

## Various Causes of Early menses

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**Abstract** -The phenomenon of early menses, or premature menarche, defined as the onset of menstruation before the age of 8, has shown an arising trend globally, attributed to multiple factors. This condition is shaped by a complex interplay of genetic, environmental, and socio-cultural influences. Key contributors include improved nutrition, which accelerates physical development; increased prevalence of childhood obesity, which alters hormonal pathways; and exposure to endocrine-disrupting chemicals, such as those found in plastics and pesticides, which interfere with hormonal regulation. Additionally, familial predisposition and genetic factors play a significant role, as a maternal history of early menarche often correlates with earlier onset in daughters.

Socio-economic conditions and lifestyle changes, including urbanization and reduced physical activity, further influence the timing of puberty. Psychological stress and early exposure to sexualized media have also been implicated in triggering early pubertal milestones. Understanding these multifaceted causes is crucial for addressing the rising incidence of early menses and its associated health risks. This growing trend calls for targeted interventions, awareness campaigns, and further research into modifiable factors to mitigate its long-term physical and psychological impacts.

### Keywords-

Early menses, premature Menarche, genetic factor, socio-economic factor, Endocrine-disrupting chemicals (EDCs), Familial history,

## 1- INTRODUCTION

Early menses, also known as premature menarche, refers to the onset of menstruation before the age of 8. In recent years, it has gained attention due to its increasing prevalence. Research indicates a downward shift in the average age of menarche over the

past few decades, influenced by factors such as better nutrition, higher rates of childhood obesity, and exposure to endocrine-disrupting chemicals. Early menarche is a significant milestone in pubertal development and is associated with various physical, psychological, and reproductive health implications.

It has been linked to an elevated risk of chronic conditions later in life, including type 2 diabetes, cardiovascular diseases, and breast cancer. Psychologically, early menarche can be challenging, as it marks a critical biological transition in a girl's life. Girls who mature early may experience emotional distress, body image issues, and social difficulties due to developing physically ahead of their peers.

Understanding early menses requires examining environmental, genetic, and socio-cultural factors that contribute to this trend. Researchers emphasize the need for early interventions, educational efforts, and psychological support to reduce the potential negative outcomes. Raising awareness among healthcare providers, parents, and educators is essential in addressing this phenomenon and supporting affected individuals effectively (1).

## 1.1 CAUSES OF EARLY MENSES

### 1.1.1 Genetics

Early onset of menstruation, also known as precocious puberty, can be influenced by various factors, including genetic causes. Below is a detailed explanation of the genetic factors that may contribute to early menses:

#### 1.1.1.1 Familial Trends and Inheritance Patterns

**1.1.1.1.1 Hereditary Patterns:** Early menstruation often runs in families. If a mother or sister experienced menarche (the first menstrual period) at an earlier age, it is more likely for a girl in the same family to also experience early

menarche.

**1.1.1.1.2 Genetic Predisposition:** S regulating specific genetic variations or mutations can influence the timing of puberty. Variations in genes the production of sex hormones and their receptors can affect the age of menarche.

**1.1.1.2 Key Genes Involved in Pubertal Timing**

**1.1.1.2.2 KISS1 and KISS1R Genes:** These genes play a role in the production and regulation of inspecting, a protein crucial for initiating puberty. Variants in these genes can lead to early activation of the hypothalamic-pituitary-gonadal axis, the system that regulates reproductive hormones.

**1.1.1.2.1 LIN28B Gene:** This gene has been linked to the timing of puberty. Variants in this gene can lead to earlier puberty. It regulates the production of microRNAs, which in turn control cellular processes involved in growth and development.

**1.1.1.2.3 MKRN3 Gene (Makorin Ring Finger Protein 3):** Mutations in the MKRN3 gene are strongly associated with central precocious puberty (CPP). MKRN3 inhibits the activation of puberty, so mutations in this gene can cause early activation of the system responsible for puberty.

**1.1.1.2.4 GnRH (Gonadotropin-Releasing Hormone):** Genetic mutations affecting GnRH production or its receptor (GnRH) can also trigger early puberty. GnRH is a key hormone responsible for the release of other reproductive hormones from the pituitary gland.(2,3)

**1.1.2 Epigenetic and Environmental Interactions**

**1.1.2.1 Epigenetics:** While specific gene mutations or variants are linked to early puberty, environmental factors can influence how these genes are expressed. Factors like nutrition, body weight, and exposure to endocrine-disrupting chemicals can interact with the genetic predisposition and accelerate the onset of puberty.

