

Burn More Body Fat By Increasing Adipose Tissue Blood Flow

Contributed by Robbie Durand
Tuesday, 10 February 2009

Chi (frequently translated as "energy flow") is the ancient art of Taoist healing, longevity and meditation. The Chinese believe that chi flows through the body's energy meridians (channels) and stimulates proper cell functioning, including getting rid of toxic wastes. If chi is blocked or is reduced, the cell is deprived of its life force and becomes ill. If you look down at your stomach and see a big, protruding gut, you may have blocked chi to your stomach! Chi may not be recognized by Western medical societies, but having reduced adipose tissue blood supply is recognized as a major inhibitor of fat mobilization. Fat mobilization needs a rich supply of blood flow; blocking blood flow to adipose tissue is similar to having a kink in your hose when watering the lawn—flow is reduced. In a recent study in the *Journal of Physiology*, evidence was reported for a hormone produced from adipose tissue that can reduce blood supply to adipose and cause impaired nutritive blood flow and inhibit fat burning in abdominal adipose tissue and skeletal muscle.¹⁵ Adipose tissue was once thought of as nothing more than a storage depot for fat, however it has clearly been established that adipose tissue produces a variety of hormones that exert multiple effects.

Chi (frequently translated as "energy flow") is the ancient art of Taoist healing, longevity and meditation. The Chinese believe that chi flows through the body's energy meridians (channels) and stimulates proper cell functioning, including getting rid of toxic wastes. If chi is blocked or is reduced, the cell is deprived of its life force and becomes ill. If you look down at your stomach and see a big, protruding gut, you may have blocked chi to your stomach! Chi may not be recognized by Western medical societies, but having reduced adipose tissue blood supply is recognized as a major inhibitor of fat mobilization. Fat mobilization needs a rich supply of blood flow; blocking blood flow to adipose tissue is similar to having a kink in your hose when watering the lawn—flow is reduced. In a recent study in the *Journal of Physiology*, evidence was reported for a hormone produced from adipose tissue that can reduce blood supply to adipose and cause impaired nutritive blood flow and inhibit fat burning in abdominal adipose tissue and skeletal muscle.¹⁵ Adipose tissue was once thought of as nothing more than a storage depot for fat, however it has clearly been established that adipose tissue produces a variety of hormones that exert multiple effects.

Adipose Tissue: An Active Endocrine Tissue

To date, more than 100 products are secreted from fat tissue, covering a wide range of protein families as well as fatty acids and prostaglandins. They have been reported to be secreted by adipose tissue, which is highly vascularized and contain lots of blood vessels, which mean it has a rich blood supply. The degree of white adipose tissue vascularity or blood supply is greater than that of skeletal muscle. It has long been recognized that adipose tissue blood flow (ATBF) is not constant, and that it increases during times of stress (dieting or exercise) when the need for lipid mobilization is increased. Compared with other tissues of the body, white adipose tissue can change drastically in cellular size throughout life, depending on a person's calorie intake. If you have been hitting the Krispy Kreme doughnut shop too often and there is increased fat mass, the creation of new fat is always accompanied by an increase in blood vessels, whereas enlargement of old fat cells evokes no changes in the blood vessel formation.¹² New fat cell formation is like a new baby; new fat cells need nutrients to grow and this means new blood vessels to bring nutrients to their crying mouths. Both fat storage and mobilization are closely controlled by the adipocyte's blood supply. In order to burn body fat, adipose tissue must be able to release stored triglycerides into circulation. Interestingly, obese people have reduced blood supply to adipose tissue compared to leaner individuals, which may be the result of increased production

of a nasty little hormone called angiotensin II, which is produced in adipose tissue.^{11, 12, 13}

