History of Presenting Illness

- Short Stature
- Failure of Normal Puberty: eg. axillary hair, acne, etc...
- Polyuria and Polydipsia (diabetes insipidus secondary to ADH deficiency)
- Hypoglycemia
- Delay in tooth development.
- Microgenitalia
- Fatigue,
- Cold intolerance,
- Constipation,
- Dry skin,
- Slow growth,
- Weight gain.
- Headaches,
- Visual disturbances

Differential Diagnoses

- Adrenal Insufficiency
- Craniopharyngioma
- Diabetes Insipidus
- Growth Hormone Deficiency
- Ambiguous Genitalia and Intersexuality
- Growth Failure
- Growth Hormone Deficiency
- Hypernatremia
- Hyponatremia

Findings on Examination

- LOOK:
  - Short stature = reduced GH
  - Pallor = reduced MSH due to reduced ACTH production
  - Lack of body hair = hypogonadism
  - Finely wrinkled skin = hypogonadism
  - Absence of secondary sexual characteristics = hypogonadism

- BLOOD PRESSURE:
  - Postural hypo due to ACTH deficiency

- FACE:
  - Multiple eye wrinkles = hypogonadism
  - Hypophysectomy scars on upper lip
  - Facial hair present? should it be?

- VISUAL FIELDS:
  - Bitemporal hemianopia
  - Assess nerves 3, 4, 6 and ophthalmic branch of 5

- FUNDOSCOPY:
  - Optic nerve atrophy? Pale useless disk

- NECK:
  - Enlarged thyroid due to hypothyroidism from reduced TSH

- CHEST:
  - Hairless = hypogonadism
  - Pale = reduced MSH from reduced ACTH
  - Nipple pigment absent
  - Breast atrophy = hypogonadism

- GENITALS:
  - Loss of pubic hair = hypogonadism
  - Atrophied testes? = normally 15 to 25 ml

- ANKLE REFLEXES:
  - “Hung up” reflexes of hypothyroid

SINISTER SIGNS

- Headache
- Vomiting
- Nausea
- Convulsions
- Coma

Production of Hormones is Lost in Order:

1. GH \(\rightarrow\) Dwarfism in kids
   (Insulin sensitivity in adults)
2. Prolactin \(\rightarrow\) Failure to lactate on cue
3. Gonadotropins \(\rightarrow\) Reduced expression of secondary sexual characteristics
4. TSH \(\rightarrow\) Hypothyroidism
5. ACTH \(\rightarrow\) Hypoadrenalism and hypopigmentation

Found together by Alex Yartsev, Sorry if I used your images or data and forgot to reference you. Tell me who you are.

aleksyigorevich@gmail.com
Tests and Investigations

Serum Biochemistry: **MAINLY SODIUM:**
- looking for an elevated serum sodium, high osmolality combined with low or normal urine osmolality

**ALL HORMONES:**
- Free T4 + TSH testing for hypothyroidism
- LH for hypogonadism
- FSH for hypogonadism
- Insulin-Like Growth Factor for growth failure

**FORMAL VISUAL FIELD TESTS** for bitemporal hemianopia

**Radiography of Left Hand and Wrist for Bone Age:**
- Not very specific or sensitive → rough indication of IGF-1 activity

