

# Leptin in Obesity –A Review

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**Abstract :****Aim:**

To determine the Leptin's role in obesity.

**Objective:**

Leptin also plays a role in other physiological processes as evidenced by its multiple sites of synthesis other than fat cells.

**Background:**

Leptin hormone synthesized by adipose cells helps to regulate energy balance by inhibiting hunger. Leptin resistance occurs when leptin levels are high due to this, your brain is starved while the body gets obese. Some researchers have referred to this as brain starvation. Leptin is produced primarily in the adipocytes of white adipose tissue. It also is produced by brown adipose tissue, placenta (syncytiotrophoblasts), ovaries, skeletal muscle, stomach (the lower part of the fundic glands), mammary epithelial cells, bone marrow. Thus leptin levels correlates with obesity of an individual.

**Conclusion:**

This review shows the relationship between leptin levels and obesity.

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**INTRODUCTION:**

Obesity is a medical condition in which excess body fat has accumulated to the extent that it may have a negative effect on health.<sup>[1]</sup> People are generally considered obese when their body mass index (BMI), a measurement obtained by dividing a person's weight by the square of the person's height, is over 30 kg/m<sup>2</sup>, with the range 25–30 kg/m<sup>2</sup> defined as overweight.<sup>[1]</sup> Some East Asian countries use lower values.<sup>[2]</sup> Obesity increases the likelihood of various diseases, particularly heart disease, type 2 diabetes, obstructive sleep apnea, certain types of cancer, and osteoarthritis.<sup>[3]</sup> It is most commonly caused due to excess food intake and lack of physical activities<sup>[1,4]</sup>. A few cases are caused by genes and mental disorders.<sup>[5]</sup> On average, obese people have a greater energy expenditure than their thin counterparts due to the energy required to maintain an increased body mass.<sup>[6,7]</sup> through a combination of social changes and personal choices.<sup>[1]</sup> Changes to diet and exercising are the main treatments.<sup>[3]</sup> Diet quality can be improved by reducing the consumption of energy-dense foods, such as those high in fat and sugars, and by increasing the intake of dietary fibre.<sup>[1]</sup> Medications may be taken, along with a suitable diet, to reduce appetite or decrease fat absorption.<sup>[8]</sup> If diet, exercise, and medication are not effective, a gastric balloon or surgery may be performed to reduce stomach volume or bowel length, leading to feeling full earlier or a reduced ability to absorb nutrients from food.<sup>[9,10]</sup>

Obesity is more common in women than men.<sup>[1]</sup> Authorities view it as one of the most serious public health problems of the 21st century.<sup>[12]</sup> Obesity is stigmatised in much of the modern world (particularly in the Western world), though it was seen as a symbol of wealth and fertility at other times in history and still is in some parts of the world.<sup>[3][13]</sup> In 2013, the American Medical Association classified obesity as a disease.<sup>[14][15]</sup>

**LEPTIN IN OBESITY :**

Leptin is thought to be blood borne signal which is from adipose tissue that informs brain about the fat mass.<sup>[16]</sup> A

gene has been identified that is responsible for producing several forms of leptin receptors by splicing different segments of the gene<sup>[17]</sup>. In obesity, a decreased sensitivity to leptin occurs, resulting in an inability to detect satiety despite high energy stores.<sup>[18]</sup> Although regulation of fat stores is seemed to be the primary function of leptin, it also plays a role in other physiological processes, as evidenced by its multiple sites of synthesis other than fat cells, and the multiple cell types beside hypothalamic cells that have leptin receptors.<sup>[19, 20,21,22,23,24]</sup> As was predicted, leptin treatment, can be done by direct injection of leptin into the cerebral ventricle or hypothalamus, profoundly inhibited food intake and decreased weight and fat in animals lacking leptin<sup>[25,26,27]</sup>. Leptin levels fall rapidly in response to fasting and evoke profound changes in energy balance and hormone levels. Low leptin levels induce overfeeding and suppress energy expenditure, thyroid and reproductive hormones, and immunity<sup>[28,29]</sup>. CSF levels provide evidence for reduction in Leptin crossing the BBB and reaching obesity- relevant targets, such as hypothalamus, in obese people. The ratio of leptin in CSF compared to blood is lower in obese people compared to the normal people

