# ANOREXIA NERVOSA: CURRENT RESEARCH FROM A BIOLOGICAL PERSPECTIVE

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## ABSTRACT

Eating disorders are viewed as serious mental illnesses, carrying significant, life-threatening medical and psychiatric implications, including morbidity and mortality. According to the Academy of Eating Disorders, anorexia nervosa has the highest mortality rate of any psychiatric disorder. The American Psychiatric Association (2004) claims that approximately three percent of the United States female population has a clinically relevant eating disorder. Risk of premature death is 6-12 times higher in women with anorexia as compared to the general population, and it has become the third most common form of chronic illness among adolescent women aged 15 to 19 years. Although the prevalence and seriousness of this problem have gained increasing attention in recent years, relatively little is known about the role that leptin plays in this disorder. Leptin is a starvation hormone as well as a satiety hormone that plays a role in the diagnoses, duration, and recovery of this devastating disease. The review of the research will attempt to define the etiology of the endocrine events and the significant physiological impact on the body's structures relative to this disease. The diagnosis and treatment will address and reflect the physiological effects caused by the semi-starvation state produced by anorexia nervosa. Anorexia is triggered by psychological problems that transform into biological issues. Profound physiological changes brought about by the semi starvation state cause a domino effect. The biological ramifications of the disease should be cured before psychological counseling is attempted.

## INTRODUCTION

Diagnosable eating disorders, such as anorexia nervosa, are not uncommon, occurring in approximately three percent of the United States female population (American Psychiatric Association [APA] 2004). According to the Academy for Eating Disorders (2011), eating disorders have become the third most common form of chronic illness among adolescent women aged 15 to 19 years. Anorexia Nervosa (AN) is classified in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) as refusal to maintain a minimally normal body weight (i.e. below 85% medically ideal body weight), profound fear of weight gain, body image disturbance, and amenorrhea (i.e. absence of menses) (American Psychiatric Association 2004). According to the American Psychiatric Association, anorexia nervosa has the highest mortality rate of any psychiatric disorder (Yager, 2000). Even when feeling hungry, afflicted individuals severely limit their food intake based on their irrational fear of gaining weight, due to the distorted perception they have of their body as perpetually being overweight. Despite their dwindling weight, those suffering from anorexia nervosa will always see themselves as fat. It is because of their skewed self-image and irrational fear of obesity that anorexia nervosa is considered a disease that is psychiatric in nature.

## HISTORY OF TREATMENT AND PERCEPTION OF ANOREXIA NERVOSA

Anorexia nervosa is not a new phenomenon. Although the disease did not receive its name until recently, its classic symptoms have been around of centuries. Recorded cases of symptoms that appear to be the disorder first appear in 1689. Two case studies by Dr. Richard Morton illustrate that although the symptoms and effects were physical, physicians usually treated the patients as if it was a purely psychological disorder. This often led to disastrous and, at times, fatal results. The first case Morton presents is that of a young woman who exhibited extreme weight loss, distorted self-image, and loss of menarche (three of the four of the current criteria for anorexia nervosa in the DSM-IV (APA 2004). It was recorded that the patient's flesh was flaccid and loose and extremely pale. However, Dr. Morton framed the problem as stemming from "a multitude of cares and passions of her mind." Dr. Morton

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concluded that it was a psychological disorder, that she could be as "different" as she wanted to be, and that this is not a doctor's area of expertise. The young woman died two months later. In another case, a young man displayed similar symptoms. Here too, Dr. Morton concluded that the young man was suffering from "passions of the mind" and prescribed some rest and relaxation in the countryside. The young man died shortly thereafter (Kendall 2011).

These cases constitute just two of many that illustrate how physicians in the past ignored the biological symptoms and effects of the disease. Any psychological condition was dismissed as one having a weak mind or lack of strength, and thus untreatable. No attempts were made to understand the harrowing condition. It was not until the late ninteenth century that anorexia nervosa was to be widely accepted by the medical profession as a recognized condition. In 1873, Sir William Gull, one of Queen Victoria's personal physicians, published a seminal paper which established the term anorexia nervosa and provided a number of detailed case descriptions and treatments. In the same year, French physician Ernest-Charles Lasègue similarly published details of a number of cases in a paper entitled *De l'Anorexie Histerique*. The physicians began to hospitalize and attempt to stabilize the patients physiologically.

During the late twentieth century, the disorder became classified as a purely psychological disease. By the time most patients were diagnosed, they were already close to death. More were forcefully hospitalized and received psychiatric treatment. This method of therapy has been largely ineffective at helping individuals suffering from the disease in recovering long-term. Perhaps the strongest proof of this is that anorexia nervosa has the highest mortality rate of all psychiatric conditions. Long-term data indicate that the mortality rate is 5-10 percent, with only 50 percent of patients regaining their normal weight (Mehler et al. 1999).