**MRI of Sella Turcica** looking for macroadenoma

### MALE TANNER STAGING

<table>
<thead>
<tr>
<th>Tanner Stage 1 (Prepubertal)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Height</strong> increases at basal rate: 5-6 cm/year</td>
<td></td>
</tr>
<tr>
<td><strong>Testes</strong> Smaller than 4 ml or long axis &lt;2.5 cm</td>
<td></td>
</tr>
<tr>
<td><strong>Pubic Hair</strong> No coarse, pigmented hair</td>
<td></td>
</tr>
<tr>
<td><strong>Penis Stage</strong> No growth</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tanner Stage 2</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Height</strong> increases at basal rate: 5-6 cm/year</td>
<td></td>
</tr>
<tr>
<td><strong>Testes</strong> Size 4 ml or long axis 2.5 to 3.2 cm</td>
<td></td>
</tr>
<tr>
<td>Age 11.5 years (age 9.5 to 13.5 years)</td>
<td></td>
</tr>
<tr>
<td><strong>Pubic Hair</strong> Minimal coarse, pigmented hair at base of penis</td>
<td></td>
</tr>
<tr>
<td>Age 12.0 years (age 9.9 to 14.0 years)</td>
<td></td>
</tr>
<tr>
<td><strong>Penis Stage</strong> Earliest increased length and width</td>
<td></td>
</tr>
<tr>
<td>Age 11.5 years (age 10.5-14.5 years)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tanner Stage 3</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Height</strong> increases at accelerated rate: 7-8 cm/year</td>
<td></td>
</tr>
<tr>
<td><strong>Testes</strong> Size 12 ml or long axis 3.6 cm</td>
<td></td>
</tr>
<tr>
<td>Age 14.0 years (11.5-16.5 years)</td>
<td></td>
</tr>
<tr>
<td><strong>Pubic Hair</strong> Dark, curly hair spread over the pubis</td>
<td></td>
</tr>
<tr>
<td>Age 13.1 years (11.2-15.0 years)</td>
<td></td>
</tr>
<tr>
<td><strong>Penis Stage</strong> Increased length and width</td>
<td></td>
</tr>
<tr>
<td>Age 12.4 years (10.1-14.6 years)</td>
<td></td>
</tr>
<tr>
<td><strong>Other Changes</strong> Gynecomastia may occur (age 13.2 years) Voice breaks (age 13.5 years); Muscle mass increases</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tanner Stage 4</th>
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</thead>
<tbody>
<tr>
<td><strong>Height</strong> increases at peak rate: 10 cm/year (age 13.8)</td>
<td></td>
</tr>
<tr>
<td><strong>Pubic Hair</strong> Hair of adult quality Not spread to junction of medial thigh with perineum</td>
<td></td>
</tr>
<tr>
<td>Age 13.9 years (12.0-15.8 years)</td>
<td></td>
</tr>
<tr>
<td><strong>Penis</strong> Continued growth in length and width</td>
<td></td>
</tr>
<tr>
<td>Age 13.2 years (11.2-15.3 years)</td>
<td></td>
</tr>
<tr>
<td><strong>Testes</strong> Length 4.1 to 4.5 cm</td>
<td></td>
</tr>
<tr>
<td><strong>Other Changes</strong> Axillary hair (age 14.0 years) Voice changes (age 14.1 years)</td>
<td></td>
</tr>
<tr>
<td>Acne Vulgaris (age 14.3 years)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tanner Stage 5</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No further height increases after age 17 years</td>
<td></td>
</tr>
<tr>
<td><strong>Pubic Hair</strong> Adult pubic hair distribution (15.3 years) Pubic hair spreads to medial thigh No hair spread to linea alba</td>
<td></td>
</tr>
<tr>
<td><strong>Penis</strong> Mature genital size by 16.5 years</td>
<td></td>
</tr>
<tr>
<td><strong>Testes</strong> Length &gt;4.5 cm</td>
<td></td>
</tr>
<tr>
<td><strong>Secondary sexual characteristics</strong> Facial hair present on sexes; Mature male physique Gynecomastia disappears</td>
<td></td>
</tr>
</tbody>
</table>

### FEMALE TANNER STAGING

<table>
<thead>
<tr>
<th>Tanner Stage 1 (Prepubertal)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Height</strong> increases at basal rate: 5-6 cm/year</td>
<td></td>
</tr>
<tr>
<td><strong>Breast</strong> :Papilla elevation only</td>
<td></td>
</tr>
<tr>
<td><strong>Pubic Hair</strong> : Villus hair only ; No coarse, pigmented hair</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Tanner Stage 2</th>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>Height</strong> increases at accelerated rate: 7-8 cm/year</td>
<td></td>
</tr>
<tr>
<td><strong>Breast</strong> Breast buds palpable and areolae enlarge</td>
<td></td>
</tr>
<tr>
<td>Age 10.9 years (8.9-12.9 years)</td>
<td></td>
</tr>
<tr>
<td><strong>Pubic Hair</strong> Minimal coarse, pigmented hair mainly on labia</td>
<td></td>
</tr>
<tr>
<td>Age 11.2 years (9.0-13.4 years)</td>
<td></td>
</tr>
<tr>
<td><strong>Other Changes</strong> Based on increasingly earlier Puberty White: Stage 2 changes may appear one year earlier Black: Stage 2 changes may appear two years earlier</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Tanner Stage 3</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Height</strong> increases at peak rate: 8 cm/year (age 12.5)</td>
<td></td>
</tr>
<tr>
<td><strong>Breast</strong> Elevation of breast contour; areolae enlarge</td>
<td></td>
</tr>
<tr>
<td>Age 11.9 years (9.9-13.9 years)</td>
<td></td>
</tr>
<tr>
<td><strong>Pubic Hair</strong> Dark, coarse, curly hair spreads over mons pubis</td>
<td></td>
</tr>
<tr>
<td>Age 11.9 years (9.6-14.1 years)</td>
<td></td>
</tr>
<tr>
<td><strong>Other changes</strong> Axillary hair develops (13.1 years) <strong>Acne Vulgaris</strong> develops (13.2 years)</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Tanner Stage 4</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Height</strong> increases at 7 cm/year</td>
<td></td>
</tr>
<tr>
<td><strong>Breast</strong> Areolae forms secondary mound on the breast</td>
<td></td>
</tr>
<tr>
<td>Age: 12.9 years (10.5-15.3 years)</td>
<td></td>
</tr>
<tr>
<td><strong>Pubic Hair</strong> of adult quality</td>
<td></td>
</tr>
<tr>
<td>No spread to junction of medial thigh with perineum</td>
<td></td>
</tr>
<tr>
<td>Age: 12.6 years (10.4-14.8 years)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Tanner Stage 5</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No further height increases after age 16 years</td>
<td></td>
</tr>
<tr>
<td><strong>Breast</strong> Adult breast contour Areola recesses to general contour of breast <strong>Pubic hair</strong> Adult distribution of hair Pubic hair spreads to medial thigh Pubic hair does not extend up linea alba</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other Milestones</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adrenarche</strong> : Age 6 to 8 years</td>
<td></td>
</tr>
<tr>
<td><strong>Menarche</strong> : Age 12.7 years (10.8-14.5 years)</td>
<td></td>
</tr>
<tr>
<td>Delayed &gt;1 year if low body fat (e.g. athlete)</td>
<td></td>
</tr>
</tbody>
</table>

