11-9-2023

Adipose Tissue Dysregulation leads to Chronic Systemic Inflammation

Jamie Rausch PhD, RN

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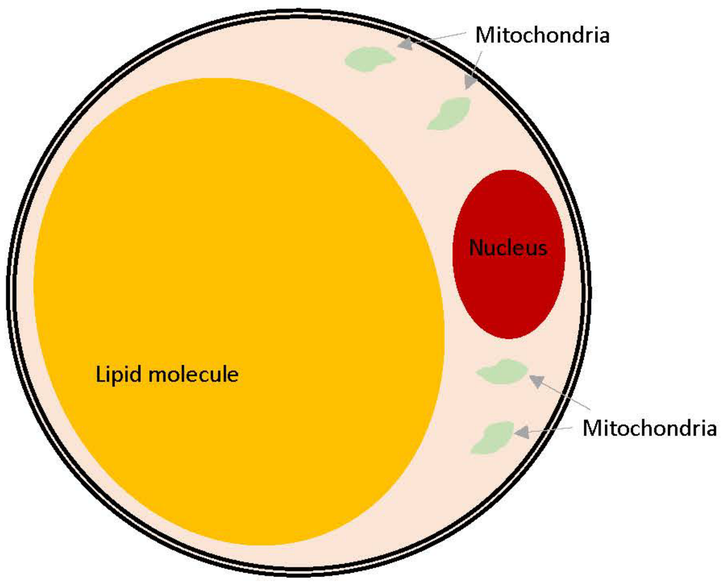
1. What Is Adipose Tissue and what is it composed of?

Adipose cells…

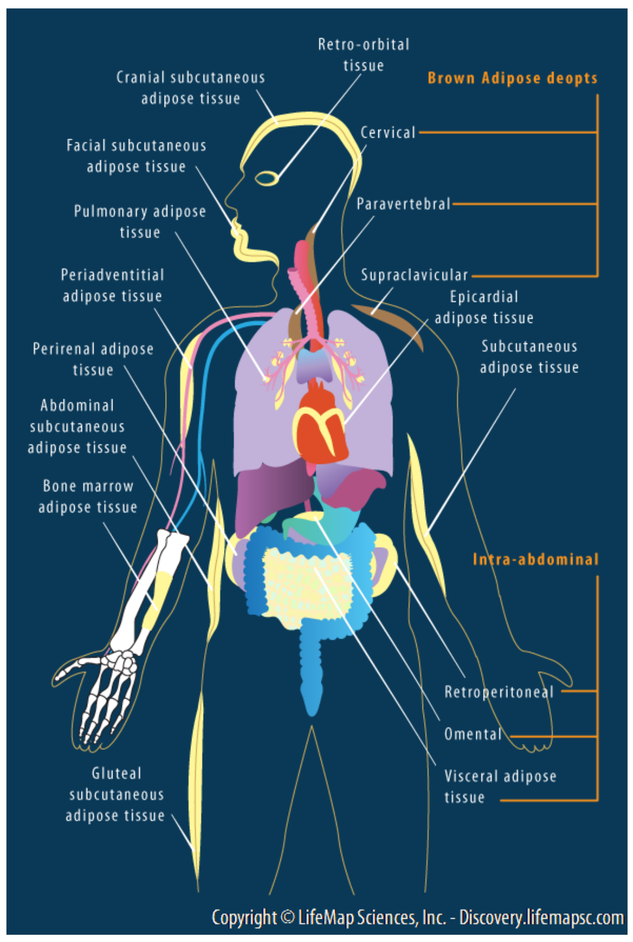


Commonly known as fat tissue or just fat, adipose tissue is a connective tissue composed mostly of adipocytes.
In healthy weight individuals, adipose tissue consists of about 25% of total body weight.
Small blood vessels, immune cells, extracellular matrix or ECM, and stromal cells are also found in adipose tissue.

