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Changes in Sexual Maturity (Puberty): A Narrative Literature Review

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A B S T R A C T

The process of sexual maturation, or puberty, is marked by the development of secondary sexual characteristics, rapid body growth, and, ultimately, the ability to reproduce. Various congenital and endocrine disorders can interfere with the timing of sexual maturation, causing delayed puberty or precocious puberty. This literature review aimed to describe puberty and its disorders and influencing factors. The age of puberty is multifactorial, involving genetic and environmental components. Delayed puberty is a physiological (constitutional) delay in which hormonal levels are normal, and the hypothalamic-pituitary-gonadal (HPG) axis is intact, but maturation occurs slowly. Precocious puberty can be partial, complete, or mixed type and can be further categorized into central (GnRH dependent) and peripheral (GnRH dependent). In conclusion, congenital and endocrine disorders can interfere with the timing of sexual maturation, causing delayed puberty or precocious puberty.

1. Introduction

The process of sexual maturation, or puberty, is marked by the development of secondary sexual characteristics, rapid body growth, and, ultimately, the ability to reproduce. Various congenital and endocrine disorders can interfere with the timing of sexual maturation, causing delayed puberty or precocious puberty. Both scenarios involve impaired production of sex hormones by the gonads.

The age of puberty is multifactorial, involving genetic and environmental components. The normal range for the onset of puberty is now 8 to 13 years and appears to be decreasing for girls. Girls of African descent and Hispanic/Latina girls may start puberty up to 1 year earlier than the average young girl. This earlier onset occurs primarily with breast development, not at menarche, and 5% of whites and 15% of all girls will start puberty before the age of eight. Both precocious and delayed puberty have implications for a child's social life and interactions. In addition, obesity has been shown to accelerate the onset of puberty, making it difficult to determine the impact of race on the timing of puberty.[1-5] This literature review aimed to describe puberty and its disorders and influencing factors.

Delayed puberty

About 2% of children in North America have delayed development of secondary sex characteristics. In girls, the onset of puberty is usually marked by thelarche, or breast development, which usually begins by age 13. Delayed puberty is diagnosed when there is no breast development by age 13, which is 2 to 2.5 standard deviations greater than the mean. Puberty age. Pubic hair may be present, as it is largely

dependent on adrenal rather than gonadal function. A clinical diagnosis can be made in the absence of menarche at age 15 or 16. Although delayed, puberty may have significant psychosocial implications and carry risks of inadequate bone development and mineralization. Puberty is a time of rapid bone growth, with the majority of bone development and mineralization being achieved during adolescence. Estrogen plays a major role in this process and a lack of circulating estrogen places individuals at risk for inadequate bone density in adulthood.[6-8]

In most cases, delayed puberty is a physiological (constitutional) delay in which hormonal levels are normal, and the hypothalamic-pituitary-gonadal (HPG) axis is intact, but maturation occurs slowly. This physiological delay tends to be familial, occurs less frequently in girls than boys, and is often diagnosed retrospectively after pubertal development has been completed. Although the exact incidence of constitutional delay in growth and puberty (CDGP) is unknown, sentinel and leading studies on the subject report that approximately 30% of girls with delayed puberty eventually progress through puberty normally and spontaneously. An additional 19% of girls had functional hypogonadotropic hypogonadism (FHH), essentially an underlying condition or disease (unrelated to gonadal function) that is responsible for the developmental delay (e.g., anorexia nervosa) (Table 1). Treatment of FHH includes correction of the underlying condition, with possible initiation of hormone therapy if prolonged recovery is projected. Treatment for CDGP includes expectant management or the initiation of hormone therapy in small doses to promote pubertal development and reduce the risk of poor bone growth and mineralization.[9-11]

Table 1. Frequency and common causes of delayed puberty.

Causes of delayed puberty	**Hypergonadotropic Hypogonadism**	**Hypogonadotropic Permanent hypogonadism**	**Hypogonadotropic Functional hypogonadism**
	Frequency (%)		
Boy	5-10	10	20
Girl	25	20	20
Common causes	• Turner syndrome • Dysgenesis gonad • Chemotherapy • Radiation therapy	• Tumor or infiltrative disease of the central nervous system • Gonadotropin hormone deficiency (isolated hypogonadotropic hypogonadism, Kallmann's syndrome) • Pituitary hormones combined	• Systemic disease (inflammation of the intestine, celiac disease, anorexia nervosa, or bulimia) • Hypothyroidism • Excessive exercise

In other cases, disruption of the HPG axis is the main cause of delayed puberty. The human gonadal function is partly controlled by luteinizing hormone (LH) and follicle-stimulating hormone (FSH), the release of which is regulated by pulsatile secretion from the hypothalamus of gonadotropin-releasing hormone (GnRH). The G protein-coupled receptor 54 (GPR54) has been identified as a gatekeeper gene for the activation of the GnRH axis. GPR54 is required for the normal function of this axis, and data suggest that the kisspeptin-1 ligand may act as a neurohormonal regulator of the GnRH axis.

The mechanisms of inhibition of GnRH release and activation in childhood are poorly understood but appear to involve feedback inhibition by sex steroids and possibly another central nervous system (CNS) pathways. Given the many etiologies that contribute to delayed puberty, a thorough evaluation should be performed, which includes a physical examination and medical and family history, specifically targeting known contributors to delayed puberty.

