SCHOOL OF MEDICINE AND HEALTH SCIENCES
DISCIPLINE OF BIOCHEMISTRY AND MOLECULAR BIOLOGY
PBK SEMINAR
SOME CHANGES ASSOCIATED WITH PUBERTY – An Overview

What is Puberty?

- Puberty can be defined in a **very simplistic** way as the period between childhood and "adolescence", when **Hormonal body changes** produce **development** of the **Secondary Sexual Characteristics**.
- **From a biological perspective:**
  - Puberty is the stage of Physical Maturation in which an Individual becomes physiologically capable of Sexual Reproduction.
  - Some of the biological changes that occur during puberty include:
    - Neuro-secretary factors and/or hormones, all of which modulate Somatic Growth, the development of the Sex Glands and the Endocrine as well as Exocrine secretions.
    - The resultant increase in Sex Steroid production induces the appearance and maintenance of Sexual characteristics and the capacity for reproduction.

What are some of the changes that indicate onset of maturation?

- In females, the onset of Menstruation and the Development of the Breasts mark this maturation.
- In males, the biological markers of puberty are the Enlargement of the External Genitalia and the production of Semen.
- In both sexes, the development of these Primary Sexual Characteristics is accompanied by the onset of a variety of Secondary Sexual Characteristics.
  - In males, these include the appearance of Facial and other body hair, including in the Pubic area and in the Armpits, as well as the Deepening of the Voice Tone.
  - In females, hair develops in the Pubic area and in the Armpits, and the Hips begin to Broaden.
  - For both sexes this is also a period of Rapid development of the Sweat glands.
- Generally, these changes prepare the body for Sexual reproduction, but they also have important social and emotional aspects.

What is adolescence?

- In a very simplistic way, Adolescence can be said to be a socially defined period of Psychological development that is Socio-cultural.
- Adolescence is also the period of body growth and mental development that takes place between the onset of Puberty and the attainment of Physical and Emotional Maturity.
- During adolescence the entire endocrine system is altered.
  - It is essentially the activation of the Hypothalamic-Pituitary-Gonadal Axis (HPG axis) that induces and enhances the progressive Ovarian and Testicular Sex Hormone secretion that are responsible for the profound Biological, Morphological, and Psychological changes to which the Adolescent is subjected.

Is Puberty the same as Adolescence?

- Puberty should not to be confused with adolescence.
- Unlike Puberty, which is more of a biological and metabolic phenomenon, adolescence is more of a socio-cultural phenomenon.
- Puberty may or may not coincide with adolescence.

HORMONAL CHANGES OF PUBERTY

What is the biochemical concept of Puberty?

- From the Biochemical point of view Puberty is a Centrally Mediated Mechanism controlled by changes in Feedback Sensitivity to Testosterone and Estrogen
- The major endocrine axis that is involved is the **Hypothalamus – Anterior pituitary – Gonadal axis (HPG Axis**).

How is the HPG-axis activated during onset of Puberty?

- The Primary triggering mechanism that initiates the activation of the HPG-axis at Puberty is still hypothetical.
- The following sequence has been suggested:
    - In childhood the concentration of Sex Hormones is low, though exogenous Gonadotropins increase production; therefore, in female the Immature Ovary has the capacity to synthesize Estrogen.
    - It is thought that these low levels of Sex hormones inhibit Gonadotropin production in Pre-Pubertal Girls.
    - At Puberty the Hypothalamic-Pituitary system becomes less sensitive to suppression by the low levels of sex hormones.
    - At Puberty, the pulsatile release of Gonadotropin Releasing Hormone (Gn-RH) begins stimulating Luteinizing hormone (LH) and this causes a dramatic increase of Ovarian Hormone production.
    - Follicle Stimulating Hormone (FSH), the main stimulus for Estrogen secretion, stimulates a Follicle to ripen, and ovulation ensues.

Briefly outline the (hypothetical) sequence for activation of HPG axis at onset of Puberty.