**1.1.2.2 Imprinting Disorders:** Some imprinting disorders, such as Prader-Willi syndrome and Silver-Russell syndrome, involve genetic regions that can affect pubertal timing through altered gene expression.

**1.1.3 Endocrine Disruptors**

Endocrine disruptors are chemicals that interfere with the normal functioning of the endocrine system, which is responsible for regulating hormones in the body. These chemicals can mimic, block, or alter the normal hormonal signals that regulate processes such as growth, development, metabolism, reproduction, and mood. The endocrine system consists of glands (e.g., thyroid, adrenal, pituitary) and hormones (e.g., estrogen, testosterone, insulin, cortisol) that act as chemical messengers. Hormones regulate a wide range of bodily functions by binding to specific receptors on cells. This system is finely tuned, and even small changes in hormone levels or receptor activity can have significant effects on health.

**1.1.3.1 Mechanisms of Action of Endocrine Disruptors:**

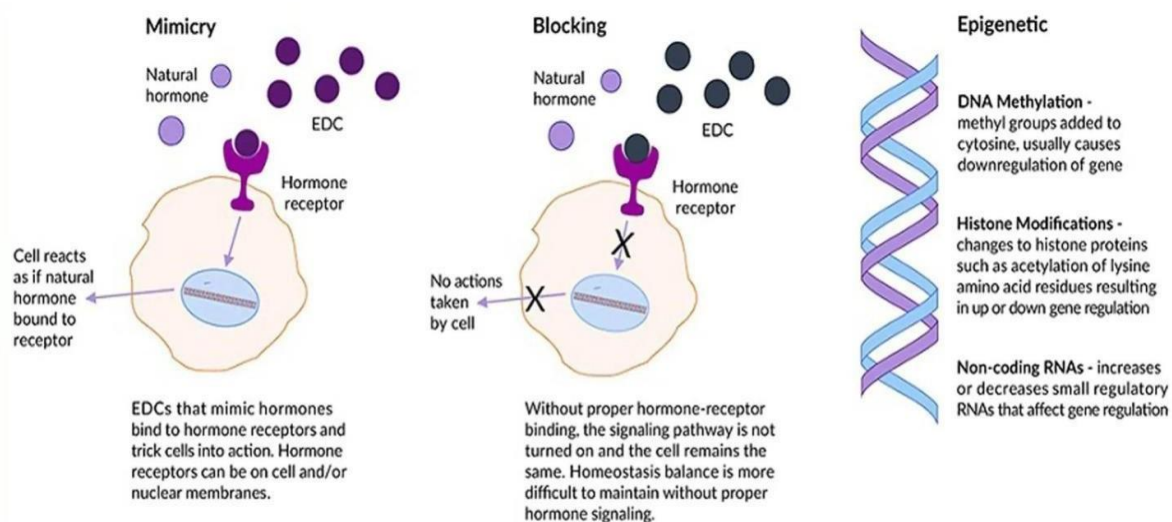
**1.1.3.1.1 Endocrine disruptors interfere with the endocrine system in several ways:**

**1.1.3.1.1.1 Mimicking Hormones:** Some disruptors can mimic natural hormones by binding to their receptors. For example, chemicals like bisphenol A (BPA) can mimic estrogen, leading to overstimulation of estrogenic activity in the body.

**1.1.3.1.1.2 Blocking Hormones:** Some disruptors block hormone receptors, preventing natural hormones from binding and exerting their normal effects. For instance, certain pesticides can block the androgen receptor, inhibiting the action of testosterone.

**1.1.3.1.1.3 Altering Hormone Production and Metabolism:** Disruptors can interfere with the synthesis, breakdown, or transport of hormones. For example, phthalates are known to interfere with testosterone synthesis, affecting reproductive development.

**1.1.3.1.1.4 Disruption of Feedback Loops:** Some disruptors interfere with the feedback loops that regulate hormone levels. For example, they may cause the body to produce too much or too little of a hormone, disrupting homeostasis.(4)



FigNo.1.EndocrineDistrupor

### 1.1.3.2 Common Endocrine Disruptors

There are many chemicals identified as endocrine disruptors. Some of the most well-known include Prostaglandins, which are produced in the endometrium, play a significant role in menstruation. They are involved in inducing uterine contractions to facilitate the shedding of the endometrial (lining). High levels of prostaglandins can also cause menstrual cramps (dysmenorrhea).