2. What are the types of adipose tissue and where can they be found?

There are three main types of adipose tissue:

White, Brown, and Beige or Brite

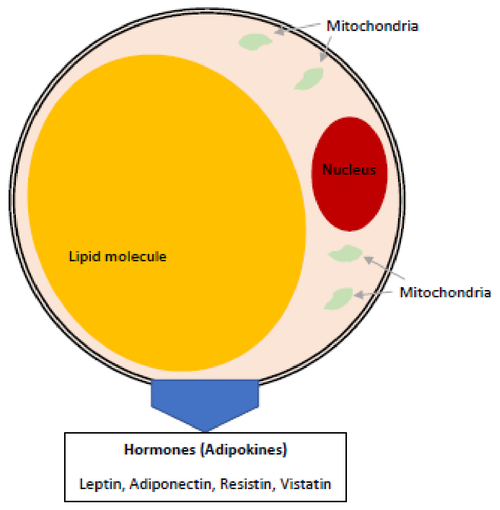


3. What is the normal function of adipose tissue?

Historically…

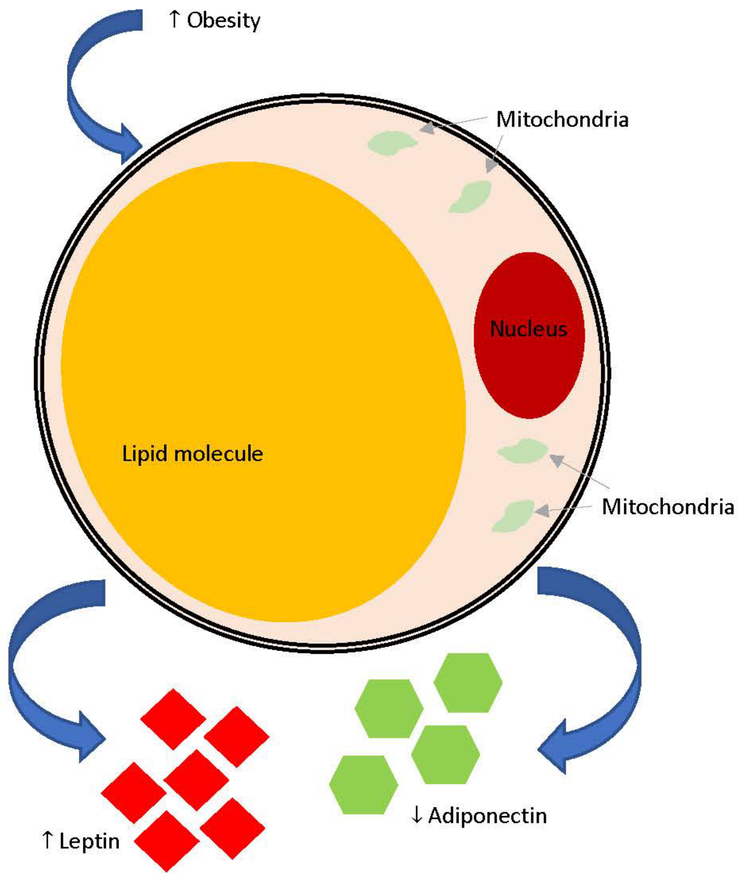
Cushion for organs, insulation, and storage unit

Recent discoveries indicate a new function…



Hormone production!

4. How does adipose tissue become dysregulated?



5. What are the consequences of adipose tissue dysregulation?

Consequences

- Insulin Resistance
- Increased Inflammation
- Dyslipidemia
- Increased thrombosis
- Atherosclerosis
- Cellular Proliferation

Increased Risk of Chronic Disease

Such as: Type II Diabetes, CVD, HTN, Depression, Arthritis, Cancer, etc.

6. What are the future directions for research?

- *Reference values for all ages, BMIs, and both sexes for leptin, adiponectin, and the leptin-to-adiponectin ratio.*
- *The extent of which and the exact mechanisms that Covariates (e.g., estrogen, testosterone, medications, sex, and age) influence leptin and adiponectin production.*
- *If leptin and adiponectin levels correlate in different human biological substances (such as hair, urine, blood/serum, saliva).*
- *Optimal dose and duration of anti-inflammatory interventions (such as EPA+DHA) for improvement in leptin and adiponectin levels.*

References:

Agostinis-Sobrinho, Mendes, Moreira, Abreu, Lopes, Oliveira-Santos, J., Skurvydas, A., Mota, J., & Santos, R. (2017). Association between Leptin, Adiponectin, and Leptin/Adiponectin Ratio with Clustered Metabolic Risk Factors in Portuguese Adolescents: The LabMed Physical Activity Study. *Annals of Nutrition and Metabolism*, *70*(4), 321–328. https://doi.org/10.1159/000477328

Angın, Arslan, & Kuralay. (2014). Leptin-to-adiponectin ratio in obese adolescents with nonalcoholic fatty liver disease. *The Turkish Journal of Pediatrics*, *56*(3), 259–266.

