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VitalLongevity™

Logo: Life's blood flows through the hourglass; the stopcock represents the alteration of aging and disease as biomedical research progresses.

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Abdominal Obesity

How We Get Fat

Although in the past obesity was considered a sign of prosperity and good fortune, it is now recognized that obesity comes with a heavy price in terms of health hazards.

Also in the past, it was assumed that all obesity came from either over-consumption of food or from metabolic defects. Today, additional causes of obesity are recognized. For example, being born small for gestational age portends obesity in adult life. Certain drugs or toxins act as obesogens, that is, promote fat deposition. Diabetes drugs like the glitazones (Avandia® and Actos®), and corticosteroids, used for the treatment of inflammatory conditions including autoimmune diseases, can cause substantial weight gain. More recently, environmental toxins such as tin-based compounds used as antifouling agents on ships and as plasticizers have been shown to promote the formation of fat depots in animal models. Because these compounds are environmentally widespread, although their use has been curtailed in recent years, the role of these persistent compounds in the current obesity plague is being investigated. How many other of the numerous environmental toxins have similar effects remains to be studied. Surprisingly, even an infectious cause of obesity has been suggested by studies linking adenovirus-36 with being overweight. And finally, the kinds and relative abundance of various microbes colonizing the lower intestine (gut microflora) can aid and abet the extraction of calories from food, thereby tipping energy balance enough to cause slow but insidious weight gain

Kinds of Obesity

Obesity can be divided into two principal types: 1) central or visceral, characterized by fat depots surrounding organs deep in the abdominal area, and 2) subcutaneous (SC), superficial fat depots under the skin which can occur anywhere including the abdomen (Figure 1). Although both contain numerous adipocytes, fat cells laden with fat droplets, they are biochemically very different. Subcutaneous depots provide for long-term energy storage

whereas the visceral depot provides short-term storage and allows rapid access to calories for processing by the liver. Since visceral obesity is more dangerous from a health standpoint, the rest of this report will be confined to this type of fat.

Distribution of fat can vary widely even among persons with the same amount of total body fat. However, a waist circumference exceeding 35 inches in women or 40 in men provides a fairly good indication of substantial amounts of visceral fat.

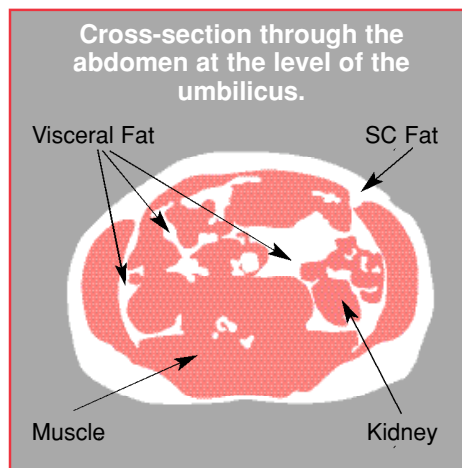


Figure 1.

Both environmental and genetic factors influence how much visceral fat an individual produces. Men and postmenopausal women have greater propensity to store visceral fat. Smoking, physical inactivity, excessive alcohol intake, and stress compound the problem. On the other hand, moderate alcohol consumption may inhibit the development of visceral fat, and the glitazones, although tending to increase total body fat, redirect fat from the visceral to the subcutaneous depot.

Negative Consequences

A partial list of problems either caused or made worse by visceral obesity includes: fatty liver disease, gall stones, sleep apnea, psoriasis, chronic heart failure, cognitive decline and dementia, prostate cancer (probable), and post-menopausal breast cancer, as well as the cluster of risk factors comprising Metabolic Syndrome and its associated morbidity and mortality.

Metabolic Syndrome

Abdominal obesity lies at the heart of the Metabolic Syndrome, a state of profound insulin resistance that carries increased risk of both diabetes and cardiovascular disease. One reason visceral fat is so detrimental is because it functions much like an endocrine organ capable of secreting a wide variety of metabolic and hormonal products that regulate or interfere with other organ functions. To make matters worse, blood drainage from visceral fat occurs through the portal venous system that delivers products directly into the liver and pancreas. For example, visceral adipocytes readily undergo lipolysis (fat breakdown) releasing fatty acids in the process and causing a high fatty acid concentration in the liver. This both impedes insulin activity and stimulates the liver to

produce glucose and fat, resulting in the characteristically high fasting glucose and triglyceride levels of Metabolic Syndrome.

