Puberty – Normal and Abnormal

Dr. B.V. Reddy
Professor of Physiology
Puberty

• Disorders of puberty constitute one of most common referrals to paediatric endocrine clinics
• Careful history and examination paramount
• Ensure sensitivity at all times
• Chaperone during pubertal examination
Puberty

• Physiological transition from childhood to reproductive maturity

• Associated with:
  – Growth spurt
  – Appearance of both primary and secondary sexual characteristics in children

  – Occurs between 8 and 14yrs in girls
  – Occurs between 9 and 14yrs in boys
Puberty

• Important to understand
  – Range of normal
  – Population differences
Normal Puberty: Endocrine control

• Onset of puberty signalled by the secretion of pulses of Gonadotrophin Releasing Hormone (GnRH)
• Prior to puberty: hormonal feedback / central neural suppression of GnRH release suppress onset of puberty
• Hypothalamo-pituitary-gonadal axis starts working in foetus. After birth, sex hormones and gonadotrophins (FSH, LH) found in adult levels
• Levels reduce in months after birth; pulsatile GnRH reduces in childhood and increases in frequency and amplitude before puberty
• For 2 yrs before puberty, rise in adrenal androgens ➔ early pubic hair and spots
The Hypothalamic - Pituitary - Gonadal Axis

- Testosterone
- Inhibin
- LH+FSH
- Progesterone
- Oestrogen
- Inhibin

- Hypothalamus
- Pituitary
- Testes
- Ovary
Physiology of Puberty

• Activation of the hypothalamic – pituitary – gonadal axis

  – Induces and enhances progressive ovarian and testicular sex hormone secretion

  – Responsible for the profound biological, morphological and psychological changes which adolescents experience
Influencing Factors

• Genetics: 50-80% of variation in pubertal timing

• Environmental factors e.g. nutritional status

• Leptin → regulates appetite and metabolism through hypothalamus. Permissive role in regulation of timing of puberty

• Adrenarche: development of pubic and axillary hair, body odour and acne
Adrenal Steroids

• DHEA, DHEA-S, Androstenedione
  – Begins before rise in gonadotrophin secretion
  – Responsible for appearance of axillary hair and in part for appearance of pubic hair (adrenarche)
Changes during puberty
Physical Changes

• 5 stages from childhood to full maturity
• Marshall and Tanner (P1 – P5)
• Reflect progression in changes of the external genitalia and of sexual hair
• Secondary sexual characteristics
  – Mean age 10.5yrs in girls
  – Mean age 11.5 – 12yrs in boys
Puberty: Girls

- Breast enlargement usually first sign.
- Thelarche
- Often unilateral
- Menarche usually 2-3 yrs after breast development
- Growth spurt peaks before menarche
- Pubic and axillary hair growth: sign of adrenal androgen secretion
- Starts at similar stage of apocrine gland sweat production and associated with adult body odour
Examination: Girls

- Examine in supine position. Helps differentiate between true breast enlargement vs adiposity.
- Genital exam: pubic hair, changes in vaginal mucosa.
- Cliteromegaly suggests androgen excess and virilisation.
- Mild acne normal in early puberty but rapid onset and progression may suggest androgen excess.
- Vaginal exam only if sexually active.
- NEVER rectal exam.
Pubertal Stages (Tanner) Female

- **P1** Prepubertal
- **P2** Early development of subareolar breast bud +/- small amounts of pubic and axillary hair
- **P3** Increase in size of palpable breast tissue and areolae, increased dark curled pubic/axillary hair
- **P4** Breast tissue and areolae protrude above breast level. Adult pubic hair but no spread to medial thighs.
- **P5** Mature adult breast. Pubic hair extends to upper thigh
Menarche

- During puberty oestradiol levels fluctuate widely (reflecting successive waves of follicular development that fail to reach ovulatory stage)
- Endometrium affected by oestradiol. Undergoes cycles of proliferation and regression until point where withdrawal of oestrogen results in the first menstrual bleed (menarche)
- Increase of only 4% of final height after menarche
Ovarian development

• Rising levels of plasma gonadotrophins
• Stimulate ovary to produce increasing amounts of oestradiol
• Oestradiol ➤ secondary sex characteristics
  – Breast growth and development
  – Reproductive organ growth and development
  – Fat redistribution (hips, breasts)
  – Bone Maturation
Ovarian development

