tissue lipid storage capacity has emerged as a critical determinant of cardiometabolic alterations.
- Lipolytic responsiveness of visceral adipocytes to positive stimuli is increased in visceral obesity, but most studies support a reduced inhibitory response to insulin in visceral adipocytes compared with subcutaneous adipocytes.
- Visceral obesity and high lipolytic rates are closely related to macrophage infiltration and inflammation.
- The pathophysiology of metabolic disorders in severe obesity may no longer be related solely to excess visceral fat and/or visceral adipocyte hypertrophy.

Mechanisms and Consequences of Ectopic Fat Accumulation

Written by Rita Buckley

Ectopic fat is defined as storage of triglycerides in tissues other than adipose tissue, such as the liver, skeletal muscle, heart, and pancreas [Snel M et al. *Int J Endocrinol* 2012]. Marja-Riitta Taskinen, MD, University of Helsinki, Helsinki, Finland, discussed ectopic fat accumulation and cardiometabolic risk.

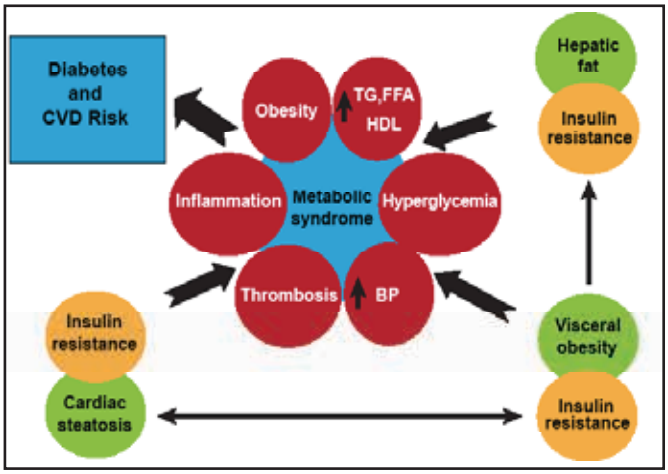
Excess body adiposity, especially abdominal obesity and ectopic fat accumulation, is a key risk factor in the development of a number of chronic diseases [Thomas EL et al. *Nutr Res Rev* 2012]. It can interfere with cellular functions, and, hence, organ functions, and is associated with insulin resistance [Snel M et al. *Int J Endocrinol* 2012].

Adipose tissue dysfunction is largely characterized by large adipocytes and secretion of adipokines with a proinflammatory profile, ultimately leading to ectopic fat deposition (among others) [Blüher M. *Exp Clin Endocrinol Diabetes* 2009].

Although visceral fat accounts for only 10% to 15% of ectopic fat accumulation, 82% to 97% is stored as subcutaneous fat. Other major sites of ectopic fat accumulation include the heart (0% to 3%), the liver (5% to 30%), and skeletal muscle fat (10% to 15%).

Ectopic fat is an important predictor of metabolic (in particular, insulin resistance) and cardiovascular disease (CVD), carrying more risk than general fat accumulation. Recent studies have shown a link between ectopic fat accumulation, as cardiac (epicardial or intramyocardial fat) and/or visceral and/or hepatic fat, and development of atherosclerosis, coronary heart disease, and hypertension (Figure 1) [Gastaldelli A, Basta G. *Nutr Metab Cardiovasc Dis* 2010].

Figure 1. Ectopic Fat and Cardiometabolic Risk.



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According to Dr. Taskinen, fatty liver produces a plethora of risk factors for CVD. The mediators that may link it and CVD include glucose, very low-density lipoprotein (VLDL), high-density lipoprotein (HDL), alanine aminotransferase and aspartate aminotransferase, fibrinogen, factor VII and plasminogen activator inhibitor-1, angiotensinogen, C-reactive protein and serum amyloid A, and tumor necrosis factor-α and interleukin-6. The atherogenic lipoprotein triad (increased large VLDL, increased small dense LDL, and decreased HDL-C) and hepatic steatosis lead to an increased risk of coronary artery disease.

Although obesity increases the risk of CVD and premature death, not all obese people (20% to 30%) develop the metabolic abnormalities associated with