New and future drugs that target intra-abdominal fat include second-generation peripheral cannabinoid 1 antagonists, 11 β hydroxysteroid dehydrogenase inhibitor, glucagon-like peptide (GLP)-1 analogs/mimetics, sodium glucose cotransporter (SGLT)-2 inhibitors, and leptin-pramlintide combination.

In an investigation of the effects of GLP-1 analog liraglutide, Inoue et al. [*Cardiovasc Diabetol* 2011] found that liraglutide significantly reduced estimated visceral fat compared with no significant change before medication induction ($p<0.005$). A study on dapagliflozin, a SGLT-2 inhibitor, showed a decrease in total body weight at Week 24, predominantly by reducing fat mass, VAT, and subcutaneous adipose tissue in patients with type 2 diabetes inadequately controlled by metformin [Bolinder J et al. *J Clin Endocrinol Metab* 2012].

Resolution of type 2 diabetes is known to be an additional benefit of surgical treatment for severe obesity [Pories WJ et al. *Ann Surg* 1995], with glycemic control often occurring long before significant weight loss [Mingrone G et al. *Diabetologia* 1997]. Buchwald et al. [*JAMA* 2004] reported 98.9% resolution of diabetes with the biliopancreatic diversion or duodenal switch technique and 83.7% for gastric bypass. Data from a subanalysis of the European Hepatic and Adipose Tissue and Functions in the Metabolic Syndrome project found decreases of 25.4±5.9% in weight (kg) and 50±8% in VAT (cm) after bariatric surgery (Table 1) [Van Gaal LJ et al. Subanalysis of EU HEPADIP Project].

Table 1. Visceral Fat Loss After Weight-Loss Surgery.

	Baseline	Follow-up	Change	% Change
Weight (kg) n=20	132.3±38.1	99.4±33.0	-32.9±10.1	-25.4±5.9
VAT (cm^2) n=19	206.0±101.0	120.0±72.0	-100.0±46.0	-50.0±8.0

VAT=visceral adipose tissue.

Sugar-Sweetened Beverages Linked to Multiple Health Risks

Written by Rita Buckley

Limiting intake of sugar-sweetened beverages is one simple change that could have a measurable impact on weight control and the risk of diabetes and other metabolic diseases in the general population, according to Frank Hu, MD, PhD, Harvard School of Public Health, Harvard Medical School, Boston, Massachusetts, USA. Dr. Hu presented data on sugar-sweetened beverages and their impact on public health.

Dr. Hu said sugar-sweetened beverages, such as sodas, fruit drinks, energy drinks, and sports drinks, are as common and familiar as they are dangerous to our health, and adults are as vulnerable as children. Between 1965 and 2002, per capita consumption of daily calories from sugar-sweetened beverages increased steadily in adults and children, while consumption of milk declined [Duffey KJ, Popkin BM. *Obesity* 2007]. By 2005 to 2006, daily consumption of sugar-sweetened beverages was approximately 172 kcal for children and 175 kcal for adults [Brownell KD et al. *N Engl J Med* 2009]. Global trends in the total volume of carbonated soft drinks consumed between 2002 and 2007 show a similar pattern [Global soft drinks: Finding value in carbonates. *Euromonitor* 2008].

In China, rising consumption of sugar-sweetened beverages [Kleiman S et al. *Obes Rev* 2012] mirrors an increased incidence of diabetes [Pan XR et al. *Diabetes Care* 1997; Gu D et al. *Diabetologia* 2003; Yang W et al. *N Engl J Med* 2010]. Currently, more than 60% of the world's diabetic population is in Asia [Ramachandran A et al. *World J Diabetes* 2012].

Strong evidence backs claims that sugar-sweetened beverages contribute to weight gain. In an analysis of 3 separate US cohorts that included 120,877 men and women, Mozaffarian et al. [*N Engl J Med* 2011] found that increased daily servings of sugar-sweetened beverages were among the individual dietary components most strongly associated with 4-year weight gain.

Temporal patterns over the past 3 to 4 decades have shown a close parallel between the rise in sugar intake and the incidence of global obesity and type 2 diabetes. These patterns, combined with observational and experimental data, suggest causality between the intake of sugar-sweetened beverages and type 2 diabetes [Malik VS, Hu FB. *Curr Diab Rep* 2012].

Other adverse cardiometabolic conditions have been attributed to consumption of caloric beverages. In the Coronary Artery Risk Development in Young Adults [CARDIA; NCT00005130] study, higher consumption of sugar-sweetened drinks (across quartiles) was associated with increased risk of high waist circumference (p for trend <0.001), cholesterol (p for trend=0.018), triglycerides (p for trend=0.33), and hypertension (p for trend=0.023) [Duffey KJ et al. *Am J Clin Nutr* 2010].

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

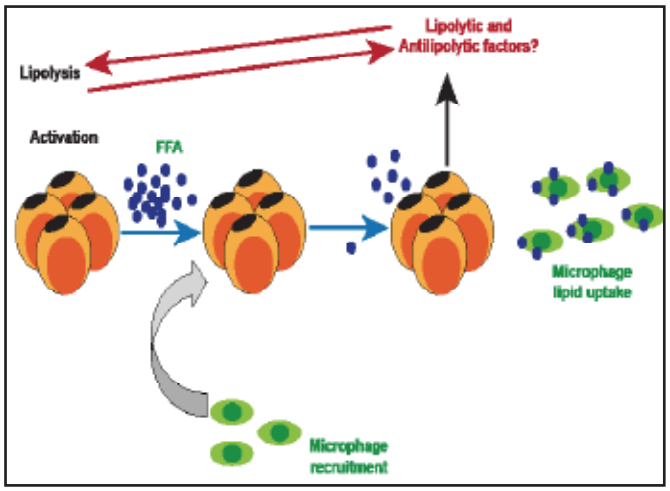
Abdominal obesity is a marker of dysfunctional adipose tissue [Després JP, Lemieux I. *Nature* 2006]. André Tchernof, PhD, Université Laval, Québec City, Québec, Canada, provided an overview of alterations in visceral and subcutaneous adipose tissue function in individuals with visceral obesity, with 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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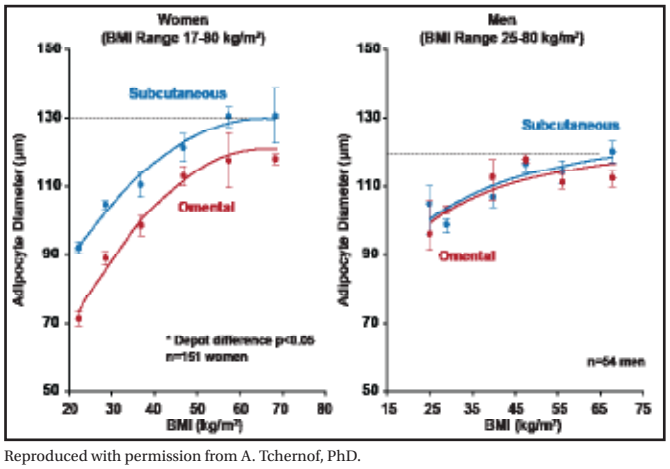
Regarding the correlations of fat cell size with obesity and fat distribution, all adiposity measures, including body mass index (BMI) and total body fat mass, as well as adipose tissue areas measured by computed tomography, are strongly and positively correlated with subcutaneous and omental adipocyte 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