



## Effect of Thyroid Hormone on Menstrual Cycle

MANSI GUPTA  
PG student

Isabella Thoburn College, Lucknow, UP, India

DR. CHITRA SINGH  
Department of Zoology,

Isabella Thoburn College, Lucknow, UP, India

### Abstract:

*For proper functioning of the female reproductive function thyroid hormones are essential as they regulate development of uterus, ovarian and placental tissue and maintains metabolism. In both women and animals' hypo and hyperthyroidism may result in subfertility and fertility. Many studies have been conducted with thyroid dysfunction and female reproduction, as well as hypo and hyperthyroidism using experimental animal's models related to ovarian, uterus and placental tissues. Previous studies have been conducted that women's suffering from hyperthyroid and hypothyroidism experienced menstrual disturbances as compared to euthyroid women's but reasons for this is not known and studies of thyroid among euthyroid women's are lacking. In an euthyroid women, this study signifies the interrelation between thyroid hormone concentration and predicted menstrual function outcomes. Before the menstrual function study begins, the serum thyroid hormone was measured. FSH and urinary estrogen and progesterone metabolites were measured and adjusted for creatinine.*

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**Keywords:** *Thyroid hormones, Menstrual cycle, Metabolism*

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### 1. Introduction

Thyroid gland is considered as endocrine gland in vertebrate or we can say that; it regulates our body system. It is of 2 inches long and situated in front of throat below the thyroid cartilage, also known as Adam's apple.

The Thyroid gland has 2 sides known as lobes and these lobes are situated on either side of windpipe which is usually connected by isthmus. Thyroid gland is considered as endocrine gland of vertebrates which produces, stores and releases hormones into bloodstream that maintain proper functioning. Thyroid gland is usually associated with iodine absorption from the food which we eat and produces two vital hormones:

T3 (Triiodothyronine)

T4 (Thyroxine)

T3 and T4 are regulated by Hypothalamus and Pituitary gland which are situated in brain. When T3 and T4 levels are low in blood then, pituitary releases more TSH, so that thyroid gland produces more Thyroid hormones. Or in blood, when T3 and T4 levels are high, then Pituitary releases less TSH so that Thyroid produces less hormones.

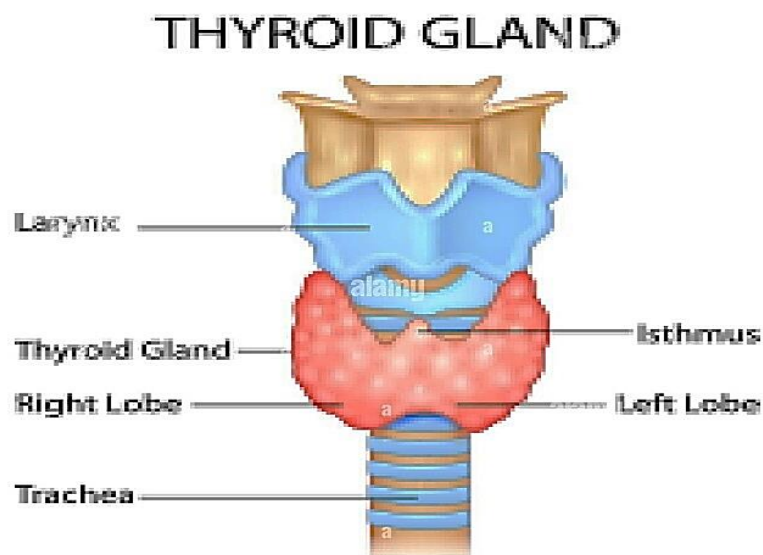
T3 and T4 travel in bloodstream and reach every cell in the body, as they regulate the speed with which the cell/metabolism works, like it regulates our heart rate and also checks that how our intestine work in case of processing food. If T3 and T4 levels are lower than normal rate then heart rate can be slower, and, if T3 and T4 levels are higher than normal rate it can cause rapid heart rate. That's why it is said that effects of too much or too little T3 and T4 in our body can be injurious to our health.

