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# Eating Disorders: The Hidden Hormonal Effect On Fertility

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## Abstract

Women who have a history of eating disorders, specifically anorexia nervosa, are more prone to suffer from infertility. There are several hormones which are the driving force in this system and are therefore responsible for this. Fortunately, there are treatments which can help women with a history of eating disorders to reproduce. Using information found on Pubmed and Touro College's database, this paper will discuss why the body cannot reproduce when it is lacking proper nutrition, as well as the various dynamics in the human reproductive system which are compromised when the body is not properly nourished.

## Introduction: Eating Disorders

The term "eating disorders" constitutes a range of disorders including anorexia nervosa, bulimia nervosa, binge eating disorder, and other unnamed eating disorders. Overall, these disorders are characterized by a distorted body image and abnormal behaviors pertaining to food intake or weight loss that lead to decreased quality of life and extreme distress.

Up to 24 million people in the United States suffer from an eating disorder (National Association, 2014). For years it was believed that eating disorders typically affect white, wealthy, well-educated females living in major cities. However, new studies are proving otherwise (Mitchison & Hay, 2014). Eating disorders are commonly found in adolescents; 13.4% of female teenagers display signs of a disorder, while 7.1% of males exhibit those signs (Treasure et al., 2010). Overall, eating disorders are slightly more predominant in individuals of lower socioeconomic status, and bulimia is more common among minorities. Education, marital status, and urbanicity, studies find, do not play a significant role in eating disorders. It is also evident that individuals who participate in specific sports, such as aesthetic (e.g. dancing and gymnastics) and leanness- or weight-related (e.g. wrestling), have a higher prevalence of developing an eating disorder. Modeling is associated with an increased incidence of anorexia and subclinical anorexia. Individuals who live with a great amount of stress report higher incidence of eating disorders. While not thoroughly studied, evidence is emerging that even minor stresses such as moving to a new house or a change in family dynamic may lead to the development of an eating disorder. With this new research, scientists have come to a general understanding about the demographics of eating disorders; however, they still admit that there are some limitations to the studies that have been performed on epidemiology, and they may never know the true prevalence of eating disorders (Mitchison & Hay, 2014).

Much of the information about individuals with eating disorders comes from those who are treated. However, many patients are embarrassed about their condition and do not seek treatment. For example, males with eating disorders tend to be ashamed, as it is more accepted for a female to be diagnosed with an

eating disorder, and they therefore do not seek help (National Association, 2014). In addition, teenagers living at home may be brought to a doctor by their parents, whereas adults or the elderly who live alone have no one looking after them and forcing them to get help. Therefore, much of the research fails to include those who do not seek treatment, which may skew statistics (Mitchison & Hay, 2014).

There are various factors that cause an individual to develop an eating disorder. Some theories suggest that the root of eating disorders is possibly biological, genetic, and psychological in nature. Treasure et al. in their article explore the biological causes and believe that the structure of the appetite system and the way it functions can cause eating disorders. They believe that the three components of the appetite system can aid in the understanding of eating disorders.

The first component of the appetite system involves a homeostatic system that is primarily situated in the hypothalamus and brainstem. This system utilizes signals from the gastrointestinal tract and specific metabolic markers to affect hunger and satiety. The second component is the drive system that registers the reward value associated with food, such as the pleasure or energy obtained from eating, and also helps motivate a person to want to eat and therefore look for suitable food. This drive system is comprised of striatum with afferent inputs from sense organs, neural structures that are involved in memory and learning, and neural circuitry that is distributed throughout the mesolimbic cortex. The third component is a self-regulation system which controls appetite and lets a person how much he needs to eat. When there are abnormalities in any of these three components, an individual is at risk of developing an eating disorder or of maintaining and exacerbating a pre-existing disorder (Treasure et al., 2010).

Despite the fact that eating disorders are often referred to as a whole, each type is characterized by distinguishing features that differentiate one from another. Since eating disorders are largely classified as psychological in nature, they are included in the

Diagnostic and Statistical Manual of Mental Disorders (DSM), the standard classification of mental disorders used by mental health professionals in the United States (DSM, 2014).

### Anorexia Nervosa

The most recent update of the DSM, DSM-5, has published changes to the previously-used classification system of eating disorders. According to DSM-5, a patient must exhibit the following symptoms to be appropriately diagnosed with anorexia:

1. Patient has low body weight relative to age, gender, physical health, and developmental trajectory; this is due to limited energy intake compared to what is actually required.
2. The patient is underweight; however, he/she has constant unrealistic worry about weight gain or becoming fat.
3. Patient denies his/her low body weight as problematic; patient is overly concerned with the way his/her body looks to the point it affects the way he/her thinks about him/herself – he/she has a false perception about the way his/her body looks (The alliance for eating disorders awareness, 2014).

Anorexia has a higher mortality rate than any other psychological disease (National Association, 2014) and is associated with a host of devastating metabolic changes to the body. Patients may experience dangerous arrhythmias due to low potassium levels, seizures due to sodium or fluid depletion from constant vomiting or diarrhea, thyroid problems, increased infections due to decreased white blood cells, dehydration, tooth decay, and reawakening of the bones. An obvious result of anorexia is malnutrition (Anorexia nervosa, 2014).

Approximately 75% of anorexia patients are female making 25% of the cases belong to the male gender, however there is not much known about the anorexic male population. (Wooldridge & Lytle, 2012).

Eating disorders negatively affect the skeletal system; growth retardation, bone loss, and osteoporosis are common. Weight gain will improve the bone density and reduce these effects. In addition, many patients with anorexia suffer from concomitant psychological ailments such as depression and anxiety due to hormonal imbalance (Misra & Klibanski, 2014).

The brain is the most important organ affected by eating disorders. The brain uses approximately 20% of the calorie intake and is also very dependent on the glucose from food. Therefore, when the body has poor nutrition, the brain is not receiving the correct amount of glucose and other nutrients. Most cases of eating disorders occur during adolescence, and this can be a major problem because this is the time of optimum growth and development.