**1.1.3.2.1 Bisphenol A (BPA):** Used in the production of plastics, BPA can mimic estrogen and has been linked to reproductive disorders, early puberty, and metabolic disorders.

**1.1.3.2.2 Phthalates:** These are chemicals found in plastics, personal care products, and cosmetics. Phthalates interfere with testosterone production and are associated with reproductive abnormalities, particularly in males.

**1.1.3.2.3 Polychlorinated Biphenyls (PCBs):** These industrial chemicals have been banned in many countries but persist in the environment. They can disrupt thyroid hormone regulation and have been linked to cognitive deficits and developmental delays.

**1.1.3.2.4 Dioxins:** Produced as by-products of industrial processes, dioxins interfere with estrogen and androgen receptors and are linked to

reproductive and immune system (5,6)

### 1.1.3.3 Sources of Exposure

Humans can be exposed to endocrine disruptors through various routes:

**1.1.3.3.1 Food and Water:** Many endocrine disruptors, such as BPA and phthalates, leach from plastic containers and food packaging. Pesticide residues on fruits and vegetables, and contaminants in water (like atrazine and PFAS), also contribute to exposure.

**1.1.3.3.2 Air and Dust:** Flame retardants and other chemicals found in household products can accumulate in household dust, leading to inhalation or ingestion.

**1.1.3.3.3 Personal Care Products:** Cosmetics, shampoos, lotions, and perfumes can contain phthalates, parabens, and other endocrine disruptors, which are absorbed through the skin.

**Occupational Exposure:** People working in industries like agriculture, manufacturing, or chemical plants may be at higher risk of exposure to endocrine disruptors.

### 1.1.3.3 Health Effects of Endocrine Disruptors

Endocrine disruptors can have a wide range of adverse health effects, depending on the timing, level, and duration of exposure. Key health impacts include:

### 1.1.3.3.1 Reproductive Health:

Disruptors like BPA, phthalates, and dioxins are linked to infertility, reduced sperm quality, and birth defects. In females, they are associated with early puberty, menstrual irregularities, and polycystic ovary syndrome (PCOS).

### 1.1.4 premature Thelarche and Adrenarche

Puberty marks a series of biological changes leading to sexual maturity. The key events include

Thelarche (breast development), Adrenarche (onset of adrenal gland maturation), puberties (pubic hair development), and menarche (onset of menstruation). Premature thelarche and adrenarche refer to the early activation of these processes, often occurring before the typical age of puberty. Understanding these premature conditions is essential, as they can lead to early menarche (onset of menses), which can have long-term physical, psychological, and metabolic consequences.

#### 1.1.4.1 Premature Thelarche

refers to the isolated breast development in girls before the age of 8 without other signs of puberty. It usually occurs between infancy and early childhood. The exact cause of premature thelarche is unclear but may involve transient hormonal activation or increased sensitivity to circulating estrogen. This condition is generally benign and self-limiting, but in some cases, it can be a precursor to central precocious puberty (CPP), leading to early menarche.

#### 1.1.4.1.1 Causes of Premature Thelarche

##### 1.1.4.1.1.1 Transient Gonadotropin Activation:

A temporary rise in gonadotropin-releasing hormone (GnRH) could stimulate breast tissue growth without initiating full puberty.

**1.1.4.1.1.2 Peripheral Estrogen:** Some girls may have increased sensitivity to low levels of circulating estrogen, causing early breast tissue development without systemic puberty.

**1.1.4.1.1.3 Exogenous Estrogen Exposure:** Environmental factors like exposure to endocrine disruptors or medications could mimic the effects of estrogen on breast tissue. (7,8)

#### 1.1.4.2 Premature Adrenarche

Premature adrenarche is characterized by the early maturation of the adrenal glands, resulting in the production of androgens (e.g., dehydroepiandrosterone [DHEA] and DHEA sulfate

[DHEA-S]) earlier than usual. This leads to the early appearance of pubic hair, body odor, and sometimes acne. Premature adrenarche typically occurs in children between the ages of 5 and 8. While premature adrenarche itself does not directly cause early menarche, it can be a sign of early activation of the hypothalamic-pituitary-adrenal (HPA) axis, which may overlap with early pubertal changes.