This paper will focus on an alternative to a purely psychological approach by concentrating on a biological perspective. The diagnosis and treatment will address and reflect various physiological ramifications caused by the semi-starvation state produced by anorexia nervosa, signaled by hypoleptimia.

## METHODS

The materials used in this research paper included the Anatomy and Physiology and Biological Psychology course textbooks. Further, the author utilized the Touro College library search engine and retrieved journal articles from EBSCO as well as Google and Google Scholar to find basic information and peer reviewed articles on the topic.

## DISCUSSION

There are four criteria that must be satisfied to be considered anorexia by the DSM-IV (APA 2004). Two of these criteria are psychiatric conditions: distorted body image and the irrational fear of gaining weight and/or becoming fat. The other two are biological concerns brought about by the first two factors. Body Mass Index, calculated from a person's weight and height, provides a reliable indicator of body fat. For most people, it is used to screen for weight categories that may lead to health problems (Centers for Disease Control and Prevention 2011). The third criterion is refusal to maintain a weight of at least 85 percent of that expected for height. This can be translated into the fifth-tenth body mass index percentile. Figuring for body mass index, as opposed to merely weight, is vital because weight alone does not tell the full picture. If someone is five feet one inch and 105 pounds, the individual is not underweight. If someone is five feet eleven inches, the individual is severely underweight at 105 pounds. "Adults should normally have a body mass index between 18.5 and 24.9… a body mass index of under 17.5 is indicative of anorexia nervosa" (Blows 2011). A body mass index below 17.5 means the body is now in a semi-starvation mode. It is scrambling to survive and will use and conserve whatever physiological reserves it possesses in order to remain alive and functioning. There is a cascading effect of short-term and long-term physical effects in the body. One of the effects is amenorrhea. Amenorrhea is the absence of a menstrual period in a woman of reproductive age. The

presence of amenorrhea is the fourth criterion, and it is purely physical and biological. The fact that a state that can only exist in women is one of the four criteria for anorexia is telling. Psychologically, there are many reasons why, according to the National Association of Anorexia Nervosa and Associated Disorders (2013), approximately 90-95 percent of anorexia patients are women. Because their fat distribution is higher, women's systems rely on leptin levels more heavily than men. Women, having higher leptin levels than men, are thus more susceptible, because when leptin levels are lowered, the effects are more rapidly and radically felt by women.

The point at which the disorder transforms from a purely psychiatric issue into a biological one is complex. Acute calorie deprivation for 2-3 days results in a significant decrease in leptin concentration before major changes in bodyweight or fat mass go up 20-30 percent (Chan et al. 2005). Thus, the body's leptin levels are significant. It begins when the caloric intake is decreased so much as to decrease the resting energy expenditure, also known as resting metabolic rate. This represents the amount of calories required in a 24-hour period by the body during a non-active period. At what point is the body considered to have entered the semi starvation state? The consensus seems to be that when a person decreases the total caloric intake of less than 50 percent of what the body requires, a semi starvation mode ensues. The metabolic rate is significantly lowered and begins to make significant changes in the body's functions. These adaptations are controlled processes involving apoptotic shutdown and organ hypotrophy that can delay death. In the early stages of malnutrition, there is scope for tightening the efficiency of various metabolic functions and for closing down some that are non-essential in the short term (e.g. reproduction). As the malnutrition worsens, long-term decisions must be made by the body to keep the individual alive. Before all those changes can be made, the resting energy expenditure must drop. What tells the metabolic rate that there is not enough caloric intake to survive and it must begin to make changes? What acts as the peripheral signal to change the body actually into the semi starvation mode and lower the resting energy expenditure?

One such signal is leptin, which has two functions. One function is as a pleiotropic hormone that relays information about peripheral energy storage and availability to the brain (Kumar et al. 2010). Its complete role as both a starvation and satiety hormone is illustrated in Figure 1. Leptin is a lipoprotein, which can pass the blood-brain barrier. It is made by adipose cells and inhibits the production of fat and increases the individual's physical activity potential. Leptin is twice as high in human beings that are obese, and this is related to their fat mass and high rate of leptin production by the body.