- Prepuberty volume – 0.3 – 0.9 cm³
- > 1.0 cm³ indicates puberty has begun
- During puberty – rapid increase in size
- Mean post pubertal volume 4 cm³
Ovulation

- First ovulation occurs 6 – 9 mths after menarche
- Plasma progesterone remains at low levels even if secondary sexual characteristics have appeared
- Rising progesterone after usually ovulation
- Plasma testosterone rise during puberty (not as much as in male)
Development of Uterus

• Prepubertal uterus is tear-drop shaped
• Neck and isthmus account for up to 66% of uterine volume
• Following production of oestrogens – uterus becomes pear shaped
• Uterine body increases in length (max 5 – 8cm) and thickness (proportionately more than cervix)
Puberty: Boys

- First signs often go unnoticed
- Testicular enlargement (12-13 yrs)
- Prepubertal testis – 2mls diameter
- Puberty begins when volume reaches 4mls
- Penile and scrotal enlargement occur approx 1 yr after testicular enlargement. Pubic hair appears at same time
Pubertal Growth Spurt: Boys

- Occurs later than in females
- Testosterone less of a stimulus to GH responsiveness than oestradiol
- Testosterone required in larger concentrations to produce same anabolic effect
- Greater and later growth spurt in boys
Examination: Boys

- Testicular growth: associated with enlargement of seminiferous tubules, epididymis, seminal vesicles and prostate
- Testicular enlargement: FSH dependant
- Prader orchidometer: assessment of testicular volume
- Signs of androgen excess without commensurate increase in testicular volume: worrisome e.g CAH, testicular tumour
- Penile growth, scrotal changes, pubic hair occur 1-2 yrs after testicular enlargement
- 50% of males varying degrees of breast hypertrophy
- Later signs: growth spurt, acne, voice deepening, facial hair
Pubertal Stages (Tanner) Male

- P1 Prepubertal, testicular volume < 2mls
- P2 Enlargement of scrotum and penis. Scrotum slightly pigmented. Few long dark pubic hairs
- P3 Lengthening of penis. Further growth of testes and scrotum. Pubic hair darker, coarser and more curled
- P4 Penis increases in length and thickness. Increased pigmentation of scrotum. Adult pubic but no spread to medial thighs
- P5 Genitalia adult in size and shape. Pubic hair spread to thighs
Puberty: Male genital development

Stage 1

Stage 2

Stage 3

Stage 4

Stage 5
Secondary sexual development

• First signs of puberty
  – Testicular volume of 4mls
  – Slight progressive increase in scrotal folds
  – Slight increase in scrotal pigmentation
Testicular Volume

Orchidometer
Used to measure testicle size and track sexual development in boys.

<table>
<thead>
<tr>
<th>Childhood</th>
<th>Early Puberty</th>
<th>Mid Puberty</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>10</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Late Puberty</th>
<th>Adulthood</th>
</tr>
</thead>
<tbody>
<tr>
<td>14</td>
<td>16</td>
</tr>
<tr>
<td>18</td>
<td>25</td>
</tr>
</tbody>
</table>

Testicle volume measured in mL

1 Inch
Final height

- Puberty usually completed within 3 - 4 yrs of onset
- Left wrist x-ray to assess bone age
- Final adult height results from complete fusion of epiphyses
  - Occurs approx 2yrs after menarche
Assessment of abnormal puberty

- Many causes
- Aim of assessment: determine whether underlying pathological abnormality vs constitutional and benign pubertal changes
- NB: recognise abnormal timing and progression of puberty
What is abnormal?

- Delayed Puberty
- Early or Precocious Puberty
  - More common in females
  - Uncommon in males (usually pathological)
  - < 8yrs in females
  - < 9yrs in males
  - May be associated with a growth spurt
Assessment 1

- Full history of previous growth and development
- Record timing and sequence of physical milestones and behavioural changes of puberty
- Full medical and surgical history
- If underweight: take full nutritional history
- Family hx of early or delayed puberty
- Family hx of any genetic disease
Assessment 2

- Plot height, weight, BMI and growth velocity
- Compare with old measurements if available
- Examine all systems: endocrine / neurology NB
- Optic fundi, visual fields, sense of smell
- Genitalia, body habitus, stage of puberty
Delayed Puberty: Hypogonadotrophic