Angiotensin II: A Major Vasoconstrictor Of Blood Vessels

Becoming overweight and fat is associated with many metabolic disorders, but a common medical problem with obesity is high blood pressure. With increasing weight gain and increases in adipose tissue, the body tries to maintain a desirable bodyweight by increasing catecholamines or adrenaline to burn body fat. It's well recognized that adrenaline or catecholamines not only increase fat mobilization, but will increase blood pressure through increased activation of the nervous system. Long-term activation of the sympathetic nervous system is thought to be one of the key mechanisms underlying obesity-associated hypertension.¹ A powerful hormone that increases blood pressure by inducing vasoconstriction (i.e., narrowing of blood vessels. When blood vessels constrict, the flow of blood is restricted or slowed.) is angiotensin II (ANG II). Many people with high blood pressure are prescribed what's called ACE inhibitors, which are medications that slow the activity of the enzymes, which decrease the production of ANG II. As a result, the blood vessels enlarge or dilate, and the blood pressure is reduced.

Angiotensin II: A Major Inhibitor Of Adipose Tissue Blood Supply

It has recently been documented that ANG II is expressed also in both white and brown adipose cells.^{2, 3} In a recent study, injections of ANG II into subcutaneous adipose tissue led to an inhibition of fat mobilization in healthy volunteers.⁴ So what the hell is going on in adipose tissue that would inhibit fat mobilization? ANG II could be nicknamed the "python hormone" because it squeezes blood vessels, allowing less blood flow, which is bad news for burning body fat. When you want to increase fat burning, having a rich blood supply will facilitate lots of fats being mobilized from adipose tissue. It has been shown that when ANG II is infused into the forearm during exercise, it reduces blood supply to the forearm. Now, the results can be carried over to adipose tissue as well. This reduced fat-burning effect could be at least partly dependent on ANG II's vasoconstricting ability (reducing blood supply) in abdominal subcutaneous adipose tissue.^{14, 15, 16}

ANG II reduces adipose tissue blood flow in a dose-dependent manner (the more ANG II produced by adipose tissue, the lower the adipose tissue blood flow¹⁵). It's interesting that adipose tissue blood flow has been reported to be lower in obese individuals, and weight reduction was followed by an increase in adipose tissue blood flow.⁵ Furthermore, weight loss by approximately 5 percent led to a reduction in ANG II in adipose tissue by 20 percent.⁶ Reducing ANG II with pharmacological blockade by ANG II inhibitors will not only reduce blood pressure in obese people, but it also increases blood flow in adipose tissue and causes weight loss.¹⁴ ANG II not only reduces blood supply to adipose tissue and inhibits fat burning, but may also stimulate fat-mass gain through the following mechanisms:

- ANG II causes stimulation of alpha₂-adrenoceptors, which inhibit fat mobilization.⁹ The alpha₂-receptors on fat cells are like the "Soup Nazi" character from the "Seinfeld" series. Once activated, they say: "No fat mobilization for you!" An increase in alpha receptors result in increased fat storage.

- ANG II also increases the activity of fat-storing enzymes (glycerol-3-phosphate dehydrogenase and fatty acid synthase).¹⁰

- ANG II causes insulin resistance in large fat cells and causes increased storage of lipids. Administration of ACE inhibitors (block ANG II production) has been shown to enhance insulin sensitivity and reduce fat mass.⁴

- ANG II levels are increased by plasma cortisol, smoking, high-fat diets and estrogen.

Nitric Oxide And Adrenaline Increases Adipose Tissue Blood Flow

Increasing ATBF may have importance in the extraction of triglycerides (TGs) from adipose tissue and increased fat mobilization. Increasing adrenaline with caffeine and thermogenic supplements increases adrenergic stimulation of fat cells, which also increases fat mobilization and ATBF.¹⁸ Nitric oxide (NO) increases blood flow to muscles and is also a major vasodilator in adipose tissue.¹⁹ NO, a signaling molecule that regulates nutrient metabolism, is produced from the amino acid L-arginine. It has been found that dietary supplementation with L-arginine reduces fat mass and enhances expression of key genes responsible for glucose uptake in muscle, increased insulin sensitivity, and increased fat oxidation.^{26,27,28,29}

In a recent study in the American Journal of Physiology-Endocrinology and Metabolism, the use L-arginine (8.3 grams per day) for 21 days combined with diet and exercise in obese subjects resulted in a two-fold greater reduction in waist circumference compared with those just using diet and exercise.³¹ Additionally, the L-arginine group lost 100 percent fat and retained all their muscle mass, while the group using just diet and exercise lost both muscle and fat. Using a NO supplement may be useful for enhancing fat oxidation by opening up blood vessels to adipose tissue and increasing fat mobilization.