Ayina, Endomba, Mandengue, Noubiap, Ngoa, Boudou, Gautier, Mbanya, & Sobngwi. (2017). Association of the leptin-to-adiponectin ratio with metabolic syndrome in a sub-Saharan African population. *Diabetology & Metabolic Syndrome*, *9*, 66. https://doi.org/10.1186/s13098-017-0265-6

Bluher, M. (2009). Adipose Tissue Dysfunction in Obesity. *Experimental and Clinical Endocrinology & Diabetes*, *117*(6), 241–250. https://doi.org/10.1055/s-0029-1192044

Brown, J. C., Harhay, M. O., & Harhay, M. N. (2017). Anthropometrically-predicted visceral adipose tissue and mortality among men and women in the third national health and nutrition examination survey (NHANES III). *American Journal of Human Biology: The Official Journal of the Human Biology Council*, *29*(1). https://doi.org/10.1002/ajhb.22898

Cannon, B., & Nedergaard, J. (2004). Brown adipose tissue: Function and physiological significance. *Physiological Reviews*, *84*(1), 277–359. https://doi.org/10.1152/physrev.00015.2003

Cannon, B., & Nedergaard, J. (2008). Developmental biology: Neither fat nor flesh. *Nature*, *454*(7207), 947–948. https://doi.org/10.1038/454947a

Carlson, N. S., Hernandez, T. L., & Hurt, K. J. (2015). Parturition dysfunction in obesity: Time to target the pathobiology. *Reproductive Biology and Endocrinology: RB&E*, *13*, 135. https://doi.org/10.1186/s12958-015-0129-6

Cawthorn, W. P., Scheller, E. L., Learman, B. S., Parlee, S. D., Simon, B. R., Mori, H., Ning, X., Bree, A. J., Schell, B., Broome, D. T., Soliman, S. S., DelProposto, J. L., Lumeng, C. N., Mitra, A., Pandit, S. V., Gallagher, K. A., Miller, J. D., Krishnan, V., Hui, S. K., … MacDougald, O. A. (2014). Bone marrow adipose tissue is an endocrine organ that contributes to increased circulating adiponectin during caloric restriction. *Cell Metabolism*, *20*(2), 368–375. https://doi.org/10.1016/j.cmet.2014.06.003

CDC. (2020). *Defining Adult Overweight and Obesity | Overweight & Obesity | CDC*. https://www.cdc.gov/obesity/adult/defining.html

Chen, Chen, Chiu, Lin, Li, & Lu. (2018). Leptin/Adiponectin ratio as a potential biomarker for metabolic syndrome in patients with schizophrenia. *Psychoneuroendocrinology*, *92*, 34–40. https://doi.org/10.1016/j.psyneuen.2018.03.021

Chou, Hsu, Wu, Teng, Sun, & Ko. (2014). Leptin-to-Adiponectin Ratio is Related to Low Grade Inflammation and Insulin Resistance Independent of Obesity in Non-Diabetic Taiwanese: A Cross-Sectional Cohort Study. *Acta Cardiologica Sinica*, *30*(3), 204–214.

Cinti, S. (2005). The adipose organ. *Prostaglandins, Leukotrienes, and Essential Fatty Acids*, *73*(1), 9–15. https://doi.org/10.1016/j.plefa.2005.04.010

Fantuzzi, & Mazzone (Eds.). (2014). *Adipose tissue and adipokines in health and disease* (Second edition). Humana Press.

