

A Comprehensive Review of Factors Contributing to Precocious Puberty

Aeysha Sultan, Irum Shahzadi, Bukhtawar Sultan, Maryam Zahra, Musarat Ijaz Roberto Acevedo

Department of Chemistry, University of Education, Lahore, Pakistan

A Comprehensive Review of Factors Contributing to Precocious Puberty

Introduction

Precocious puberty refers to the unusually early onset of secondary sexual characteristics—before eight years in girls and nine years in boys. Over recent decades, the global rise in early puberty has raised concerns among clinicians, researchers, and public health experts. This shift reflects complex interactions between genetic predisposition, environmental chemical exposure, dietary patterns, psychosocial stressors, and circadian disruption. Early sexual maturation not only influences physical growth but is also associated with multiple health risks, including increased vulnerability to metabolic syndrome, psychological issues, and hormone-related cancers later in life.

Understanding the multifactorial origins of precocious puberty allows for earlier detection, appropriate intervention, and focused prevention. This review provides an extensive, interconnected, and updated account of biological, environmental, lifestyle, psychosocial, and technological influences contributing to its development.

Physiological Basis of Pubertal Onset

Puberty is governed by activation of the hypothalamic–pituitary–gonadal (HPG) axis. During childhood, the axis remains suppressed through inhibitory neuroendocrine pathways. The initiation of puberty begins when this restraint is lifted, leading to pulsatile secretion of gonadotropin-releasing hormone (GnRH) from the hypothalamus.

GnRH stimulates the anterior pituitary to secrete luteinizing hormone (LH) and follicle-stimulating hormone (FSH), which in turn promote gonadal maturation and the production of sex steroids—estrogens in girls and testosterone in boys. In precocious puberty, this cascade begins prematurely.

Recent research indicates that kisspeptin, neurokinin B, and dynorphin neurons play critical roles in modulating GnRH activity. Overactivation of the KNDy neuron network can lead to early GnRH pulsatility. Additionally, heightened sensitivity of GnRH receptors, aberrant synaptic pruning during early childhood, and epigenetic alterations influenced by environmental factors can all alter the timing of puberty.

Nutritional and Metabolic Influences

Rising Childhood Obesity and Metabolic Acceleration

Obesity is one of the strongest predictors of early puberty, particularly in girls. Excess adiposity increases aromatase activity, leading to greater peripheral conversion of androgens to estrogens. High leptin levels—characteristic of obesity—signal energy sufficiency to the hypothalamus, reducing the threshold for GnRH activation.

Furthermore, insulin resistance elevates circulating insulin and IGF-1 levels, both of which stimulate ovarian steroidogenesis and accelerate the maturation of reproductive tissues.

Malnutrition and Endocrine Imbalance

Paradoxically, chronic malnutrition can also disturb hormonal homeostasis. Reduced IGF-1, altered ghrelin secretion, and overall energy imbalance may prompt adaptive mechanisms that influence HPG axis reactivation. Historical and population-based studies reveal that both undernutrition and overnutrition disrupt normal pubertal timing.

Dietary Patterns and Chemical Intake Through Food

In recent decades, changes in diet composition and food processing have introduced new factors that affect hormonal balance, particularly involving estrogen metabolism and endocrine function. These dietary elements interact complexly with the gut microbiota and endocrine systems, collectively impacting hormone regulation.

1. Ultra-Processed Foods and Gut Microbiota Alteration

Ultra-processed foods are commonly enriched with preservatives, emulsifiers, and artificial additives designed to extend shelf life and improve texture. These compounds can disrupt the gut microbial ecosystem, known as the **gut microbiota**, which plays a critical role in metabolizing estrogens. The gut bacteria express enzymes such as β -glucuronidase that regulate the **estrobolome**—the collection of microbial genes capable of metabolizing estrogens.

Disruption of this microbial balance (dysbiosis) can lead to altered estrogen metabolism, influencing the levels of circulating estrogens and their activity in the body. Such shifts may contribute to hormonal imbalances that can affect reproductive health and potentially increase risks for estrogen-sensitive conditions.