It seems that fasting ATBF is primarily under NO tone and to some extent under adrenergic control. After meal consumption, there is an increase in ATBF to fat cells, which are controlled principally by the adrenergic system. The level from which this enhancement takes place is strongly influenced by the NO tone.²⁰ NO is present in virtually all cells and plays an important role in fat metabolism.²⁴ Leptin, which is secreted from adipose tissue, is a powerful mediator of fat oxidation. Leptin-induced fat mobilization directly increases NO production in adipose tissue. When NO is blocked pharmacologically, the powerful stimulatory fat-mobilizing effects of leptin are reduced.²⁷ These findings suggest that NO is an important regulator of fat mobilization by enhancing the actions of leptin. It has also been proven that if NO synthesis is blocked by drugs that inhibit NO production, it causes increased body fat mass.²⁵ Reducing blood supply to adipose tissue limits the amount of fat that can be mobilized out of fat cells. For example, administration of drugs that cause vasoconstriction of adipose tissue blood supply results in inhibited fat mobilization.²⁰ If you are taking a thermogenic supplement, it should contain a yohimbine extract, as yohimbine causes vasodilation in adipose tissue and enhanced ATBF. NO not only increases fat oxidation by allowing greater blood flow, but also increases fat oxidation by other mechanisms.

NO Increases Fat-Burning Mitochondria And Increases Insulin Sensitivity

The mitochondrion is considered the powerhouse of the cell and is an important site for the fat oxidation, where the released chemical energy is for ATP synthesis. Therefore, mitochondria play a crucial role in regulating energy balance in the cell. Because NO stimulates the formation of metabolically active new mitochondria, the production of NO is of great interest regarding its effect on the treatment of obesity. Fat burning requires fat mobilization and then the delivery of fatty acids into the mitochondria of the muscle cell, where they can be burned as fuel. The more mitochondria a cell has, the greater the potential to burn more fat.

Other nutritional factors (e.g., omega-3 polyunsaturated fatty acids, antioxidants and phytochemicals) that increase NO synthesis also will enhance fat oxidation, energy expenditure and insulin sensitivity. Insulin sensitivity is also of crucial importance for fat burning and increasing adipose tissue blood flow. Increasing insulin sensitivity increases fat burning, as adipose tissue fat metabolism is sensitive to insulin; any elevation in insulin due to insulin resistance results in reduced fat metabolism. Increasing insulin sensitivity will also increase blood flow in adipose tissue. Studies have shown that ATBF is directly related to insulin sensitivity in adipose tissue, regardless of bodyweight.³⁰ Conversely, factors (e.g., high-fat diet, oxidative stress and protein malnutrition) that reduce NO synthesis will likely lead to reduced adipose tissue

blood flow and increased fat mass. NO supplements may not only help you get a better pump in the gym, but will enhance adipose tissue blood flow and increase fat mobilization. Talk about a great added benefit!

Key Points:

- ANG II is a major vasoconstrictor of adipose tissue blood flow and inhibits fat mobilization.
- Reduced adipose tissue insulin sensitivity reduces adipose tissue blood flow and reduces fat burning.
- Nitric oxide increases blood flow to not only muscle, but adipose tissue as well.
- Nitric oxide, catecholamines and yohimbine all increase blood flow to adipose tissue and increase fat oxidation.

