put together by Alex Yartsev: Sorry if i used your images or data and forgot to reference you. Tell me who you are.
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Hypopituitarism and Puberty

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**

SINISTER SIGNS
→ Headache
→ Vomiting
→ Nausea
→ Convulsions
→ Coma

PRODUCTION OF HORMONES IS LOST IN ORDER:

1. **GH** → dwarfism in kids (insulin sensitivity in adults)
2. **PROLACTIN** → failure to lactate on cue
3. **GONADOTROPINS** → reduced expression of secondary sexual characteristics
4. **TSH** → hypothyroidism
5. **ACTH** → hypoadrenalism and hypopigmentation

Differential Diagnoses

Adrenal Insufficiency
Craniopharyngioma
Diabetes Insipidus
Growth Hormone Deficiency
Ambiguous Genitalia and Intersexuality
Growth Failure
Growth Hormone Deficiency
Hypernatremia
Hyponatremia
Histiocytosis
Hypoglycemia
Hypogonadism
Hypothyroidism
Hyposomatotropism
Microphallus

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

Tests and Investigations

Serum Biochemistry: MAINLY SODIUM:

- looking for an **elevated serum sodium, high osmolality** combined with **low or normal urine osmolality** } **DIABETES INSIPIDUS**

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

Tanner Stage 1 (Prepubertal)

Height increases at basal rate: 5-6 cm/year
Testes Smaller than 4 ml or long axis <2.5 cm
Pubic Hair No coarse, pigmented hair
Penis Stage No growth

Tanner Stage 2

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

Tanner Stage 3

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

Tanner Stage 4

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

Tanner Stage 5

No further height increases after age 17 years
Pubic Hair Adult pubic hair distribution (15.3 years)
Pubic hair spreads to medial thigh
No hair spread to linea alba
Penis Mature genital size by 16.5 years
Testes Length >4.5 cm
Secondary sexual characteristics
Facial hair present on sides; Mature male physique
Gynecomastia disappears

Growth in Boys

Peak height velocity: Age 13.5 (11.7-15.3 years)
Basal growth occurs up until Tanner Stage 3
Basal Growth rate: 5.0 to 6.0 cm per year
Pubertal Growth
Boys who mature average time: 9.5 (7.1-11.9) cm/yr
Boys who mature early: 10.3 (7.9-12.5) cm/yr
Boys who mature late: 8.5 (6.3-10.7) cm/yr

FEMALE TANNER STAGING

Tanner Stage 1 (Prepubertal)

Height increases at basal rate: 5-6 cm/year
Breast :Papilla elevation only
Pubic Hair : Villus hair only ; No coarse, pigmented hair

Tanner Stage 2

Height increases at accelerated rate: 7-8 cm/year
Breast Breast buds palpable and areolae enlarge
Age 10.9 years (8.9-12.9 years)
Pubic Hair Minimal coarse, pigmented hair mainly on labia
Age 11.2 years (9.0-13.4 years)
Modifications based on increasingly earlier Puberty
White: Stage 2 changes may appear one year earlier
Black: Stage 2 changes may appear two years earlier

Tanner Stage 3

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

Tanner Stage 4

Height increases at 7 cm/year
Breast Areolae forms secondary mound on the breast
Age: 12.9 years (10.5-15.3 years)
Pubic Hair Hair of adult quality
No spread to junction of medial thigh with perineum
Age: 12.6 years (10.4-14.8 years)

Tanner Stage 5

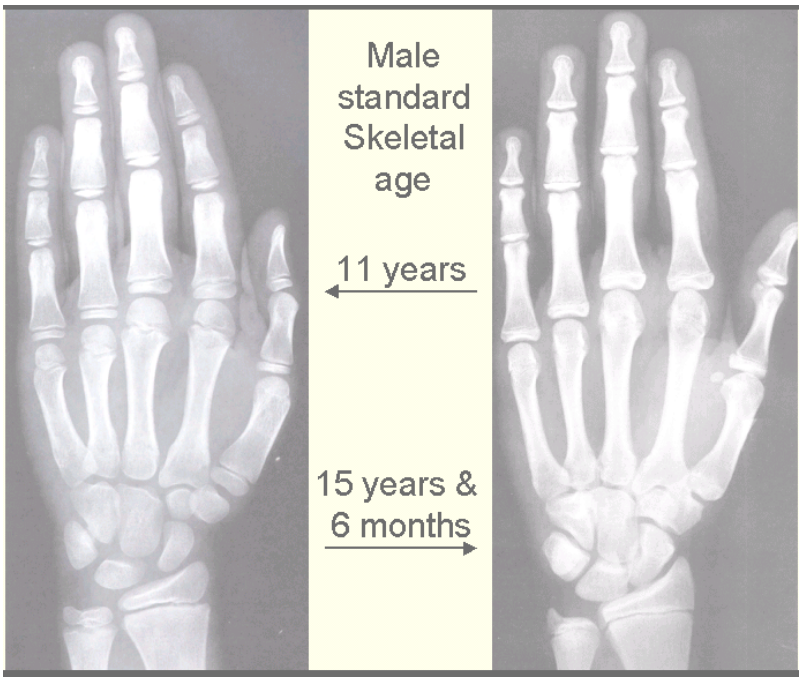
No further height increases after age 16 years
Breast Adult breast contour
Areola recesses to general contour of breast
Pubic hair Adult distribution of hair
Pubic hair spreads to medial thigh
Pubic hair does not extend up linea alba