2. Pesticide Residues with Estrogenic and Anti-Androgenic Activities

Fruits and vegetables, even when healthy in general, may carry residues of pesticides known as **endocrine-disrupting chemicals (EDCs)**. Many pesticides act as **xenoestrogens**—chemicals that mimic or interfere with natural estrogens—and some exhibit anti-androgenic effects, inhibiting male hormone activity. These compounds can bind to hormone receptors, disrupting normal hormone signaling pathways, thereby altering reproductive hormone balance, fertility, and possibly contributing to developmental and metabolic disorders.

3. Excessive Consumption of Phytoestrogens

Phytoestrogens are naturally occurring plant compounds found in foods like soy, flaxseed, and legumes. These compounds, including isoflavones and lignans, structurally resemble human estrogens and can bind to estrogen receptors, though with much weaker affinity.

When consumed in very high amounts, phytoestrogens may exert **mild estrogenic effects**, which could influence hormone-sensitive tissues. While moderate intake is generally considered beneficial, excessive consumption might affect menstrual cycles, fertility, or the risk of hormone-related cancers in susceptible individuals.

4. High Sugar Diets and Insulin-Mediated Hormonal Effects

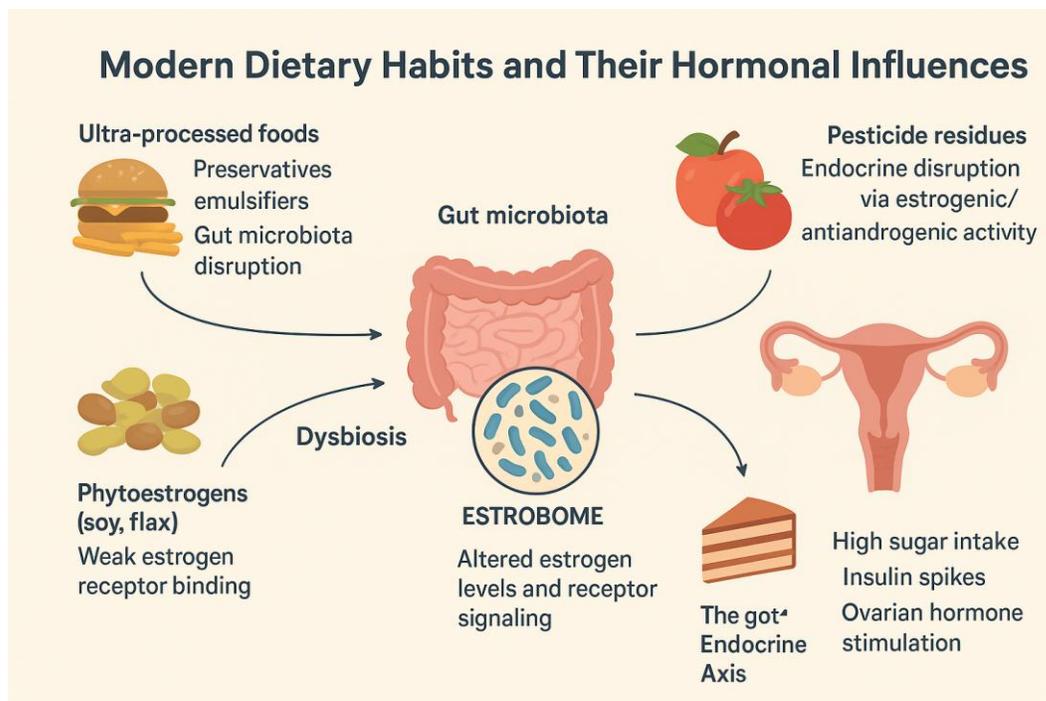
Diets high in refined sugars and simple carbohydrates cause rapid spikes in blood glucose, leading to increased insulin secretion. Insulin, beyond its metabolic role, acts as a hormone that can influence the **hypothalamic-pituitary-ovarian axis** by stimulating ovarian theca cells to produce androgens, which are then converted to estrogens by granulosa cells.

Chronic hyperinsulinemia may thus elevate ovarian hormone production, contributing to conditions such as polycystic ovary syndrome (PCOS) characterized by hormonal imbalance, irregular menstruation, and infertility.