When a person starves his brain, his brain is actually shrinking from lack of nutrition. This can lead to several behavioral and psychosocial disturbances. If a person would regain his lost weight and restore the brain mass to its normal level, his condition would most likely improve (Treasure et al., 2010).

Another important body system which is affected by eating disorders is the reproductive system. Since reproduction and nutrition are connected, severe weight loss will inhibit the cycle of reproduction from functioning properly. The records of a number of infertility clinics were reviewed to determine the various sources of these women's infertility. Almost 17% of the patients in the clinics were suffering from eating disorders in general, including 7.6% suffering from anorexia and bulimia (Stewart et al., 1990). In a London-based study, 11,088 pregnant women were questioned. Of those women, 171 (1.5%) said they had a history of anorexia, and 199 (1.8%) had suffered from bulimia at some point. Eighty-two women (0.7%) suffered from both. These women were compared with the remaining 10,636 women (96%). The following statistics were recorded: 39.5% of those who suffered from an eating disorder took over 6 months more to conceive than did the 25% of the general population. Of those women with a history of anorexia or bulimia who did become pregnant, 6.2% said they had undergone treatment to help them get pregnant, while in the general population the number was only 2.7% (Easter et al., 2011).

A hindrance in the reproductive system due to a lack of nutrition can be seen from Holocaust survivors who lived to tell the tale of those terrible times. One lady, who was hiding in Siberia, hardly ate anything for the few years she was there because of the lack of food. This caused her menstrual cycle to stop for those years that she was not receiving proper nutrition. Another lady was in the Auschwitz concentration camp, where she was literally starving; the inmates were given potato peels and moldy bread to eat. This caused her to also experience a cessation of her monthly periods. Both of their menstrual cycles resumed within a few years after the war, and with that, each of them was able to begin a family. This paper will go on to explain in detail why this is so. What is the connection between these two aspects? What are the underlying factors which cause a lack of nutrition to lead to an inability to become pregnant? While infertility caused by eating disorders was once thought to be untreatable, new research is identifying various hormones, such as GnRH, Kisspeptin, and Leptin, which boost LH and FSH to make it possible for women with anorexia to conceive. How do these three hormones regulate the reproductive system?

### Methods

The question above will be answered based on the information compiled from various articles and reviews. These references were obtained through Pubmed and Touro College's database which connected further to a variety of medical journals and

publications. The information was narrowed down to those directly relevant to the topic at hand. Once all the information was in place, an attempt could be made to answer the question regarding these specific hormones and their involvement in the reproductive system when adequate nutrition is and is not present.

### Discussion

The two hormones, FSH and LH?

Follicle-stimulating hormone, better known as FSH, is a hormone which controls and maintains development, maturation, and all reproductive processes in the human body. In males, a low FSH level can result in a cessation of normal sperm development, while in females it can halt the reproductive cycle. The Luteinizing hormone, or LH, is a hormone that triggers ovulation. When there is an LH surge in the female body, this indicates that ovulation will occur within the next 24-48 hours. (When a woman is pregnant, there is a decreased level of LH since a similar hormone, HCG, takes over. HCG is the hormone which helps preserve the uterine lining in pregnancy and will further produce progesterone.) A deficiency in LH will cause the same effects as the FSH deficiency does in both males and females (Barker et al., 2012).

### The menstrual cycle

The menstrual cycle is on average a 28-day cycle of various hormones and activities circulating the female reproductive system. The goal of the menstrual cycle is to produce eggs and to prepare the uterus for pregnancy. In cases where pregnancy is not achieved, the uterus will shed the eggs. The endocrine system is in charge of the cycle because of the various hormonal changes. At the beginning of the cycle, there is an increased level of estrogen and the lining of the uterus thickens, forming what is called the corpus luteum. Various hormones assist with the development of follicles in the ovary. Eventually, only one will become dominant while the others die. At mid-cycle, there is a surge in LH; this occurs when the egg has matured and the estradiol, or estrogen, begins to stimulate the production of LH from the anterior pituitary gland, initiating a surge of LH. This surge causes the dominant follicle to release an egg, an event known as ovulation. Unless it is fertilized to become an embryo, this egg will survive only up to 24 hours. FSH and LH aid the formation of the uterine lining from the remains of the dominant follicle, and this produces progesterone. This increased amount of progesterone leads to a rise in estrogen levels. If pregnancy is achieved, the embryo will implant itself within the uterus for the duration of the pregnancy. If, however, the egg is not fertilized, then approximately two weeks later, the corpus luteum will begin to disintegrate. The uterine lining will atrophy, causing the progesterone and estrogen hormones directly influencing the FSH and LH levels to diminish. As a result, there will be a large drop in the estrogen and progesterone levels, which will then cause the uterus to shed its corpus luteum and egg, bringing about another menstrual cycle (Chrousos, 2009).

### GnRH, Gonadotropin-releasing hormone

"In mammals, a sparsely populated and widely dispersed network of hypothalamic neurons, the Gonadotropin-releasing hormone (GnRH) neurons, serve as the pilot light of reproduction via coordinated secretion of GnRH" (Balasubramanian et al., 2010).