Other Milestones

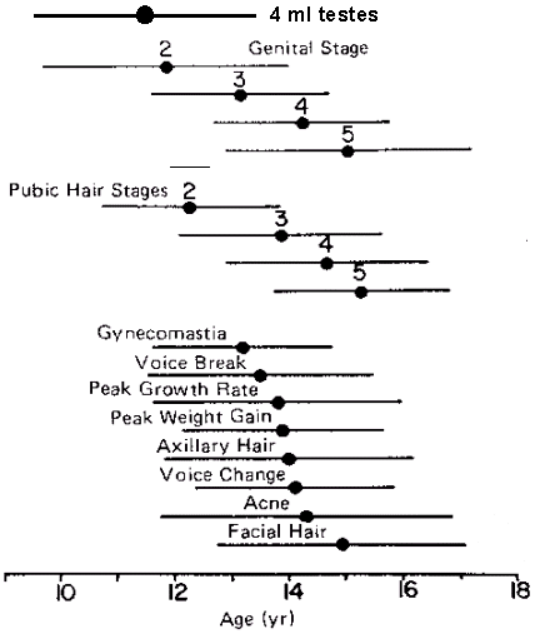
Adrenarche: Age 6 to 8 years
Menarche: Age 12.7 years (10.8-14.5 years)
Delayed >1 year if low body fat (e.g. athlete)

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



THERE IS NO EVIDENCE THAT MALE GENITAL PUBERTY IS BEING ACHIEVED AT AN EARLIER TIME: CHICKEN ESTROGEN THEORIES ARE WRONG AT LEAST AS FAR AS BOYS ARE CONCERNED



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: transspehnoidal 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

Parents and health professionals rate the child as having more problems than the children demonstrate on formal testing.

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.
less 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%),**
- **thyrotrope 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 (!!)**

achievement of optimal growth depends upon
- **nutrition,**
- **general health,**
- **emotional health,**
- **genetic factors**
- **hormones.**

- **!! 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.

the **two year delay** before the onset of the male growth spurt + 3 cm greater total growth during puberty accounts for the average 13 cm difference in final height between males and females. Thus, males spend longer in childhood growth phase, and their puberty is slightly more effective

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 youre 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

RELEASE 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

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

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

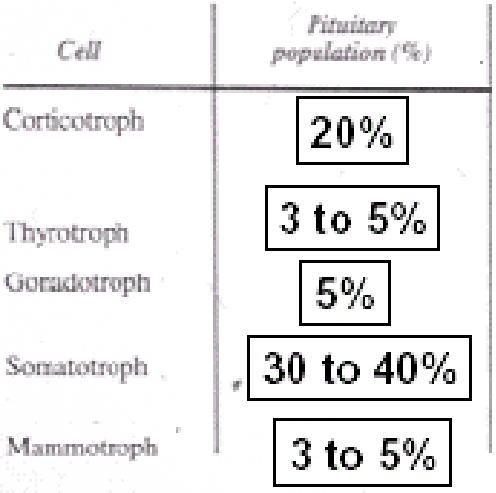
SOMATOMEDINS INDUCE INDIRECT CHANGES in most tissues
Anabolic + Mitogenic:
- INCREASE of amino acid uptake, thus
- INCREASE of protein synthesis
- THUS cartilage bone and muscle growth

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

glycoproteins



MICRO-ANATOMY

Pars distalis	winding cords of epithelial cells & fenestrated capillaries (helps hormone delivery into blood)	**Acidophils** (red stain) Lactotropes **(PRL)** somatotropes **(GH)** **Basophils** (blue) gonatotropes **(LH, FSH)** thyrotropes **(TSH)** corticotropes **(VPR)**
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