The Gut–Endocrine Axis: A Crucial Mediator

Emerging research highlights the **gut–endocrine axis**, where gut microbiota interacts with the endocrine system to regulate hormone levels and actions. The **estrobolome** subset of gut bacteria is particularly involved in estrogen metabolism by deconjugating estrogens excreted into the gut, allowing their reabsorption and recycling (enterohepatic circulation).

Dysbiosis, or an imbalance in gut microbiota, can impair estrobolome function, resulting in disrupted estrogen recycling. This leads to altered systemic estrogen levels, impacting reproductive health, metabolic regulation, and susceptibility to hormone-related diseases.



Environmental and Chemical Exposures

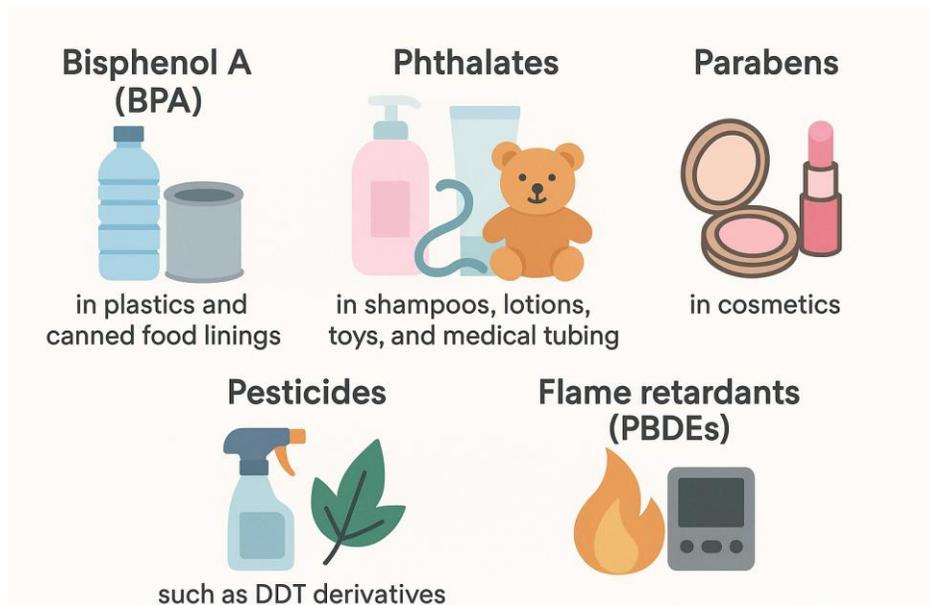
Endocrine-Disrupting Chemicals (EDCs)

Endocrine-disrupting chemicals (EDCs) are synthetic or naturally occurring substances that interfere with the normal functioning of the endocrine system—the body’s complex network responsible for hormone production, regulation, and signaling. Hormones regulate a wide range of physiological processes, including growth, metabolism, reproduction, and immune responses. When EDCs enter the body, they can disrupt hormone balance by mimicking natural hormones, blocking hormone receptors, altering hormone synthesis, or modifying hormone metabolism and clearance. This disruption can lead to adverse health effects such as reproductive disorders, developmental abnormalities, metabolic syndromes, immune dysfunction, and even increased risk of certain cancers.

EDCs are pervasive in the environment due to widespread industrial and agricultural use, as well as their presence in everyday consumer products. Some of the most common and well-studied EDCs include:

- **Bisphenol A (BPA):**
BPA is a chemical primarily used in manufacturing polycarbonate plastics and epoxy resins. It is commonly found in food and beverage containers, such as water bottles and the linings of canned foods and beverages. BPA can leach into food and drinks, especially when containers are heated or damaged. Structurally similar to estrogen, BPA can bind to estrogen receptors, disrupting normal hormonal signaling. Studies have linked BPA exposure to reproductive abnormalities, altered brain development, and increased risk of metabolic disorders.
- **Phthalates:**
Phthalates are a group of chemicals used as plasticizers to increase the flexibility and durability of plastics. They are commonly found in personal care products like shampoos, lotions, and perfumes, as well as in children’s toys, medical tubing, and packaging materials. Phthalates can interfere with androgen hormones, critical for male reproductive development. Exposure has been associated with reduced fertility, developmental defects in male reproductive organs, and potential impacts on thyroid function.
- **Parabens:**
Parabens are preservatives widely used in cosmetics, toiletries, and some food products to prevent microbial growth. Common parabens include methylparaben and propylparaben. They possess weak estrogenic activity and can mimic natural estrogen by binding to estrogen receptors. Chronic exposure to parabens has raised concerns about their potential role in breast cancer development and endocrine-related reproductive issues.
- **Pesticides (such as DDT derivatives):**
Certain pesticides, including dichlorodiphenyltrichloroethane (DDT) and its breakdown products, are potent endocrine disruptors. Despite bans or restrictions in many countries, these persistent organic pollutants remain in the environment due to their long half-lives. DDT and related compounds can mimic estrogen or interfere with androgen signaling, leading to reproductive abnormalities, developmental delays, and wildlife population declines. Pesticide exposure has also been linked to neurodevelopmental disorders in children.
- **Flame Retardants (Polybrominated Diphenyl Ethers, PBDEs):**
PBDEs are used in furniture, electronics, textiles, and building materials to reduce flammability. These compounds bioaccumulate in the environment and in human tissues. PBDEs can disrupt thyroid hormone homeostasis, which is critical for brain development and metabolism. Exposure

to PBDEs has been associated with cognitive impairments, behavioral changes, and thyroid dysfunction.



These chemicals accumulate over time. Even low-dose, chronic exposure during early childhood—or even in utero—can alter epigenetic markers that regulate puberty-related genes.

Indoor Air Quality and Urban Exposure

In modern lifestyles, children tend to spend a significant portion of their time indoors—in homes, schools, and recreational centers—where they are exposed to a variety of indoor pollutants. Unlike outdoor air pollution, which has been extensively studied, indoor pollutants often reach higher concentrations due to confined spaces and limited ventilation. These pollutants include volatile organic compounds (VOCs), microplastic particles, secondhand smoke, and airborne phthalates. Emerging evidence indicates that these compounds can interfere with critical hormone pathways, particularly adrenal steroidogenesis and estrogen metabolism, which are pivotal in regulating puberty and overall endocrine function.

- **Volatile Organic Compounds (VOCs):**
VOCs are a large group of carbon-based chemicals emitted as gases from products like furniture, paints, varnishes, adhesives, and cleaning agents. Common VOCs include formaldehyde, benzene, and toluene. When inhaled, VOCs can enter the bloodstream and influence hormone-producing glands such as the adrenal glands and ovaries. Specifically, VOC exposure can disrupt adrenal steroidogenesis—the process by which adrenal glands synthesize steroid hormones like cortisol and androgens—which play a role in the timing of puberty and stress responses. Moreover, VOCs can affect enzymes involved in estrogen metabolism, leading to altered levels of circulating estrogens.
- **Microplastic Particles:**
Microplastics are tiny plastic fragments (less than 5 millimeters) that result from the breakdown of larger plastic items or are directly introduced through consumer products. Indoors, microplastics can accumulate in dust and air. Due to their small size, these particles can be inhaled or ingested, carrying with them chemical additives such as plasticizers and flame retardants. These additives often have endocrine-disrupting properties, capable of interfering with hormone receptors or

altering hormone synthesis. Exposure to microplastics and their associated chemicals has been linked to disturbances in reproductive hormone balance.

- **Secondhand** **Smoke:**
Tobacco smoke contains thousands of chemicals, many of which are toxic and hormonally active. Children exposed to secondhand smoke indoors absorb substances that can interfere with adrenal and gonadal hormone production. Components of smoke can inhibit or stimulate enzymes that regulate steroid hormone synthesis, thereby disrupting normal pubertal development. Studies have shown associations between secondhand smoke exposure and altered timing of puberty, as well as increased risk of respiratory and metabolic disorders.
- **Airborne** **Phthalates:**
Phthalates are plasticizers commonly found not only in products but also as airborne contaminants indoors, especially in dust and aerosols. Inhalation of airborne phthalates leads to systemic absorption, where they interfere with hormone signaling. Phthalates are known to disrupt estrogen and androgen pathways, and in children, this interference can skew the delicate hormonal balance that governs puberty onset. Research has linked phthalate exposure to premature thelarche (early breast development) and other signs of early puberty.