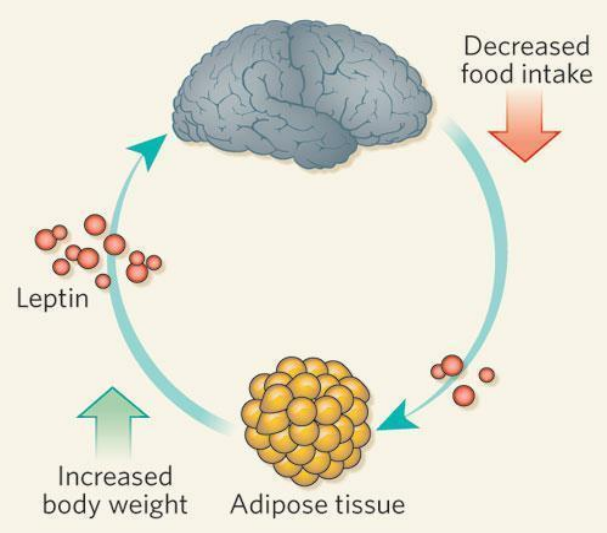
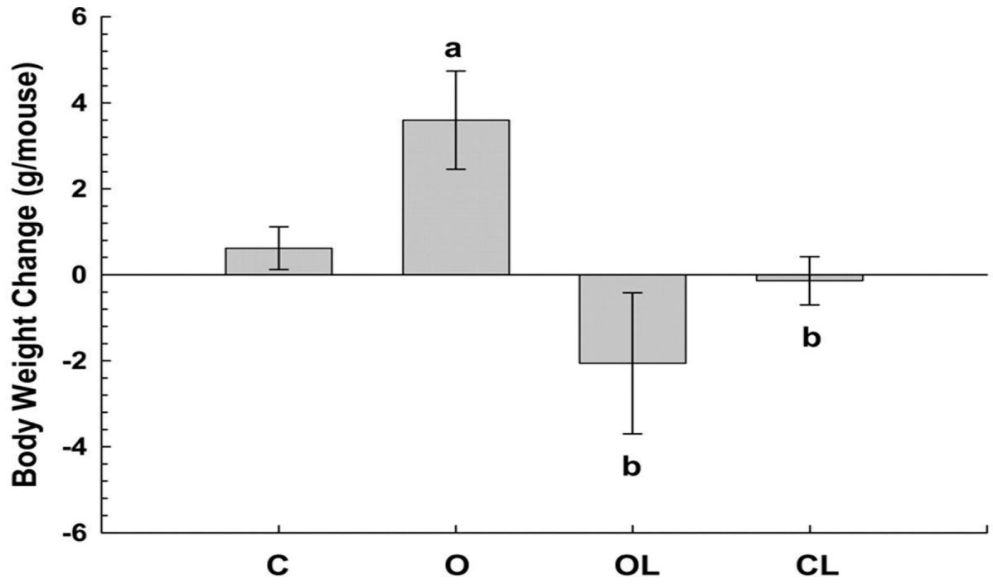



**Figure 1**: Cycle of Leptin production in the body. Source: Friedman 2009

This figure shows that an increase in body weight also increases the amount of leptin produced. Leptin then crosses over the blood brain barrier and inhibits the brain, which leads to a decrease in food intake of the body. Once synthesized, leptin is secreted through a constitutive pathway and not stored in the cell. Chan and his colleagues (2005) describe leptin as a 167 amino acid protein product of the ob gene that was discovered in 1994 through positional cloning in the ob/ob obsese mouse, a model of morbid obesity resulting from the absence of leptin due to a gene mutation. It is secreted in a pulsatile fasion and has a substantial diurnal variation with an increase of about 50 percent in the late evening and early morning hours that might be related to an intrinsic circadian component, meal timing, and the sleep-wake cycle. The original study and research was conducted using mice as illustrated in Figure 2. Severely obese mice were observed and discovered to have a mutation that did not allow them to produce the leptin hormone. When artificial leptin was administered, the mice began to slim down.

**Figure 2**: The Effect of leptin on body weight changes in C57BL/6J (control) and ob/ob (leptin-deficient) mice. Source: Claycombe et al. 2008




C, control; O, obese; OL, obese with leptin treatment; CL, control with leptin treatment

Schematic illustrations show of the effect of leptin on body weight changes *ob*/*ob* (leptin-deficient) mice. Mice were weighed at day zero before the start of leptin and saline injection. Body weight measurements were gathered daily for the next seven days, and the amount of leptin injected was adjusted accordingly. The mean values were calculated by averaging daily body weight differences for each mouse for all groups. Leptin treatment occurred over the span of seven days. As shown, the bar with letter *a* is significantly different from the control group. The bars with letter *b* are significantly different from the obese group. The hypothesis was that this satiety hormone could be a possible treatment of individuals suffering from obesity. Because individuals with anorexia do not eat proper meals and are on an incorrect cycle, leptin levels can be severely affected as well. However, researchers realized how complex, not only obesity is, but leptin as well. When studying obese individuals, they found that many had enough leptin. The theory was that although these obese individuals had enough leptin to signal their hypothalamus that they are not hungry, the body did not perceive the proper amounts of the hormone due to a default in their receptors. Therefore, leptin is not

the key to unlocking the mystery of causation and treatment of obesity. Although this theory proved to have some faulty hypothesis, the discovery of leptin is vital in the study of weight and anorexia as a disorder and its role as a satiety and starvation hormone. It was realized that leptin might be more important at the other end of the energy homeostasis spectrum, i.e. energy deprivation. In this context, studies in mice, as well as people, have shown that leptin has a role in the neuroendocrine adaptations to starvation which includes changes in hormone concentration that have a protective effect for patients with anorexia. Energy deficient conditions such as anorexia reflect low leptin levels, which could play a vital part in their pathophysiology ad potentially their treatment.