All ant. pituitary hormones use cAMP 2e messenger system

GH	*somatotropin*	(high %)
Prolactin	*mammotrop*	
LH	*lutropin*	
TSH	*thyrotropin*	
ACTH	*corticotropin*	
FSH	*follitropin*	

TSH

stim: **TRH**
also/ - cold weather
- pregnancy

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

effects: stimulates **thryoid gland** to release TH

excess: Grave's disease
defic: (child) cretinism
(adult) myxedema

GROWTH HORMONE

stim: ↓[GH]
also/
- estrogen
- hypoglycaemia
-↑ blood aa's
-↓ fatty acids
- exercise & stress
(all trigger **GHRH**)

inhib: ↑ GH and IGF (fb)
also/
- hyperglycaemia
- hyperlipidaemia
- emot. 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**
- fever (all trigger CRH)
- stress
- hypoglycemia

inhib: glucocorticoids (fb) inhib CRH

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

excess: Cushing's disease
cycle: peaks morning after rising (stress)

Gonadotropins

	FSH	LH
stim:	GnRH	GnRH
inhib: (fb)	♀ oestrogen ♂ testosterone inhibin	♀ oestrogen progesterone ♂ testosterone

effects: ovaries & testes

♀ ovarian follicle maturation
oestrogen production
♂ sperm production

♀ triggers ovulation
stim ovarian oestrogen & progesterone
♂ testosterone production (acts on Leydig cells)

excess: ♂ sexual dysfn / gynaecomastia
defic: no puberty
cycle: absent pre-puberty,
↑ puberty causing gonad maturation
↑↑ menopause

PROLACTIN

stim: oestrogens (♀) } → **PRH** → prolactin
contraceptive pill }
opiates }
lactation }

inhib: PIH (dopamine)
(predominates in non-pregnant life ♀ & ♂)
PRL (fb)

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: ♀ prolactin varies w oestrogen levels
↑ pre-menstrual period (breast swelling, tender)
pregnancy: oestrogens & progesterone counter PRL,

OXYTOCIN (OT)

oxytocia = childbirth

stim: cervical/uterine stretch } → hypothal → sythesis
suckling } →pit. Release

inhib: lack of stim

effects:
uterus: stim contractions (used to induce labour)
breast: triggers milk ejection
sensory signals (breast) → hypothal nuclei → ↑OT ↑VP → mammary gland
coitus: ↑ secretion, uterine contrxn propels semen
behaviour: "cuddle" hormone, nurture

cycle: ↑ seceretion & receptor no. at birth

POSTERIOR PITUITARY HORMONES

Storage of hormones made in hypothalamus and forwarded thru neurons.
Secreted in response to hypothalamic stimulus.

VASOPRESSIN, VP
(Antidiuretic hormone, ADH)

actions:

↑ blood osmolarity* → osmoreceptors (hypothal) → SON & PVN → ↑VP
↓
kidney tubules
← resorb water
-'ve fb ←

(V2r)

↓BP (baro-receptors) → hypothal → V1 (vascular sm musc) → ↑ bl vol ↓ urine → ↑ Ca DAG/IP3 → ↑ periph resist*

[*2% ↓ body water / 25% blood vol = max VP secretion]
[*VP also lowers HR, so no dramatic ↑ BP]
pressure drop is key, not volume

other stim: pain, drugs (nicotine)
inhib: alcohol, adequate hydration

defic: **Diabetes insipidus** – cell body destruction in hypothal / mutation VP gene (head trauma pts need monitoring in case damage to hypothal) (pit removal won't disrupt)
Px = thirst, freq urination
Rx = nasal VP

excess: childhood meningitis / post neuroSx / hypothal Ix / tumour
= **inappropriate ADH secretion syndome**
→ hypo-osmolar blood, brain oedema
→ fluid retention, headache, disorientation

