

## Overview

- Puberty refers to a *collection* of physiological, morphological and behavioural changes in the individual as the gonads change to an adult condition.
- In girls, a definitive sign is *menarche* (the first menstrual bleeding), which indicates that the ovary has secreted sufficient oestradiol and progesterone to induce uterine development. In boys, the first *ejaculation* indicates similar maturity (though is harder to date as it often occurs nocturnally). However, these events do not signify *fertility*. In early puberty the ovary does not ovulate and the seminal plasma lacks spermatozoa.
- Changes are initiated 2–4 years before this throughout the body, and depend on gonadal and adrenal sex steroids.
- **Physical changes.** The *adolescent growth spurt* is an acceleration of growth (from minimum growth velocity to peak height velocity, PHV) followed by a deceleration (→ cessation of growth at epiphyseal fusion). All areas of the body are involved, but sex differences in regional growth enhance sexual dimorphism (e.g. more shoulder growth in boys, more hip growth in girls).
- The growth spurt depends on growth hormone as well as sex steroids.
- Body composition alters. Prepubertal girls and boys have virtually identical lean body mass and body fat. Adult men have 1.5× the lean body mass of women, 1.5× the skeletal mass and 0.5× the body fat. These changes are among the earliest, beginning at 6y (girls) and 9y (boys).
- **Secondary sexual characteristics.** Breasts, genitalia, pubic hair. (There are clinical staging systems for these.) Axillary hair. Masculine beard growth and laryngeal enlargement (deepening of the voice).
- In males, androgens regulate these changes. In females, ovarian oestrogens regulate growth of the breast and female genitalia, but androgens (ovarian and adrenal) control pubic and axillary hair growth.
- The precise age and tempo at which these changes occur varies greatly with individuals, but the sequence of change is fixed.

## Hormonal changes

- Physical changes largely controlled by gonadal and adrenal steroids, together with some adenohipophyseal hormones.
- **Gonadotrophins** present at or soon after birth at low levels, rise & fall intermittently for first 1/2 years, then remain low until puberty. Then FSH & LH levels rise gradually to adult levels.
- **Prolactin:** increases in late puberty in girls. No change in boys. (Oestradiol enhances prolactin secretion in females.)
- No evidence of circadian rhythm of FSH or LH in adults or prepubertal children. In early to mid puberty, magnitude (+frequency?) of LH pulses increases: **sleep-augmented LH secretion**. In late puberty, daytime LH pulses increase but less than those occurring at night, until adult pattern (higher basal levels with no daily variation) achieved.
- **Testosterone** levels low (<0.1ng/ml) in boys and girls, except in boys aged 3-5 months when pubertal levels are seen. Early puberty: testosterone levels rise at night with LH secretion, but increase occurs steadily through puberty (inc. daytime). Greatest change in pubertal Stage 2 (0.2 up to 2.4 ng/ml). Smaller but consistent increases in girls (stages P1-P4).
- **Oestrogen** v. high in all fetuses (from placental conversion of fetal+maternal steroids). **Oestradiol** and **oestrone** levels soon drop and remain low until puberty. In girls oestradiol levels rise through puberty up to normal cyclical levels (50pg/ml follicular phase, 150pg/ml luteal phase). In boys oestrone higher than oestradiol, but both lower than girls' levels during comparable pubertal stages. In male, about ½ the oestradiol is from extraglandular aromatization of testosterone, and ≤¼ from testicular secretion.
- **Adrenal androgens** (notably dehydroepiandrosterone and its sulphate) begin to show progressive increase by 8y which continues until 13-15y in boys and girls. This change considerably precedes changes in gonadotrophins and gonadal steroids. **“Adrenarche”** (one of the first pubertal endocrine events; significance obscure). What is clear is that they promote pubic/axillary hair growth. Adolescent growth spurt does not require them. Hyper/hyposecretion *not* clearly associated with early or delayed puberty.