#### 1.1.4.2.1 Causes of Premature Adrenarche

**1.1.4.2.1.1 Early Adrenal Maturation:** The adrenal glands begin producing androgens earlier than the typical timeline, possibly due to genetic or environmental influences.

**1.1.4.2.1.2 Obesity and Insulin Resistance:** Children with premature adrenarche often have a higher body mass index (BMI), which may contribute to insulin resistance. Insulin can stimulate androgen production, further accelerating pubertal changes.

#### 1.1.5. Increase caloric intake and improved nutrition

##### 1.1.5.1 Increased Caloric Intake

##### 1.1.5.1.1 Energy Balance and Puberty:

Review studies have consistently highlighted the role of increased caloric intake in promoting early pubertal onset. Increased energy availability leads to the accumulation of body fat, which is essential for the activation of the hypothalamic-pituitary-gonadal (HPG) axis, the system responsible for regulating puberty.

**1.1.5.1.2 Leptin and Adipose Tissue:** Fat tissue produces the hormone leptin, which plays a critical role in regulating energy balance and signaling the brain to initiate puberty, suggest that higher leptin levels due to increased body fat lead to earlier activation of the HPG axis, thereby advancing the onset of menstruation.

**1.1.5.1.3 Obesity Link:** There is a well-documented relationship between obesity and early menarche. Higher body mass index (BMI) in childhood is correlated with earlier puberty onset. Confirm that obese girls, due to higher caloric intake, often experience menarche earlier than their normal-weight peers.

##### 1.1.5.2 Improved Nutrition

##### 1.1.5.2.1 Nutrient Availability and Growth:

Improved access to better-quality nutrition, including proteins, vitamins, and minerals, accelerates overall physical growth and development.

This, in turn, influences pubertal timing, that improved nutrition contributes to more rapid growth during childhood, which correlates with earlier menarche.

**1.1.5.2.2 Micronutrients and Reproductive Health:** Specific micronutrients, such as iron, zinc, and vitamin D, are essential for healthy reproductive development. Rich in these nutrients support early maturation, indirectly contributing to the earlier onset of menstruation.

#### **1.1.6 Thyroid dysfunction:**

Chemicals like PFAS and flame retardants interfere with thyroid hormones, leading to hypothyroidism or hyperthyroidism, particularly hypothyroidism and hyperthyroidism, has been implicated in the abnormal timing of puberty, including early menarche. Thyroid hormones are crucial regulators of growth, metabolism and overall development of which influence pubertal timing. (9,10,11)

#### **1.1.6.1 Thyroid Function and Pubertal Development**

The thyroid gland produces hormones, primarily thyroxine (T4) and triiodothyronine (T3), that regulate metabolism, growth, and development. These hormones interact with the hypothalamic-pituitary-gonadal (HPG) axis, which controls the onset and progression of puberty. Disruptions in thyroid function can lead to alterations in the timing of menarche.

#### **1.1.6.2 Hypothyroidism and Early Menarche Role of Hypothyroidism:**

Hypothyroidism, characterized by low thyroid hormone levels, can paradoxically cause early menarche in some cases. The exact mechanism is complex, but it is believed that the deficiency in thyroid hormones leads to increased secretion of thyrotropin-releasing hormone (TRH) from the hypothalamus. TRH stimulates the release of both thyroid-stimulating hormone (TSH) and prolactin from the pituitary gland. Elevated prolactin levels, a condition known as hyperprolactinemia, can interfere with the normal regulation of reproductive hormones, leading to early or irregular menarche.

**1.1.6.2.1 Evidence from Review Studies:** hypothyroid girls often experience premature sexual development, including early menarche. This is linked to the high levels of prolactin seen in hypothyroid patients, which

disrupts the normal feedback mechanism in the HPG axis. Additionally, prolonged hypothyroidism can cause ovarian cyst formation, contributing to premature menstrual cycles. (12)

#### **1.1.6.2.2 Subclinical Hypothyroidism:**

Even mild or subclinical hypothyroidism can lead to early menarche that even in cases where thyroid hormone levels are not severely deficient, subtle disruptions in the endocrine balance may influence the timing of menarche. **7.5.3 Hyperthyroidism and Early Menarche** Hyperthyroidism and Accelerated Puberty: While hyperthyroidism (excess thyroid hormone production) is more commonly associated with delayed puberty, some studies suggest that it can lead to accelerated growth and earlier pubertal onset in rare cases. Hyperthyroid conditions can increase metabolism and growth rates, indirectly influencing the early onset of puberty, including menarche.