Leptin is initially produced by the adipose tissue and is secreted into circulation. It crosses the blood-brain barrier with the help of a transporter protein to bind to leptin receptors in the arcuate nucleus of the hypothalamus (Blows 2011). The nervous and endocrine systems act together to coordinate functions of all body systems as illustrated in Figure 3. The endocrine system helps regulate virtually all types of body cells. For many years, the pituitary gland, or hypophysis, was thought to be the master endocrine gland because it secretes several hormones that control other endocrine glands. We now know that the pituitary gland has a grand master as well: the hypothalamus. This small region of the brain below the thalamus is the major link between the nervous and endocrine systems.

At the point when the body mass index hits below 17.5, leptin signals the hypothalamus to go into semi-starvation mode. Three main brain axes are affected by the semi-starvation mode: the hypothalamus-pituitary-gonadal, hypothalamus-pituitary adrenal, and hypothalamus-pituitary thyroid axis. The metabolism slows down, and the first system that is shut down is the reproductive system.

**Figure 3:** Energy balance is regulated through complex interactions of factors in the body and the brain among which the hormone leptin plays an essential role. Source: Hofbauer & Huppertz 2002

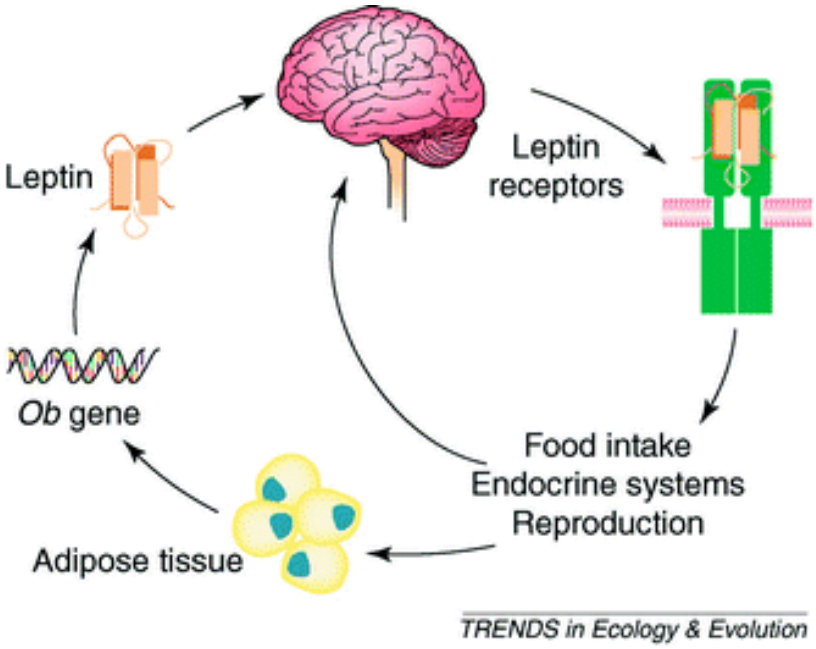



Figure 3 illustrates leptin and energy balance. Leptin is encoded by the Ob gene, which is expressed in white adipose tissue. Leptin is similar in structure to cytokines, which are heterogeneous group of endogenous, bioactive peptides released mainly from inflammatory tissue and cells of the immune system. It is secreted into the blood and crosses the blood-brain barrier, probably via a carrier system which has a limited maximum transport system. In the hypothalamus, leptin acts on specific receptors of the class I cytokine receptor subtype. Through stimulatory or inhibitory effects on downstream effector systems, leptin reduces appetite. However, in its semi starvation mode, it also influences various endocrine systems, such as adrenocortical and gonadal hormones. In the long term, decreased food intake leads to a reduction in adipose tissue and consequently a diminished production of leptin, which then increases food intake. The fourth criterion of the DSM-IV is met when the body enters amenorrhea. Like a domino effect, energy becomes more and more scarce throughout the body, triggering numerous hormonal cascades. Each cascade hits a specific axis. However, each cascade works along the same series of steps. The initial trigger is hypoleptimia, which will signal the hypothalamus to secrete either a releasing or inhibitory hormone. Each axis will react differently and, therefore, need a different type of hormone. At this point, the pituitary gland will release a specific hormone. Although the hormone will differ at each axis, its ultimate result will remain the same. This releasing hormone will trigger a specific endocrine gland to secrete yet another hormone, which will directly affect one of the critical homeostatic ranges of the body. This is turn will disrupt one of the vital metabolic processes that keep the organism alive. The same initial trigger, leptin, and ultimately the same devastating results (having affected homeostatic ranges) are observed.