Base of Skull: Home of the Cavernous Sinus

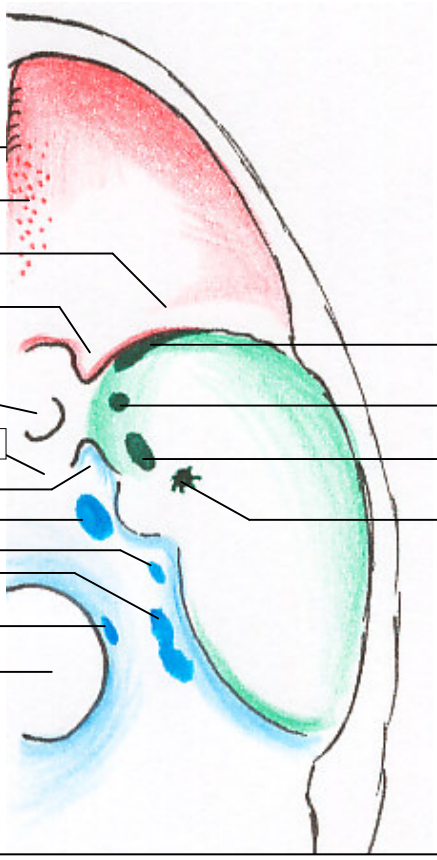
Anterior Cranial Fossa

- Crista Galli: Is the Anterior Attachment of Falx Cerebri
- Cribiform plate
- Lateral crest: deep inside lateral fissure
- Anterior Clinoid Process: Optic nerve emerges from under this process

Posterior Cranial Fossa

- Sella Turcica
- Dorsum sellae
- Posterior Clinoid Process
- Foramen Lacerum, for Internal Carotid
- Internal Acoustic Meatus
- Jugular Foramen
- Hypoglossal Canal
- Foramen Magnum

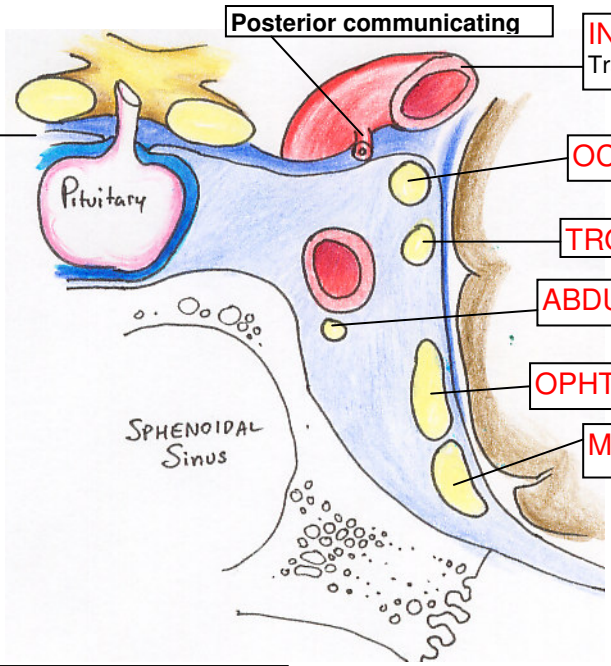
*PFC is roofed by the Tentorium Cerebelli



Middle Cranial Fossa

- Supraorbital fissure, for CNs 3, 4, 6 , + the opthlamic branch of CN 5
- Foramen Rotundum for Maxillary nerve (5)
- Foramen Ovale for Mandibular (5) + Lesser Petrosal (parasympathetic)
- Foramen Spinosum: for the **MIDDLE MENINGEAL ARTERY**

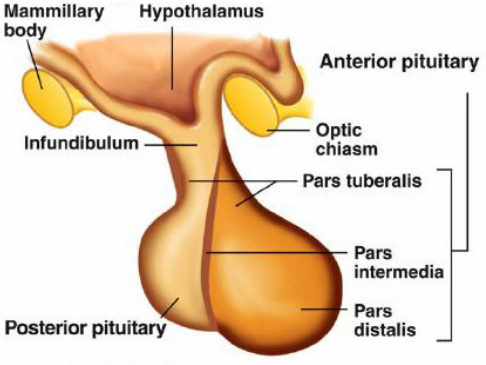
Roof of the pituitary fossa is the Sellar Diaphragm: Stretched between the clinoid processes like a trampoline.
ABOVE THAT: Chiasm, hypothalamus, 3rd ventricle



- **Posterior communicating**
- INTERNAL CAROTID Travels inside the sinus!
- OCULOMOTOR nerve
- TROCHLEAR nerve
- ABDUCENS nerve
- OPHTHALMIC branch of CN 5
- MAXILLARY branch of CN 5

NOW ABOUT THAT SINUS:

- **2 layers of dura**
- **Venous blood between**
- Contains numerous important things and frequently gets into trouble



