FUTURE OF PEDIATRICS TALKS!
A VIRTUAL SUMMER SERIES

Pediatric Health Network
A few notes about today’s Webinar

• All lines are muted throughout the webinar.
• Please use the Q&A box to ask questions or make comments.
• Today’s Webinar recording and slides will be posted to the PHN website following the presentation. You can find past FOP presentations on our website at https://pediatricrealthnetwork.org/future-of-pediatrics/
Speakers

Nadia Merchant, MD

No conflicts to disclose:

- No financial or business interest, arrangement or affiliation that could be perceived as a real or apparent conflict of interest in the subject (content) of their presentation.
- No unapproved or investigational use of any drugs, commercial products or devices
# Upcoming FOP Talks!

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<td>Abnormal Thyroid Labs in the Primary Care Setting</td>
<td>Priya Vaidyanathan, MD</td>
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<td>A Pediatrician's Approach to a Young Child With Joint Effusion</td>
<td>Bita Arabshahi, MD</td>
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<td>July 29</td>
<td>Allergic Reactions: When to Refer?</td>
<td>Amaziah Coleman, MD</td>
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<td>Claire Boogaard, MD</td>
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<td>Dermatologic Manifestations of COVID-19</td>
<td>Anna Kirkorian, MD</td>
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<td>August 12</td>
<td>Obstructive Sleep Apnea: Primary Care Management and When to Refer</td>
<td>Claire Lawlor, MD</td>
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<td>Neuropsychological Evaluations: What are they, when are they needed and how can I get them for my patients?</td>
<td>Kristina Hardy, PhD, Laura Kenealy, PhD</td>
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<td>August 26</td>
<td>Meeting Teens Where They Are: the Contraception Discussion</td>
<td>Brooke Bokor, MD, MPH</td>
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<td>School’s Out: Supporting School Attendance and Distance Learning Engagement</td>
<td>Asad Bandealy, MD, Heidi Schumacher, MD</td>
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PHN Webinars

July 7th – 12PM PCP Town Hall: Back to School Guidance featuring Nathaniel Beers, MD
https://childrensnational.org/healthcare-providers/refer-a-patient/covid/covid-19-webinars

July 8th – 12PM: PHN Office Manager and Practice Administrator Steering committee presents Practice Management: Road to Recovery Series
Link to register: https://cvent.me/mq8XxD or email PHN@childrensnational.org if you are interested in attending.

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<th>July 8</th>
<th>Reports andRecalls</th>
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<td>July 22</td>
<td>Payment Collection</td>
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<td>August 5</td>
<td>Best Practices: New Initiatives and Implementing Change</td>
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<td>August 19</td>
<td>Managing a COVID-19 positive Employee and Wellness In Your Workplace</td>
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Normal and Abnormal Variation in Pubertal Development

Nadia Merchant, MD
Assistant Professor of Pediatrics
Division of Endocrinology and Diabetes
Objectives

• Discuss the clinical signs of puberty, usual sequence of appearance, and typical rate of progression
• Identify benign and pathologic variations in pubertal development
• Understand evaluation and treatment options for early or delayed puberty
• Identify indications for an endocrine referral for a child with a pubertal variation
When is Puberty Normal?

- AAP recommends a complete physical examination at every health supervision visit that includes evaluating and documenting pubertal development.
- Accurate and consistent tracking of the timing, tempo, and sequence of pubertal development can aid in early identification and treatment of pubertal disorders.
Physiology of Puberty

Normal Puberty and Tanner Staging

- Normal puberty begins between the ages of 8 and 13 years in girls and between 9 and 14 years in boys.
- Mean age of peak height velocity 12.2 years in girls and 13.8 years in boys.

Potential Adverse Outcomes of Pubertal Variations

Abnormal timing of pubertal development may result in a variety of undesirable outcomes, such as the following:

- Short adult stature
- Adverse psychosocial outcomes, including engagement in exploratory behaviors at an earlier age than adolescents maturing within the normal range or later (early puberty)
- Decreased sports involvement (delayed puberty)
- Delayed acquisition of normal bone density (delayed puberty)
- Symptoms of emotional tension and psychosomatic complaints
- Feeling different from peers about masculinity or femininity
- Teasing or bullying
Precocious Puberty
Benign Variations of Pubertal Development: Premature Thelarche

• Frequent in female infants and toddlers.
• Breast development usually begins before 2 years, over time there is little or no progression and sometimes regression, and a normal rate of linear growth in observed.
• The cause is unknown but may be due to transient appearance of functioning ovarian cysts.
• It is usually benign.
• The risk of central precocious puberty is greater if breast growth begins after 3 to 4 years of age.
Breast Development

Median age at onset of breast stage 2 was 8.8, 9.3, 9.7, and 9.7 years for African American, Hispanic, white non-Hispanic, and Asian participants, respectively. Girls with greater BMI reached breast stage 2 at younger ages.