The first axis cascade, of the hypothalamic-pituitary gonadal axis, begins by a state of hypoleptimia, and this causes a reduction in gonadotropic-releasing hormones (the inhibitory hormone secreted by the hypothalamus). At the same time, there is sequential reduction in the follicle stimulating hormone (FSH) and luteinizing hormone (LH), which is normally secreted by the anterior pituitary. The luteinizing hormone is responsible for the ovarian-follicle growth that leads to ovulation. With the reduction of the ovarian function, ovulation and reproductive functions cease, including menstruation (Usdan et al. 2008). Estrogen is a key factor in ovulation because the amount must reach a certain level

for ovulation to be triggered. Without enough estrogen, ovulation will not occur. Estrogen levels decrease dramatically in women with anorexia nervosa because one of the components of estrogen is cholesterol, which is derived from fat. With little to no fat being consumed in one's diet, there are simply not enough raw materials to create the necessary estrogen.

Any factor causing an organism's condition to waver away from homoeostasis can be interpreted as stress. In such instances an organism's fight or flight response recruits the body's energy stores and focuses attention to overcome the challenge at hand; thus, stress throws off nearly all the homeostatic ranges in the body. Cortisol is one of the stress hormones produced in high levels as a result of severe caloric restriction, and it helps the body manage stress when a person is in semi-starvation mode. Cortisol, which is produced by the adrenal gland, metabolizes fat and sugar into energy as its primary function. Anorexia catapults the body into starvation mode, and the body interprets a shift of homeostatic ranges as extreme stress. Cortisol levels spike, and the body shifts to fight or flight mode to survive. This leads into the second hormonal cascade.

The hypothalamic-pituitary-adrenal axis is affected next. As glucose becomes scarcer with the continued severe restriction of carbohydrates, the hypothalamus triggers a rise in corticotropin-releasing hormone (CRH) which, in turn, triggers the pituitary to increase adrenocorticotropic hormone (ACTH) secretion. This raises the cortisol levels of the adrenal gland. At this point, the autonomic nervous system takes over, particularly the sympathetic portion, shifting from voluntary to involuntary, and the fight or flight response becomes activated. As this is occurring, the rising level of cortisol triggers lipolosis and gluconeogenesis. Any other available raw materials that are not specifically carbohydrates are converted into glucose to provide energy from the body to survive. The first step the body takes is moderate, using raw materials other than carbohydrates to maintain the energy required. As the disease progresses and there is less raw material available, the body begins to consume itself (i.e. muscles) in a further attempt to keep homoeostatic ranges and the essential body systems running.