- Immediately prior to the Onset of Puberty, the sensitivity of Gonadotrophin (FSH and LH) production to Feedback Inhibition by Sex hormones (Testosterone and Estrogen) falls dramatically.
- At Puberty the GnRH producing cells in the Hypothalamus becomes less susceptible to Feedback Inhibition by sex hormones.
- Pulses of GnRH are carried in the portal blood to target cells (Gonadotropes) of the Anterior Pituitary, causing the release of both FSH and LH.
- The FSH then binds to receptors on the ovarian follicle stimulating the synthesis and secretion of 17-beta-estradiol (female sex hormone) and maturation of the Follicle and Ovum.
- Other proteins such as **Inhibin** are also synthesized. Inhibin is a negative feedback regulator of FSH production in the Anterior Pituitary.

- When the Follicle reaches full maturation and the Ovum also is matured, LH binds to its cognate receptor and together with other factors such as Prostaglandin, plays a role in Ovulation.
- The residual Follicle remaining after Ovulation becomes the functional Corpus Luteum under primary control of LH.

TAKE NOTE:

- As central mechanisms become less sensitive to feedback inhibition, Sex hormone levels rise and Puberty is entered.
- The pattern of release of Hypothalamic GnRH, which stimulates FSH and LH release from the Anterior Pituitary, is highly relevant physiologically. **Why?**
- Because it is involved in the Control of Sexual Development and Maturation through Puberty, and the subsequent attainment of Fertility.

What are some of the Specific Changes that occurs during Puberty?

- **Changes associated with GnRH**:
    - In Pre-Pubertal children, no significant LH or FSH response to intravenous or subcutaneous administration of GnRH is observed.
    - During adolescence, the LH response to GnRH increases progressively in both sexes.
    - The increase of FSH is much less marked than that of LH.
    - One of the important Neuro-Endocrine mechanisms that control the onset of puberty is probably an increase in the frequency of GnRH pulse stimulation of the Pituitary.
    - Whatever the mechanism, the process is not abrupt but develops over several years, as evidenced by slowly rising plasma concentrations of the Gonadotropins and Testosterone or Estrogens.

- **Changes associated with Gonadotropins (LH and FSH)**:
    - The first demonstrable biological change of puberty is the appearance of pulsatile LH release during sleep.
    - As puberty progresses, the Frequency and Amplitude of secretion of LH during sleep increases, although increase secretions are also found during the wake period.
    - At the end of puberty, the difference between sleep and wake LH secretary patterns disappears.

    - **In girls**:
        - Circulating FSH levels increase progressively from 10 to 11 years of age, approximately 1 year prior to those of LH.
        - Thereafter, Gonadotropins continue to increase throughout puberty, but important fluctuations are observed during the menstrual cycle.

    - **In boys**:
        - Significant increase in both plasma FSH and LH is also found from the onset of puberty, closely linked to the rapid increase in testicular size characteristic of this pubertal stage.
        - A further significant increase in circulating Gonadotropins is also observed at late puberty.

- **Changes associated with Prolactin**:
  - Serum Prolactin concentrations increase modestly during female puberty but remain stable in boys.
  - Physiological role of Prolactin in the course of puberty, if any, is not fully known.

- **Changes associated with Adrenal Steroids**:
  - Adrenal Androgens vary from infancy through Adolescence: A phenomenon is called **Adrenarche**
  - In girls:
    - Dehydroepiandrosterone (DHEA) and Dehydroepiandrosterone sulfate (DHEAS) increase as early as 6 to 7 years of age, followed within 1 to 2 years by a corresponding increase in Androstenedione.

  - In boys:
    - DHEA and DHEAS increase as early as 8 to 9 years of age, followed by Androstenedione 1 to 2 years later.

  - Adrenarche begins before the rise in Gonadotropin secretion.
  - The adrenal androgens are responsible for the appearance of Axillary hair and, in part, for the appearance of Pubic hair in the Adolescent; however they do not appear to play a decisive role in determining the initiation of Puberty.

- **Changes associated the Ovary:**
  - The rising levels of plasma Gonadotropins stimulate the ovary to produce increasing amounts of Estradiol.
  - Estradiol is responsible for the development of Secondary Sexual characteristics, that is:
    - Growth and development of the breasts and reproductive organs,
    - Fat redistribution (Hips, Breasts), and
    - Bone maturation.