The combined exposure to these indoor pollutants creates a biochemical environment in children that can accelerate the onset of puberty. Disruption of **adrenal steroidogenesis** affects the production of hormones like dehydroepiandrosterone (DHEA) and its sulfate (DHEAS), which are involved in adrenarche—the early phase of puberty. Meanwhile, alterations in **estrogen metabolism** influence the timing of puberty is not solely dictated by genetics and physical health but is also significantly influenced by psychosocial and emotional environments. Stress and early life adversity play a pivotal role in modulating neuroendocrine systems that control pubertal onset.

Stress, Trauma, and Early Life Adversity

Chronic stress leads to sustained elevations in cortisol, the primary stress hormone produced by the adrenal glands. Cortisol is regulated by the hypothalamic-pituitary-adrenal (HPA) axis, which closely interacts with the hypothalamic-pituitary-gonadal (HPG) axis responsible for reproductive development. When cortisol levels remain elevated over time due to adverse psychosocial conditions, the balance between these two axes is disrupted, accelerating pubertal maturation.

Children exposed to stressful environments such as: Family conflict, Parental absence, Emotional neglect, Physical or emotional trauma and/or Socioeconomic instability, often demonstrate earlier pubertal milestones, such as premature breast development, accelerated growth spurts, and earlier menarche. From an evolutionary biology perspective, early maturation in response to environmental stressors may represent an adaptive mechanism to maximize reproductive success in unpredictable or harsh environments. Essentially, early puberty might be the body's way of increasing reproductive potential when the future appears uncertain.



Parenting, Attachment, and Family Dynamics

The quality of parenting and family relationships significantly impacts children’s stress responses and hormonal regulation. Warm, secure, and emotionally supportive environments foster stable oxytocin and cortisol patterns that help maintain a balanced neuroendocrine state, delaying premature puberty.

Conversely, harsh, inconsistent, or neglectful parenting styles can dysregulate stress hormone pathways. Altered oxytocin levels—known for their role in social bonding—and heightened cortisol secretion indirectly affect the secretion of gonadotropin-releasing hormone (GnRH), the key hormone triggering puberty. This hormonal imbalance can lower the threshold for pubertal initiation, leading to earlier onset.

Circadian Rhythm, Light Exposure, and Pubertal Timing

Biological rhythms governed by the circadian clock play a crucial role in coordinating hormonal secretions necessary for normal growth and development, including puberty.

Melatonin Suppression and Artificial Light

Melatonin, a hormone secreted by the pineal gland during darkness, suppresses GnRH secretion in childhood, helping delay pubertal onset. However, exposure to artificial light—especially blue light emitted by screens (smartphones, tablets, computers) and LED lighting—can reduce melatonin production.

The consequences of reduced melatonin include:

- **Earlier sleep disruption** due to difficulty falling asleep or fragmented sleep
- **Nocturnal hormonal imbalance** as the natural nighttime surge of melatonin diminishes
- **Increased adrenal activation** from stress-related pathways during night hours

Together, these changes lower the physiological threshold for initiating puberty, pushing pubertal development earlier than expected.

Screen Time, Sleep Loss, and Neuroendocrine Effects

Excessive evening screen use further exacerbates circadian disruption by impacting:

- **REM sleep cycles**, essential for brain development and hormonal regulation
- **Melatonin amplitude**, reducing its overall nighttime availability
- **Cortisol regulation**, potentially causing elevated nighttime cortisol levels
- **Growth hormone secretion**, which predominantly occurs during deep sleep phases and is crucial for normal growth and development

Children suffering from chronic sleep deprivation or irregular sleep patterns exhibit a higher prevalence of early puberty. Sleep loss effectively stresses the neuroendocrine system, accelerating pubertal processes and influencing physical and emotional health.

Genetic and Congenital Determinants

Heritable Factors

The timing of puberty is strongly influenced by genetic factors, with studies showing a high degree of heritability. Specific genes have been identified that play crucial roles in regulating the initiation and progression of puberty. For example, *KISS1* and its receptor *KISS1R* encode kisspeptin and its receptor, which are essential for stimulating gonadotropin-releasing hormone (GnRH) neurons in the hypothalamus. This stimulation triggers the cascade of hormonal changes leading to puberty. Variations or mutations in these genes can either advance or delay pubertal onset. Similarly, the *TAC3* gene and its receptor *TACR3* regulate neurokinin B, a neuropeptide that modulates GnRH secretion. Mutations in *GNRHR*, which encodes the GnRH receptor itself, can impair or alter the hormonal signaling necessary for puberty. Lastly, *LIN28B* is implicated in timing biological developmental events, including puberty, and polymorphisms in this gene have been linked to variations in pubertal age. Families with histories of early puberty often display these genetic variants across multiple generations, indicating a strong hereditary influence.