Foks, A. C., & Kuiper, J. (2017). Immune checkpoint proteins: Exploring their therapeutic potential to regulate atherosclerosis. *British Journal of Pharmacology*, *174*(22), 3940–3955. https://doi.org/10.1111/bph.13802

Fruhbeck, Catalán, Rodríguez, Ramírez, Becerril, Salvador, Portincasa, Colina, & Gómez-Ambrosi. (2017). Involvement of the leptin-adiponectin axis in inflammation and oxidative stress in the metabolic syndrome. *Scientific Reports*, *7*(1), 6619. https://doi.org/10.1038/s41598-017-06997-0

Golbahar, Das, Al-Ayadhi, & Gumaa. (2012). Leptin-to-adiponectin, adiponectin-to-leptin ratios, and insulin are specific and sensitive markers associated with polycystic ovary syndrome: A case-control study from Bahrain. *Metabolic Syndrome and Related Disorders*, *10*(2), 98–102. https://doi.org/10.1089/met.2011.0075

Gonzalez-Periz, A., & Claria, J. (2010). Resolution of Adipose Tissue Inflammation. *Thescientificworldjournal*, *10*, 832–856. https://doi.org/10.1100/tsw.2010.77

Hajer, G. R., van Haeften, T. W., & Visseren, F. L. J. (2008). Adipose tissue dysfunction in obesity, diabetes, and vascular diseases. *European Heart Journal*, *29*(24), 2959–2971. https://doi.org/10.1093/eurheartj/ehn387

Harms, M., & Seale, P. (2013). Brown and beige fat: Development, function and therapeutic potential. *Nature Medicine*, *19*(10), 1252–1263. https://doi.org/10.1038/nm.3361

Huether, S. E., McCance, K. L., & Brashers, V. L. (2020). *Understanding pathophysiology*.

Juge-Aubry, Henrichot, & Meier. (2005). Adipose tissue: A regulator of inflammation. *Best Practice & Research Clinical Endocrinology & Metabolism*, *19*(4), 547–566. https://doi.org/10.1016/j.beem.2005.07.009

Larsen, Isaksen, Moen, Wilsgaard, Remijn, Paulssen, Florholmen, & Goll. (2018). Leptin to adiponectin ratio – A surrogate biomarker for early detection of metabolic disturbances in obesity. *Nutrition, Metabolism and Cardiovascular Diseases*, *28*(11), 1114–1121. https://doi.org/10.1016/j.numecd.2018.06.020

Lekva, Michelsen, Aukrust, Henriksen, Bollerslev, & Ueland. (2017). Leptin and adiponectin as predictors of cardiovascular risk after gestational diabetes mellitus. *Cardiovascular Diabetology*, *16*(1), 5. https://doi.org/10.1186/s12933-016-0492-4

Marieb, E. N., & Hoehn, K. (2008). *Anatomy & physiology* (3rd ed). Pearson/Benjamin Cummings.

Mayo Clinic Labs. (n.d.-a). *FADIO - Clinical: Adiponectin*. Retrieved March 3, 2021, from https://www.mayocliniclabs.com/test-catalog/Clinical+and+Interpretive/75607

Mayo Clinic Labs. (n.d.-b). *FLEP - Clinical: Leptin*. Leptin. Retrieved March 3, 2021, from https://www.mayocliniclabs.com/test-catalog/Clinical+and+Interpretive/91339

McCance, K. L., Huether, S. E., Brashers, V. L., & Rote, N. S. (2019). *Pathophysiology: The biologic basis for disease in adults and children*.

Montague, C. T., & O'Rahilly, S. (2000). The perils of portliness: Causes and consequences of visceral adiposity. *Diabetes*, *49*(6), 883–888. https://doi.org/10.2337/diabetes.49.6.883

Monteiro, R., & Azevedo, I. (2010). Chronic Inflammation in Obesity and the Metabolic Syndrome. *Mediators of Inflammation*, *2010*. https://doi.org/10.1155/2010/289645

Opatrilova, R., Caprnda, M., Kubatka, P., Valentova, V., Uramova, S., Nosal, V., Gaspar, L., Zachar, L., Mozos, I., Petrovic, D., Dragasek, J., Filipova, S., Büsselberg, D., Zulli, A., Rodrigo, L., Kruzliak, P., & Krasnik, V. (2018). Adipokines in neurovascular diseases. *Biomedicine & Pharmacotherapy*, *98*, 424–432. https://doi.org/10.1016/j.biopha.2017.12.074

Park, Y.-M., Myers, M., & Vieira-Potter, V. J. (2014). Adipose tissue inflammation and metabolic dysfunction: Role of exercise. *Missouri Medicine*, *111*(1), 65–72.