  - Maturation of the ovary at Adolescence correlates well with Estradiol secretion and the stages of Puberty.
  - During Puberty plasma Estradiol levels fluctuates widely, probably reflecting successive waves of follicular development that fail to reach the ovulatory stage.
  - The Uterine Endometrium is affected by these changes and undergoes cycles of Proliferation and Regression, until a point is reached when substantial growth occurs so that withdrawal of Estrogen results in the First Menstruation (Menarche).
  - Plasma Testosterone levels also increase at Puberty although not as markedly as in males.
  - Plasma Progesterone remains at low levels even if secondary sexual characteristics have appeared.
  - A rise in Progesterone after Menarche is, in general, indicative that Ovulation has occurred.
  - The first ovulation does not take place until 6-9 months after Menarche because the positive feedback mechanism of Estrogen is not developed.

- **Changes associated with Testis**:
    - The increase in Testicular size observed during Pre-Puberty and Puberty results essentially from the development of the Seminiferous Tubules under the stimulating effect of FSH.
    - Long-standing pulsatile LH secretion induces the differentiation of interstitial cells into Testosterone-secreting Leydig cells, which, in turn, exert a negative feedback control on LH secretion.
    - As puberty progresses, Spermatogenesis is initiated and then sustained by FSH and by Testosterone produced by the Leydig cells under LH control.
    - Dihydrotestosterone shows a pattern similar to that of Testosterone, and the proportion of Dihydrotestosterone to Testosterone decreases gradually until adulthood, when Dihydrotestosterone levels are approximately 10% of those of Testosterone.

What are the roles of Growth hormone (GH), Insulin-like Growth Factor-I (IGF-I), and Insulin in Puberty?

- Puberty of patients with isolated GH deficiency is frequently delayed, Leydig cell function is diminished, and the response to Chorionic Gonadotropins is decreased.
- GH administration can restore testicular responsiveness to LH and Leydig cell Steroidogenesis.
- Growth hormone-releasing factor (GRF) levels and GH secretion increase considerably during puberty, mainly at night.
- The amplitude of GH peaks increases early in puberty.
- IGF-I is an important modulator of growth during childhood and adolescence.
- Adrenal Androgens seem to have no physiological role in normal growth.
- The characteristic pubertal growth spurt results mainly from the synergetic effect of Sex steroids, Growth hormone, and IGF-I production, with all showing a significant increase at the time of pubertal growth acceleration.
- Insulin is also important for normal growth.
- Plasma insulin levels increase throughout childhood, but the rise is particularly pronounced during puberty with a strong positive correlation with IGF-I.

What are some of the other Biochemical changes that occur during puberty?

- Several Biochemical changes take place in the composition of body fluids between infancy and puberty.
- Most of the changes are gradual, and there are rarely abrupt changes to adult concentrations.
- Some of these changes include the following:
    - Serum activity of most enzymes which are high during childhood decrease to adult values by Puberty or earlier, although the activity of Alanine Aminotransferase (ALT) may continue to rise, at least in men until middle age.
    - Serum Alkaline Phosphatase (ALP) activity is higher in infancy but decreases during childhood, and rises again with growth before puberty.

- ALP activity is better correlated with skeletal growth and sexual maturity than with chronological age; it is greatest at the time of maximum osteoblastic activity occurring with bone growth.
- ALP activity decreases rapidly after puberty, especially in girls.
- Serum Creatinine concentration increases steadily from infancy to puberty parallel to development of skeletal muscle; until puberty, there is little difference in the concentration between sexes.
- Serum Uric Acid concentration decreases from its high at birth until age 7 to 10 years, at which time it begins to increase, especially in boys, until 16 years.
- In general, under normal Physiological Conditions, the concentrations of most test constituents remain quite constant between Puberty and Menopause in women and between Puberty and middle age in men.

Reference:

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2. Harper's Biochemistry, By R. K. Murray et al. Pages 568, 573, 574
3. Textbook of Biochemistry with Clinical Correlations. 4th Edition. Edited by T. M. Devlin, Pages 866- 869.