← 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

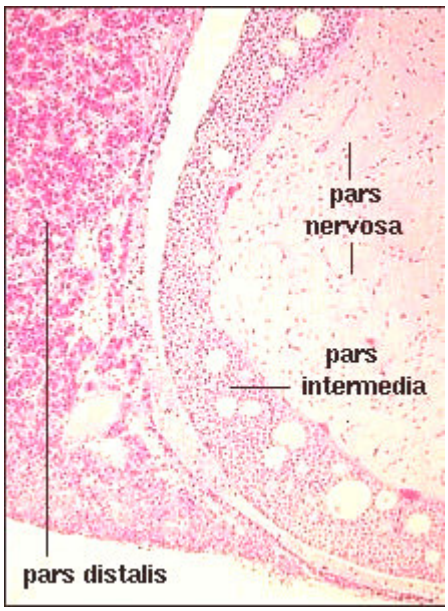
POSTERIOR: "pars nervosa" = contains axons of hypothalamic neurons and some glial cells

HORMONES STORED AT AXON TERMINALS

ANTERIOR: "pars Distalis" = glandular tissue, localised

hormone production

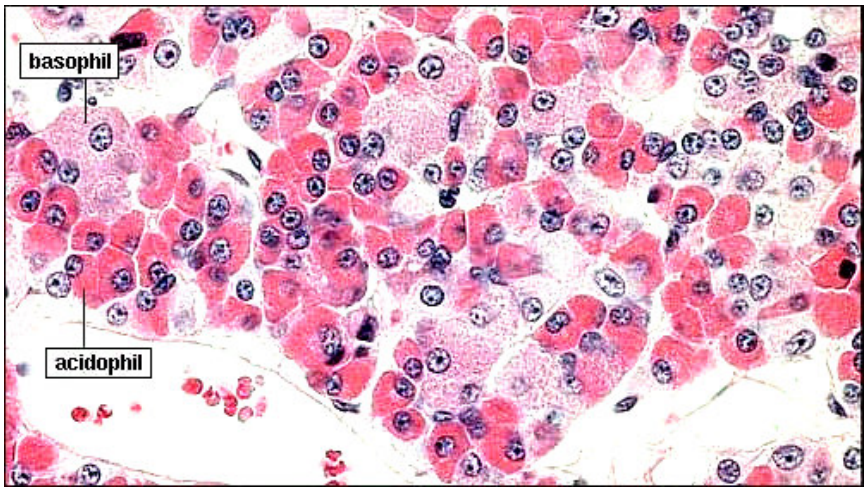
HISTOLOGY OF THE PITUITARY GLAND



ANTERIOR: pars distalis

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

BASOPHILS:	**ACIDOPHILS:**
Gonadotroph Thyrotroph Corticotroph	Lactotroph **Somatotroph**



pars intermedia contains large pale 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:

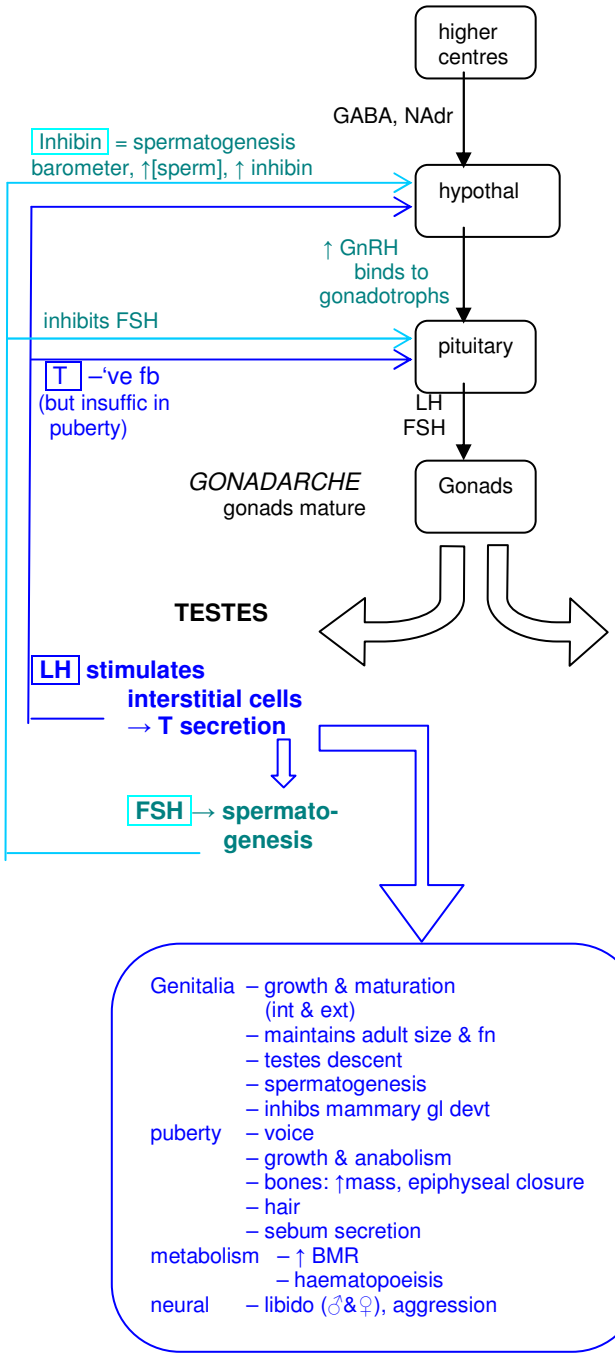
Stage	Normal growth	1° Determinants
PRENATAL: 9m	50cm (rapid) * 30% total linear growth achieved in utero 5% adult weight	foetal nutrition placental function maternal health in-utero infxn toxins genetics
INFANTILE: 1-3y	(rapid deceleration) rapid weight gain: birth wt x3 by 1y	nutrition genetics hormones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