#### **1.1.6.3 Thyroid Hormone's Role in Growth:**

Since thyroid hormones regulate metabolic and growth processes, excess thyroid hormone can stimulate rapid skeletal growth, potentially advancing pubertal milestones. However, most studies focus on hypothyroidism as the more common cause of early

#### **1.1.7 Socioeconomic and Psychosocial Stress**

Environmental stressors such as poverty, family conflict, or the absence of a biological father have been associated with earlier menarche. These stressors can influence the hypothalamic-pituitary-gonadal axis, leading to early puberty.

Increased caloric intake and improved nutrition in regions where nutrition has improved significantly, the average age of menarche has declined, as better health and growth patterns may accelerate puberty. (13)

#### **1.1.8 Ethnicity**

Some studies have found that African-American and Hispanic girls tend to experience earlier menarche compared to Caucasian or Asian girls, although this is also influenced by other factors such as socioeconomic status and body composition.

Ethnicity plays a crucial role in the timing of menarche, with significant variations observed across different ethnic and racial groups. Numerous studies have found that ethnic background, often intertwined with genetic, environmental, and socioeconomic factors, can significantly influence when girls begin menstruating. In this review-based explanation, we explore how ethnicity affects the onset of menarche and the underlying factors

associated with these differences.

#### **1.1.8.1 BMI and Ethnicity:**

Body Fat Composition: Ethnic differences in body fat composition and BMI significantly contribute to variations in menarche timing. African American and Hispanic girls tend to have higher BMI and greater body fat percentages compared to White and Asian girls. Since body fat plays a critical role in triggering puberty, this difference in fat distribution contributes to the earlier onset of menarche. (14,15,16)

### **1.2 PREVENTION AND MANAGEMENT**

Preventing early menses (precocious puberty) involves addressing underlying causes, promoting a healthy lifestyle, and minimizing exposure to potential triggers.

#### **1.2.1 Environmental and Hormonal Triggers:**

1.2.1.1 Avoid endocrine-disrupting chemicals (EDCs):

Reduce exposure to substances like bisphenol A (BPA), phthalates, and pesticides, often found in plastics, cosmetics, and non-organic produce.

Use BPA-free containers and avoid microwaving plastic. Choose organic foods when possible.

Limit processed foods and animal products with added hormones:

Opt for hormone-free dairy, meat, and poultry to avoid ingestion of synthetic hormones. (17,18)

#### **1.2.2 Obesity and Weight Management:**

1.2.2.1 Encourage a balanced diet:

Promote whole grains, fruits, vegetables, lean proteins, and healthy fats.

1.2.2.2 Maintain regular physical activity:

Encourage at least 60 minutes of physical activity daily to maintain a healthy weight and regulate hormonal balance..

#### **1.2.3 Genetic and Familial Factors:**

1.2.3.1 Understand family history

If early puberty runs in the family, consult a healthcare provider to monitor signs early and consider medical advice on managing symptoms. (19,20,21,22)

#### **1.2.4 Stress Management:**

1.2.5.1 Provide emotional support:

High stress levels can disrupt hormone regulation. Ensure children have a supportive environment at home and school.

1.2.5.2 Teach coping strategies:

Encourage relaxation techniques, mindfulness, or therapy if needed. (23,24,25)

#### **1.2.5 Chronic Medical Conditions:**

1.2.6.1 Manage underlying health conditions:

Treat conditions like hypothyroidism or adrenal disorders promptly, as these can influence early puberty.

Limit processed foods and animal products with added hormones:

Opt for hormone-free dairy, meat, and poultry to avoid ingestion of synthetic hormones.

#### **1.2.6 Obesity and Weight Management:**

1.2.6.1 Encourage a balanced diet:

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Encourage at least 60 minutes of physical activity daily to maintain a healthy weight and regulate hormonal balance.

#### **1.2.7 Genetic and Familial Factors:**

1.2.7.1 Understand family history:

If early puberty runs in the family, consult a healthcare provider to monitor signs early and consider medical advice on managing symptoms. (23,26)

#### **1.2.8 Stress Management:**

1.2.8.1 Provide emotional support:

High stress levels can disrupt hormone regulation. Ensure children have a supportive environment at home and school.

1.2.8.2 Teach coping strategies:

Encourage relaxation techniques, mindfulness, or therapy if needed.

