Puberty in children with cerebral palsy

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Overview

• Normal pubertal processes
• Abnormal puberty
• Precocious puberty
• Hypogonadotrophic hypogonadism
• Bone health
Puberty

• The process by and the period during which sexual maturation occurs and reproductive capacity is attained.

• Cultural influences on puberty include nutrition, the quality of health care and living conditions.

• In the developed world the biologic age of menarche has declined over the past centuries from 16.6 years in 1840 to 12.5 years by 1980.
Puberty

- There is a wide normal range in pubertal development.
- Early maturation is a positive experience for boys but may be negative for girls.
- Height compromise may psychologically affect boys more later on.
- Late maturation is usually more difficult for boys than for girls.
- Peer pressure may lead to psychological sequelae.
Regulation of puberty
Pubertal assessment - Tanner staging

- Tanner developed a scale in 1962 that divides the pubertal staging into 5 classes based on:
  - pubic hair and breasts in females
  - pubic hair and genitalia in males
Timing of onset of puberty

- **Boys**
  
  Testicular volume 4 mls:
  
  - 97\textsuperscript{th} centile: 10 years
  - 3\textsuperscript{rd} centile: 14 years

- **Girls**
  
  Breast stage 2:
  
  - 97\textsuperscript{th} centile: 9 years
  - 3\textsuperscript{rd} centile: 13 years
Breast staging in girls

Average age for initial breast development onset is 10.5 years.

95% of girls developing breast buds between 8 & 13 years.

Growth peak growth rate – stage 2-3
## Puberty in Females

<table>
<thead>
<tr>
<th>Stage</th>
<th>Breast development</th>
<th>Pubic hair</th>
<th>Other changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Prepubertal</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>Breast bud</td>
<td>Minimal hair around labia</td>
<td>Growth spurt</td>
</tr>
<tr>
<td>3</td>
<td>Enlargement of breast and areola</td>
<td>Darker and extends across the midline</td>
<td>Peak growth, axillary hair</td>
</tr>
<tr>
<td>4</td>
<td>Secondary mound of areola and papilla</td>
<td>Increased but less than adult pattern</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Adult size and shape</td>
<td>Adult distribution including medial thighs</td>
<td><strong>Menarche</strong></td>
</tr>
</tbody>
</table>
Between stages 4 and 5 there is the peak Pubertal growth spurt

<table>
<thead>
<tr>
<th>Stage</th>
<th>Genital development</th>
<th>Pubic hair</th>
<th>Testicular size</th>
<th>Other changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Prepubertal</td>
<td>None</td>
<td>&lt;4mls</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>Early penile and scrotal growth</td>
<td>Minimal hair at base of penis</td>
<td>4-8mls</td>
<td>None</td>
</tr>
<tr>
<td>3</td>
<td>Increased penile length, further scrotal rugosity</td>
<td>Darker extending across midline</td>
<td>10-15mls</td>
<td>Light facial hair, growth spurt</td>
</tr>
<tr>
<td>4</td>
<td>Increased penile width, scrotal pigmentation</td>
<td>Increased but less than adult pattern</td>
<td>15-20mls</td>
<td>Sideburns</td>
</tr>
<tr>
<td>5</td>
<td>Adult size and shape</td>
<td>Adult distribution including medial thighs</td>
<td>20-25mls</td>
<td>Facial hair and change in voice</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>Further spread of pubic hair</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Secondary sexual characteristics in puberty

- **Female**:
  - Linear growth velocity
  - Menarche
  - Breast development
  - Pubic hair

- **Male**:
  - Linear growth velocity
  - Penis
  - Testis
  - Pubic hair

The graphs illustrate the mean age at onset for each characteristic in both genders.
Abnormal Puberty

- Early or “precocious”
  - <9 years in boys
  - <8 years in girls
- Delayed
  - >14 years in boys
  - >13 years in girls
- Abnormal pattern/Incomplete
  - Premature thelarche
  - Premature adrenarche
- Consonant v non-consonant
- 23 x Commoner in girls – sinister in boys.
Non-consonant development I