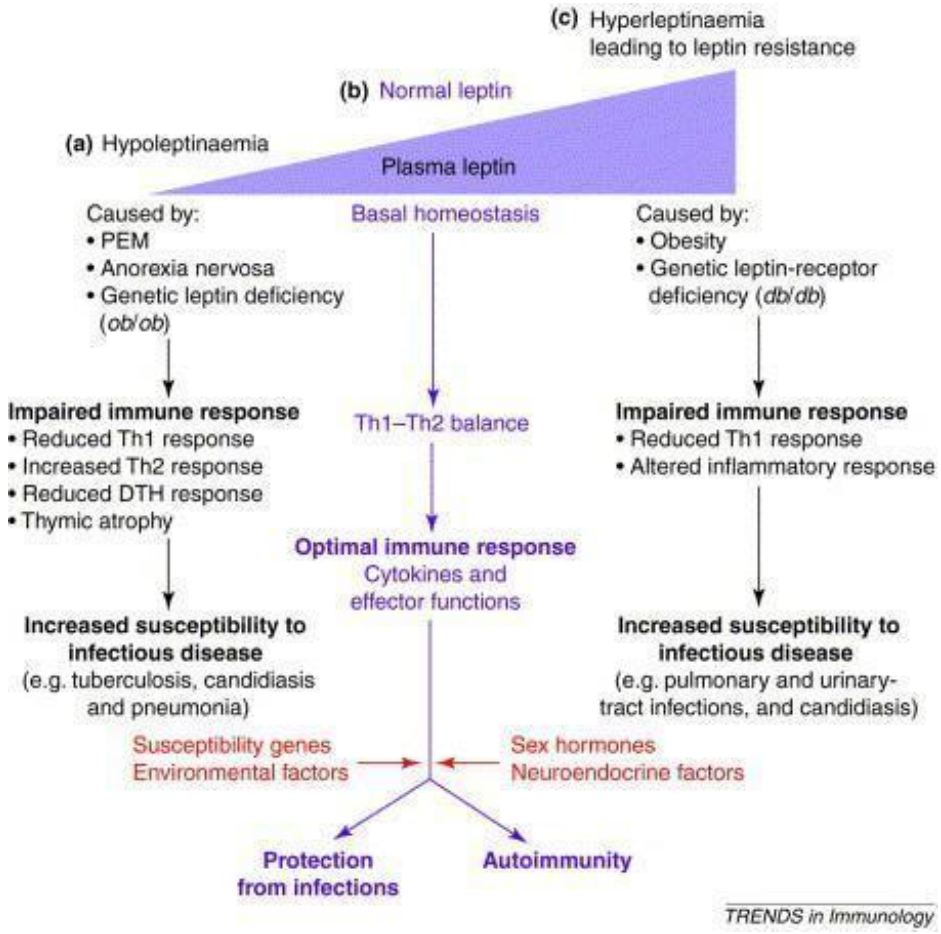
The rising cortisol level and the semi-starvation state elicit a response from the hypothalamic-pituitary-thyroid axis, the third main brain axis. The thyrotropin-releasing hormone (TRH) from the hypothalamus is decreased, prompting a decrease in the thyroid-stimulating hormone (TSH) from the pituitary gland. This, in turn, decreases the release of T3 and T4 and the overall function of the thyroid. This is significant because while most hormones require specific receptors within cells to affect them, the thyroid gland produces hormones that can interact and affect almost every cell in the body. While thyroid irregularity is not fatal, it does throw the body into disarray. The patient cannot sustain health because thyroid hormones contribute to so many important physiological processes, such as development, growth, and metabolism. Because of this hypothyroidism, the whole metabolic rate is lowered and can go into hypothermia. Since the appetite cannot be appropriately controlled, glucose will not be absorbed properly, as hypothyroidism mimics the exact initial symptoms of anorexia (i.e. lack of food intake). At this point, hypothyroidism is a symptom of a progression of the disease.

As discussed, the body initially attempts moderate measures to continue its upkeep, regardless of the severe decrease of nutrition, and eventually moves on to more radical measures. Reproduction activity ceases and the body begins inhibiting production of hormones responsible for growth stimulation, focusing on increasing hormones that help maintain bone, tissue, and muscle already present. The body attempts to preserve the raw materials it already possesses. An example of this is that the body decreases the production of insulin-like growth factors which are responsible for the promotion of cell proliferation. Insulin-like growth factor is thought to be a primary growth factor and is required to achieving maximal growth. In contrast, there is a significant increase in growth hormone, which is a peptide hormone that stimulates regeneration in humans .One of the functions of the growth hormone is to help maintain muscle and bone mass of the adult body. It promotes healing of injuries and tissue repair. It also helps convert all reserves other than glucose, such as fats and amino acids into energy the body can use to survive.

Bone mass is lost early on in the course of the disorder. The body's desperate attempt for survival causes it to shut down bone formation, in order to conserve its small energy reserve. The body's desperate attempt for survival causes it to shut down bone formation, in order to conserve its small energy reserve. "Recently bone has been recognized as a highly metabolic tissue requiring energy such that new bone formation is appropriately suppressed with inadequate nutrition" (Sum et al. 2011). Until the point of decreased bone mass, with proper refeeding, the negative cascade of biological disarray wreaked on the body by starvation is reversible. Decreased bone mass, however, is a permanent loss, as bone cannot replenish itself. Bone regeneration is an active area of research. This impact of cessation of bone formation has an especially devastating effect on adolescents with anorexia. Anorexia patients, regardless of age, often have a very early onset of osteopenia, and as high as 25% of the patients develop osteoporosis. The body is now focused on trying to maintain a homeostatic range of calcium to keep the normal metabolic processes operating. Bone health in a normal, healthy adult is maintained through bone remodeling, which occurs in two phases: bone formation and bone resorption. Both are necessary to maintain health calcium homeostasis. Bone formation causes calcium to be extracted from the blood and uses it to form new bone. Bone resorption is when the body breaks down bone to extract the calcium needed for other body functions, such as neurotransmission. "Women with anorexia have increases in markers of bone resorption with decreases in markers of bone formation" (Sum et al. 2011). Not only is new formation not occurring, but bone is being broken down constantly for the needed calcium. This leads to extremely porous bones. Any slight tap can lead to fractures, so much so that it can be a cause of "sevenfold increases incidence of spontaneous fractures" (Hebebrand et al. 2007). Estrogen is also essential to bone formation, and with the drastically reduced levels, as previously mentioned, it maintains the state of bone resorption and cannot begin bone formation. This point is illustrated in menopausal women. They have a very high rate of osteoporosis due to their natural drastic decrease of estrogen.