A network of approximately 1500 GnRH neurons is found in the hypothalamus. These neurons originate elsewhere in the body and migrate to the brain during embryological development. Scientists tested rodents to investigate the origin of these GnRH neurons and found that they originate in the nose, outside of the CNS, and migrate into the brain, where they scatter throughout the hypothalamus. It is obvious from the neurons' specific path from the olfactory placode to the preoptic area of the hypothalamus that they play a large part in a number of body systems which ultimately transfer data, including body weight and nutritional status, over to the reproductive system. GnRH is initially secreted from early fetal life until a few months of infancy. It is then quiet until the child reaches puberty, when it is once again secreted, resulting in sexual maturation. Since this neural network spurs the reproductive system in mammals, the GnRH neurons will determine, upon receipt of information, whether it is the right time and place and under the right body conditions for the reproductive system to prompt fertility. Once in the hypothalamus, the neurons bundle together to pass chemical signals to each other, causing the release of GnRH. In order for GnRH to be emitted, the neurons must extend their axon projections into the median eminence of the hypothalamus, the part of the hypothalamus that connects it to the pituitary glands (Balasubramanian et al., 2010). GnRH is then secreted in a coordinated, pulsatile manner into the pituitary gland, where it activates its own receptor, GnRHR, to release the gonadotrophin hormones, Luteinizing hormone (LH) and Follicle-stimulating hormone (FSH), from the gonadotrope cells located in these glands (Counis et al., 2009). This unique pulsatile pattern in which the GnRH is released is directly responsible for the degree of LH and FSH produced; low-frequency GnRH pulses lead to FSH release, while high-frequency pulses stimulate LH release (Jayes et al., 1997). In males, the GnRH pulses are constant, but in females, the pulses vary throughout the monthly menstrual cycle, and a large surge of GnRH occurs just before ovulation. Thus, LH is released prior to ovulation due to the large surge (Chrousos, 2009). The fact that the gonadotropes react to the fluctuations in the GnRH pulses demonstrates that these pulses are critical for the reproductive system to function properly. This further proves a strong correlation between a healthy neuroendocrine system and a properly-functioning reproductive system (Counis et al., 2009). Therefore, GnRH is a neurohormone that mediates brain control of the reproductive system; all of human reproductive activity is generated by GnRH and the network of neurons in the hypothalamus.

### Kisspeptin

There is a neuropeptide in the hypothalamus known as Kisspeptin, whose role is to regulate the GnRH neurons. In the last decade, studies have been done to prove the role that Kisspeptin plays in the reproductive system. This further enhanced scientists' understanding of neuroendocrine regulation of reproduction (De Roux et al., 2003). Kisspeptin was originally discovered in 1996 in Hershey, Pennsylvania and was amusingly named after the famous Hershey "Kisses" that were produced in this town (Skorupskaite et al., 2014).

"Kisspeptin is now recognized as a crucial regulator of the onset of puberty, the regulation of the sex hormone-mediated secretion of gonadotropins, and the control of fertility" (Pinilla et al., 2012, in Skorupskaite et al., 2014 article).

It does so by stimulating the hypothalamus to secrete GnRH at the appropriate time, thereby maintaining a homeostatic environment in the body. In order for the reproductive system to function properly, there must be a balance of energy, and the Kisspeptin neurons ensure this. They signal to the GnRH neurons to release GnRH, which stimulates the secretion of LH and FSH from the gonadotropes (Clark & Cummins, 1985). The secretion of LH is much greater than that of FSH (Dhillon et al., 2005). In this way, Kisspeptin plays a key role in fertility; it activates the GnRH neurons and locates itself near the GnRH neuron which stimulates LH release. Because Kisspeptin plays a large role in reproduction, it is evident that it can help individuals who are in a state of negative energy. During a study, when Kisspeptin was administered to a group of starving rats, their LH and FSH levels rose (De Bond & Smith, 2013). Kisspeptin accomplishes this by sensing the energy storage and initiating the secretion of GnRH, providing a connection between nutrition and reproductive function. This demonstrates the possibility of using Kisspeptin to restore reproductive activity in individuals who are in a negative state of energy, as in cases of anorexia nervosa (Skorupskaite et al., 2014).

Most GnRH neurons contain a receptor for the Kisspeptin neurons (Kiss1r). However, there are many other Kisspeptin receptors located in different areas of the brain. This suggests that Kisspeptin does not only play a role in controlling the energy balance in reproduction, but has other functions, as well. (De Bond & Smith, 2013).

### Leptin

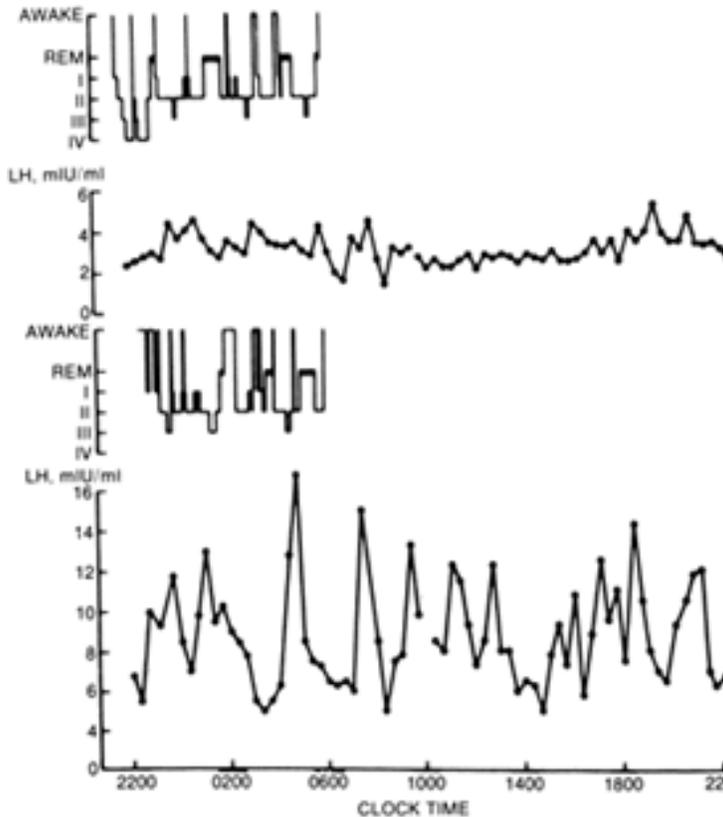
Leptin is a hormone derived from the adipose tissue. It comes from the Greek word "Leptos" meaning thin (Meier & Gressner, 2004). It is a recently-discovered hormone from the OB gene (Grasemann et al., 2004). It regulates energy balance along with hunger and metabolism, and it tells the brain when the body has enough energy and when it needs more food to provide energy. Due to its role in regulating food intake, Leptin is sometimes