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

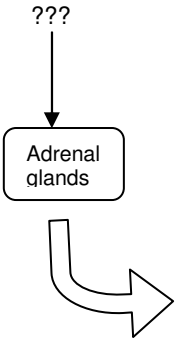
PUBERTY

= attainment of 2° sexual characteristics & reproductive capabilities

♀ : 8 – 13.5y
♂ : 9.5 – 14y



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 ♀

hair → pubic
→ axillary
acne
oily skin & hair
perspiration odour

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

MALE :

~ 9.5

- **emotional changes**
  metabolism: ↑ protein
  ↓ fat
  bone mineralisation
  ↑ **BP**
- **acne**
- **voice breaks**
  vocal cords lengthen
  enlarg't : larynx
  cricothyroid cartilage
  laryngeal mm

13.5

- **growth spurt** (max)
- **sperm production**
- **hair**: pubic → axillary → facial

endpoints:
voice changes
shaving
male musculature
epiphyseal closure

(1) testes 1-3ml (prepuberty)

(2) testes 4-8ml (early testicular)
penile & scrotal growth

Testicular changes
growth Seminiferous tubules
Sertoli cells mature
Seminal vesicles enlarge
↑ blood flow
penis 6.2cm → 12.4 cm

(3) testes 10-15ml
(4) testes 15-20ml
early sideburns

(5) testes 25ml
beard

DISORDERS OF PUBERTY

PRECOCIOUS PUBERTY (< 9.5y)

	True / Complete → [a] hypo-pit-gonads	**Pseudo** → [suppression] h-p-g	**Incomplete** → immature h-p-g
Cause:	CNS abn Genetic Idiopathic	ingestion sex steroids adrenal (tumour, CAH) gonadal tumour	
Px:	↑ LH, FSH, T large testes	↓ LH, FSH ↑ T small testes	premature adrenarche (virilisation) LH, FSH, T prepubertal small testes ~↑ DHEAS

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** (3° hypogonadism)	**Pituitary** (2°)	**Gonadal** (1°)
	- familial - childhood sickness - lesion affecting GnRH damage (tumour / trauma / infxn) - genetic GnRH defx	- lesion (tumour/trauma) - genetic defic	- lesion (torsion / trauma) - chromosomal - radiation / chemo - cryptorchidism
PX:	↓ LH, FSH, T (rise in LH, FSH with GnRH stim)	all ↓ (no rise with stim)	↑ LH, FSH ↓ T

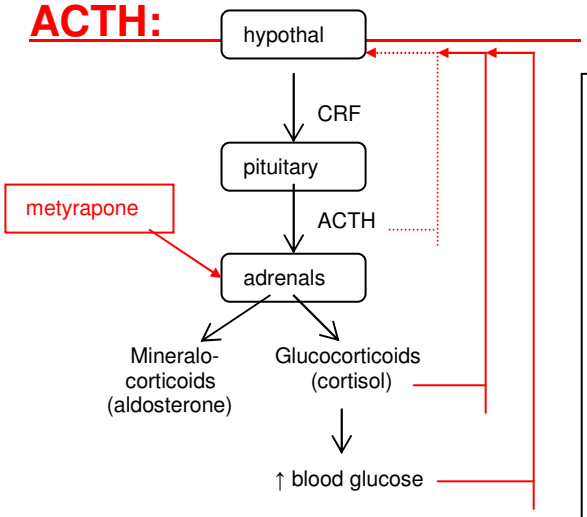
GYNAECOMASTIA

types:
- 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

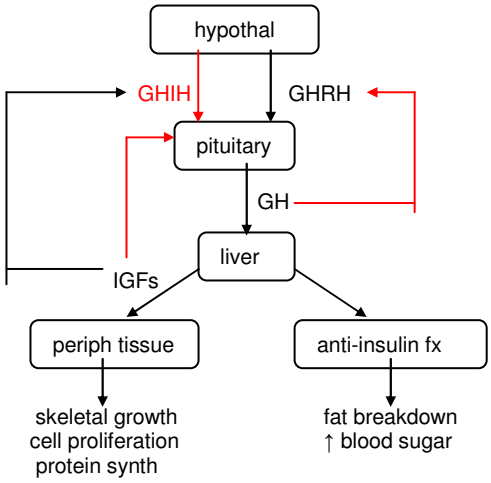
Insulin → -'ve feedback health
↓ blood glucose