Hypertension

Excess abdominal fat both predicts future hypertension and contributes to existing high blood pressure, another defining characteristic of Metabolic Syndrome, and it does so even in individuals who do not weigh enough to be considered obese.

Visceral fat cells produce and release more of a precursor molecule of the potent blood pressure increasing vasoconstrictor angiotensin II than do subcutaneous fat cells. In addition, visceral obesity increases intra-abdominal pressure, which can affect the kidneys resulting in greater sympathetic activity (the flight or fright arm of the nervous system) and higher blood pressure.

Inflammation

A feature of adipocytes is to secrete chemokines, circulating molecules that affect white blood cells. One such chemokine—monocyte/macrophage chemoattractant protein -1 (MCP-1)—attracts macrophages, a type of white blood cell, into visceral fat. Thus, as obesity increases macrophages infiltrate the fat depot until they become a significant fraction of the total numbers of cells present. These resident macrophages secrete many of the cytokines and hormones (Table 1) associated with obesity-induced inflammation including the eotaxins-1 and -2 whose concentrations correlate with body mass index (BMI), waist-hip ratio, and the inflammatory biomarker C-reactive protein (CRP). While the relative contribution of the various cell types present in visceral fat to the secretion of these inflammatory precursors remains unclear, it is quite certain that obesity generates a chronic, mild inflammatory state in the body. Chronic inflammation promotes atherosclerotic changes in blood vessels and

cardiovascular disease, increases risk of diabetes and pancreatic cancer, and plays an important role in a variety of autoimmune disorders like rheumatoid arthritis.

Among the other compounds secreted from visceral fat that promote diverse undesirable effects are resistin (promotes insulin resistance), plasminogen activator inhibitor-1 (PAI-1) (raises risk of blood clots), tumor necrosis factor-alpha (TNF- α) (one of the most potent pro-inflammatory compounds), and acute phase serum

amyloid A (ASAA). ASAA, produced in adipocytes and secreted into the blood, induces inflammatory responses and thus serves as a molecular link between obesity and its comorbidities. It can be reduced by major weight loss or by glitazones. Thus, visceral fat can be considered a true endocrine organ and not just inert tissue.

Some of the many secretory products of visceral fat.

Name	Site	Properties
Adipokines		
ASAA	Adipocytes	Proinflammatory; lipolytic; increased in obesity; decreased by weight loss or glitazones
Resistin	Adipocytes + Macrophages	Causes insulin resistance; 400% higher in visceral fat vs. subcutaneous fat; high in human visceral fat
PAI-1	Adipocytes	Affects blood clotting and lysis
TNF- α	Adipocytes + Macrophages	Major pro-inflammatory adipokine systemically, but protective within the fat mass
Chemokines		
MCP-1	Adipocytes	Attracts macrophages into visceral fat
Eotaxin -1, -2	Macrophages	Specific chemoattractant for eosinophils

Table 1.

Fighting Fat

One piece of good news in all of this is that visceral fat, relatively speaking, is somewhat labile. Generally, one does not need to shed all excess weight to reduce this depot. Visceral fat tends to go early in a diet and exercise program so that a loss of as little as 7% to 10% of body weight can result in marked improvement in metabolism.

Supplementation with 50 mg of DHEA daily (see VitaLongevity December 2005) can help decrease visceral obesity and increase insulin sensitivity. Several other supplements are worth trying in conjunction with diet and exercise, which are still the best ways to combat abdominal obesity. N-acetyl cysteine (NAC) (600 mg/day) appears to have some visceral fat-specific fighting ability by inhibiting the formation of new fat cells. Conjugated linoleic acid (CLA) (3 gm/day), a component of beef and milk, enhances burning of fat while at the same time inhibiting fat deposition. The percentage of CLA in dairy products keep dropping due to changing feeding patterns of livestock and most Americans get inadequate amounts in their diet.

Information for Donors

The Orentreich Foundation for the Advancement of Science, Inc., was founded in 1961. OFAS is a non-profit institution dedicated to biomedical research to prevent, halt, or reverse those disorders that decrease the quality or length of life. It is duly registered with the US Internal Revenue Service as an Operating Private Foundation under Section 4942(j)(3).

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