referred to as the satiety hormone. Each person has a set Leptin threshold that is specific to him, which is believed to be genetically determined. When the Leptin level is above the threshold, such as after a person eats a sufficient amount of food, the brain receives a message that it has enough energy to expend on daily activities, such as exercising and eating, and on expansive metabolic activities, such as pregnancy and puberty. However, the Leptin level is low due to a food deprivation, the brain senses this and goes into starvation mode, and basic metabolic processes are halted due to a lack of energy. The pituitary gonadal axes become suppressed and other critical neuroendocrine axes malfunction. It is believed that Leptin affects the neuroendocrine system because it suppresses neuropeptide Y (NPY) production and prevents its secretion from neurons in the arcuate nucleus. NPY strongly stimulates appetite and regulates many of the hormones that are secreted by the pituitary gland, such as stimulating the pituitary adrenal axes, suppressing growth hormone by stimulating somatostatin, and suppressing gonadotropins (Meier & Gressner, 2004). A decrease in Leptin levels demonstrates a lack of energy; this will lead to a non-operative reproductive system, since it requires a lot of energy to function properly. Women with anorexia generally have low amplitude secretion levels of Luteinizing hormone, similar to those in young women who have not yet reached puberty or just begun it. This may be due to the decreased amount of fat mass and the alterations of the hormones produced by the adipocytes, such as Leptin. Leptin is an important factor in the timing of puberty, and as such, it facilitates the secretion of normal gonadotrophic hormones. Therefore, when an anorexia patient has reduced levels of Leptin due to the lack of necessary energy, her menses can be affected (Misra & Klibanski, 2014). A study done on rodents proved that in a state of starvation they displayed a reduction in LH pulse frequency, and when Leptin was administered, these rodents experienced an LH surge prior to ovulation as well as restored menstrual cycles, which led them to be fertile once again. The lack of energy present in patients with anorexia nervosa resulted in low Leptin and gonadotropin levels. These levels were restored with the aid of administering Leptin and adding nutrition to the patients' diets. There is a hypothesis that Leptin initiates puberty, since studies indicate that a critical amount of body fat is required in order for a person to begin maturation. This suggests a positive correlation between the energy stored up in a human's body and the onset of puberty (Elias & Purohit, 2012).

Leptin concentration is based on BMI. Therefore, in patients with anorexia and bulimia, Leptin levels are low, leading to a starvation state in which menstrual cycles are disrupted and fertility is severely affected (Meier & Gressner, 2004). However, these studies indicate that Leptin is not the only component necessary in puberty. A study in Jackson Laboratories observed Leptin-deficient mice. It was discovered that even though these mice's gonads and gonadotropes were fully developed and ready for puberty, they were GnRH deficient. Based on this piece of information,

**Figure 1:**

LH pattern in an anorexia case vs LH pattern in a normally-functioning system (Boyar et al., 1974).



LH concentration in a patient with anorexia nervosa (upper) is drastically lower than it is in a normal pattern when the patient is in remission (lower) (Boyar et al., 1974).

scientists theorize that Leptin affects the hypothalamic part of the brain by stimulating GnRH secretion (Elias & Purohit, 2012).

“It is now well-accepted that Leptin is a key metabolic cue that signals energy sufficiency to control adequacy and timing of reproductive function” (Elias & Purohit, 2012).

**Reproductive issues that anorexia can cause**

In the DSM IV, amenorrhea is listed as a criterion for the diagnosis of anorexia nervosa; however, this obviously does not include the male population who make up 10% of the anorexic patients, which is the reason that amenorrhea is not included as a criterion in the DSMV. (Misra & Klibanski, 2014).

Hypothalamic oligoamennhorhea, a symptom of anorexia nervosa in which a woman’s menstrual cycle is infrequent due to the decreased available energy, can lead to infertility. However, fertility can be restored once the body weight is stabilized and a normal period cycle resumes (Misra & Klibanski, 2014).

Hypothalamic Amenorrhoea: Amenorrhea is defined as the cessation of a regular monthly period for more than six months. 68-89% of women with anorexia reported an absence of their monthly period for at least 3 months (Hoffman et al., 2011). This signifies that there is a lack of normal ovarian activity, probably due to a disturbance in the proper secretion of hormones. This condition occurs when the GnRH pulse is low because the hypothalamus is not functioning as it should be and cannot produce GnRH, thereby causing a decline in LH and FSH secretion and follicular activity. This demonstrates the importance of a normally-operating hypothalamus, as all ovarian activity and hence the menstrual cycle is completely dependent on its smooth functioning. Some functional defects which can interfere with the normal operating system can include eating disorders, stress, and exercise, since they can all potentially decrease GnRH secretion, which will lead to reduction of the other hormones (Baird, 1997).

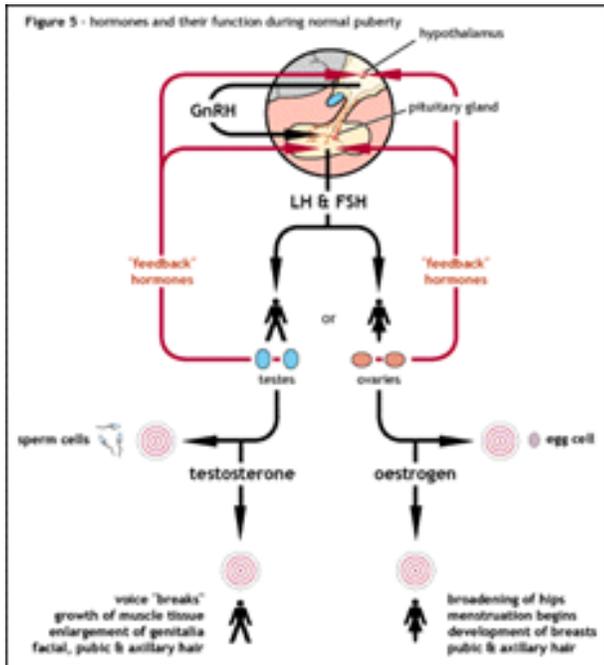
Kallman’s Syndrome: a genetic condition which affects three to five times more males than females and is associated with the inability to conceive. This hypogonadotropic hypogonadism disorder occurs because there is a low amount of sex hormones (testosterone in males, and estrogen and progesterone in females) circulating in the body. The low levels of these hormones are due to a low level of FSH and LH which is caused by the hypothalamus not releasing GnRH properly. This could be a result of a defect in any part of the GnRH neurons’ migration from the olfactory placode to the hypothalamus, or it may be a failure of the pituitary gland to secrete GnRH. Without GnRH secretion, LH and FSH will not be secreted and therefore they will not “turn on” the ovaries or the testes, and eggs and sperm will not be produced (Mitchell et al., 2011). This concert of events is illustrated in Figures 2 and 3.