*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

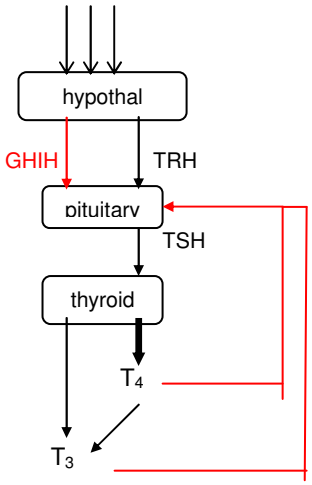
GHRH → pituitary health
L-dopa → " "

↓ 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



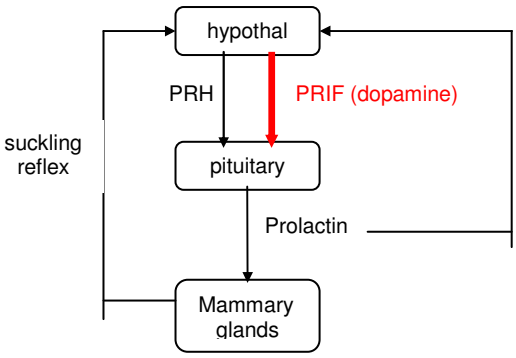
INDICATIONS:
diagnosis / screening thyroid disorder
monitor → hormone Rx
→ ♀ infertility probs

TSH → pit & thyroid health
T3 (may be spot-checked as less pulsatile secretion)
T4
TRH stimulation → pituitary health

↑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

PROLACTIN :



INDICATIONS:
↑ prolactin signs
investigs → infertility (♂ & ♀)
→ ↓ testosterone (♂)

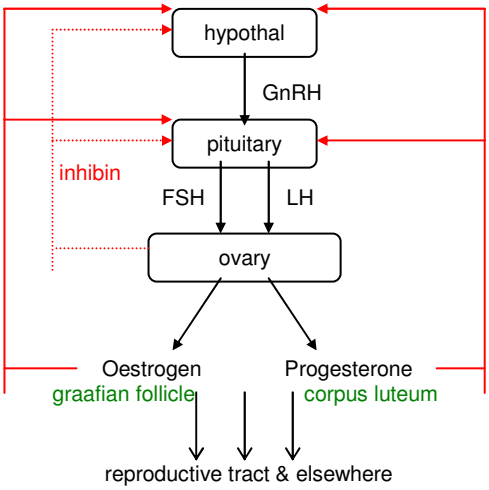
Prolactin → pituitary health
(spot test)

PRH → pit health

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

GONADOTROPINS

female :



INDICATIONS:
suspicion thyroid disorder
infertility
irreg menstruation
early/late puberty
menopause confirm

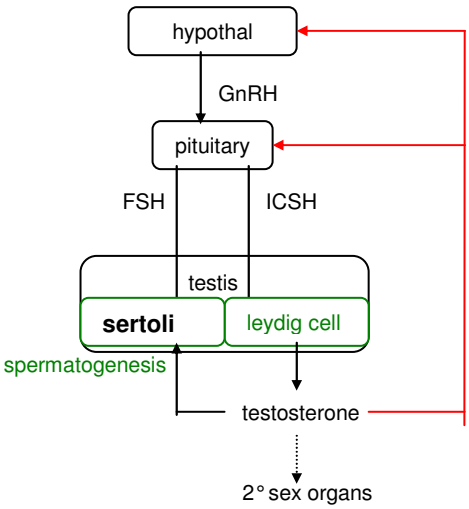
FSH, LH (ICSH) levels → gonad health
→ pituitary health

GnRH stimulation → pituitary health

↑FSH, LH → hypersecretion → pituitary adenoma (rare)
→ ovary failure → devt dfx → agenesis
→ chromosomal (Turner's)
→ steroidogenesis dfx
→ damage → radiation / chemoRx
→ autoimmune
→ failure to ovulate → polycystic ovary
→ thyroid disease
→ adrenal disease
→ tumour
→ menopause