Congenital and Pathological Causes

Certain congenital disorders and pathological conditions can precipitate early puberty by disrupting normal hormonal pathways:

- **Congenital Adrenal Hyperplasia (CAH)**: This inherited enzyme deficiency leads to excess production of adrenal androgens from birth. Elevated androgens can cause premature development of secondary sexual characteristics, such as early pubic hair and accelerated growth.

- **Hypothalamic Hamartomas:** These benign, tumor-like malformations in the hypothalamus can secrete GnRH independently of the body's normal regulatory mechanisms, triggering precocious puberty.
- **Central Nervous System (CNS) Lesions or Tumors:** Tumors affecting the hypothalamus or pituitary gland can disrupt normal endocrine control, causing early activation of the HPG axis.
- **Chronic Endocrine Disorders:** Conditions such as hypothyroidism or other hormonal imbalances can interfere with pubertal timing.
- **Thyroid Dysfunction:** Both hypothyroidism and hyperthyroidism affect metabolism and hormonal homeostasis and have been associated with altered pubertal onset.

Advanced neuroimaging, especially magnetic resonance imaging (MRI), has enabled detection of subtle hypothalamic anomalies in children with idiopathic precocious puberty (where no clear cause is identified), aiding diagnosis and treatment.

Medical, Maternal, and Iatrogenic Influences

Maternal Environment

The prenatal environment critically shapes the development of the fetal endocrine system. Several maternal factors have been linked to altered programming of the child's hormonal axis, influencing the timing of puberty:

- **Maternal Obesity:** Excess maternal adiposity increases circulating leptin and inflammatory markers, which may cross the placenta and affect fetal neuroendocrine development, predisposing children to earlier puberty.
- **High Fat or High Sugar Diet:** Diets rich in unhealthy fats and sugars during pregnancy can lead to metabolic alterations in the fetus, including insulin resistance and altered adipokine signaling, which in turn influence puberty.
- **Smoking and Alcohol Use:** Both are known teratogens that disrupt fetal brain and endocrine development, increasing risk for earlier pubertal onset.
- **Chronic Stress:** Maternal stress elevates cortisol levels, which can cross the placental barrier and program the fetal hypothalamic-pituitary-adrenal (HPA) axis, potentially altering later stress responses and puberty timing.
- **Gestational Diabetes:** Elevated maternal glucose affects fetal insulin and growth factor pathways, which are important regulators of growth and development, including puberty.

While some researchers have hypothesized that repeated prenatal ultrasound exposure might influence fetal hormone milieu, current evidence is insufficient to confirm a causal relationship.

Pharmaceuticals and Medical Devices

Children exposed to certain medications or medical devices over prolonged periods may experience altered pubertal timing due to endocrine-disrupting effects:

- **Hormonal Medications:** Long-term use of medications containing estrogens, progestins, or androgens can artificially modify the timing of puberty.
- **Steroid-Containing Creams:** Topically applied corticosteroids can be absorbed systemically, especially with frequent or large-area application, potentially suppressing or altering endogenous hormone production.
- **Phthalate-Containing IV Tubing:** Phthalates are known endocrine disruptors that can leach from medical tubing into the body during intravenous therapy, interfering with hormone synthesis and signaling.
- **Certain Antiepileptic Drugs:** Some anticonvulsants can alter liver metabolism of sex steroids or influence neuroendocrine regulation, thereby affecting pubertal onset.

Careful monitoring is warranted for children on these treatments to detect any changes in pubertal development.

