

The Science on Fat Loss: Lipolysis and Fat Burning

Written by Dan Gwartney, M.D.

Fat Attack

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It is peak time for making New Year's resolutions. As it has been every year, losing weight sits on or near the top of the list for the majority of people. Given the economic conditions, it may have taken a back seat to financial goals (save more, pay off debt, eat at home, etc.)— but it remains a perennial favorite.

Of course, health clubs and weight loss centers depend upon this annual parade of lemming-like couch potatoes, with the month of January accounting for nearly 50 percent of new membership enrollments in established clubs.¹ Invariably, the advice of eat fewer calories, perform cardiovascular exercise to burn fat, and lift weights to build muscle (and bone if you are a woman) is given in an office furnished with a Steelcase[®] desk, flat screen monitor, and those blue fabric chairs.

The charming early-20s trainer, upbeat music, as well as the digital flashiness and iPod[®] compatibility of the machines are designed to motivate and inspire members to meet their goals. Unfortunately, fat loss does not occur because one wishes it will. Fat loss is the result of a series of chemical reactions.

Fat Storage

Before talking about fat loss, it may help to understand fat storage. Ask most people where fat is stored and they will grab the skin around the navel as though there is a Tupperware[®]

container of Crisco[®]

belted around the belly. In part, this is true at the cellular level. Body fat is thought of by many as being unsightly lumps and bumps; in the U.S., this often lowers one's social standing. To the body, fat is wealth, as it represents energy reserves that will allow a person to withstand days to months of famine; it also allows for long periods of low-to-moderate activity between meals. To the mitochondria (the power factories of living tissue), stored fat is like cash in the bank.

Unlike wealth, the display of a fortune in body fat is neither envied nor advantageous as is the opulence of financial wealth. Let's face reality; people turn green with envy when they see a multi-millionaire being chauffeured in a Maybach 62 S. Conversely, very few in the U.S. demonstrated the same response when they see the body of a person with a 10-year savings account of adipose (fat). A million calories of stored fat is not as wonderful as a million dollars.

Of course, millionaires don't carry their cash on them in bundles of \$10 bills. Ironically, one gram of fat has nine calories and a million calories of fat would weigh 244 pounds. A million dollars in \$10 bills (as close as one can get to a \$9 bill) would weigh a little more than 220; coincidentally, a \$10 bill also weighs a gram.

Despite the abhorrence most have towards morbid obesity, and the epidemic of increased deaths and disease that accompany this degree of fat accumulation, the human body is still designed to absorb and store as many calories as possible. This seems inappropriate in today's society here in the U.S., but traveling to many parts of the world will confirm that starvation and famine remain common. Even in the venerable U.S., food rationing and soup kitchens were a national way of life 60-80 years ago. Global genetic adaptation (evolution) to discourage rather than promote the storage of fat is unlikely to occur for many, many generations, if ever.

Body fat is primarily stored in specialized cells called white adipose tissue (WAT).²

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Folklore suggested that people are born with a set number of fat cells and individuals are stuck with those cells for life; the same was also said of brain cells. Medical science has proven this is not true. Fat cells arise from a self-replenishing pool of precursor stem cells—the same precursor cells that can also turn into skeletal muscle.

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Contrary to another folktale, even though muscle and fat arise from the same pre-cursor, muscle does not and cannot turn into fat when a person stops exercising. Instead, muscle atrophies (shrinks or wastes away) if a person stops training and fat stores increase due to the decrease in physical activity, often in the setting of overeating.

Calories are consumed in the diet. The focus used to be on dietary fat as being the source of body fat. It made sense to the general public and marketing agencies across the nation; if fat is being stored, then it must come from fat that is being consumed. Then the Atkins Diet diverted blame onto carbohydrates and their wicked habit of raising insulin, which in turn promoted fat storage. Now, the public is back to not knowing what to think.

Breaking it Down

Fat is a generic term—it can be a relative comparison; refer to either tri-acyl-glycerides or specific fatty acids; or if spelled P-H-A-T describe a particularly attractive woman. For the purposes of this article, the term fat refers to tri-acyl-glycerides (TAG), a chemical class of molecules defined as three fatty acids bonded to a common glycerol atom. To make it an easy visual, hold your hand out and extend only three fingers (pointer, middle, and ring fingers). The hand is glycerol and each finger represents a fatty acid. There are many different fatty acids in the diet and in stored fat. Many are familiar with the terms saturated and unsaturated fat (fatty acids). Omega-3 fatty acids are a subset of unsaturated fatty acids, as is oleic acid—a monounsaturated fat rich in olive oil. The differentiation between saturated and unsaturated is not important for the purposes of this discussion.

When dietary fat is consumed in a meal, it is commonly in the form of a TAG. TAG will form big globules in the watery environment of the stomach and intestines; drop some cooking oil into a bowl of water for a demonstration. To break up these globules, the gallbladder secretes bile acids, which make the TAG form smaller globules so that enzymes can attack. Lipases are enzymes that break down TAG to 2-monoglycerol and fatty acids.⁴ These digested fragments are taken up or absorbed in the small intestine and re-formed into TAG, packaged with cholesterol in lipoproteins, and transported through lymphatic ducts before entering the bloodstream. Some free fatty acids and TAG directly enter the bloodstream and can be taken up by exercising muscle and other active tissue (e.g., heart) for energy or to be stored in those

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tissues as an immediate source of long-term energy.

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TAG are packaged in the liver for transport to adipocytes (fat cells), where they are again broken down into fatty acids by a fat-cell bound enzyme called lipoprotein lipase (LPL).⁶ High concentrations of insulin increase the number of LPL in fat cells, increasing fat uptake for storage rather than as energy for muscle, heart, etc.