- Abnormal patterns of gonadotrophin secretion
  - premature thelarche (isolated breast development)
  - thelarche variant, slowly progressive variants of CPP
  - hypothyroidism
Non-consonant development II

- Sexual precocity due to adrenal androgens (Non-Consonant)
  - adrenarche
  - adrenal enzyme defects e.g. congenital adrenal hyperplasia
  - adrenal tumours: Cushing syndrome, virilizing tumour

- Gonadal tumours secreting sex steroids
- Exogenous sex steroids
Central precocious puberty. Premature activation of the GnRH pulse generator (LH and FSH detectable)

Signs of early pubertal development

Consonant with puberty? ie breasts, genitalia, pubic hair and a growth spurt

Yes

Central precocious puberty. McCune-Albright syndrome, testotoxicosis

No

Gonadotrophin-independent precocious puberty (GIPP). Lack of consonance. No gonadotrophins detectable

Isolated PV bleeding

Isolated breast development

Isolated pubic/axillary hair, acne

McCune-Albright syndrome, testotoxicosis

Isolated menarche

Thelarche

Early precocious puberty

Abuse

Urinary tract infection (UTI), PV infection

Adrenarche,
Central precocious puberty (CPP) - Causes

- Gonadotrophin-dependent precocious puberty (Consonant)
  - Idiopathic central precocious puberty (CPP)
  - Secondary CPP

- Congenital anomalies, neoplasia eg gliomas, hamartomas, cysts, hydrocephalus, post-infection. post-trauma, post-cranial radiotherapy, neurofibromatosis, adoption, HCG-producing neoplasms eg. choriocarcinoma, hepatoblastoma, mediastinum, germ cell tumours
Assessment of sexual precocity 1

- Height vs parental targets
- Pubertal staging
- Neurological examination
- Rate of progress
Assessment of sexual precocity 2

- Basal gonadotrophins
- Thyroid function, prolactin
- Sex steroids – oestradiol or testosterone
- Adrenal androgens, 17 OHP
- bHCG and AFP tumour markers (optional)
- LHRH test
- Pelvic USS in girls
- Bone age xray
- Neuroimaging especially in boys.
- Imaging of adrenals
Interpretation of LHRH test

- Pubertal response- LH>5mU/l and LH>FSH

Gonadal steroid secretion stimulated by pituitary gonadotrophins

- LH predominates
  - Centrally mediated precocious puberty
  - Slowly developing variants of central precocious puberty
  - Thelarche variant
  - Premature thelarche

- FSH predominates
Puberty in CP

- Puberty begins earlier but ends later in white children with CP.
- Girls with CP entered puberty earlier than boys with CP.
- Caucasian girls with CP developed pubic hair earlier, but breast development was similar to the general population.
- Menarche occurs later in white girls with CP (median age 14yrs, 1.3 yrs later)
- Sexual maturation was associated with more body fat in caucasian girls (the opposite for boys)

Worley et al, 2002 Pediatrics
Early puberty – the concerns?

• Child failing to understand their changing body.
• Loss of childhood and vulnerability as an adult.
• Mood swings and behavioural changes esp in the non-verbal.
• Onset of menstruation and toileting.
• Height outcomes – not so in CP.
• Masturbation in the socially disinhibited.
Causes of increased irritability

- Growing pains in limbs.
- Rapid breast development.
- Developing breasts rubbing against harnesses.
- Abdominal pain – premenstrual syndrome.
Advantages of pubertal progression

• Improvement in physical strength – increased ability with lifting and position shifts.
• Improvement in psychological maturity.
• Reduction in risk of fracture due to accruement of bone density through pubertal hormones.
• Eventual completion of growth – permanent fittings for equipment or wheelchairs.
Treatment of early puberty

- LHRH agonist
  - if given at regular intervals will stem the progression of puberty, preserve final height.
  - Subcutaneous depot injections 1-3 monthly.
  - May be an issue in the very lean.
  - Should only be used for a fixed amount of time to avoid metabolic bone health compromise. (Girls 12 years).
  - Pubertal progression will recommence after discontinuation.
Treatment to of early puberty II