#### **1.2.9 Chronic Medical Conditions:**

1.2.9.1 Manage underlying health conditions:

Treat conditions like hypothyroidism or adrenal disorders promptly, as these can influence early puberty.

1.2.9.2 Ensure routine check-ups:

Regular pediatric check-ups can help detect and manage potential health issues early. (27)

#### **1.2.10 Exposure to Sexual Content and Media :**

1.2.10.1 Monitor media consumption: Limit exposure to age-inappropriate content that might psychologically or hormonally influence a child.

1.2.10.2 open communication:

Discuss media content and encourage critical thinking.

1.2.10.3 Adequate Sleep and Lifestyle Habits :

1.2.11. 1 Promote good sleep hygiene:

Ensure children get enough sleep for their age, as insufficient rest can disrupt hormonal balance.(28)

### CONCLUSION

Early onset of menstruation, or precocious puberty, arises from a complex interplay of genetic, environmental, hormonal, and lifestyle factors. Contributing factors include exposure to endocrine-disrupting chemicals, increased rates of childhood obesity, chronic stress, underlying medical conditions, and hereditary influences. Modern lifestyle changes, such as higher consumption of processed foods and greater exposure to environmental toxins, have further heightened the occurrence of this condition.

Effectively addressing early menses requires a comprehensive approach that combines prevention, early diagnosis, and targeted treatment. Public health initiatives should prioritize reducing exposure to harmful chemicals, encouraging healthy dietary and exercise habits, and ensuring timely medical evaluations when symptoms arise. Continued research into the contributing factors is essential to advance prevention and treatment methods. Raising awareness and promoting education among parents, healthcare professionals, and policymakers are crucial for minimizing the immediate and long-term effects of early menses on children's physical and emotional wellbeing.

Addressing the issue of early menses demands a holistic, multidisciplinary approach. This involves implementing preventive strategies, ensuring early detection, and providing appropriate interventions. Public health measures should focus on minimizing exposure to harmful chemicals, fostering healthier dietary and exercise practices, and promoting routine medical evaluations to identify potential issues early. Further research is critical to unravel the intricate interactions among these causative factors and to develop innovative approaches to prevention and treatment.

Moreover, enhancing awareness and educating parents, caregivers, healthcare providers, and policymakers is vital to reducing the immediate and long-term effects of precocious puberty on children's health, development, and overall quality of life.

### REFERENCE

[1]. McCarthy B, O'Neill S, O'Brien S. The

menstrual cycle: A comprehensive review. *Am J Obstet Gynecol.* 2020;223(4):446–55. Doi:10.1016/j.ajog.2020.05.001.

[2]. Marvin ML, Saldana R, Vázquez A. Menstrual health: A systematic review of the literature. *Int J Womens Health.* 2021;13:393–409. Doi:10.2147/IJWH.S299365.

[3]. Kruit MC, Launer LJ, Ferrier IN, et al. Menstrual-related migraines: A systematic review of the literature. *Cephalalgia.* 2021;41(1):17–27. Doi:10.1177/03331024209664.

[4]. Varyani F, Bhandari S, Pappas T, et al. Dysmenorrhea: A review of the evidence and current management. *Am J Obstet Gynecol.* 2020;223(4):528–38. Doi:10.1016/j.ajog.2020.05.018.

[5]. Petersen K, Moller N, Kreiner S, et al. Premenstrual syndrome: A review of the literature. *Acta Obstet Gynecol Scand.* 2021;100(6):1042–50. Doi:10.1111/aogs.14018.

[6]. Fraser IS, McCarron G, Hapangama D, et al. Menorrhagia: A review of the literature. *Obstet Gynecol Surv.* 2019;74(10):611–22. Doi:10.1097/OGX.0000000000000641.

[7]. Sommer M, Caruso BA, Sahin M, et al. A global review of menstrual hygiene management among adolescent girls. *J Pediatr Adolesc Gynecol.* 2016;29(4):309–15. Doi:10.1016/j.jpag.2016.04.

[8]. Khan ME, Sinha S. Menstrual health: A review of the literature on the stigma and its effects. *Indian J Community Med.* 2020;45(1):1–6. Doi:10.4103/ijcm.IJCM\_94\_19.

[9]. Baird DD, Wilcox AJ. Future prospects for research on the menstrual cycle. *Environ Health Perspect.* 1985;61:145–8. Doi:10.1289/ehp.8561145.