## 2. Disease and Disorders Associated with Thyroid

There are many diseases associated with thyroid gland. This can develop at any stage and can cause injury, disease or dietary deficiency for instance. Some common thyroid disorders are;

- 1. Goiters:** It is caused due to deficiency of iodine and it is a bulge in the neck. Toxic goiter is associated with hyperthyroidism and a non-toxic goiter, we can say a simple or endemic goiter. If this is left untreated it can cause severe problems.
- 2. Hypothyroidism:** It can be described as an underactive thyroid condition in which Thyroid gland doesn't produce enough certain crucial hormones, When Hypothyroidism occurs in infants, the condition is known as Cretinism. It is a very serious condition, including abnormal bone formation and mental retardation. If hypothyroidism takes place in adults, one may experience symptoms like: Obesity, joint pain, infertility, heart problems, fatigueness, dry skin, sensitivity to cold temperature, frequent and heavy periods, thinning of hairs, muscle weakness and weight gain.
- 3. Hyperthyroidism:** It can be described as an overproduction of thyroid hormones. If hyperthyroidism takes place, one may experience many symptoms like: Anxiety, increased metabolism, irritability, sweating, sensitivity to high temperature, hand trembling, hair loss, missed or light menstrual periods.
- 4. Thyroid cancer:** It is a very rare, but their long-term survival rates are excellent. It can affect anyone at any age, but it has been noticed that mostly women and people who are above thirty are most likely to develop Thyroid cancer. Symptoms include Hoarseness, neck pain, and enlarged lymph nodes.

## 3. Cause of Menstruation



*Reference: Illustration of health care and medical education of human Thyroid gland*

The menstrual cycle refers to natural change occurs due to production of hormones Also the structure of the uterus and ovaries of the female reproductive system changes, so as to make pregnancy possible. The ovarian cycle regulates the production and release of eggs and also the cyclic release of estrogen and progesterone. The function of uterine cycle is to prepare and maintain the lining of uterus (womb) to receive a fertilized egg. This menstrual cycle considered as concurrent, and co-ordinated normally lasts between 21 and 35 days in adult women, with a median length of 28 days. It continues to 45-50 years.

It is estimated that 1% of female population is suffering from hypothyroidism. Thyroid has an intense effect on menstrual functioning and reproductive health. In the reproductive age group, the menstrual disturbance is a common issue faced by women's, in which they experience heavy pain, discomfort,

and awkwardness. It can be determined as the first sign of thyroidism (Wiliansky DL; Griesman 1992). Timely detection of thyroid dysfunctioning with menstrual irregularities in women's and their proper management can be prevented with proper diagnostic and therapeutic courses.

#### 4. Thyroid dysfunction and female reproduction

Numerous investigators signify a link between autoimmune thyroid disorders and reproductive physiology /pathology. The successive facts suggest the role of thyroid hormone in the female reproductive physiology/pathology. In recent studies it has been found that T4 enhance the action of FSH and LH. In the follicular fluid T3 and T4 are found. In granulosa cells TSH receptors are found. These hormones and their prospective effects on immune system plays an important role and develop autoimmune thyroid disorder. Against the thyroid, the polygonal immunoglobulins are produced which create a spectrum of autoimmune thyroid disease and effects reproductive function.

Some studies have been shown that in mice, excessive level of thyroid cause early maturation of reproductive tract and early opening of the vagina whereas, hypothyroidism in mice causes ovaries lacking cholesterol. In human embryos no changes have been observed.

**Hypothyroidism** – women who are suffering from hypothyroidism have low level of sex hormone binding globulin (SHBG) and have low level of estrogen and testosterone. They also have probability of menstrual disturbances such as oligomenorrhea, amenorrhea and menorrhagia. Thyroid regulating hormone (TRH) induction causes disturbances in hyperprolactinemia which alters pulsatile GnRH secretion and partially defects homeostasis with low level of blood clots.

**Hyperthyroidism (thyrotoxicosis)** – Thyrotoxicosis or hyperthyroidism causes various symptoms ranging from normal menstrual irregularities such as menorrhagia, oligomenorrhea, amenorrhea, and reduced fertility. Women's who are suffering from grave's disease, have 2-3 times higher level of estrogen and LH, during all phases of menstrual cycles, apparently due to high level of SHBG (hormone binding globulin). It is also observed that the production of testosterone and androstenedione is also increased in these women.

#### 5. Thyroid Disorder and Obesity

Obesity and hypothyroidism are the two most important circumstances that are closely linked together. Thyroid hormone plays an important role in maintaining metabolism, thermogenesis, lipid and glucose metabolism. Hypothyroidism is connected with decrease thermogenesis, decrease metabolic rate and obesity. While hyperthyroidism is connected with increase in metabolic rate. Marzullo et al indicate that thyroid autoimmunity is a risk factor for obesity. Further large studies show the association between leptin, thyroid autoimmunity and the consecutive development of hypothyroidism.