### Growth in Girls
- Peak height velocity: 11.5 years (9.7-13.3 years) Basal growth occurs up until Tanner Stage 2 Basal Growth rate: 5.0 to 6.0 cm per year **Pubertal Growth** Girls who mature average time: 8.3 (6.1-10.4) cm/yr Girls who mature early: 9.0 (7.0-11.0) cm/yr Girls who mature late: 7.5 (5.4-9.6) cm/yr
Disease Definition
The tumour results in destruction of normal pituitary tissue resulting in reduced hormone production. The most obvious hormone deficiency is growth hormone resulting in decreased growth velocity and short stature. Decreased thyroid hormone and gonadotrophins contribute to short stature and delayed puberty.

Management
- depends on the symptoms and the extent of disease

Asymptomatic microadenoma → periodic follow-up until symptoms appear

SURGERY: transsphehnoidal microsurgery
( unless extended into the subfrontal, retrochiasmatic or middle cranial fossae = need a transcranial route)

Incomplete Excision (positive margins) = RADIOTHERAPY

A choice of
- EXTERNAL BEAM,
- BRACHYTHERAPY or
- isotope labelled radiopharmaceuticals.

SIDE EFFECTS: treats the whole sella turcica.

Prolactinomas:
Bromocriptine, a dopamine agonist, is the most widely used medical treatment for prolactinomas because of its efficacy in inhibiting synthesis and release of prolactin and reducing the level of serum prolactin.

Growth hormone secreting tumours:
Octreotide is an analogue of somatostatin and has been associated with decrease in growth hormone levels an tumour size.

Corticotropin secreting tumours:
Ketoconazole, an anti-fungal agent which inhibits adrenal steroidogenesis, is commonly used, however medical therapy is usually reserved for patients unsuitable for surgery or for patients with recurrent tumour after surgery or radiation.

Craniopharyngeomas:
Surgery can result in partial or almost complete removal of the lesion. Regrowth may occur.

!! Replace whichever hormones are lacking
Epidemiology
There is no correlation with either race or sex. Neither for age, as there are both congenital and acquired forms. Frequency in the population: ~ 1 in 4000 for growth hormone deficiency ~ 3 in 1,000,000 for panhypopituitarism

Behavioural science: short stature and social development

**SUPPORT GROUPS:**
- offer psychological support,
- disseminate information,
- lobby for special consideration
- offer practical help suggestions

eg:
- Little People’s Association

**SHORT STATURED PEOPLE OF AUSTRALIA (INC), (9642 5046).**

Care is usually managed through special multi-disciplinary clinics associated with teaching hospitals.

It is more important for a short child to acquire coping skills than to buy inches through pharmacological means".

**Psychological consequences**
- lack of self-esteem
- Depression
- underachievement

**HEIGHT AGE influences responses more than CHRONOLOGICAL AGE:**

Teachers, peers may regard the short person as being younger
This may lead to reduced expectations and fewer demands than are placed on the child's age peers.

**NEED TO RECONFIGURE ENVIRONMENT FOR PROPER DEVELOPMENT:**
Reachable Shelves, low chairs to allow the feet to touch the floor

**PITUITARY TUMOURS**

- Common Autopsy Findings: 6 to 23% of people have one when they die
- 20% of “normal” glands look tumourous on MRI
- rarely metastasise but may be locally invasive.

lesser than 1 cm in diameter are microadenomas,
greater than 1 cm are macroadenomas.

**Symptoms of Compression or invasion:**
- headache from stretching of the dura mater, or with very large tumours,
- CSF obstruction and hydrocephalus;
- visual field disturbances from optic nerve compression, classically a bitemporal hemianopia;
- IIIrd, IVth or VIth cranial nerve palsies;
- CSF rhinorrhoea from erosion of the sella turcica.

**The principal tumour types:**
- non-functioning adenoma (32%),
- prolactinoma (27%),
- growth hormone producing adenoma (13%),
- corticotrope adenoma (10%),
- gonadotrope adenoma (9%),
- combined GH and prolactin producing adenoma (8%),
- thyro trope adenoma (1%).

Non-functioning adenomas do in fact frequently stain positive for one or more glycoprotein hormones, in particular gonadotropins, a subunit or the b subunit of LH, FSH or TSH, and ACTH. However, they are non-secretory or secrete only biologically inactive hormones, such as a subunit.
Normal Growth in Childhood

...is LINEAR but in 4 stages:

- **Prenatal growth**: 30% of total linear growth; 5% of weight (!!) - RAPID!! 50 cm in 9 months. is largely independent of foetal and maternal hormonal control.