As calcium levels drop significantly in anorexics, neurotransmitter releases drop tremendously as well. Serotonin (a key neurotransmitter) production drops significantly. Levels also fall because serotonin is synthesized from carbohydrates that we intake through our diets. Since there are not enough raw materials to create the hormone, it is not present. As a result of serotonin deficiency, the individual feels satiated without eating the proper amount of food. This is a transformation in which anorexics no longer control their food intake purely by choice. It becomes a physical condition in which, as opposed to ignoring messages and feelings of hunger their bodies send them, they really are not hungry. As the disease progresses, the amygdala and hypocampus of the limbic system atrophy. Emotions are now affected and biology takes over even the emotional aspect of food and eating. Memory and feelings about food, which effect how much and what a person chooses to eat, are distorted and they no longer can make proper choices. A complex and life-threatening physical problem has taken over.

**Figure 4:** Body Moving from Hypoleptinaemia to Hyperleptinaemia. Source: Matarese et al.




In traditional treatment, the first step is hospitalization and refeeding, usually force-feeding. An important initial step, however, is a blood test to check leptin levels. This is important because the degree of hypoleptinaemia in acute anorexia nervosa is an indicator of the severity of the disorder; thus, pronounced hypoleptinaemia is not only indicative of an exceedingly low fat mass, but also reveals that the neuroendocrine adaptation to semi-starvation has maximally progressed in such critically ill patients (Hebebrand et al. 2007). As the refeeding process progresses, the leptin levels are going to move from hypoleptinaemia (starvation hormone) to hyperleptinaemia (satiety hormone) as depicted in Figure 4.

During the course of a normal pattern of life in a person without anorexia, leptin levels constantly fluctuate, but within certain limits. The danger of refeeding is that the levels move from zero to 60 in a very short period. The leptin in the anorexic patients have become a satiety hormone, and biologically, the patients cannot eat because they feel full. This is yet another example of the disease and treatment being biologically based. In spite of all the therapy patients receive, if they are not hungry, they cannot force down the food. To prevent this issue, doctors should begin refeeding extremely slowly, i.e. moving from 600 up to 700 calories a day, as opposed to the normal 1800 calories. Another danger of refeeding too quickly is throwing the person's electrolytes out of balance because of drastic fluid shifts, which can cause cardiac arrhythmia. Furthermore, introducing too many

carbohydrates very quickly is problematic because it creates a large influx of insulin and "the introduction of insulin to the starved system poses a variety of severe hemodynamic and electrolyte consequences…. The sodium retention caused by increased insulin levels can lead to hypervolemia and resultant cardiac and respiratory failure" (Usdan et al. 2008).

The leptin levels should be monitored several times a day, particularly after meals, to ensure that they are increasing but not dramatically into a state of hyper (which causes its own set of biological problems). The leptin levels will also tell the doctors how soon they can introduce more calories as well as how much they should be increasing the caloric intake at each interval, i.e. if moving from 600 to 750 calories produced a dramatic increase in leptin, it should perhaps be reduced to 700.

Moreover, small amounts of leptin should also be artificially given to patients with anorexia to slowly bring up their levels. The purpose is twofold. The first reason is to stop the cascade; it will fool the body into thinking that it is not in a semi-starvation state, and the other reactions, i.e. bone loss and amenorrhea, will not be triggered. If leptin levels are monitored properly, i.e. given artificially when necessary and used to dictate refeeding amounts and schedules, it can take about six months or more to normalize and stabilize their leptin levels. That will allow the patient's biological condition to improve dramatically by stopping many of the processes that began because of extremely low levels, i.e. hypothyroidism. If the leptin is introduced prior to the domino-like effects produced by the semi-starvation and before resting energy expenditure levels drop, the underlying psychological causes of anorexia can be addressed, as opposed to dealing with the near death physical conditions and complications of the disease. Once the refeeding process is near completion and normal body mass index and body fat ranges are attained, leptin levels must still be monitored closely. This is important to ensure that leptin transitions from the energy expenditure regulator role caused by anorexia and semi-starvation back into the satiating hormone of a healthy body. Additionally, research has shown that for the first six months, leptin levels in anorexia patients that have achieved a proper and healthy weight are often higher than people with normal, healthy weights and eating habits. Consequently, the leptin, in the satiety position, can hinder their weight maintenance because of this false feeling of fullness. (Hebebrand et al. 2007)

Due to the importance of leptin and the information that it provides in diagnosis, treatment, and prevention, it can be argued that determination of leptin levels should be included in the DSM-IV as part of the criteria for anorexia nervosa (American Psychiatric Association 2000). Hypoleptinaemia is integral in diagnosing how far the disease has progressed and what form of treatment is needed. It is believed that if doctors use leptin levels properly to diagnose and treat patients with anorexia, mortality rates can and should decrease.