#### 6. Classification of thyroid Disorders

**Euthyroid** – T3 (NORMAL) T4 (NORMAL) TSH (NORMAL)

**Hyperthyroid** – T3 (ELEVATED) T4 (ELEVATED) TSH (LOW)

**Hypothyroid** – T3 (LOW) T4 (LOW) TSH (ELEVATED)

**Subclinical Hypothyroidism** – T3 (NORMAL) T4 (NORMAL) TSH (ELEVATED)

**Subclinical Hyperthyroidism** – T3 (NORMAL) T4 (NORMAL) TSH (LOW)

#### 7. Physiology of menstruation

The menstrual cycle occurs due to simultaneous integrated events which occurs in ovaries (oogenesis) as well as the uterine endometrium (endometrial preparation).

#### 8. Endometrial differentiation during menstrual cycle

**The uterine wall consists of 3 layers:** a thin lining endometrium, a muscular layer myometrium and serosa. Endometrium is the innermost portion of uterus and it is divided into 2 layers: - 1) upper

functional layer (Blastocyst implantation takes place) 2) Basal layer (Endometrium monthly regeneration takes place).

The monthly preparation of the endometrium for implantation occurs during the menstrual cycle. During the menstrual cycle endometrium effects hormones which is produce by ovary, i.e., estrogen (E) and progesterone (P). Menstrual cycle is divided into 3 phases due to endometrial changes,

1. Degenerative phase which is known as menstrual phase.
2. Proliferative phase which communicates with ovarian follicular phase.
3. Secretory phase which communicates with the ovarian luteal phase.

The first day of menstrual cycle is initial day decline and exclusion of the endometrium. The follicular phase is identified by secretion of estrogen and growing follicles. Increasing estrogen level during the follicular phase encourages expansion of the endometrium, which becomes thicker as number of glands increases. During the luteal phase, endometrium is arranged for blastocyst implantation. Degeneration of endometrium starts if pregnancy does not occur. After 2 weeks the corpus luteum forms corpus albicans. The secretion of estrogen and progesterone decreases which shows endometrium degeneration.

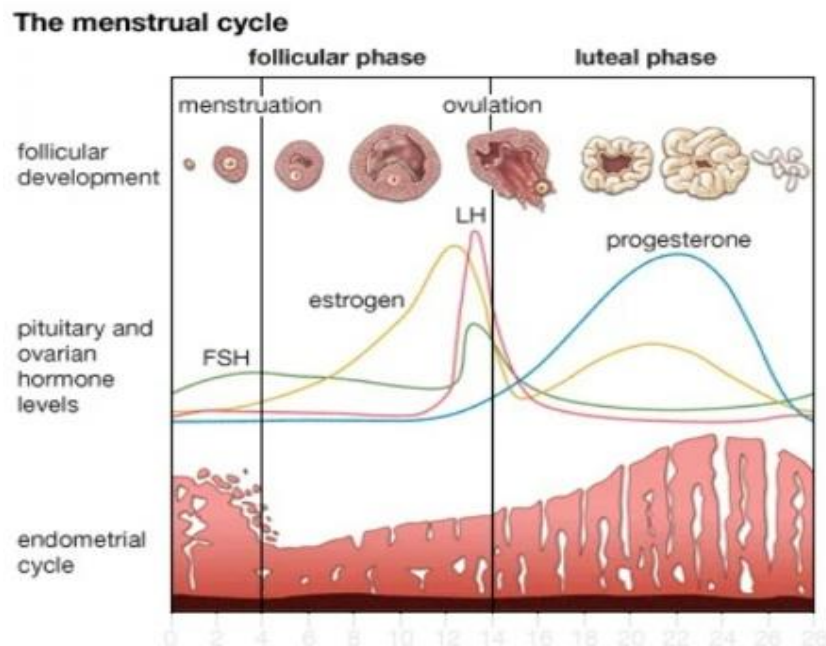
**Follicular phase:** span – from 1<sup>st</sup> day of menses till ovulation. The primary objective of this phase is to develop a viable follicle which is capable of undergoing ovulation. The early growth of follicle occurs over the several spans of menstrual cycle, but the ovulatory follicle is considered as the companion of follicle which is enrolled at the time of luteal -follicular transition. The total duration to attain preovulatory status is of about 85 days. Early follicular development is autonomous of hormonal control. Thus, follicles are constant available (2-5mm in size) for feedback to FSH. Estrogen exerts an antagonistic effect on FSH, as a growth of all follicles is prohibited except the one imminent to become dominant follicle. A flow of LH occurs former to ovulation, the positive action of estrogen modifies the gonadotropin molecule; which increases the quality as well as quantity of FSH and LH during the late follicular phase, which excite the androgen production in the theca.