- Major regulators include:
  - foetal nutrition
  - placental function
  - maternal health
  - intra uterine infections
  - toxins
  - genetic factors.

- **Postnatal growth**: (3 phases) approximately 113 (females) - 126 (males) cm
  - infantile phase for the first 3 years: triple weight in 1 year!!
  - rapidly decelerating
  - largely dependent upon nutrition and genetic factors.
  - The endocrine hormones and other growth factors have a contributory role.

- **Childhood growth**: from age 3 to onset of puberty: Weight gain is steady
  - slowly decelerating
  - is largely regulated by genetic factors and growth hormone.

- **The pubertal growth spurt**: accelerated increase in weight
  - approximately 30 cm in males and 27 cm in females
  - dependent upon sex steroids and growth hormone.
  - Females have a significant increase in body fat,
  - Males have a greater increase in lean tissue
  - Males continue to accrue lean tissue until their early 20's.
  - Bone mineral increases parallel to height and weight growth curves
  - peak bone mass is attained within a few years of completing the growth spurt

---

**GENETICS are most responsible for variations between individuals.**

i.e: if your genes determine you to be tall, you will grow faster during childhood.

**BUT NEVER AT THE SAME RATE!!**

consistently slow or fast growth velocities = an underlying disorder of growth or puberty.

---

**GROWTH HORMONE ENDOCRINOLOGY:** all actions are via G-protein coupled cAMP 2ndary messages

**STIMULATED by**

- Somatoliberin, GHRH
  - decrease in blood sugar
  - exercise
  - stress
  - excess amino acids in blood stream
  - deficit of free fatty acids

**INHIBITED by**

- Somatostatin, GHIH
  - hyperglycaemia
  - hyperlipidaemia
  - obesity
  - malnutrition

**RELASE OF GH (somatotropin)**

- From somatotroph cells @ anterior pituitary (acidophilic)

**DIRECT EFFECTS:**

- Response is from most tissues:
  - Lipolysis, and subsequently
  - Release of free fatty acids
  - Decreased uptake of fatty acids from the blood stream
  - INSULIN RESISTANCE: reduced uptake of glucose
  - Increased gluconeogenesis

**NEGATIVE FEEDBACK** back to hypothalamus and pituitary occurs via direct concentrations of GH and IGF-1, plus via the increase in concentrations of free fatty acids, amino acids and glucose

**LIVER, MUSCLE, CARTILAGE and BONE** respond by PRODUCING IGFs (Insulin-like Growth factors) aka. SOMATOMEDINS

**SOMATOMEDINS INDUCE**

- INDIRECT CHANGES in most tissues
  - Anabolic + Mitogenic:
    - INCREASE of amino acid uptake, thus
    - INCREASE of protein synthesis
    - THUS cartilage bone and muscle growth

---

Growth hormone secretion is cyclical, pulsatile, and is greatest during SLEEP
ANTERIOR PITUITARY and its HORMONES

CELL TYPES | HORMONE | STAINING
---|---|---
Somatotrop | somatotropin (GH) | acidophil
Mammotrop | prolactin | acidophil
Corticotrop | corticotropin | basophil
FSH-gonadotrop | follitropin (FSH) | basophil
LH-gonadotrop | lutropin (LH) | basophil
Thyrotrop | thyrotropin (TSH) | basophil

**MICRO-ANATOMY**

<table>
<thead>
<tr>
<th>Pars</th>
<th>Winding cords of epithelial cells &amp; fenestrated capillaries</th>
<th>Acidophils (red stain)</th>
<th>Lactotropes (PRL)</th>
<th>Somatotropes (GH)</th>
<th>Basophils (blue)</th>
<th>Gonatotropes (LH, FSH)</th>
<th>Thyrotropes (TSH)</th>
<th>Corticotropes (VPR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pars distalis</td>
<td>(helps hormone delivery into blood)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>
| Pars nervosa | Unmyelinated axons, glial cells, fenestrated capillaries | Herring bodies: bulges nr axon endings containing stored hormones.OT and VPR bound to neurophysins (carrier protein) Near capillaries.
| Pars intermedia | Large pale cells among follicles | Melanocyte-stimulating hormone predominates |

**GROWTH HORMONE**

**stim:**
- TRH
- Cold weather
- Pregnancy

**inhib:**
- TH (acts at pit & hypothal)
- GHIH (from TH at hypothal)

**effects:**
- Stimulates thyroid gland to release TH

**excess:**
- Grave’s disease
- (child) cretinism
- (adult) myxedema

**defic:**
- (child) myxedema

**TSH**

**stim:**
- TRH
- Cold weather
- Pregnancy

**inhib:**
- TH (acts at pit & hypothal)
- GHIH (from TH at hypothal)

**effects:**
- Stimulates thyroid gland to release TH

**excess:**
- (child) cretinism
- (adult) myxedema

**defic:**
- (child) myxedema

**GROWTH HORMONE**

**stim:**
- [GH]
- Estrogen
- Hypoglycaemia
- ↑ Blood aa’s
- ↑ Fatty acids
- ↓ Exercise & stress
- (all trigger GHRH)

**inhib:**
- ↑ GH and IGF (fb)
- Hyperglycaemia
- Hyperlipidaemia
- Emol. deprive.
- Obesity & malnutrition
- (all trigger GHIH)