- Progestogen
  - Oral (POP) or depot injections (Depot provera)
  - Thins the endometrium and stops periods.
  - Does not prevent bone age advancement or preserve height.
Treatments to manage menstruation

• Combined oral contraceptive pill (COC)
  - Oral medication in monthly cycles
  - Can be used in ‘back to back’ packets for up to 3 months in a row to reduce menstruation to 4 bleeds a year.
  - Risk of venous thrombosis particularly in the immobile and limb contractures.
  - Increased metabolism in those on anticonvulsants.
  - Benefit of contraception.
  - Weight gain.
  - May improve mood swings.
Treatments to manage menstruation II

• Long acting progestogen (Depo provera)
  - IM
  - Effective in stopping periods in those responsive to POP and contraceptive
  - May switch off HPO axis and reduce oestrogen production.
  - Leads to increased risk of fracture and therefore may need to be given with oestrogen supplementation.

• Low dose progestogen implant
  - 3 years contraception, light regular bleeds
  - May cause disordered bleeding requiring removal.
Treatments to manage menstruation

III

• **Progesterone-bearing intra-uterine device (IUD) – Mirena coil**
  - Inserted under GA in adolescents PV
  - May last up to 5 years - stops menstruation and acts as contraception.
  - May fall out spontaneously.
  - May take up to 6 months to work properly.
  - May cause disordered bleeding.
Delayed puberty

- Hypogonadotrophic hypogonadism
  - likely in those with midline brain structural abnormalities.
  - May be associated with other pituitary hormone deficiencies.
  - Raised prolactin due to hypothalamic dysregulation can also delay puberty.

- Constitutional delay - chronic illness related.
Disadvantages of delayed puberty

• Reduction in growth be it transient.
• Delay in psychological maturation.
• Increased risk of fragility fractures particularly in the immobile.
Treatment for delayed puberty

- Considered if puberty very late (> 14 years for girls, > 15 years in boys)
- Induction of puberty or ‘kickstart’ with:
  - ethinyloestradiol (oral) or oestradiol (patches) in girls
  - testosterone (oral, gel or IM) in boys (usually for 4 months)
- In some, continued induction for the full course is required.
Bone health in people with disability

- Assessment of bone mineral density (BMD) is of particular importance in the immobile to prevent longer term osteoporosis.
- 40-50% of bone mass is acquired during puberty
- Peak bone mineral density reached at age 22-25 years.
Factors affecting bone health in CP

- **Mobility**
  - Immobility decreases muscle bulk and tension on bones, reducing bone quality.
  - Bone turnover rates are slower in the chronically immobilised. Sudden immobilisation increases turnover and bone loss.
  - Use of standing frames increase vertebral but not necessarily limb BMD (Caulton et al., 2004).

- **Calcium** intake reductions and feeding problems.

- **Vitamin D** deficiency – CP patients may have reduced sun exposure.

- **Anticonvulsants** – may interfere with Vitamin D metabolism
Methods

• **Xray** – simplest method to demonstrate bone shape and structure (gracility), osteopenia, fracture, vertebral height and structural abnormalities such as kyphoscoliosis.

• **Bone mineral density (BMD)** – x-rays of 2 wavelengths passed through a bone to assess amount of bone within area.
  - Must account for bone size / area (BMAD)
  - Children need to be still, difficult to assess with contractures or spinal curvatures
  - DEXA – minimal radiation, enables VFA
Fractures in CP

- Prevalence of fracture (mainly in long bones) 12-23% (Mergler et al., DMCN 2009)
- Causes of fracture - Moving and handling, Falls, Physiotherapy, Severe muscle spasm / seizures
- Increased fracture risk – low BMD, feeding difficulties, anticonvulsants, previous fracture.
- Implications – unrecognised pain, loss of mobility, muscle wasting, missed schooling, litigation and suspected NAI.
How to improve bone health

• Monitoring and awareness of fracture risk.
• Calcium and Vitamin D supplementation if required.
• Weight bearing and physiotherapy.
• Ensuring timely pubertal processes and adequate hormones.
• ? Vibration therapy
• ? Bisphosphonates
References

- Caulton et al., *ACDC* 2002.