**LEPTIN DIET :**

There are some rules which you should not take snacks after the dinner and take your dinner before seven before you go to bed. Eat three times a day, but no snacks. Do not take large meal when you are quite full. The Leptin diet encourages you to eat fresh, organic foods whenever possible. On this diet, you neither religiously count calories nor totally ignore them. Coming to the breakfast. Breakfast on the Leptin diet. This meal should include 20 to 30 grams of protein. To fulfill this hefty requirement, you could eat steak and an egg; a scrambled egg has 6 grams of protein, while 3 ounces of top round supplies 20 grams. Or try something lighter like oatmeal with almond milk and whey protein powder. For a breakfast-to-go, whip up one of the approved smoothies, like Lemon Basil, Berry Green or Coco Spice. For lunch salad is the best for the Leptin diet

quinoa and lentil salad and goat cheese salad are good choice for lunch eating quinoa will give you 8 grams of proteins and having lentil salad will give 18 grams of proteins and also have a cup of soup. Coming to dinner part chicken steak, salmon and seafood are the best options for dinner on the Leptin diet, include coconut rice with grilled shrimp, chicken cutlets and turkey burger. These are all the main Leptin diet.<sup>[30]</sup>

#### ROLE OF LEPTIN IN DISEASES:

Leptin levels and expressions are associated with the body adiposity and body mass index in both experimental animals and humans<sup>[31,32]</sup>. Leptin provides important feedback mechanism, which is necessary for the precise regulation of long-term energy balance. Leptin levels do not increase rapidly. Leptin is mainly responsible for large decrease in food intake that accompanies satiety. Leptin has a variety of important central and peripheral actions to regulate energy balance and metabolism, fertility, and bone metabolism that are mediated by specific cell surface leptin receptors.<sup>[33,34]</sup> Importantly, leptin may also exert actions related to cardiovascular homeostasis that are potentially atherogenic, thrombotic, and angiogenic.<sup>[35,36]</sup> Leptin has peripheral actions to stimulate vascular inflammation, oxidative stress, and vascular smooth muscle hypertrophy that may contribute to pathogenesis of type 2 diabetes mellitus, hypertension, atherosclerosis, and coronary heart disease.

#### LEPTIN AND INSULIN:

Leptin increases insulin sensitivity in rats and may improve vascular responses to insulin in states of insulin resistance.<sup>[37]</sup> Leptin increases free fatty acid oxidation in isolated mouse soleus muscle by 42%, whereas insulin decreases this by 40%. When both hormones are administered, leptin is reduced in both the antioxidative and lipogenic effects of insulin by 50%.<sup>[38]</sup> Leptin attenuates the antioxidative, lipogenic actions of insulin on muscle free fatty acid metabolism via a peripheral mechanism, whereas the effects of leptin in modulating insulin-stimulated glucose disposal appear to occur via a central mechanism.<sup>2</sup> Recombinant mouse leptin inhibits glycogen synthesis in soleus muscle of ob/ob mice in the presence of insulin.<sup>[39]</sup> By contrast, leptin increases glycogen synthesis in cultured C2C12 muscle cells.<sup>[40]</sup>

#### LEPTIN IN HYPERTENSION :

Correlations between leptin and blood pressure are influenced by gender. Despite higher serum leptin levels in women, leptin and blood pressure associations have been reported more frequently in men than in women, regardless of hypertension and adiposity.<sup>[41]</sup> Ethnic and racial background may also influence the relationship between leptin and blood pressure. We did not observe significant correlations between plasma leptin levels and blood pressure before efonidipine therapy.<sup>[42]</sup>

#### CONCLUSION:

Leptin concentration and body composition were previously observed were previously observed<sup>[43,44]</sup> and

Prepubertal children<sup>[45]</sup>. The important finding is the energy expenditure in children and physical activity in correlated with plasma leptin concentration. Leptin plays an important role in the energy expenditure in humans<sup>[46,47]</sup>. Leptin may intervene energy expenditure in humans and, more specifically, physical activity, perhaps by activation of the sympathetic nervous system. Leptin may therefore be important in regulating energy balance, not only by controlling food intake, but also by increasing total daily energy expenditure.