Although this paper mainly discusses the effects of malnutrition and fertility in females, the instabilities in the reproductive system in males with anorexia have also shown to affect male fertility. This is an effect of the low leptin, gonadotropin (LH and FSH), and testosterone secretion levels. A study done to demonstrate the levels of fertility in anorexic males and females shows that from 140 women with anorexia, 50 women had a total of 86 children, and none of 11 anorexic men had children. As shown, anorexia can affect male fertility, but the extent is not documented thoroughly (Misra & Klibanski, 2014).

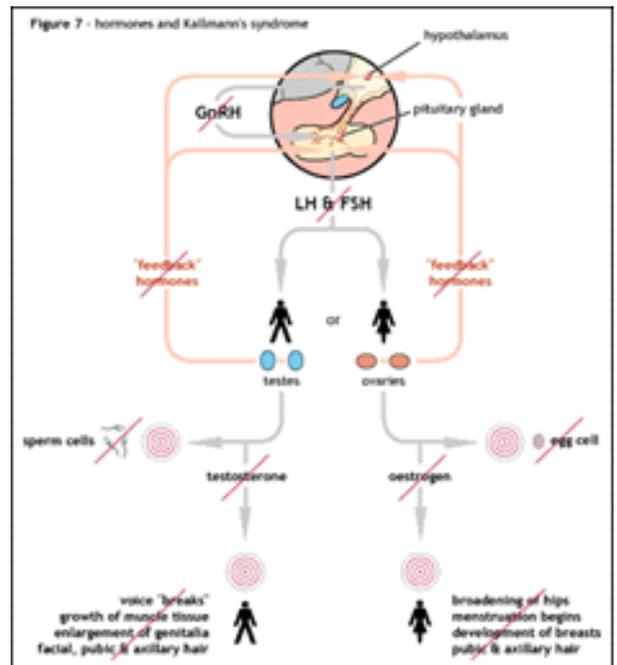
**Treatments**

An increase in fat mass has proven to be a key role in restoring the menstrual cycle. Figure 4 shows a study done on adolescents suffering from anorexia nervosa which demonstrates that the menses returned to girls with body fat greater than 24%, while in those with less than 18% body fat, it did not (Misra & Klibanski, 2014).

## Eating Disorders: The hidden hormonal effect on fertility

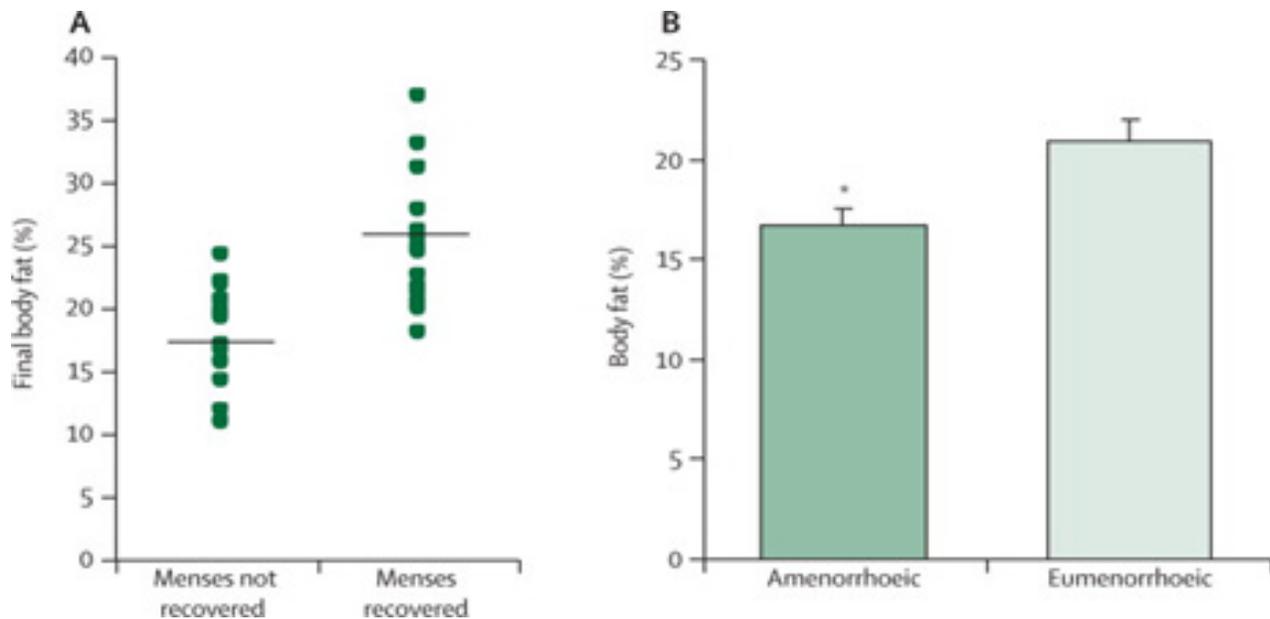


**Figure 2:** Hormones and their function during normal puberty; the release of GnRH, LH, and FSH from the hypothalamus and pituitary glands and their effect on the ovaries and testes (Smith, 1995).