Pietzner, M., Kaul, A., Henning, A.-K., Kastenmüller, G., Artati, A., Lerch, M. M., Adamski, J., Nauck, M., & Friedrich, N. (2017). Comprehensive metabolic profiling of chronic low-grade inflammation among generally healthy individuals. *BMC Medicine*, *15*(1), 210. https://doi.org/10.1186/s12916-017-0974-6

Pond, C. M. (1998). *The fats of life*. Cambridge University Press.

Porter, S. A., Massaro, J. M., Hoffmann, U., Vasan, R. S., O'Donnel, C. J., & Fox, C. S. (2009). Abdominal subcutaneous adipose tissue: A protective fat depot? *Diabetes Care*, *32*(6), 1068–1075. https://doi.org/10.2337/dc08-2280

Rausch, J. A., Gillespie, S., Orchard, T., Tan, A., & McDaniel, J. C. (2021). Secondary data analysis investigating effects of marine omega-3 fatty acids on circulating levels of leptin and adiponectin in older adults. *Prostaglandins, Leukotrienes, and Essential Fatty Acids*, *170*, 102302. https://doi.org/10.1016/j.plefa.2021.102302

Rausch, J., Gillespie, S., Orchard, T., Tan, A., & McDaniel, J. C. (2020). Systematic Review of Marine-derived Omega-3 Fatty Acid Supplementation effects on Leptin, Adiponectin, and the Leptin-to-Adiponectin Ratio. *Nutrition Research*.

Rius, B., López-Vicario, C., González-Périz, A., Morán-Salvador, E., García-Alonso, V., Clària, J., & Titos, E. (2012). Resolution of inflammation in obesity-induced liver disease. *Frontiers in Immunology*, *3*. https://doi.org/10.3389/fimmu.2012.00257

Rosenwald, M., Perdikari, A., Rülicke, T., & Wolfrum, C. (2013). Bi-directional interconversion of brite and white adipocytes. *Nature Cell Biology*, *15*(6), 659–667. https://doi.org/10.1038/ncb2740

Samuelson, I., & Vidal-Puig, A. (2020). Studying Brown Adipose Tissue in a Human in vitro Context. *Frontiers in Endocrinology*, *11*, 629. https://doi.org/10.3389/fendo.2020.00629

Sarray, Madan, Saleh, Mahmoud, & Almawi. (2015). Validity of adiponectin-to-leptin and adiponectin-to-resistin ratios as predictors of polycystic ovary syndrome. *Fertility and Sterility*, *104*(2), 460–466. https://doi.org/10.1016/j.fertnstert.2015.05.007

Snel, M., Jonker, J. T., Schoones, J., Lamb, H., de Roos, A., Pijl, H., Smit, J. W. A., Meinders, A. E., & Jazet, I. M. (2012). Ectopic fat and insulin resistance: Pathophysiology and effect of diet and lifestyle interventions. *International Journal of Endocrinology*, *2012*, 983814. https://doi.org/10.1155/2012/983814

Stocco, C. (2012). Tissue physiology and pathology of aromatase. *Steroids*, *77*(1–2), 27–35. https://doi.org/10.1016/j.steroids.2011.10.013

Szalay, J. (2015, September 30). *Inflammation: Causes, Symptoms & Anti-Inflammatory Diet*. Live Science. https://www.livescience.com/52344-inflammation.html

Thomas, L. W. (1962). The chemical composition of adipose tissue of man and mice. *Quarterly Journal of Experimental Physiology and Cognate Medical Sciences*, *47*, 179–188. https://doi.org/10.1113/expphysiol.1962.sp001589

World Health Organization. (2020). *Obesity and overweight*. World Health Organization - Obesity and Overweight. https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight

Zhang, M., Cheng, H., Zhao, X., Hou, D., Yan, Y., Cianflone, K., Li, M., & Mi, J. (2017). Leptin and Leptin-to-Adiponectin Ratio Predict Adiposity Gain in Nonobese Children over a Six-Year Period. *Childhood Obesity (Print)*, *13*(3), 213–221. https://doi.org/10.1089/chi.2016.0273

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