The association between leptin concentrations and energy expenditure in children does not prove a causal relationship whereby leptin produces an increase in energy expenditure. However, it is unlikely that energy expenditure actually elevates leptin concentrations since it is known that elevated levels of physical activity increase sympathetic nervous system activity. Leptin seems to increase energy expenditure and physical activity in children<sup>[48]</sup>. Leptin resistance in obese people is a normal part of mammalian physiology and possibly, could confer a survival advantage.<sup>[49]</sup> Leptin resistance (in combination with insulin resistance and weight gain) is seen in rats after they are given unlimited access to palatable, energy-dense foods.<sup>[50]</sup> This effect is reversed when the animals are put back on a low-energy diet.<sup>[51]</sup> This also may have an evolutionary advantage: allowing energy to be stored efficiently when food is plentiful would be advantageous in populations where food frequently may be scarce.<sup>[52]</sup>

#### REFERENCES:

- 1.) Obesity and overweight Fact sheet N°311". WHO. January 2015. Retrieved 2 February 2016.
- 2.) Kanazawa, M; Yoshiike, N; Osaka, T; Numba, Y; Zimmet, P; Inoue, S (2005). "Criteria and classification of obesity in Japan and Asia-Oceania". World review of nutrition and dietetics 94: 1–12. doi:10.1159/000088200. PMID 16145245.
- 3.) Haslam DW, James WP (2005). "Obesity". Lancet (Review) 366(9492): 1197–209. doi:10.1016/S0140-6736(05)67483-1. PMID 16198769.
- 4.) Yazdi, FT; Clee, SM; Meyre, D (2015). "Obesity genetics in mouse and human: back and forth, and back again". PeerJ3: e856. doi:10.7717/peerj.856. PMC 4375971. PMID 25825681.
- 5.) Bleich S, Cutler D, Murray C, Adams A (2008). "Why is the developed world obese?". Annu Rev Public Health (Research Support) 29: 273–95. doi:10.1146/annurev.publhealth.29.0
- 6.) Oxford Handbook of Medical Sciences (2nd ed.). Oxford: OUP Oxford. 2011. p. 180. ISBN 9780191652295.
- 7.) Kushner, Robert (2007). Treatment of the Obese Patient (Contemporary Endocrinology). Totowa, NJ: Humana Press. p. 158. ISBN 1-59745-400-1. Retrieved April 5, 2009.
- 8.) Novski SZ, Yanovski JA (Jan 1, 2014). "Long-term drug treatment for obesity: a systematic and clinical review.". JAMA: the Journal of the American Medical Association (Review) 311 (1): 74–86. doi:10.1001/jama.2013.281361. PMC 3928674. PMID 24231879.
- 9.) Colquitt, JL; Pickett, K; Loveman, E; Frampton, GK (Aug 8, 2014). "Surgery for weight loss in adults". The Cochrane database of systematic reviews (Meta-analysis, Review) 8: CD003641. doi:10.1002/14651858.CD003641.pub4. PMID 25105982.
- 10.) Imaz I, Martínez-Cervell C, García-Alvarez EE, Sendra-Gutiérrez JM, González-Enríquez J (July 2008). "Safety and effectiveness of the intragastric balloon for obesity. A meta-analysis". Obes Surg 18 (7): 841–6. doi:10.1007/s11695-007-9331-8. PMID 18459025.
- 11.) Encyclopedia of Mental Health (2 ed.). Academic Press. 2015. p. 158. ISBN 9780123977533.
- 12.) Dibaise JK, Foxx-Orenstein AE (July 2013). "Role of the gastroenterologist in managing obesity". Expert Review of Gastroenterology & Hepatology (Review) 7 (5): 439–51. doi:10.1586/17474124.2013.811061. PMID 23899283.