**Figure 3:** Hormones and the Kallmann's syndrome; the failure of the hypothalamus to release GnRH and this will eventually result in a non- functioning testes and ovaries (Smith, 1995).

**Figure 4:** Proportion of body fat and relation to menstrual function (Misra, MD & Klibanski, MD, 2014)



Menstrual cycles resume in individuals with an increase in body fat. For individuals with a low body fat (<18%) menses did not resume to its normal state (Misra, MD & Klibanski, MD, 2014).

### GnRH pumps

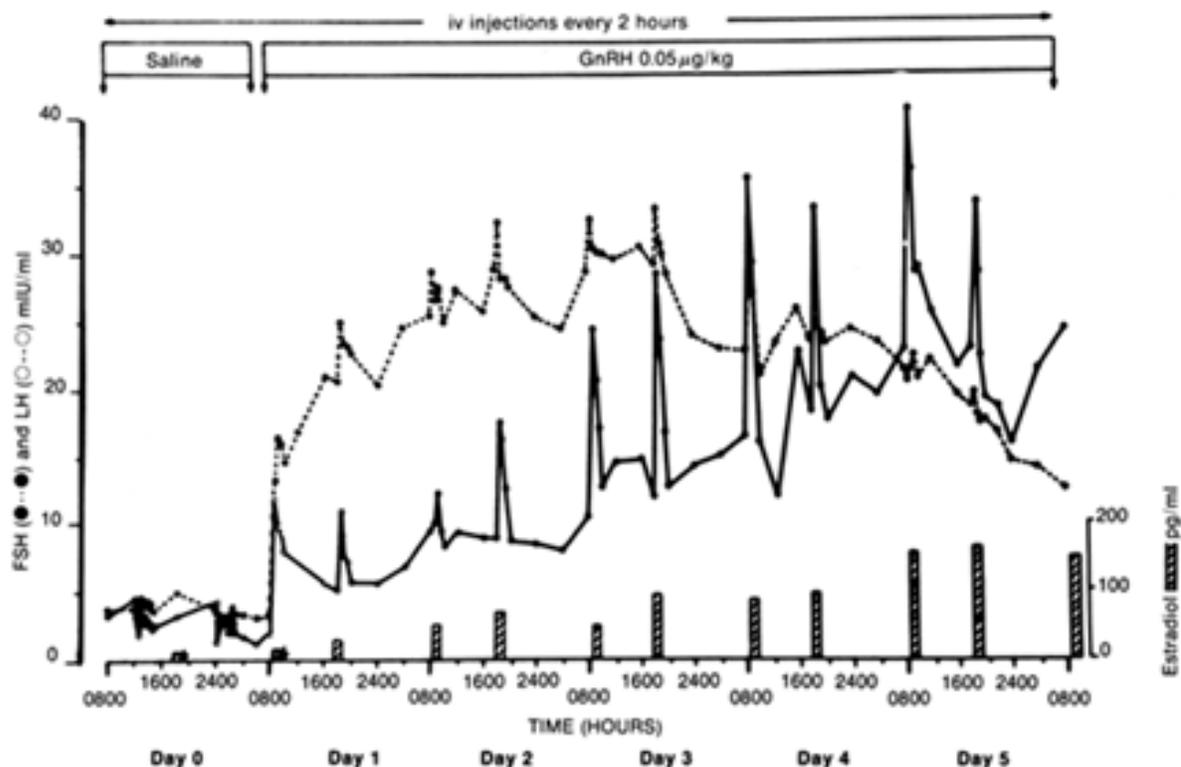
The Southern Ontario Fertility Technologies (S.O.F.T.) was faced with several cases of hypothalamic amenorrhea, and since treatments with gonadotropins are expensive, they sought a more affordable option. In 2011, they purchased two pumps to help alleviate the agony of these childless couples. Because hypothalamic amenorrhea is caused by a lack of GnRH, reinstating GnRH seemed like the most practical solution. The only catch is that GnRH has to be released in pulses because a constant flow will desensitize the hypothalamus and pituitary gland. Pulses of GnRH will cause a release of LH and FSH which will then target the ovaries and testes and achieve the desired results of producing eggs and sperm. The pulses are emitted through a device called a GnRH pump, which is a small battery-operated machine. There is a programmable timer attached in order to emit the GnRH in pulses every 90-120 minutes. The pump is worn around the waist or thigh the entire time that the drug is being administered, usually starting from day three of the menstrual cycle until the time the woman ovulates. This form of treatment has been proven to be very successful, with a success rate of 90% in people with Kallmann's syndrome. These fortunate women became pregnant within six months of beginning this treatment. For women with hypothalamic amenorrhea, their success rate of achieving pregnancy per cycle with this treatment is 25% (Martin J., 2011). In women suffering from hypothalamic amenorrhea, this therapy resembles the beginning of puberty and these women will begin to

experience normal menstrual cycles with the follicular maturation, ovulation, and corpus luteum formation. Once this is achieved, these women have a pregnancy rate comparable to those with healthy and normal cycles. The side effects of this pulse therapy are mild. Multiple pregnancies are a common occurrence as a result of the GnRH pulse level being too high for the required amount of that specific ovulation (Martin J., M.D., 2011). The GnRH pulse generator accomplishes its goal because it imitates the dynamics of a normal menstrual cycle; it releases GnRH at various frequencies throughout the period over which it is performed (Santoro et al., 1986).

Hypothalamic amenorrhoea can be corrected by injecting Kisspeptin-54 twice a day for two weeks at a dosage of 6.4 nmol/kg. This will result in a tenfold increase of LH secretion and a 2.5-fold increase in FSH secretion. However, ovarian activity is not necessarily restored (Jayasena et al., 2009). Kisspeptin has proven to be a very useful therapy in restoring a normal LH level from a relatively high or low LH pulse (Skorupskaite et al., 2014).

When Leptin was administered to females suffering from hypothalamic amenorrhea due to weight loss and excessive exercise, it was found that Leptin increased the LH volume and created a more favorable environment for reproduction (Elias & Purohit, 2012).