↓FSH, LH → pituitary / hypothal failure

Male :



INDICATIONS:
cause of ↓ sperm count
infertility
early/late puberty

↑FSH → no –'ve fb → testicular failure → devt defx → agenesis
→ chromosomal (Klinefelter's)
→ viral infxn (mumps)
→ trauma
→ radio / chemoRx
→ autoimmune
→ tumour

↓FSH → ↓ secretion → pit / hypothal prob

* ↑ FSH, ↑LH in children → precocious puberty

General:

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

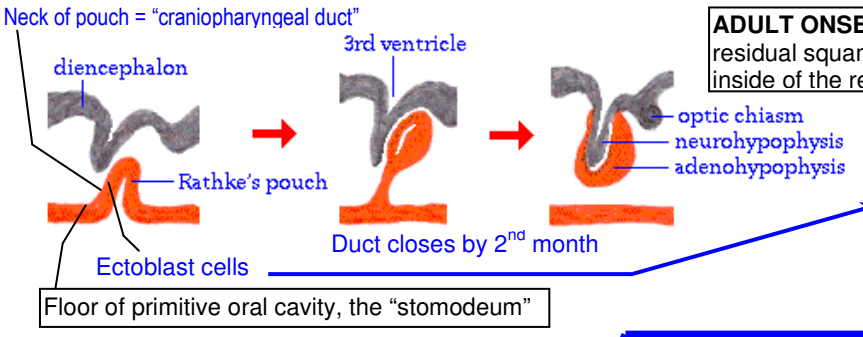
Adrenal → MRI / CT

Thyroid → ultrasound
→ radioactive I scan
→ FNAB

Gonads

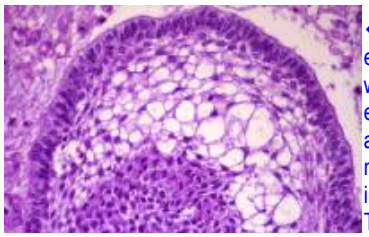
USE OF HORMONE TESTING
- diagnosis of disorder
- long term monitoring of Rx
- tumour recurrence monitoring (post-op)

Mechanism of Craniopharyngioma and Hypopituitarism 7.02



ADULT ONSET: metaplasia of residual squamous cells on the inside of the remaining duct

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.



← complex histology: epithelial-looking cells with palisading at the edges of the lesion and scattered nodules of "wet" immature keratin. The surrounding brain parenchyma is filled with densely packed glial filaments, which is apparently a normal astrocyte response to chronic compression. THE BLOOD BRAIN BARRIER IS BROKEN.

~ENDOCRINOPATHY~

Invading 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

→ **CHUBBYNES**

MUSCLES:
- Reduced protein synthesis

→ **LETHARGY & WEAKNESS**

LIVER
Reduced protein synthesis
Reduced gluconeogenesis (pro-insulin activity)
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**

Tissues in general:
DECREASED RATE OF DNA & RNA SYNTEHSIS and thus REDUCED RATE OF MITOSIS
Therefore:
REDUCED TISSUE GROWTH and ORGAN SIZE

Low TSH

Thus: tertiary HYPOTHYROIDISM→
Reduced fat mobilisation via lipolysis
Reduced heart rate
Reduced metabolic rate
!! reduced adrenoceptor expression and activity !!
THUS:
Reduced attention
Reduced alertness
Reduced memory formation

→ **POOR SCHOOL PERFORMANCE**

Low LH+ FSH

Both sexes: Reduced secretion of TESTOSTERONE

MALE: Cant produce normal sperm
FEMALE: Cant ovulate

No androgens except what the maturing adrenals can produce (weak androgens, "gonadocorticoids")
THUS → NO PUBERTY

NO PUBIC HAIR
TINY USELESS TESTES
NO CHANGE IN VOICE
NO SEXY MAN-STINK
(hypothetically, no pheromones)

MICROADENOMA: Incomplete filling of the sella; therefore no tell-tale neuro signs

MACROADENOMA: Over 10mm→ Compression of the suprasellar diaphragm and **OPTIC CHIASM:**

→ **BITEMPORAL HEMIANOPIA**

TUMOUR > 1.5cm
→ mass effects cause headache (increase in pressure by 20mmHg is enough to cause headache by compressing soft venous walls

LOCAL INVASION:
→ into the cavernous sinus:
THUS → cranial nerve signs

→ into hypothalamus
THUS → autonomic dysf(n)

→ through the wall of the 3rd ventr.
THUS → hydrocephalus

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