**effects:**
- *Receptors present on most tissues

**DIRECT (anti-insulin fx)**
- Fats as fuels:
- (Adipose release & lipolysis)
- Spare glucose:
- (↓ uptake, glycogenolysis liver)

**INDIRECT (anabolic, mitogenic)**
- Stim liver, skeletal m, bone, cartilage release
- of IGFs (somatomedins)
- → ↑ cartilage & skeletal growth
- → ↑ protein synth, cell growth & prolif

**cycle:**
- Peaks at sleep (early phase), adolescence

**excess:**
- (Child) gigantism (epiphyseal plates still open)
- (Adult) acromegaly: enlarged extremities

**defic:**
- (Child) pituitary dwarfism
**ACTH**

- **stim:** CRH (all trigger CRH)
- **stim:** fever, stress, hypoglycemia
- **inhib:** glucocorticoids (fb) inhibit CRH

**Effects:**
- 1.) Stimulates adrenal cortex to release glucocorticoids & mineralocorticoids (ie. Cortisol: stress fighter) and androgens
- 2.) Controls adrenal size

**Cycle:** Cushing’s disease

---

**Gonadotropins**

**FSH**

- **stim:** GnRH
- **inhib:** oestrogen (fb)

**LH**

- **stim:** GnRH
- **inhib:** oestrogen, progesterone

**Effects:**
- Ovaries & testes
  - ♀ ovarian follicle maturation
  - Oestrogen production
  - ♂ sperm production
  - Testosterone production

**Cycle:**
- ♀ Pre-puberty, ↑ pubertal maturation, ↑↑ menopause
- ♂ Pre-puberty, ↑ puberty causing gonad maturation

---

**Prolactin**

- **stim:** oestrogens, contraceptive pill, lactation
- **inhib:** PIH (dopamine), prolactin

**Effects:**
- Promotes lactation in breasts
- Enhances testosterone production

**Excess:** galactorrhoea (also caused by loss of doaminergic neurons in hypothal)
- ♀ Cessation menses, infertility
- ♂ Impotence, gynaecomastia

**Cycle:**
- ♀ pre-menstrual period (breast swelling, tender)
- Pregnancy: oestrogens & progesterone counter PRL,

---

**Oxytocin (OT)**

- **stim:** cervical/uterine stretch, suckling
- **inhib:** lack of stim

**Effects:**
- Uterus: stimulates contractions (used to induce labour)
- Breast: triggers milk ejection
- Coitus: ↑ secretion, uterine contractions, semen

**Behaviour:** “Cuddle” hormone, nurtures

**Cycle:** ↑ secretion & receptor no. at birth

---

**Vasopressin, VP**

(Antidiuretic hormone, ADH)

**Actions:**
- ↑ blood osmolarity → osmoreceptors → SON & PVN → ↑VP (hypothal)
- ↑ VP → ↑ Ca → ↑ DAG/IP3 → ↑ periph resist
- ↓ BP (baro receptors) (vascular sm musc)
- ↑ VP → ↑ urine
- ↑ water resorption

**Other stim:** pain, drugs (nicotine)

**Inhib:** alcohol, adequate hydration

**Deficit:** Diabetes insipidus → cell body destruction in hypothalamic tissue, VP gene (trauma pts need monitoring in case damage to hypothal)

**Pressure drop is key, not volume**

**Excess:**
- Childhood meningitis / post neuroSx / hypothal Ix / tumour = inappropriate ADH secretion syndrome
- Hypo-osmolar blood, brain oedema
- Fluid retention, headache, disorientation

---

**Posterior Pituitary Hormones**

Storage of hormones made in hypothalamus and forwarded thru neurons. Secreted in response to hypothalamic stimulus.
Anterior Cranial Fossa
- Crista Galli: the Anterior Attachment of the Falx Cerebri
- Lateral crest: deep inside lateral fissure
- Anterior Clinoid Process: Optic nerve emerges from under this process
- Sella Turcica

Posterior Cranial Fossa
- Dorsum sellae
- Foramen Lacerum, for Internal Carotid
- Internal Acoustic Meatus
- Hypoglossal Canal
- Foramen Magnum

*PFC is roofed by the Tentorium Cerebelli

Middle Cranial Fossa
- Supraorbital fissure, for CNs 3, 4, 6, + the opthalmic branch of CN 5
- Foramen Rotundum for Maxillary nerve (5)
- Foramen Ovale for Mandibular (5) + Lesser Petrosal (parasympathetic)
- Foramen Spinosum

Base of Skull: Home of the Cavernous Sinus

NOW ABOUT THAT SINUS:
- 2 layers of dura
- Venous blood between
- Contains numerous important things and frequently gets into trouble

Roof of the pituitary fossa is the Sellar Diaphragm: Stretched between the clinoid processes like a trampoline.