Figure 5: LH and FSH response to injections of GnRH every two hours (Marshall & Kelch, 1979).



The FSH (dotted line) and LH (solid line) patterns increase significantly when administered with injections of GnRH; these pulses are much greater with GnRH than they are with a saline (Marshall & Kelch, 1979).

There is more pertinent information available on the connection of infertility with specifically anorexia nervosa than with any other eating disorder. Whether bulimia nervosa has an effect on fertility is unknown, even though patients tend to display various menstrual irregularities. A study done on 173 women with bulimia provides information on this area. At first, 38.2% of these women were experiencing regular menstruation, while 4.6% had amenorrhea. 10-15 years later, the rate of amenorrhea was much higher at 13.9%. However, when the study was first conducted, 34.7% of the women had been pregnant at least once, while 10-15 years later this number rose to 74.6%, with only 1.7% of the women experiencing infertility. This demonstrates that while bulimia may be associated with menstrual dysfunction, it does not seem to have much of an effect on ability to conceive (Crow et al., 2002). For those who have struggled with infertility, the cause is most probably menstrual irregularities, because infertility from anorexia is a result of a dysfunctional menstrual cycle. The same treatments which help alleviate the anxiety caused by anorexia would likely be appropriate for these individuals who are suffering from infertility due to bulimia.

### Conclusion

This paper describes the importance of a proper nutrition to encourage a healthy reproductive system. Whenever the body is lacking necessary energy, as it is in cases of anorexia nervosa, there are alterations in the endocrine axis to help divert the energy that is present to perform the key body functions instead (Misra & Klibanski, 2014). There are various hormones present in every female body which will help boost LH, the chief hormone in a healthy menstrual cycle, in order to enable a malnourished body to conceive. GnRH, Kisspeptin, and Leptin are such hormones which will work together to help achieve a healthy pregnancy in individuals suffering from eating disorders.

If people knew that there are treatments for fertility affected by eating disorders, they would not be so embarrassed and ashamed to seek help. Since the success rate of the treatments has been proven to be quite high, people should be made aware of the various treatment options. Unfortunately, in today's society, the prevalence of eating disorders is very great, and there is no real way to stop this trend. Therefore, it is important that people become aware of the ways they can improve their situation to ensure themselves a healthier future. Once people are diagnosed with an eating disorder, their physician should administer Kisspeptin, GnRH, and Leptin to prevent the damage that eating disorders can cause. Based on research which highlights the importance of these hormones on the reproductive system, the additional dosage of these can only be beneficial for them.

### Abbreviations

DSM	Diagnostic and Statistical Manual of Mental Disorders
CNS	Central Nervous System
GnRH	Gonadotropin-releasing hormone
LH	Luteinizing hormone
FSH	Follicle-stimulating hormone
BMI	Body Mass Index
HCG	Human chorionic gonadotropin

### References

- Anorexia nervosa. Medline plus Updated: February 26, 2014. Available at <http://www.nlm.nih.gov/medlineplus/ency/article/000362.htm>. Accessed May 5, 2014.
- Anorexia nervosa. National association of anorexia nervosa and associated disorders. Available at: <http://www.anad.org/get-information/get-informationanorexia-nervosa/>. Accessed: May 5, 2014.
- Baird DT. Professor. Amenorrhoea. *The Lancet*. 1997; 350:275- 79. ProQuest Biology Journals.
- Balasubramanian R, Dwyer A, Seminara SB, Pitteloud N, Kaiser UB, Crowley Jr., WF. Human GnRH deficiency: A unique Disease Model to unravel the ontogeny of GnRH neurons. *Neuroendocrinology*. 2010; 92: 81- 99. Doi: 10.1159/000314193.
- Barker NM, Flyckt R, Seftel AD, Hurd WW. Luteinizing Hormone Deficiency. *Medscape*. Updated: March 23, 2012. Accessed: May 25, 2014. Available at: <http://emedicine.medscape.com/article/255046-overview>
- Boyar RM, Katz J, Finkelstein JW et al: Anorexia nervosa: Immaturity of the 24-hour luteinizing hormone secretory pattern. *N. Engl J Med*. 1974; 291:861.
- Chrousos GP. Gonadal hormones and Inhibitors. *Basic and Clinical Pharmacology*. (11th ed). Katzung BG, Masters SB, Trevor AJ., editors. New York. McGraw Hill, 2009; pp 700-701
- Clarke, JJ, Cummins JT. GnRH pulse frequency determines LH pulse amplitude by altering the amount of releasable LH in the pituitary glands of ewes. *J. Reprod. Fertil*. 1985; 2: 425-431
- Counis R, Garrel G, Laverriere JN, Simon V, Bleux C, Magre S, Cohen-Tannoudji J. The GnRH receptor and the response of gonadotrope cells to GnRH pulse frequency code. A story of an atypical adaptation of cell function relying on a lack of receptor homologous desensitization. *Folia Histochemica Et Cytobiologica*. 2009; 47 (5); S81-S87.
- Crow SJ, Thuras P, Keel PK, Mitchell JE. Long-Term Menstrual and Reproductive Function in Patients with Bulimia Nervosa. *Am J Psychiatry*. 2002; 159:1048- 1050. doi:10.1176/appi.ajp.159.6.1048

De Bond JAP, Smith JT. Kisspeptin and Energy Balance in reproduction. <http://www.reproduction-online.org/content/147/3/R53.long#sec-3>. Published 2013. Accessed 2014.

De Roux N, Genin E, Carel JC, Matsuda F, Chaussain JL, Milgrom E. hypogonadotropic hypogonadism due to loss of function of the kiss-1 derived peptide receptor GPR54. *Proc Natl Acad Sci USA*. 2003; 19:10972- 10976.