References:

1. Pausova Z. From big fat cells to high blood pressure: a pathway to obesity-associated hypertension. *Curr Opin Nephrol Hypertens*, 2006 Mar;15(2):173-8. Review.
2. Shenoy, U. and L. Cassis. Characterization of renin activity in brown adipose tissue. *Am J Physiol*, 272: C989-999, 1997.
3. Cabassi A, Coghi P, Govoni P, Barouhiel E, Speroni E, Cavazzini S, Cantoni AM, Scandroglio R, Fiaccadori E. Sympathetic modulation by carvedilol and losartan reduces angiotensin II-mediated lipolysis in subcutaneous and visceral fat. *J Clin Endocrinol Metab*, 2005 May;90(5):2888-97.
4. Boschmann M, Ringel J, Klaus S, Sharma AM. Metabolic and hemodynamic response of adipose tissue to angiotensin II. *Obes Res*, 2001; 9:486-491.
5. Blaak EE, van Baak MA, Kemerink GJ, et al. Beta-adrenergic stimulation and abdominal subcutaneous fat blood flow in lean, obese, and reduced-obese subjects. *Metabolism*, 1995; 44:183-187.
6. Engeli S, Bohnke J, Gorzelnik K, Janke J, Schling P, Bader M, Luft FC, Sharma AM. Weight loss and the renin-angiotensin-aldosterone system. *Hypertension*, 2005 Mar;45(3):356-62.
7. Lonroth P, Smith U. Intermediary metabolism with an emphasis on lipid metabolism, adipose tissue, and fat cell metabolism: a review. In: Bjorntorp P, Brodoff BN, editors. *Obesity*, Philadelphia: Lippincott; 1992. pp. 3-14.
8. Goossens GH, Blaak EE, van Baak MA. Possible involvement of the adipose tissue renin-angiotensin system in the pathophysiology of obesity-related disorders. *Obes Rev*, 2003; 4:43-55.
9. English V, Cassis L. Facilitation of sympathetic neurotransmission contributes to angiotensin regulation of body weight. *J Neural Transm*, 1999; 106:631-644.
10. Kim S, Dugail I, Standridge M, et al. Angiotensin II-responsive element is the insulin-responsive element in the adipocyte fatty acid synthase gene: role of adipocyte determination and differentiation factor 1/sterol-regulatory-element-binding protein 1c. *Biochem J*, 2001; 357:899-904.
11. Boschmann M, Adams F, Schaller K, Franke G, Sharma AM, Klaus S, Luft FC, Jordan J. Hemodynamic and metabolic responses to interstitial angiotensin II in normal weight and obese men. *J Hypertens*, 2006 Jun;24(6):1165-71.
12. Di Girolamo M, Skinner NS, Hanley HG, Sachs RG. Relationship of adipose tissue blood flow to fat cell size and number. *Am J Physiol*, 1971; 220:932-937.
13. Virtanen KA, Lonroth P, Parkkola R, Peltoniemi P, Asola M, Viljanen T, et al. Glucose uptake and perfusion in subcutaneous and visceral adipose tissue during insulin stimulation in non-obese and obese humans. *J Clin Endocrinol Metab*, 2002; 87:3902-3910.