- 13.) Woodhouse R (2008). "Obesity in art: A brief overview". *Front Horm Res. Frontiers of Hormone Research* 36: 271–86. doi:10.1159/000115370. ISBN 978-3-8055-8429-6. PMID 18230908.
- 14.) Pollack, Andrew (June 18, 2013). "A.M.A. Recognizes Obesity as a Disease". *New York Times*. Archived from the original on June 18, 2013.
- 15.) Weinstock, Matthew (June 21, 2013). "The Facts About Obesity". H&HN. American Hospital Association. Retrieved June 24, 2013.
- 16.) Zhang Y, Proenca R, Maffei M, Barone M, Leopold L, Friedman JM. Positional cloning of the mouse obese gene and its human homologue. *Nature* 1994;372:425-32.
- 17.) Lee G-H, Proenca R, Montez JM, Carroll KM, Darvishzadeh JG, Lee JI, et al. Abnormal splicing of the leptin receptor in diabetic mice. *Nature* 1996;379:632-5.
- 18.) Brennan AM, Mantzoros CS (2006). "Drug Insight: the role of leptin in human physiology and pathophysiology—emerging clinical applications". *Nat Clin Pract Endocrinol Metab* 2 (6): 318–27. doi:10.1038/ncpendmet0196. PMID 16932309.
- 19.) Halaas JL, Gajiwala KS, Maffei M, Cohen SL, Chait BT, Rabinowitz D, Lallone RL, Burley SK, Friedman JM (July 1995). "Weight-reducing effects of the plasma protein encoded by the obese gene". *Science* 269 (5223): 543–6. doi:10.1126/science.7624777. PMID 7624777.a
- 20.) Campfield LA, Smith FJ, Guisez Y, Devos R, Burn P (July 1995). "Recombinant mouse OB protein: evidence for a peripheral signal linking adiposity and central neural networks". *Science* 269 (5223): 546–9. doi:10.1126/science.7624778. PMID 7624778.
- 21.) Pelleymounter MA, Cullen MJ, Baker MB, Hecht R, Winters D, Boone T, Collins F (July 1995). "Effects of the obese gene product on body weight regulation in ob/ob mice". *Science* 269 (5223): 540–3. doi:10.1126/science.7624776. PMID 7624776.
- 22.) Maffei M, Halaas J, Ravussin E, Pratley RE, Lee GH, Zhang Y, Fei H, Kim S, Lallone R, Ranganathan S (November 1995). "Leptin levels in human and rodent: measurement of plasma leptin and ob RNA in obese and weight-reduced subjects". *Nat. Med.* 1 (11): 1155–61. doi:10.1038/nm1195-1155. PMID 7584987.
- 23.) Considine RV, Considine EL, Williams CJ, Nyce MR, Magosin SA, Bauer TL, Rosato EL, Colberg J, Caro JF (June 1995). "Evidence against either a premature stop codon or the absence of obese gene mRNA in human obesity". *J. Clin. Invest.* 95 (6): 2986–8. doi:10.1172/JCI118007. PMC 295988. PMID 7769141.
- 24.) Considine RV, Sinha MK, Heiman ML, Kriauciunas A, Stephens TW, Nyce MR, Ohannesian JP, Marco CC, McKee LJ, Bauer TL (1996). "Serum immunoreactive-leptin concentrations in normal-weight and obese humans". *N. Engl. J. Med.* 334 (5): 292–5. doi:10.1056/NEJM199602013340503. PMID 8532024
- 25.) Zhang, Y., et al. 1994. Positional cloning of the mouse obese gene and its human homologue [erratum 1995, 374:479]. *Nature*. 372:425–432.
- 26.) Morton, G.J., et al. 2006. Central nervous system control of food intake and body weight. *Nature*. 443:289–295
- 27.) Flier, J.S. 1998. Clinical review 94: what's in a name? In search of leptin's physiologic role. *J. Clin. Endocrinol. Metab.* 83:1407–1413.
- 28.) Ahima, R.S., et al. 1996. Role of leptin in the neuro-endocrine response to fasting. *Nature*. 382:250–252.
- 29.) Welt, C.K., et al. 2004. Recombinant human leptin in women with hypothalamic amenorrhea. *N. Engl. J. Med.* 351:987–997.
- 30.) Menus for the Leptin Diet Last Updated: Dec 11, 2015 | By Paula Martinac
- 31.) Maffei M, Halaas J, Ravussin E, et al. (1995) Leptin levels in human and rodent: measurement of plasma leptin and ob mRNA in obese and weight-reduced subjects. *Nat Med* 1: 1155±1161
- 32.) Considine R, Sinha MK, Heiman ML, et al. (1996) Serum immunoreactive-leptin concentrations in normal-weight and obese humans. *N Engl J Med* 334: 292±295
- 33.) Margetic S, Gazzola C, Pegg GG, Hill RA. Leptin: a review of its peripheral actions and interactions. *Int J Obes Relat Metab Disord.* 2002; 26: 1407–1433. CrossRefMedline
- 34.) Seufert J. Leptin effects on pancreatic beta-cell gene expression and function. *Diabetes.* 2004; 53 (suppl 1): S152–S158. Abstract/FREE Full Text