Health Consequences and Long-Term Implications

- **Accelerated Bone Aging and Reduced Final Height:** Early puberty causes premature closure of growth plates (epiphyseal fusion) in bones, leading to a shorter window for height gain and consequently reduced adult stature.
- **Increased Risk of Obesity and Insulin Resistance:** Early hormonal changes can alter fat distribution and insulin sensitivity, increasing the risk of obesity and metabolic syndrome.
- **Higher Likelihood of Type 2 Diabetes:** Insulin resistance associated with early puberty predisposes individuals to type 2 diabetes later in life.
- **Increased Risk of Polycystic Ovary Syndrome (PCOS) in Girls:** Early exposure to estrogens and androgens may disrupt ovarian function, increasing the likelihood of PCOS, which involves hormonal imbalance and fertility issues.
- **Elevated Lifetime Estrogen Exposure and Breast Cancer Risk:** Early menarche extends the duration of estrogen exposure over a woman's lifetime, increasing the risk of hormone-dependent cancers like breast cancer.
- **Emotional Distress, Anxiety, and Self-Esteem Issues:** Early physical maturation often mismatches emotional and cognitive development, leading to psychological challenges, social difficulties, and increased risk for anxiety and depression.
- **Early Initiation of Risky Behaviors:** Children undergoing early puberty may engage sooner in behaviors such as substance use, sexual activity, and delinquency, due to social pressures and hormonal influences.

Management, Prevention, and Lifestyle Interventions

Medical Therapies

- **GnRH Analogue Therapy:** The gold standard treatment for central precocious puberty involves administering synthetic GnRH analogues, which desensitize the pituitary gland and temporarily halt puberty progression. This treatment allows children to maintain normal growth rates and improves final adult height. It is reversible and well-tolerated when carefully managed.

Lifestyle and Environmental Measures

- **Reducing Exposure to Plastics, Pesticides, and Cosmetic Chemicals:** Many everyday products contain endocrine-disrupting chemicals (EDCs) such as phthalates, parabens, and BPA. Limiting the use of plastic containers, avoiding pesticides on foods, and choosing EDC-free cosmetics can reduce the chemical burden that may hasten puberty.
- **Improving Diet Quality with Whole, Unprocessed Foods:** Diets rich in fruits, vegetables, whole grains, and lean proteins support healthy metabolism and reduce exposure to additives and excess sugars that can disrupt endocrine function.
- **Promoting Physical Activity:** Regular exercise helps regulate body weight, insulin sensitivity, and hormonal balance, thereby supporting normal pubertal timing.
- **Regulating Sleep and Limiting Screen Exposure:** Proper sleep hygiene and reduced exposure to artificial light, especially blue light from screens, maintain normal melatonin rhythms, which play a role in delaying puberty onset.
- **Creating Emotionally Stable Home Environments:** Reducing chronic stress through supportive parenting and stable family dynamics can normalize cortisol and oxytocin levels, reducing the risk of early puberty.

Public Health and Policy-Level Actions

- **Stricter Regulation of Endocrine Disrupting Chemicals (EDCs):** Governments can enforce bans or limits on harmful chemicals in consumer products, improving overall population health.
- **Improved Food Labeling:** Clear information about pesticide residues and chemical additives empowers consumers to make safer dietary choices.
- **Urban Air Quality Measures:** Reducing air pollution can lower children's exposure to airborne endocrine disruptors.
- **Early Screening in High-Risk Populations:** Identifying children at risk for precocious puberty through medical history or environmental exposures enables timely intervention and reduces adverse outcomes.

Conclusion

Precocious puberty results from a complex interplay of genetic, biological, environmental, nutritional, and psychosocial factors. Its increasing prevalence in recent decades mirrors shifts in modern lifestyles, widespread exposure to endocrine-disrupting chemicals, and evolving social and familial dynamics. Addressing this multifaceted condition demands a comprehensive, multidisciplinary strategy that integrates effective medical interventions with targeted lifestyle modifications, proactive environmental reforms, and robust psychological support.

Such an integrated approach not only mitigates the physical health consequences of early puberty but also fosters emotional resilience and supports healthy developmental trajectories. By deepening our understanding of these interconnected determinants, clinicians, educators, policymakers, and families can collaborate more effectively to recognize early signs, implement timely interventions, and develop prevention strategies. This collective effort is critical to safeguarding children's long-term well-being and confronting precocious puberty as an emerging public health challenge with lasting societal impact.