ABOVE THAT: Chiasm, hypothalamus, 3rd ventricle

NOW ABOUT THAT SINUS:
- The PITUITARY gland: a pea on a stalk
  Stalk: INFUNDIBULUM: contains portal veins and UNMYELINATED AXONS from the hypothalamus; + send inhibiting signals to ant. pituitary
  POSTERIOR: “pars nervosa” = contains axons of hypothalamic neurons and some glial cells
  HORMONES STORED AT AXON TERMINALS
  ANTERIOR: “pars Distalis” = glandular tissue, localised hormone production

INTERNAL CAROTID Travels inside the sinus!

OCULOMOTOR nerve
TROCHLEAR nerve
ABDUCENS nerve
OPHTHALMIC branch of CN 5
MAXILLARY branch of CN 5
### HISTOLOGY OF THE PITUITARY GLAND

#### ANTERIOR: pars distalis

Winding cords of cells and fenestrated vessels:
- high surface area, rapid hormone delivery

#### BASOPHILS:
- Lactotroph
- Thyrotroph
- Corticotroph

#### ACIDOPHILS:
- Lactotroph
- Somatotroph

**pars intermedia** contains large cells that often surround follicles filled with defined "colloid". Melanocyte-stimulating hormone is the predominant hormone secreted by the pars intermedia.

#### POSTERIOR: pars nervosa

Bulging unmyelinated axons and fenestrated vessels:
- high surface area, rapid hormone delivery...

PLUS: **HERRING BODIES** = fat ends of axons, swollen with stored hormones.

**THESE HORMONES ARE BOUND to CARRIER PROTEINS**
- (neurophysins)

### GROWTH PATTERNS

4 stages of (linear) growth:

<table>
<thead>
<tr>
<th>Stage</th>
<th>Normal growth</th>
<th>1° Determinants</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRENATAL: 9m</td>
<td>50cm (rapid)</td>
<td>foetal nutrition, placental function, maternal health, in-utero infxn, toxins, genetics</td>
</tr>
<tr>
<td></td>
<td>* 30% total linear growth achieved in utero</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5% adult weight</td>
<td></td>
</tr>
<tr>
<td>INFANTILE: 1-3y</td>
<td>(rapid deceleration) rapid weight gain: birth wt x3 by 1y</td>
<td>nutrition, genetics, hormones &amp; growth factors</td>
</tr>
<tr>
<td>CHILDHOOD: 3y-puberty</td>
<td>(slow deceleration) steady wt gain</td>
<td>growth hormones, genetics</td>
</tr>
<tr>
<td>PUBERTY:</td>
<td></td>
<td>sex steroids (gonadotropins), growth hormone</td>
</tr>
<tr>
<td></td>
<td>♀ 27cm</td>
<td></td>
</tr>
<tr>
<td></td>
<td>♂ 30cm</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2yr delay for male growth spurt: taller</td>
<td></td>
</tr>
<tr>
<td></td>
<td>starting point for spurt + 3cm more growth</td>
<td></td>
</tr>
<tr>
<td></td>
<td>→ av 13cm difference between ♀ &amp; ♂</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(no gender diffs pre-puberty)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>rapid wt gain ♀ - fat</td>
<td></td>
</tr>
<tr>
<td></td>
<td>♂ - lean muscle</td>
<td></td>
</tr>
</tbody>
</table>

**General:**
- nutrition, health (phys & emotional), hormones and genetics important for max growth at all stages
- most height variability → genetic
- bone mineralisation in parallel with height & weight curves, peak bone mass within few years of completing pubertal growth spurt
- **Growth velocity** (cm/yr) Tall people = higher growth velocs. Varies thru stages. Problem if consistently high/low relative to population standards
PUBERTY

= attainment of 2° sexual characteristics & reproductive capabilities

Puberty initiated when hypothalamus resumes pulsatile GnRH secretion → GnRH pulse generator fires up neurones inter-connected via gap junctions (previously active in utero & postnatal)
Causes ↑ GnRH secretion * nocturnal peaks

ADRENARCHE
adrenal glands mature

= production of weak androgens (gonadocorticoids) from ~ age 7
♀ & ♂ equal amts
include: DHEA androstenedione
converted to → testosterone ♂
→ oestrogen ♀

Genitalia – growth & maturation
(int & ext)
- maintains adult size & fn
- testes descent
- spermatogenesis
- inhibs mammary gl devt
puberty – voice
- growth & anabolism
- bones: ↑ mass, epiphyseal closure
- hair
- sebum secretion
metabolism – ↑ BMR
- haematopoeisis
neural – libido (♂&♀), aggression

♀ : 8 – 13.5y
♂ : 9.5 – 14y
MALE:

- ~9.5:
  - testes 1-3ml (prepuberty)
  - bone mineralisation ↑BP

- 13.5:
  - testes 4-8ml (early testicular)
  - penis & scrotal growth

- 13.5:
  - testes 10-15ml
  - early sideburns

- 13.5:
  - testes 15-20ml
  - beard

- 13.5:
  - testes 25ml

DISORDERS OF PUBERTY

**VOICE BREAKS**
- vocal cords lengthen
- enlarg't: larynx
cricothyroid cartilage
laryngeal mm

**TESTICULAR CHANGES**
- growth Seminiferous tubules
Sertoli cells mature
Seminal vesicles enlarge
↑ blood flow
penis 6.2cm → 12.4 cm

**HAIR:**
- pubic → axillary → facial

endpoints:
- voice changes
- shaving
- male musculature
- epiphyseal closure

**PREOCIOUS PUBERTY (<9.5y)**

<table>
<thead>
<tr>
<th>True / Complete</th>
<th>Pseudo</th>
<th>Incomplete</th>
</tr>
</thead>
<tbody>
<tr>
<td>→ [a] hypo-pit-gons</td>
<td>→ [suppression] h-p-g</td>
<td>→ immature h-p-g</td>
</tr>
</tbody>
</table>

**Cause:**
- CNS abn
- Genetic
- Idiopathic

**Px:**
- ↑ LH, FSH, T
- large testes

<table>
<thead>
<tr>
<th>True</th>
<th>Pseudo</th>
<th>Incomplete</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓ LH, FSH</td>
<td>↓ T</td>
<td>premature adrenarche</td>
</tr>
<tr>
<td>small testes</td>
<td></td>
<td>(virilisation)</td>
</tr>
</tbody>
</table>

**RX:**
- treat 1° cause (MRI)
- 75% organic cause
- Androgen antagonist
- Steroid synth inhibitor
- GnRH superagonist (as yet unavail)

if untreated:
- short stature (long-term)
- aggression, inapprop libido (short-term)

*T = testosterone

**DELAYED PUBERTY (no changes>14y/ incomplete devt)**

- Hypogonadism no fx on adrenarche

**Cause:**
- Hypothalamic
  - familial
  - childhood sickness
  - lesion affecting GnRH
- Pituitary
  - lesion (tumour/trauma)
  - genetic defic
- Gonadal
  - lesion (torsion / trauma)
  - chromosomal
  - radiation / chemo
  - cryptorchidism

**damage**
- (tumour / trauma / infxn)
- genetic GnRH defx

**PX:**
- ↑ LH, FSH, T (rise in LH, FSH with GnRH stim)
- all ↓ (no rise with stim)
- ↑ LH, FSH
- ↓ T

**GYNAECOMASTIA**

- neonatal (1st 6m)
- pubertal (67% boys)
- congenital → Klinefelter’s
- drugs → marijuana
- tumours (feminising fx : eg. secreting aromatase – converts T to E)

**RX:**
- no signs of puberty → explore puberty → reassure / Sx
HORMONE TESTING

ACTH:

INDICATIONS: low cortisol, suspicion of pituitary / adrenal disease

Where is the problem?
(if normal response to stimulus, problem is higher up chain)

ACTH stimulation test → adrenal health
abN results may still indicate higher pit prob causing adrenal atrophy (if so, repeats will improve)

CRF stimulation → pituitary health

Metyrapone stimulation → -ve feedback health
blocks cortisol

Insulin → -ve feedback health
↓ blood glucose

*compare [ACTH] with [cortisol] to pinpoint irregularity

dexamethasone suppression → secretory pwrs of tumour

Disease:
↑ ACTH → hypersecretion → pit tumour (Cushings)
→ ectopic tumour (apical lung)
→ decreased uptake → adrenal damage (Addison’s)

↓ ACTH → decreased production → non-functional pit tumour
→ xs -ve feedback → adrenal (functional) tumour

GROWTH HORMONE:

INDICATIONS: (not routine screening)
GH abnormalities
follow-up for other abN results
monitor long-term chemoRx fx (children)

“GH stimulation”
insulin / arginine → shows hypo-pituitarism
“GH suppression”
glucose soln → shows hyper-pituitarism

IGF-1 assay → [IGF1] reflects [GH]
IGF<GH = problem higher up: → liver/kidney d, malnutrit
→ ineffective form of GH

GHRH → pituitary health
L-dopa → “ ”

↓ GH → less secretion → hypopituitarism (↓ fn) → genetic
→ damage (trauma / infxn / inflam)
→ non-functional pit tumour

↑ GH → ↑ secretion → functional pit tumour (poly/monoclonal)
**TSH:**
- cold / trauma / stress

**INDICATIONS:**
- diagnosis / screening thyroid disorder
  - monitor → hormone Rx
  - → ♀ infertility probs

**TSH →** pit & thyroid health

**T3** (may be spot-checked as less pulsatile secretion)
- TRH stimulation → pituitary health

**T4**
- ↑TSH → ↓T3, T4 → underactive thyroid (hypothyroidism)
  - (or insuffic replacement H)
  - → hypersecretion → pit tumour (rare)
- ↓TSH → ↑T3, T4 → overactive thyroid (hyperthyroidism)
  - → XS replacement H
  - → insuffic secretion → pit damage