## CONCLUSION

All body systems are affected by anorexia nervosa in a nearly domino-like effect. Severe malnutrition can ultimately lead to multi-organ failure and death. The psychiatric causes of the disease are likely to be impossible to address while a patient is extremely physically ill and in danger of losing his or her life. Physical reactions from increased leptin and serotonin levels in the body create a situation in which the patient no longer feels hungry. Thus, a truly effective cure for anorexia nervosa must take far more expertise that can be provided by a psychiatrist alone. Various medical professionals, in addition to mental health professionals, must work together to provide care in their individualized specialties in order to bring about an effective and lasting cure for this destructive and multifaceted disease. Where damage has been caused by the onset of anorexia nervosa, doctors must work together to ensure that these conditions do not continue to deteriorate, as well as work to improve them. Doctors must have a coordinated plan in order to truly cure the disease and ensure that the patient does not relapse into a state of malnutrition and disease. The false assumption of anorexia as a purely psychiatric condition has contributed to a fairly high mortality rate. Although anorexia is rooted in mental illness, its profound physiological ramifications must be dealt with first in a bottom up

approach. It is only after a biological cure is effected can the road be paved to successful psychological counseling. It is hypothesized that with more research on the biological basis of the disorder and treatment, particularly the role of leptin in diagnosing and treating this harrowing disorder, the mortality rates can be significantly reduced, and a greater understanding of anorexia nervosa can be achieved.

## REFERENCES

Academy for Eating Disorders. 2011. Eating disorders: Critical points for early recognition and medical risk management in the care of individuals with eating disorders. Retrieved from http://www.anad.org/wp-content/uploads/2011/10/AED-Medical-Risk-Management.pdf.

American Psychiatric Association. 2004. Diagnostic and statistical manual of mental disorders. 4th ed. Washington: American Psychiatric Publishing.

Blows W. 2011. The physiology of food intake regulation and eating disorders. Gastrointestinal Nursing 9(6):40-45.

Centers for Disease Control and Prevention. 2011. Body Mass Index. Retrieved from http://www.cdc.gov/healthyweight/assessing/bmi/.

Chan JL, Mantzoros CS. 2005. Role of leptin in energy-deprivation states: Normal human physiology and clinical implications for hypothalmic amenorrhea and anorexia nervosa. Lancet 366:74-85.

Claycombe K, King LE, Fraker PJ. 2008. A role for leptin in sustaining lymphopoiesis and myelopoiesis. Biological Sciences Immunology 105(6):2017-2021.

Friedman JM. 2009. Obesity: Causes and control of excess body fat. Nature 459:340-342.

Hebebrand J, Muller TD, Holtkamp K, Herpertz-Dahlmann B. 2007. The role of leptin in anorexia nervosa: Clinical applications. Molecular Psychiatry 12(1):23-35.

Hofbauer KG, Huppertz C. 2002. Pharmacotherapy and evolution. Trends in Ecology & Evolution 17(17):328-334.

Kendall J. 2011. The forgotten founding father: Noah Webster's obsession and the creation of an American culture. London, England. Penguin Books.

Kumar KK, Tung S, Iqbal J. 2010. Bone loss in anorexia nervosa: leptin, serotonin, and the sympathetic nervous system. Annals of the New York Academy of Sciences 1211:51-65.

Matarese G, La Cava A, Sanna V, Lord GM, Lechler RI, Fontana S, Zappacosta S. 2002. Balancing susceptibility to infection and autoimmunity: A role for leptin? Trends in Immunology 23(4):182-187.

Mehler PS, Eckel RH, Donahoo WT. 1999. Leptin levels in restricting and purging anorectics. The International Journal of Eating Disorders 26(2):189-194.

National Association of Anorexia Nervosa and Associated Disorders. 2013. Eating Disorders Statistics. Retrieved from: http://www.anad.org/get-information/about-eating-disorders/eating-disorders-statistics/.

Sum M, Mayer L, Warren MP. 2011. Bone mineral density accrual determines energy expenditure with refeeding in anorexia nervosa and supersedes return of menses. Journal of Osteoporosis 2011:1-7.

Usdan LS, Khaodhiar L, Apovian L. 2008. The endocrinopathies of anorexia nervosa. Endocrine Practice 14(8):1055-1063.

Yager J. 2000. The American Psychiatric Association practice guideline for the treatment of patients with eating disorders. Eating Disorders Review 11(2):1-8.