## Mechanisms of maturation of the hypothalamo-pituitary-gonadal (HPG) axis

N.B. This is a summary only. You should examine the experimental evidence.

Puberty is the process of *pituitary–gonadal activation*. There are two theories:

1. Pituitary & gonads could function in a mature manner at birth. Only requires increased output of hypothalamic GnRH to activate puberty. Result of maturation in CNS. *Good evidence*.
2. The “gonadostat” hypothesis. Accepts the first idea, but also emphasizes that negative feedback of FSH and LH regulation in boys and girls operates at a v. low threshold/set point, i.e. is very sensitive prepubertally. That is, it takes very little steroid to suppress FSH/LH secretion. The set point increases (becomes less sensitive) at puberty; hence the rise in gonadotrophins and sex steroids. Not well proven, but it is clear that the pituitary’s sensi-

tivity to GnRH does increase during puberty. Why? (a) self-priming of GnRH; (b) increased oestradiol (girls)/testosterone (boys) probably enhances this effect of GnRH on gonadotrophs. *Generally, less good hypothesis.*

### Timing of puberty

There has been a *secular trend towards an earlier menarche* in girls, and puberty in boys, in the West over the last century.<sup>1</sup> Menarche has decreased from 14–15y to 12–13y. Why?

- *Environmental factors.* Better standards of health. But more plausible are...
- *Photoperiod.* Electricity means our daily dark periods may be as short as 7h all year round. Photoperiod certainly affects the HPG axis of other species. Exposure to constant light accelerates puberty in the rat. There is little direct evidence in the human; plasma **melatonin** levels change at the onset of puberty in girls (the hormone is synthesized by the pineal gland and only at night) but blind girls experience *earlier* menarche.
- *Nutrition.* Low food intake, or low body weight, impairs adult reproductive function (anorexics have irregular menstrual cycles and often amenorrhoea). Though the age at menarche has declined over the last century, *the body weight at menarche has remained remarkably constant at ~47kg*. Perhaps a *critical metabolic mass* related to body weight triggers puberty. A similar suggestion of 55kg for boys has been made. Evidence for: moderately obese girls have earlier menarche; the amenorrhoea of anorexics begins below 47kg and ovulation resumes once their weight exceeds 47kg again; it is a logical idea – if you're <47kg, you wouldn't be capable of successful pregnancy. Evidence against: this is not *causal* evidence (perhaps puberty affects weight or some third factor affects both); it has proved difficult to *predict* age of menarche from weight...

### The CNS and puberty

- The CNS seems the place to look for processes that control puberty via hypothalamic GnRH neurons.
- *Kallman's syndrome* – delayed puberty and anosmia.<sup>2</sup> Failure of development of midline cranial structures leads to GnRH deficiency. Puberty can be initiated by exogenous GnRH; therefore the pituitary is adequately sensitive to it and GnRH must be crucial in attaining sexual maturity.
- *CNS tumours.* If the tumour does not produce gonadotrophins itself, then its *site* determines its effect on puberty. In the hypothalamus, lesions of the *anterior area* produce delayed puberty; lesions of more posterior areas are associated with precocious puberty. Tumours of the *pineal* have variable effects; it is not known whether they are due to gonadotrophin secretion by the tumour or interference with melatonin production. Tumours of the *pituitary* produce early/late puberty if they increase/decrease gonadotrophin production respectively.

... in other words, poorly understood.

(I'm sure you're familiar with the habit lecturers have of telling you facts when they understand something, and a mixture of evidence, history and anecdote when they don't.)

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<sup>1</sup> *secular*, 1. occurring once in or lasting for an age or a century; 2. lasting or going on for ages (opp. of short-term); 3. concerned with worldly affairs (not sacred, monastic or ecclesiastical), but there were *secular clergy*; 4. sceptical of religious truth or opposed to religious education.

<sup>2</sup> Inability to smell.