Laboratory studies may consist of X-ray scanning for bone age, measurement of thyroid function, determination of serum levels of prolactin and adrenal and gonadal steroids, plasma gonadotropin radioimmunoassay, and screening for systemic disorders. Adolescents with high gonadotropin levels require karyotyping to rule out a genetic cause, and those with low gonadotropin levels require skull imaging (lateral skull film, computed tomography, or MRI) to rule out pituitary or other CNS infiltrates or tumors. Treatment of delayed puberty depends on the

cause; the goals of treatment are the development of secondary sex characteristics and fertility and the promotion of growth and bone mineralization. Insufficient sex hormone secretion can be corrected with hormone replacement therapy, such as estrogen. Idiopathic hypogonadotropic hypogonadism is treated with synthetic GnRH or sex hormone administration, or both and may be lifelong.[12-15]

Precocious puberty

Early puberty is a rare event, affecting about 29 in 100,000 girls. Early puberty is defined as the onset of clinical signs of puberty (growth of breasts or pubic hair) before the age of 8 years. However, some endocrinologists have recommended that the criteria be changed to reflect trends in early puberty, suggesting that pubertal changes before age 6 years in black girls or age 7 years in white girls are more likely to reflect abnormal development.

There are many postulated causes of early puberty, including changes in genetic factors, increased obesity, increased protein consumption, and the increasing prevalence of molecular compounds known as endocrine disruptors in common household products. In addition to the premature development of secondary sex characteristics, precocious cause premature closure of the epiphyses of long bones, resulting in lifelong short stature, and often has profound psychosocial consequences. Because precocious puberty can be a sign of pathological conditions, all cases of precocious puberty require a thorough evaluation.[16-18]

Precocious puberty can be partial, complete, or mixed type and can be further categorized into central (GnRH dependent) and peripheral (GnRH dependent). Central precocious puberty results from failure of central inhibition of the GnRH pulse generator (gonadostat), often due to CNS abnormalities. However, most cases are idiopathic. Mutations in the MKRN3 gene religious recently been reported as a cause of central puberty. The diagnosis of central precocious puberty is one exception. Because CNS lesions may be missed, children with suspected central precocious puberty require long-term monitoring.

Peripheral puberty is GnRH-independent and develops when sex hormones are produced by some mechanism other than stimulation by gonadotropins and are either genetic or exogenous. Peripheral causes include adrenal hyperplasia or tumors, endocrine disruptors of environmental origin (benzene compounds), exposure to exogenous sex steroids, exogenous anabolic steroids, familial Leydig cell hyperplasia, gonadal tumors or cysts, human chorionic gonadotropin (hCG)-secreting tumors (hepatoblastomas, intracranial lesions), severe hypothyroidism, McCune-Albright syndrome, and testotoxicosis.[19]

Partial precocious puberty is the partial early development of corresponding secondary sex characteristics alone or in combination. A girl with incomplete precocious puberty may experience thelarche or pubarche and, rarely, premature menarche. Thelarche Preterm birth can be seen from 2 to 24 months of age, and in very young children, breast development is often reversed. Thelarche is considered premature if it occurs before the age of 8 years, but it is usually a normal variation and represents the end of hormone release pre-puberty higher. Bone growth and menarche in these girls occur during the normal course of life. Premature puberty tends to occur between the ages of 5 and 8. Premature puberty is usually the consequence of an early rise in adrenal androgens that causes early growth of pubic hair and possibly a temporary acceleration in bone growth and maturation that has no significant effect on the timing of puberty or final height. Sparse growth of hair on the genitals, in the absence of thelarche or menarche, does not indicate early puberty. Girls with precocious puberty and thelarche should be followed until puberty to ensure normal development; sometimes pathological conditions can contribute to premature development.[19]

Complete precocious puberty refers to the onset and development of all the features of puberty (i.e., thelarche, pubarche, and menarche). Mixed precocious puberty (virilization of girls or feminization of boys) causes a child to develop some secondary sex characteristics of the opposite sex. This condition is usually apparent at birth and rarely occurs in older children. The diagnosis and causes of premature development are often straightforward. A thorough history and physical examination are performed to determine the speed of the process and to rule out

systemic neoplasms and life-threatening nerves central, ovarian, or adrenal. A family history of events helps exclude tumors. Children with early puberty also have a tendency to be obese. Treatment for all forms of precocious puberty includes identifying and eliminating the underlying cause or administering appropriate hormones. If needed, early puberty can be reversed. Management goals include diagnosing and treating intracranial disease, stopping maturation until appropriate development, maximizing eventual adult height, and reducing emotional problems. The most common form, central precocious puberty, is usually treated with potent GnRH agonist analogs, which induce reversible, selective suppression of the HPG axis. Because many of these children are obese and childhood obesity is predictive of morbidity in adolescence and adulthood, it is important for clinicians to include the assessment and management of obesity as a component of treatment for early central puberty.[20,21]

2. Conclusion

Congenital and endocrine disorders can interfere with the timing of sexual maturation, causing delayed puberty or precocious puberty.

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