- 35.) Beltowski J. Leptin and atherosclerosis. *Atherosclerosis.* 2006; 189: 47–60.
- 36.) Werner N, Nickenig G. From fat fighter to risk factor: the zigzag trek of leptin. *Arterioscler Thromb Vasc Biol.* 2004; 24: 7–9. FREE Full Text
- 37.) Sivitz WI, Walsh SA, Morgan DA, Thomas MJ, Haynes WG. Effects of leptin on insulin sensitivity in normal rats. *Endocrinology.* 1997; 138: 3395–3401. CrossRefMedline
- 38.) Muoio DM, Dohm GL, Fiedorek FT, Tapscott EB, Coleman RA. Leptin directly alters lipid partitioning in skeletal muscle. *Diabetes.* 1997; 46: 1360–1363. Abstract/FREE Full Text
- 39.) Liu Y-L, Emilsson V, Cawthorne MA. Leptin inhibits glycogen synthesis in the isolated soleus muscle of obese (ob=ob) mice. *FEBS Lett.* 1997; 411: 351–355. CrossRefMedline
- 40.) Berti L, Kellerer M, Capp E, Haring HU. Leptin stimulates glucose transport and glycogen synthesis in C2C12 myotubes; evidence for a PI3-kinase mediated effect. *Diabetologia.* 1997; 40: 606–609.
- 41.) Mallamaci F, Cuzzola F, Tripepi G, Cutrupi S, Parlongo S, Tripepi R, Zoccali C. Gender-dependent differences in plasma leptin in essential hypertension. *Am J Hypertens.* 2000; 13: 914–920. Abstract/FREE Full Text
- 42.) Singhal A, Farooqi IS, Cole TJ, O'Rahilly S, Fewtrell M, Kattenhorn M, Lucas A, Deanfield J. Influence of leptin on arterial distensibility: a novel link between obesity and cardiovascular disease? *Circulation.* 2002; 106: 1919–1924
- 43.) Maffei, M., J. Halaas, E. Ravussin, R.E. Pratley, G.H. Lee, Y. Zhang, H. Fei, S. Kim, R. Lallone, S. Ranganathan, P.A. Kern, and J.M. Friedman. 1995. Leptin levels in human and rodent: measurement of plasma leptin levels and ob RNA in obese and weight reduced subjects. *Nat. Med.* 1:1155–1161.
- 44.) Considine, R.V., M.K. Sinha, M.L. Heiman, A. Kriauciunas, T.W. Stephens, M.R. Nyce, J.P. Ohannesian, C.C. Marco, L.J. McKee, T.L. Bauer, and J.E. Caro. 1996. Serum immunoreactive-leptin concentrations in normal-weight and obese humans. *N. Engl. J. Med.* 334:292–295.
- 45.) Hassink, S.G., D.V. Sheslow, E. de Lancey, I. Opentanova, R.V. Considine, and J.E. Caro. 1996. Serum leptin in children with obesity: relationship to gender and development. *Pediatrics.* 98:201–203.
- 46.) Pelleymounter, M.A., M.J. Cullen, M.B. Baker, R. Hecht, D. Winters, T. Boone, and F. Collins. 1995. Effects of the obese gene product on body weight reduction in ob/ob mice. *Science (Wash. DC).* 269:540–543.
- 47.) Halaas, J.L., K.S. Gajiwala, M. Maffei, S.L. Cohen, B.T. Chait, D. Rabinowitz, R.L. Lallone, S.K. Burley, and J.M. Friedman. 1995. Weight-reducing effects of the plasma protein encoded by the obese gene. *Science (Wash. DC).* 269:543–546.
- 48.) Total Energy Expenditure and the Level of Physical Activity Correlate With Plasma Leptin Concentrations in Five-Year-Old Children Arline D. Salbe, Margery Nicolson,† and Eric Ravussin Clinical Diabetes and Nutrition Section, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Phoenix, Arizona 85016-5319; and ‡AMGEN, Inc., Thousand Oaks, California 91320
- 49.) Myers MG, Cowley MA, Münzberg H (2008). "Mechanisms of leptin action and leptin resistance". *Annu. Rev. Physiol.* 70 (1): 537–556. doi:10.1146/annurev.physiol.70.113006.100707. PMID 17937601.
- 50.) Wang J, Obici S, Morgan K, Barzilay N, Feng Z, Rossetti L (December 2001). "Overfeeding rapidly induces leptin and insulin resistance". *Diabetes* 50 (12): 2786–2791. doi:10.2337/diabetes.50.12.2786. PMID 11723062.
- 51.) Enriori PJ, Evans AE, Sinnayah P, Jobst EE, Tonelli-Lemos L, Billes SK, Glavas MM, Grayson BE, Perello M, Nilni EA, Grove KL, Cowley MA (March 2007). "Diet-induced obesity causes severe but reversible leptin resistance in arcuate melanocortin neurons". *Cell Metab.* 5 (3): 181–194. doi:10.1016/j.cmet.2007.02.004. PMID 17339026.
- 52.) Obici S, Rossetti L (December 2003). "Minireview: nutrient sensing and the regulation of insulin action and energy balance". *Endocrinology* 144 (12): 5172–8. doi:10.1210/en.2003-0999. PMID 12970158.