[10]. Mcneely J, Charkoudian N. Regulation of the menstrual cycle: A review of the hormonal interactions. *Physiol Rev.* 2019;99(3):1061–93. Doi:10.1152/physrev.00017.2018.

[11]. Kelley M, Cohn L. The role of the hypothalamic-pituitary-ovarian axis in the regulation of the menstrual cycle. *Obstet Gynecol Surv.* 2020;75(5):311–9. Doi:10.1097/OGX.0000000000000712.

[12]. Tao Y, Gao S, Li Z, et al. The hypothalamic-pituitary-gonadal (HPG) axis and its role in regulating the menstrual cycle. *Front*

- Endocrinol (Lausanne). 2021;12:749728. Doi:10.3389/fendo.2021.749728.
- [13]. Klein NA, Bliithe DL, Kiefer D, et al. The physiology of the normal menstrual cycle: A review. *J Clin Endocrinol Metab.* 2019;104(3):451–9. Doi:10.1210/jc.2018-01876.
- [14]. Simpson ER, Clyne C, Rubin JB, et al. The role of estrogen in the regulation of the ovarian cycle: A review. *Endocr Rev.* 2020;41(2):115–43. Doi:10.1210/edrv/bnz006.
- [15]. Rosenfield RL. The ovarian cycle: A comprehensive review of hormonal regulation. *Horm Res Paediatr.* 2019;92(5):269–76. Doi:10.1159/000502843.
- [16]. Sullivan T, Sneddon C, Hutton M. Prostaglandins and menstrual pain: A review of the literature. *Am J Obstet Gynecol.* 2021;225(1):1–9. Doi:10.1016/j.ajog.2021.01.012.
- [17]. Bourne T, et al. The role of prostaglandins in uterine contraction and pain: A comprehensive review. *BJOG.* 2018;125(3):292–303. Doi:10.1111/1471-0528.15267.
- [18]. Aguirre M, et al. The significance of the LH surge in the ovarian cycle: A review of its physiological mechanisms. *J Clin Endocrinol Metab.* 2019;104(9):4175–86. Doi:10.1210/jc.2019-00258.
- [19]. Kumar P, et al. The luteal phase: Physiology and regulation of the corpus luteum. *Horm Res Paediatr.* 2020;93(5):311–8. Doi:10.1159/00.
- [20]. Harris H, et al. The role of hormones in the female reproductive system: A review. *Endocr Rev.* 2019;40(6):1481–93. Doi:10.1210/er.2019-00.
- [21]. Cecchino GN, et al. The ovarian follicle: A review of folliculogenesis and its regulatory mechanisms. *Reprod Biol Endocrinol.* 2019;17(1):1–12. Doi:10.1186/s12958-019-0503-9.
- [22]. Gonzalez C, et al. The role of the fallopian tubes in reproduction: Overview of function and pathology. *Fertil Steril.* 2020;113(1):84–92. Doi:10.1016/j.fertnstert.2019.08.016.
- [23]. Ibáñez L, Dimartino-Nardi J, Poteau N, Saenger P. Premature adrenarche—normal variant or forerunner of adult disease? *Endocr Rev.* 2000;21(6):671–96. Doi:10.1210/edrv.21.6.0416.
- [24]. Ahmed ML, Ong KK, Dunger DB. Childhood obesity and the timing of puberty. *Trends Endocrinol Metab.* 2009;20(5):237–42. Doi:10.1016/j.tem.2009.02.004.
- [25]. Rogers IS, Northstone K, Dunger DB, Cooper AR, Ness AR, Emmett PM. Diet throughout childhood and age at menarche in a contemporary cohort of British girls. *Public Health Nutr.* 2010;13(12):2052–63. Doi:10.1017/S1368980010001696.
- [26]. Penta L, Cappa M. Disorders of puberty in juvenile hypothyroidism: A review of the literature and personal observations. *J Endocrinol Invest.* 2001;24(8):654–62. Doi:10.1007/BF03343949.
- [27]. Palmert M, Dunkel L. Clinical practice. Delayed puberty. *N Engl J Med.* 2012;366(5):443–53. Doi:10.1056/NEJMcp1109290.
- [28]. Ahmed ML, Ong KK, Dunger DB. Childhood obesity and the timing of puberty. *Trends Endocrinol Metab.* 2009;20(5):237–42. Doi:10.1016/j.tem.2009.02.004.