Dhillon WS, Chaudhri OB, Patterson M, Thompson EL, Murphy KG, Badman MK, McGowan BM, Amber V, Patel S, Ghatei MA et al. Kisspeptin- 54 simulates the hypothalamic- pituitary gonadal axis in human males. *J Clin Endocrinol Metab*. 2005; 12: 6609- 6615.

DSM. American Psychiatric Association. 2014. Accessed: May 6 2014. Available at <http://www.psych.org/practice/dsm>

Easter A, Treasure J, Micali N. Fertility and prenatal attitudes towards pregnancy in women with eating disorders: results from the Avon Longitudinal Study of Parents and Children. *BJOG: An International Journal of Obstetrics & Gynaecology*, 2011; doi: 10.1111/j.1471-0528.2011.03077.

Elias CF, Purohit D. Leptin signaling and circuits in puberty and fertility. *Cellular and Molecular Life Sciences*. 2013; 70:841- 862. Doi: 1007/s00018-012-1095-1.

Grasemann C, Wessels HT, Knauer- Fischer S, Richter- Unruh A, Hauffa BP. Increase of serum leptin after short term pulsatile GnRH administration in children with delayed puberty. *European Journal of Endocrinology*. 2004; 150: 691- 698.

Hoffman ER, Zerwas SC, Bulik CM. Reproductive issues in anorexia nervosa. *Expert Rev Obstet Gynecol*. 2011; 6(4): 403-414.

Jayasena CN, Abbara A, Veldhuis JD, Comninou AN, Ratnasabapathy R, De Silva A, Nijher GM, Ganiyu-Dada Z, Mehta A, Todd C, Ghatei MA, Bloom SR, Dhillon WS. Increasing LH pulsatility in women with hypothalamic amenorrhea using intravenous infusion of Kisspeptin- 54. *J Clin Endocrinol Metab*. 2014; jc 20131569.

Luking- Jayes, FC, Britt JH, Esbenshade KL. Role of Gonadotropin-releasing hormone pulse frequency in differential regulation of gonadotropins in the gilt. *Biology of Reproduction*. 1997; 56:1012-1019. Retrieved November 2013.

Marshall JC, Kelch RP: Low dose pulsatile gonadotropin-releasing hormone in anorexia nervosa: A model of human pubertal development. *J Clin Endocrinol Metab*. 1979; 49:712.

Martin J, MD. The Soft Fertility Blog. Ontario, Canada. Southern Ontario Fertility Technologies (S.O.F.T.) 2011. [soft-infertility.ca/blog/hypothalamic-amenorrhea-gnrh-pump-program/](http://soft-infertility.ca/blog/hypothalamic-amenorrhea-gnrh-pump-program/)

Meier U, Gressner AM. Endocrine Regulation of Energy Metabolism: Review of Pathobiochemical and Clinical Chemical Aspects of Leptin, Ghrelin, Adiponectin, and Resistin. *Clinical Chemistry*. 2004; (50)9: 1511-1525.

Misra M, Klibanski, A. Endocrine Consequences of anorexia nervosa. *The Lancet Diabetes and Endocrinology*. 2014. Doi: 10.1016/S2213-8587(13)70180-3.

Mitchell AL, Dwyer A, Pitteloud N, Quinton R. (2011). Genetic Basis and Variable Phenotypic expression of Kallmann syndrome; towards a unifying theory. *Trends Endocrinol Metab*. 22 (7): 249-58. doi: 10.1016/j.tem.2011.03.002.

Mitchison D, Hay PJ. The epidemiology of eating disorders: genetic, environmental, and societal factors. *Clin Epidemiol*. 2014; 6:89-97. eCollection 2014.

Pinilla L, Aguilar E, Dieguez C, Millar RP, Tena- Sempere M. Kisspeptins and reproduction: physiological roles and regulatory mechanisms. *Physiol Rev*. 2012; 3: 1235- 1316.

Santoro N, Filicori M, Crowley WF. Hypogonadotropic disorders in men and women: diagnosis and therapy with pulsatile gonadotropin-releasing hormone. *Endocr Rev*. 1986; 7:11- 23.

Skorupskaite K, George JT, Anderson RA. The Kisspeptin- GnRH pathway in human reproductive health and disease. *Oxford Journals*. Published: March 9, 2014. Doi: 10.1093/humupd/dmu009.

Smith N, (figure 2:) Flow diagram showing normal hormonal control of puberty. Wikipedia. Published: 1995. Accessed: May 25, 2014. Available at: [https://en.wikipedia.org/wiki/File:Flow\\_diagram\\_showing\\_normal\\_hormonal\\_control\\_of\\_puberty.gif](https://en.wikipedia.org/wiki/File:Flow_diagram_showing_normal_hormonal_control_of_puberty.gif)

(figure 3:) Diagram showing the disruption of the hormonal pathways of puberty due to the failure of GnRH release seen in KS and HH. Wikipedia. Published: 1995. Accessed: May 25, 2014. Available at: [https://en.wikipedia.org/wiki/File:Diagram\\_showing\\_the\\_disruption\\_of\\_the\\_hormonal\\_pathways\\_of\\_puberty\\_due\\_to\\_the\\_failure\\_of\\_GnRH\\_release\\_seen\\_in\\_KS\\_and\\_HH.gif](https://en.wikipedia.org/wiki/File:Diagram_showing_the_disruption_of_the_hormonal_pathways_of_puberty_due_to_the_failure_of_GnRH_release_seen_in_KS_and_HH.gif)

Stewart DE, Robinson E, Goldbloom DS, Wright C. Infertility and eating disorders. *Am J Obstet Gynecol*. 1990; 163: 1196-1199.

The alliance for eating disorders awareness. Accessed: May 6 2014. Available at <http://www.allianceforeatingdisorders.com/portal/dsm-bed#.U3GApeDD8m8>

Treasure J, Claudino AM, Zucker N. Eating Disorders. *The Lancet*. 2010; 375:583-93. Doi: 10.1016/S0140-6736(09)61748-7.

Wooldridge T, Lytle PP. An overview of anorexia nervosa in males. *Eating Disorders*. 2012; 20(5):368-378.