### **Ovulation**

Ovulation is the process in which mature egg is released from the ovary. It usually occurs on the 14<sup>th</sup> day of menstrual cycle. It is Incited by LH surge. The oocyte which is released from the ovary into fallopian tube (by the chemotactic effect) gets fertilised by the spermatozoa in the ampulla of the fallopian tube. As the oocyte has been ejected out, the ovarian follicle which is now empty gets converted into corpus luteum, which generate progesterone in the absence of fertilization.

### **Luteal phase**

Progesterone production by the corpus luteum influences secretory changes in the endometrium. In the early luteal phase, estrogen decreases till the mid luteal phase from where it begins to rise a consequence of corpus luteal secretion. if pregnancy does not occur, the corpus luteum corrupts Oestrogen and progesterone levels and cause negative feedback at the hypothalamus which results in decrease in the level of FSH and LH hormones.



Reference: Clayton, S. George (2019, August 8). menstruation. Encyclopedia Britannica.  
<https://www.britannica.com/science/menstruation>

### 9. Irregularities associated with menstrual cycle

1. **Menorrhagia** – It is a condition in which a patient experiences a regularly timed episodes of bleeding that are excessive in amount or duration of flow
2. **Polymenorrhoea** – It is defined as menstrual cycle which is frequent but regularly timed episodes of bleeding that is shorter than 21 days.
3. **Oligomenorrhoea** – It is defined as a condition in which patient experiences infrequent or irregularly timed episodes of bleeding which occurs at an interval of 35 days or more as a result have only 4 to 9 periods each year.
4. **Hypomenorrhoea** –It is a condition in which menstruation is scanty or infrequent that are not due to underlying tissue.
5. **Amenorrhoea** – It is defined as a condition in which no menstruation occurs i.e., absence of menstruation for a period of 6 months in a woman with normal menstrual cycle or a period equal to duration of 3 cycles in irregular cycled womens.
6. **Metorrhagia** – A condition in which bleeding takes place from the uterus that occurs in between periods, or it may occur every few weeks and the flow may be heavier than usual.
7. **Menometorrhagia** – It is defined as excessive or prolonged uterine bleeding which occurs at irregular and /or frequent intervals. It occurs in womens upto aged 40-50 years.

### 10. Thyroid Dysfunction and Menstrual Disorders in Definite Conditions

1. **Anorexia Nervosa** – An eating disorder causing people to obsess about weight and what they eat. It is characterized by a distorted body image, with an intense fear of being overweight.

#### *Symptoms:*

1. Extreme weight loss or not making expected developmental Weight gains.
2. Thin appearance
3. Abnormal blood counts
4. Fatigue
5. Insomina
6. Yellowish or dry skin
7. Low blood pressure
8. Absence of menstrual cycle.



These symptoms are due to an abnormal regulation of hypothalamus mechanism. It occurs from the formation of active T3 to reverse T3 for the malnourishment.