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The fatty acids released by LPL can circulate in the blood or be taken up by the fat cell and converted once again into TAG which is stored in a fat globule in the fat cell. If a person eats a calorie-appropriate diet, the process is well-balanced, providing for immediate and long-term energy needs while avoiding excess body fat accumulation.

That may be everything and more than most wish to know about how fat gets from the lips to the hips. What is the primary concern for most is how to shed the saddlebags.

Losing It

Fat loss occurs when the fat cells are stimulated by certain hormones (growth hormone, glucagon, ACTH, etc).⁸ A common pathway stimulates the activation of several enzymes, as well as “opening doors” in the fat globule so the enzymes can deconstruct the TAG into glycerol and free fatty acids.

For some time, the scientific model held that a single enzyme was primarily responsible for most of fat breakdown and release. Further, the thought was that the freed fatty acids either fled the bondages of TAG incarceration or were re-incorporated into TAG that was confined behind the prison-like membrane of the intracellular fat globule (possibly charged with additional time for a failed escape attempt).

However— and this will probably only thrill the biology geeks for the most part— a fuller

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understanding of the processes relating to the release and breakdown of TAG stored in the intracellular fat globule of the adipocyte (fat cell) has recently been gained through ultra-fine research.⁹ Scientists have determined that stored fat is brought to the surface of the fat globule inside the cell when gateway proteins are phosphorylated (turned on).¹⁰ There, a newly-discovered/understood enzyme call desnutrin/ATGL breaks off one of the three glycerol-bonded fatty acids.

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Think back to holding three fingers from your hand to demonstrate what a TAG looks like; desnutrin/ATGL just breaks off the pointer finger. The TAG becomes DAG when it loses one fatty acid. DAG is attacked by a second enzyme called hormone-sensitive lipase (HSL) that only breaks off the ring finger; after that there is another enzyme that takes care of the remaining fat fragment called a MAG—tearing off the “middle finger” fatty acid.⁹

The three free fatty acids and the glycerol molecule that have been created by breaking apart TAG can either enter the circulating bloodstream or be converted back into fat. Yet, researchers have now found that the free fatty acids can also be used by the fat cell itself for energy. In fact, when lipolysis (fat breakdown) is turned on, the fat cell’s energy factories appear to be pushed into high gear, burning fat for energy at a higher rate.^{12,13}

It was long believed that fat cells were metabolically quiet, but the last decade has shown that they produce hormones that affect the metabolism and appetite, as well as being a place where calorie burning occurs. This agrees with recent observations that it is healthier to have a large number of small fat cells rather than relatively few fat cells that are large.¹⁴ After all, it takes more to feed a hundred hungry children (small fat cells) than a couple of sumo-wrestlers (large fat cells).

Not surprisingly, fat cells of obese people absorb fatty acids more readily than lean people and do not burn fatty acids for calories, preferring to store the energy as fat.¹⁵ It is beneficial to the body that the fat cells do use up fatty acids as they are being released to some degree as an overload of free fatty acids in the system causes a condition known as *insulin resistance*, sometimes called pre-diabetes.

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There are two relative states that directly affect the fat cell’s willingness to release and

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break down fat. When the body is fasted (has not eaten for many hours), certain hormones are elevated, promoting a lipolytic (fat breakdown) response to the fat-losing hormones and neurotransmitters, the most important being norepinephrine— an adrenalin-like chemical released from nerve endings.¹⁸ When the body is fasted, the concentration of glucocorticoids is elevated, which upregulates (similar to stimulating or promoting) the production of desnutrin/ATGL.¹⁹ In the fed state, insulin concentrations are high, which activates the enzyme that turns off the fat-loss signal generated by the adrenaline-like biochemicals and drugs. 18

There are a number of other hormones and signaling molecules that affect the fat cell's preference to store or break down stored fat.

Prostaglandins

One other recent discovery (biology geek time again) that revealed another way fat cells regulate fat storage/breakdown was reported. Prostaglandins are signaling molecules that communicate only with surrounding cells, or sometimes even just the originating cell itself. They are the biochemical equivalent to a whisper, and as all know, the most interesting information is usually told in whispers.

The fat cell has a relatively unique enzyme that generates a prostaglandin called PGE2. In the fat cell, PGE2 slows down fat loss by degrading cAMP, a chemical messenger signal that is produced when fat loss hormones/chemicals attach onto receptors located on the fat cell.¹² These fat loss hormones and drugs that circulate through the bloodstream cannot enter or turn on the fat loss mechanisms of the fat cell. That happens when cAMP is generated, carrying the fat loss message to various enzymes and proteins like an office gofer passing out memos. If the gofer is fired (or cAMP degraded), the office (or fat cell) has no direction and just sits there biding its time. If there is a cell-level version of solitaire, this is when the fat cell would be playing. PGE2 degrades cAMP (fires the gofer), slowing down fat loss.

¹²

The enzyme that produces PGE2 (called AdPLA) is turned on by insulin which is highest in the fed state.

¹²

Pretty amazing— the interaction between so many regulating processes. When one

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considers all the various hormones, drugs, enzymes, etc., involved in fat storage/breakdown, it becomes clear why one drug could never circumvent all the regulatory pathways.

This article presents a lot of science and describes (only superficially) how complex fat storage/breakdown is within fat cells. However, as the Chinese philosopher Sun Tzu wrote, "If you know the enemy and know yourself, you need not fear the result of a hundred battles." [*paraphrased*]

People know how much they eat, drink, exercise, and sleep; knowing how the body responds, especially a part of the body that many struggle to control, will help win the fat loss battle.

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