- Constitutional (familial, sporadic)
- Chronic illness (CF, Crohn's Disease, Renal failure)
- Malnutrition (Anorexia, CF, coeliac disease)
- Exercise
- PCOS
- Tumours of pituitary/hypothalamus (craniopharyngioma)
- Hypothalamic syndromes (PWS, Laurence-Moon-Biedl)
- Hypothyroidism
- Suppression $2^0$ to hyperthyroidism, hyperprolactinemia, Cushing Syndrome, CAH
- Panhypopituitarism
Delayed Puberty: Hypergonadotrophic

• Congenital
  – Turner Syndrome
  – Klinefelters Syndrome

• Acquired
  – Irradiation / Chemotherapy
  – Surgery
  – Testicular torsion, trauma
  – Infection
  – Autoimmunity
Precocious Puberty

• Onset of secondary sexual characteristics < 8yrs in girls and < 9yrs in boys

• 5 times more common in girls

• Usually benign central process – girls

• Pathological in ~ 50% in boys
Premature thelarche / pubarche

• Thelarche – beginning of breast development
• Pubarche – first appearance of pubic hair
  – (more common in certain populations e.g. asian / afro-caribbean)
• More common than true precocious puberty
• Benign variants
  – breast development in girls < 3yrs with spontaneous regression
  – Pubic hair in boys and girls < 7yrs due to adrenal androgen secretion in middle childhood

  – NB Examination normal or may be slight advance in growth curve
Precocious Puberty
Gonadotrophin dependant

- Idiopathic (sporadic / familial)
- Congenital (Hydrocephalus)
- Acquired (irradiation/surgery/infection)
- Tumours (hamartomas/gliomas)
- Hypothyroidism
- Russell Silver Syndrome
- Mc Cune Albright Syndrome
Precocious Puberty
Gonadotrophin Independant

• Normal pattern of puberty absent

  – Virilisation of female (CAH)
  – Feminisation of a boy (oestrogen producing leydig tumour)
  – Adrenal Tumour
  – Ovarian Tumour
Investigations

• Blood Tests (first line)
  – FBC
  – U&E
  – LFT’s
  – TFT’s
  – FSH/LH
  – Oest/Testosterone
  – 17 OHP / 11 DOC
  – Adrenal androgens
  – Prolactin

• Second line
  – GnRH assay
  – Beta –HCG
  – Karyotype if indicated
Diagnostic Imaging

- Pelvic USS (ovarian tumours / cysts)
- Testicular USS (tumour)
- Adrenal USS (MRI / CT better if tumour considered)
- Bone Age (if within 1yr of CA, puberty not started or only just started; if > 2yrs, puberty already started)
- Brain MRI in all males and patients with neurological signs or symptoms)
Management

• Treat systemic disease

• Psychological support

• Promote puberty / growth if necessary
  – Low dose testosterone
  – Ethinyloestradiol
Issues

• Treatment of the cause e.g. cranial neoplasm
• Behavioural difficulties – psychology
• Reduce rate of skeletal maturation (early growth spurt may result in early epiphyseal closure and reduced final adult height)
  – Halt or slow puberty (GnRH analogue)
  – Inhibit action of excess sex steroids
Growth and Puberty

- GH plays role in pubertal development
- Amplifies ovarian response to gonadotrophins
- IGF-1 enhances gonadotrophin effect on granulosa cells
- Isolated GH deficiency associated with pubertal delay, diminished Leydig cell function and decreased response to chorionic gonadotrophins
- GH administration can restore testicular responsiveness to LH and Leydig Cell steroidogenesis
Growth and Puberty

- Growth hormone-releasing factor (GRF) levels and GH secretion increase considerably during puberty, mainly at night.
- Amplitude of GH peaks increases in early puberty – growth spurt.
- IGF-1 is an important modulator of growth during childhood and adolescence.
- Adrenal androgens have little physiological role in normal growth.
Thelarche

- Absence of a growth spurt and axillary or pubic hair differentiates thelarche from precocious puberty
Ambiguous genitalia

- Range of presentations
  - Inadequately developed male to virilised female
- Most common cause is Congenital Adrenal Hyperplasia → virilised female
- Urgent identification as can cause adrenal failure in neonatal period
- Do not ascribe sex immediately
- Identify cause of intersex
- Karyotype does not indicate the sex of rearing
- Family counselling imperative
- Early surgery now less popular
Thank You

TEEN-AGER
(Labeled for convenience)

WEED-WACKED HAIR

LOOK OF APATHY

WALLET CHAIN
($20 in wallet)

SUB-STANDARD POSTURE

FUNKY TEEN-AGER ODOR

BIG-ASS PANTS