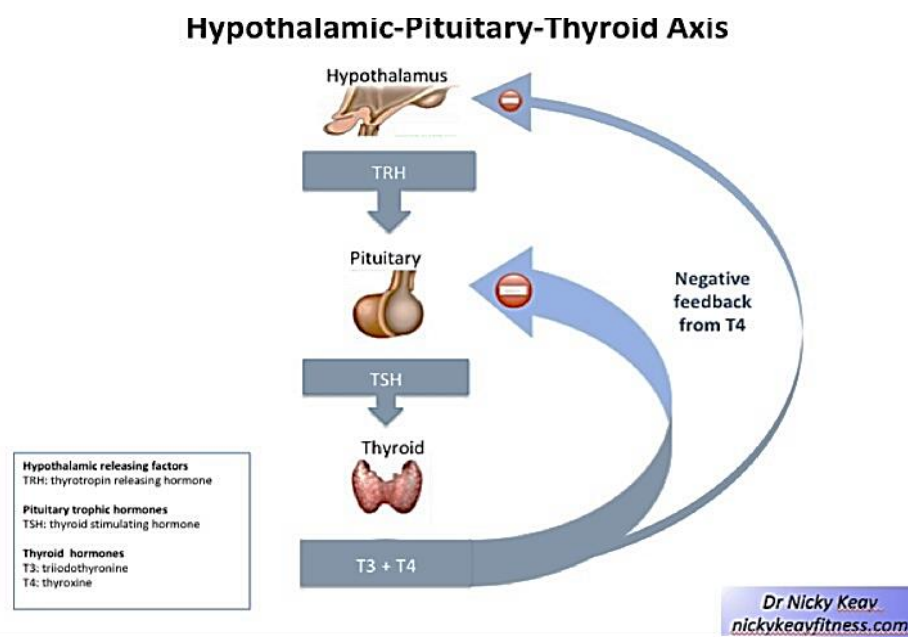
**2-Turner's Syndrome** – Women with turner syndrome have a short stature, streak gonads, primary amenorrhea, webbed neck, widely spaced nipples and various other abnormalities associated with heart and kidneys. Turner syndrome is associated with 45XO karyotype deletion of a long or short of a chromosome usually occurs. Occurrence of high autoimmune thyroid disorders with about 50% of patients with turners have antithyroglobulin (anti TG) antibody and anti-thyroid peroxidase (anti – TPO). While, about 30% patients usually develop subclinical /clinical hypothyroidism (Barbesino G et al, 1998).

**3-Postpartum thyroiditis** – The occurrence of the transient thyroid dysfunction in Womens who are euthyroid before pregnancy during the first postpartum year.

It is an increase of Underlying autoimmune thyroiditis which shows a strong interconnection with anti - Thyroperoxidase antibodies. During hyperthyroid state, beta blocker treatment is given while, during hypothyroid state thyroxine supplementation is given but anti thyroid drugs are not designated. The risk of appearance in pregnancy is upto 70%. Monitoring should continue after pregnancy and yearly thereafter.

### 11. Hypothalamic – Pituitary – Thyroid Axis

Synthesis and release of T3 and T4 are similar in humans and animals. And the Concentration of serum and some hormones are synchronised by a negative Feddback loop which involves hypothalamus, the pituitary and the thyroid. Thyrotropin is also known as TSH which is secreted by thyrotrophic cells of anterior Pituitary which controls the secretion of T3 and T4 by the thyroid. In addition, Hypothalamus secretes Thyrotropin-releasing hormone (TRA) which controls the Secretion of Pituitary TSH. Hpothalamic-Pituitary- Thyroid axis is form by TSH, TRH, and THS. T3 and T4 contains 2 tyrosyl residues, which are interconnected by an ether bond by 3 and 4 iodine residues for the synthesis of these hormones by the thyroid. Entry of iodide into the thyroid follicles is required which depends upon two transmembrane glycoproteins present in thyroid. After its entry into the thyroid follicle, iodide is oxidized by TPO to form monoiodothyronine (T1) and diiodothyronine (T2) with the formation of T3 and T4.



Reference: By Dr Nicky Keay @Nickykfitness.Com Blogs.bmj.com

### 12. Conclusion

From the above study it can be concluded that there is a distinctive interrelation between thyroid dysfunction and menstrual disorders. The development of blastocyst occurs by adding thyroid hormone

in early embryo culture. Between 2004-20014, 86 euthyroid premenopausal women's participated in a study measuring menstrual function of those women's who are not lactating or taking hormonal medications. Thyroid hormone concentration are related with subtle differences in menstrual cycle function outcomes, i.e., sex steroid hormone levels in healthy women. Some recent studies have shown that women's of age between 18-29 had longer cycle and follicular phases variability than women's of age 30's. i.e., their bleeding length and intensity decreases with age. Women's who are overweight had longer cycle than normal weight women. Women of age group 41-54 had higher FSH in late luteal phase and early follicular phase, and lower Pd3G and E13G at various time frames as compared with younger women.

Euthyroid range and thyroid level is interconnected with several menstrual cycle function outcomes among a healthy pre-menopausal woman. Therefore, T4 and T3 are related to urinary estrogen and progesterone metabolite levels across the menstrual cycle.

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