**TSH →** pit & thyroid health

**T3** (may be spot-checked as less pulsatile secretion)

**T4**

**PROLACTIN:**

**INDICATIONS:**
- ↑ prolactin signs
  - investig → infertility (♂ & ♀)
  - → ↓ testosterone (♂)

**Prolactin →** pituitary health
- (spot test)

**PRH →** pit health

**↑ PRL →** pregnancy & lactation
- → hypersecretion → pit tumour (prolactinoma = common)
GONADOTROPINS

Female:

- Hypothalamus → GnRH → Pituitary
  - Inhibin
  - FSH → Ovary
    - Graafian follicle
  - LH → Ovary
    - Corpus luteum
  - Progesterone
  - Oestrogen
  - Reproductive tract & elsewhere

Male:

- Hypothalamus → GnRH → Pituitary
  - ICSH
  - FSH → Testis
    - Leydig cell
    - Sertoli cell
    - Spermatogenesis
    - Testosterone
    - 2° Sex organs

INDICATIONS:
- Suspicion thyroid disorder
- Infertility
- Irreg menstruation
- Early/late puberty
- Menopause confirm

FSH, LH (ICSH) levels → Gonad health → Pituitary health
GnRH stimulation → Pituitary health

↑ FSH, LH → Hypersecretion → Pituitary adenoma (rare)
  → Ovary failure → Deviation → Agenesis
  → Steroidogenesis deviation → Radiation / ChemoRx
  → Autoimmune
  → Failure to ovulate → Polycystic ovary
  → Thyroid disease → Adrenal disease
  → Tumour → Menopause

↓ FSH, LH → Pituitary / Hypothal failure

INDICATIONS:
- Cause of ↓ sperm count
- Infertility
- Early/late puberty

↑ FSH → No negative feedback → Testicular failure → Deviation → Agenesis
  → Chromosomal (Klinefelter’s)
  → Viral infection (Mumps)
  → Trauma
  → Radio / ChemoRx
  → Autoimmune
  → Tumour

↓ FSH → ↓ Secretion → Pit / Hypothal prob

* ↑ FSH, ↑ LH in children → Precocious puberty
3 TYPES OF TEST-

**Stimulation tests** → deficiency (spot tests may reflect normal cyclical/pulsatile variation)
**Suppression tests** → overproduction (must prove you can’t suppress)
**Spot tests**: random sampling of hormone levels (non-stimulated)

**FOLLOW-UP**
Must investigate glands if abnormality detected

- **Pituitary**
  - MRI / CT (expansion)
  - visual fx (VER)
  - X-ray

- **Adrenal** → MRI / CT

- **Thyroid** → ultrasound
  - radioactive I scan
  - FNAB

**Gonads**

**USE OF HORMONE TESTING**
- diagnosis of disorder
- long term monitoring of Rx
- tumour recurrence monitoring (post-op)
CHILDHOOD ONSET: most comm. = “adamantinous type” Craniopharyngioma
composed of duct lining remnants, epithelioid
is cyst-like, with turbid proteinaceous material.
SLOW GROWING AND BENIGN (non-metastatic)
...BUT INVASIVE by direct extension along paths
of least resistance.

ADULT ONSET: metaplasia of
residual squamous cells on the
inside of the remaining duct
Ectoblast cells
Floor of primitive oral cavity, the “stomodeum”

- ENDOCRINOPATHY -
Intruding intra-sellar tumour
crushes the fragile pituitary tissue
Anterior pituitary suffers the most from the pressure,
→ blood supply blocked: starvation and ischaemia of pituitary
→ Secretory cells stop functioning due to direct pressure
→ portal veins are crushed and thus the hypothalamic
hormonal stimulation is blocked

Low GH

- ADIPOCYTES:
  - Reduced rate of lipolysis
  - Increased rate of glucose uptake

- MUSCLES:
  - Reduced protein synthesis

- LIVER
  Reduced protein synthesis
  Reduced gluconeogenesis
  Reduced synthesis of INSULIN-LIKE GROWTH FACTORS (somatomedins)

- CHONDROCYTES AND OSTEOBLASTS
  THUS:
  - decreased rate of collagen synthesis
  - decreased rate of cartilage formation
  - decreased protein synthesis in general
  - decreased rate of cell proliferation
  THUS: young bone age; plus → DECREASED LINEAR GROWTH

- SHORT STATURE

Low TSH

- LETHARGY & WEAKNESS

Chubbynes

CHUBBYNES

Low LH + FSH

- Both sexes:
  - Reduced secretion of TESTOSTERONE
  - No androgens except what the maturing adrenals can produce (weak androgens, “gonadocorticoids”)
  - NO PUBIC HAIR
  - NO PUBERTY
  - NO PUBIC HAIR
  - NO SEXY MAN-STINK (hypothetically, no pheromones)

- POOR SCHOOL PERFORMANCE

- Tumour Necrosis and Calcification
Due to disruption of blood-brain barrier and tissue necrosis (as the tumour chokes its own blood supply) the shreds of decomposing proteins bind calcium and become consolidated into calcified masses. Which looks lovely on CT or X-ray