Benign Variations of Pubertal Development: Premature Adrenarche (Girls or Boys)

- Typically occurs between 5 and 8 years of age.
- Caused by early increase in secretion of weak androgens from the adrenal gland.
- More common in African American and Hispanic girls and in obese children of either sex.
- Mildly elevated adrenal androgens, mainly Dehydroepiandrosterone sulfate (DHEA-S), with normal levels of testosterone and 17-hydroxyprogesterone.
- Rapid progression of pubic and axillary hair, severe acne, and rapid growth should raise concern for possible late-onset congenital adrenal hyperplasia (CAH) or an adrenal or testicular tumor.
- Similar symptoms, but with a stunted or decreased growth rate, are concerning for Cushing syndrome.
- Functional ovarian hyperandrogenism or polycystic ovarian syndrome may develop in up to 20% of girls with premature adrenarche.
Precocious Puberty

Precocious Puberty in Girls?
- Breast ≥ Tanner II and age < 8 yo
- Estrogenization of vaginal mucosa (pre = red, pubertal = pink)
- Leukorrhea or menstruation
- Growth acceleration

Precocious Puberty in Boys?
- Testicular Volume ≥ 4 cc prior to 9 years
- Scrotal thinning
- Growth acceleration

Family History
- Early or late pubertal development in parents or siblings
- Unusually short or tall stature
- Female family members with hirsutism, severe acne, or irregular menses
- Infertility
Precocious Puberty; Ladies First...

- Breast ≥ Tanner II and age < 8 yo
- Estrogenization of vaginal mucosa (pre = red, pubertal = pink)
- Leukorrhea or menstruation
- Growth acceleration

**YES?**

- Bone age
- 8 am labs: LH, FSH, estradiol, free T4, TSH
- If significant andrenarche on exam: consider DHEAS, total testosterone, 17-hydroxyprogesterone, androstendione

**High LH/FSH**

*Gonadotropin Dependent*

- Idiopathic
- Brain Tumor (Hypothalamic Hemartoma, Glioma)
- CNS Malformation, Trauma, Radiation
  *Consider Brain MRI*

**Low LH/FSH**

*Gonadotropin Independent*

- Primary Hypothyroidism
- McCune Albright Syndrome
- Ovarian Cyst/Tumor
- Exogenous Estrogen
- Adrenal (CAH)
Precocious Puberty; Now let's move on to Gentleman...

- Testicular Volume > 4 cc prior to 9 years
- Scrotal thinning
- Growth acceleration

If significant andrenarche on exam: consider DHEAS, 17-hydroxyprogesterone, androstendione

### High LH/FSH
**Gonadotropin Dependent**
- Idiopathic
- Brain Tumor (Hypothalamic Hemartoma, Glioma)
- CNS Malformation, Trauma, Radiation
  *Consider Brain MRI*

### Low LH/FSH
**Gonadotropin Independent**
- Primary Hypothyroidism
- Exogenous Testosterone
- Adrenal (CAH, adrenal tumor)
- Testicular (McCune Albright Syndrome, tumor, testotoxicosis)

Bone age
- 8 am labs: LH, FSH, testosterone, free T4, TSH
- Consider Brain MRI
Delayed Puberty
Delayed Puberty

Girls: No breast buds by 13
Boys: No testicular development > 4 cc by 14

1. Growth rate, tanner stage
2. Family History of Delayed Puberty
3. Chronic Disease, anosmia, radiation or chemotherapy, anorexia

- Bone age
- Basal serum LH, FSH, IGF-1, TSH, free testosterone or estradiol, IGF-1

Low LH, FSH
- Growth rate prepuberal
  - GnRH deficiency or constitutional delay of growth and puberty