14. Goossens GH, Blaak EE, Arner P, Saris WH, van Baak MA. Angiotensin II: a hormone that affects lipid metabolism in adipose tissue. *Int J Obes, (Lond)*. 2007 Feb;31(2):382-4.
15. Goossens GH, McQuaid SE, Dennis AL, van Baak MA, Blaak EE, Frayn KN, Saris WH, Karpe F. Angiotensin II: a major regulator of subcutaneous adipose tissue blood flow in humans. *J Physiol*, 2006 Mar 1;571(Pt 2):451-60.
16. Goossens GH, Blaak EE, Saris WH, van Baak MA. Angiotensin II-induced effects on adipose and skeletal muscle tissue blood flow and lipolysis in normal-weight and obese subjects. *J Clin Endocrinol Metab*, 2004 Jun;89(6):2690-6.
17. Sharma AM, Janke J, Gorzelniak K, Engeli S, Luft FC. Angiotensin blockade prevents type 2 diabetes by formation of fat cells. *Hypertension*, 2002 Nov;40(5):609-11.
18. Samra JS, Simpson EJ, Clark ML, et al. Effects of adrenaline infusion on the interstitial environment of subcutaneous adipose tissue as studied by microdialysis. *Clin Sci, (Lond)*. 1996;91:425-430.
19. Steinberg HO, Brechtel G, Johnson A, et al. Insulin-mediated skeletal muscle vasodilation is nitric oxide dependent: a novel action of insulin to increase nitric oxide release. *J Clin Invest*, 1994;94:1172-1179.
20. Ardilouze JL, Fielding BA, Currie JM, Frayn KN, Karpe F. Nitric oxide and beta-adrenergic stimulation are major regulators of preprandial and postprandial subcutaneous adipose tissue blood flow in humans. *Circulation*, 2004 Jan 6;109(1):47-52.
21. Galitzky J, Lafontan M, Nordenstrom J, et al. Role of vascular alpha-2 adrenoceptors in regulating lipid mobilization from human adipose tissue. *J Clin Invest*, 1993;91:1997-2003.
22. Fu WJ, Haynes TE, Kohli R, Hu J, Shi W, Spencer TE, Carroll RJ, Meininger CJ, Wu G. Dietary L-arginine supplementation reduces fat mass in Zucker diabetic fatty rats. *J Nutr*, 2005 Apr;135(4):714-21.
23. W. Jobgen, S. Fried, W. Fu, C. Meininger, G. Wu. Regulatory role for the arginine-nitric oxide pathway in metabolism of energy substrates. *The Journal of Nutritional Biochemistry*, Volume 17, Issue 9, Pages 571-588.
24. Garcia-Villafranca, J., Guillen, A. & Castro, J. (2003) Involvement of nitric oxide/cyclic GMP signaling pathway in the regulation of fatty acid metabolism in rat hepatocytes. *Biochem Pharmacol*, 65:807-812.
25. Khedara, A., Goto, T., Morishima, M., Kayashita, J. & Kato, N. (1999) Elevated body fat in rats by the dietary nitric oxide synthase inhibitor, L-N-nitroarginine. *Biosci. Biotechnol Biochem*, 63:698-702.
26. Gaudiot, N., Ribiere, C., Jaubert, A. M. & Giudicelli, Y. (2000) Endogenous nitric oxide is implicated in the regulation of lipolysis through antioxidant-related effect. *Am J Physiol*, 279:C1603-C1610.
27. Fruhbeck, G. & Gomez-Ambrosi, G. (2001) Modulation of the leptin-induced white adipose tissue lipolysis by nitric oxide. *Cell Signal*, 13:827-833.
28. Fu WJ, Haynes TE, Kohli R, Hu J, Shi W, Spencer TE, et al. Dietary L-arginine supplementation reduces fat mass in Zucker diabetic fatty rats. *J Nutr*, 2005;135:714-21.
29. Jobgen WS, Fried SK, Fu WJ, Meininger CJ, Wu G. Regulatory role for the arginine-nitric oxide pathway in metabolism of energy substrates. *J Nutr Biochem*, 2006 Sep;17(9):571-88. Epub 2006 Jan 9. Review.
30. Karpe F, Fielding BA, Ilic V, Macdonald IA, Summers LK, Frayn KN. Impaired postprandial adipose tissue blood flow response is related to aspects of insulin sensitivity. *Diabetes*, 2002 Aug;51(8):2467-73.
31. Lucotti P, Setola E, Monti LD, Galluccio E, Costa S, Sandoli EP, Fermo I, Rabaiotti G, Gatti R, Piatti P. Beneficial effects of a long-term oral L-arginine treatment added to a hypocaloric diet and exercise training program in obese, insulin-resistant type 2 diabetic patients. *Am J Physiol Endocrinol Metab*, 2006 Nov;291(5):E906-12.