Elevated FSH
- Growth rate less than prepubertal
  - Functional hypogonadotrophic hypogonadism (secondary to chronic disease, anorexia)
  - Permanent hypogonadotrophic hypogonadism or hypopituitarism

Hypergonadotropic Hypogonadism
Consider Referral

• **Premature Adrenarche**
  • Pubic or axillary hair alone in a girl < 7 years or a boy < 9 years (since the great majority of these children have premature adrenarche and need no tests or treatment, following the child in the PCP setting is also an option)
  • Rapid pubertal progression; in hair growth or other signs of virilization

• **Premature Thelarche**
  • Breast development beginning after the age 3
  • Significant thelarche (Tanner stage 3 or more)
  • Rapid linear growth and breast development
  • McCune-Albright syndrome suspected
  • Vaginal bleeding or other coincident signs of pubertal development

• **Precocious Puberty**
  • Breast development in a girl < 8 years
  • Testicular enlargement > 4 cc especially with penis enlargement in a boy < 9 years
  • Rapid linear growth
  • Rapid progression of Tanner staging

• **Delayed Puberty**
  • Lack of breast development in girls by age 13 years or no menses by 16 years
  • Lack of testicular enlargement in boys by age 14 years
Variation in Timing of Puberty

What is needed with referral...

- Try to track signs of puberty at PCP visits
- Growth charts
- If bone age obtained, please ask family to take CD for appointment
- If obtaining labs, try to obtain labs 8 am, especially LH (order 3rd generation)

- The younger the child, more rapid the progression of findings, greater the likelihood of detecting pathology
- Lots of variation in puberty, especially with different races and ethnicities → we are always willing to see a patient if there are concerns
Thank You
Central Precocious Puberty: GNRH analog

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<tr>
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<th>Leuprolide</th>
<th>Histrelin</th>
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<tr>
<td><strong>Functions</strong></td>
<td>A GnRH analog when given chronically suppresses LH and FSH production and slows pubertal progression and bone age advancement.</td>
<td>GnRH analog that is inserted by a surgeon, avoiding the need for injections.</td>
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<td><strong>Application</strong></td>
<td>Given intramuscularly monthly or every 3 months. A 6-month formulation was approved by the FDA in 2017.</td>
<td>Implanted in the inner arm subcutaneous tissue, approved for replacement every 12 months, its effect may last for 24 months.</td>
</tr>
<tr>
<td><strong>Side effects</strong></td>
<td>Sterile abscesses, rare allergic reactions, acne, or rash.</td>
<td>Rare local insertion site reactions, keloid formation, and pain.</td>
</tr>
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</table>

Once treatment is started, it is important to monitor the following:
- Progression of pubertal development
- Growth rate
- Skeletal maturity (bone age) progression
- LH and estradiol or testosterone to assess adequate suppression
### Delayed Puberty: Hormonal Therapy

#### Boys

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<th>Use</th>
<th>Administration</th>
<th>Side Effects/Cautions</th>
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<tr>
<td><strong>Testosterone (various forms)</strong>&lt;br&gt;Delayed puberty: short-term to jump-start pubertal development&lt;br&gt;Hypogonadism: higher doses for long-term replacement</td>
<td>Intramuscular: much easier to increase dose over time than with patch or gel&lt;br&gt;Transdermal (patch or gel)</td>
<td>High doses: premature epiphyseal closure&lt;br&gt;IM preparations: local reactions&lt;br&gt;Patch: local irritation</td>
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#### Girls

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<tr>
<th>Use</th>
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<th>Side Effects/Cautions</th>
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<tr>
<td><strong>Estrogens (various forms)</strong>&lt;br&gt;Not routinely recommended, but may be used in delayed puberty&lt;br&gt;Induce breast development, induce menstruation, maintain bone mass</td>
<td>Oral&lt;br&gt;Transdermal by patch</td>
<td>Liver toxicity&lt;br&gt;Potential risk of thromboembolism and hypertension</td>
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<td><strong>Progestins</strong>&lt;br&gt;Added to induce endometrial cycling. Usually necessary only if treatment continues longer than 1 to 2 years, after breakthrough bleeding</td>
<td>Oral most commonly used</td>
<td>Minor: headaches, breast tenderness, abdominal discomfort</td>
</tr>
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Once treatment is started, it is important to monitor the following:  
- Progression of pubertal development  
- Growth rate  
- Skeletal maturity (bone age) progression—to avoid excess advancement of bone age