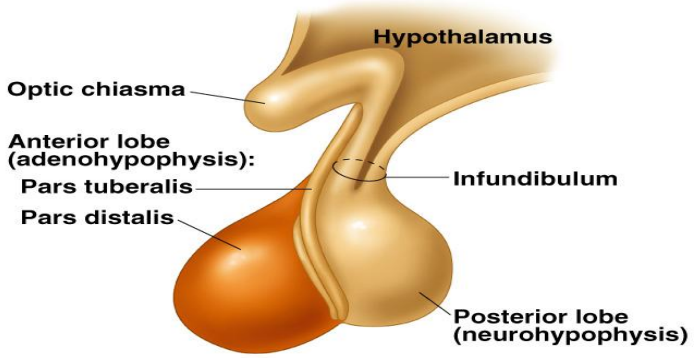
Endocrine Physiology Outlines
The Pituitary gland
The Hypothalamic control

The Pituitary gland (hypophysis):

- Master gland, as it's the site of coordination of endocrine & nervous systems.
- Small gland (≈ 1cm diameter; ≈ 0.5 to 1 gm weight)
- Lies in *sella turnica*, a bony cavity at the base of the brain.
- Connected to the hypothalamus by the pituitary stalk or (hypophysial; infundibulum).
- Structurally & functionally divided into 2 lobes:
  1) Anterior lobe (2/3),
  2) Posterior lobe (1/3).



1) The anterior pituitary lobe

- Called 'Adenohypophysis'.
- Consists of 2 parts (in adults):

  1. Pars distalis … known as the anterior pituitary

  Rounded portion & major endocrine part of the gland.

  2. Pars tuberalis … thin extension in contact with the infundibulum.

- **Pars intermedia…**

  Avascular tissue b/w anterior & posterior lobes, exists <u>in fetus</u> (no longer present in adults). Much more functional in some lower animals, such as fish, amphibians, & reptiles.

The anterior pituitary gland cells:

- Embryologically, its derived from a pouch of epithelial tissue (*Rathke's pouch*), that is derived from pharyngeal epithelium (mouth).
- Histologically, it contains many types of secretary cells (Chromophils):

  I: Acidophils (epsilon ε)
  1) Somatotropes – (hGH) … ≈ 30-40%
  2) Lactotropes – (PRL) ≈ 3-5%

  II: Basophils (delta δ)
  1) Corticotropes – (ACTH) … ≈ 20%
  2) Thyrotropes – (TSH) ≈ 3-5%
  3) Gonadotropes – gonadotropic hormones (LH, FSH) ≈ 3-5%

(at least one cell type for each major hormone)

2) The posterior pituitary lobe

- Is the neural part of the pituitary gland.
- Called 'Neurohypophysis'.
- Consists of **pars nervosa**, also called the posterior pituitary.
- Embryologically, its derived from a down growth of the hypothalamus.
- In contact with the infundibulum & adenohypophysis.

❖ Relationship between hypothalamus & pituitary gland

- Almost all secretions by the pituitary are controlled by either <u>hormonal</u> or <u>nervous</u> signals from hypothalamus.

❖ I: Hypothalamic Control of Anterior Pituitary Gland

- **Relationship between hypothalamus & anterior pituitary gland**
  - There are both anatomical & physiological relationship:

a: Anatomical relationship:

- Anterior pituitary gland is connected to hypothalamus by portal system: "hypothalamic-hypophysial portal vessels".
- <u>Remember</u>: Anterior pituitary gland is NOT innervated by hypothalamus.

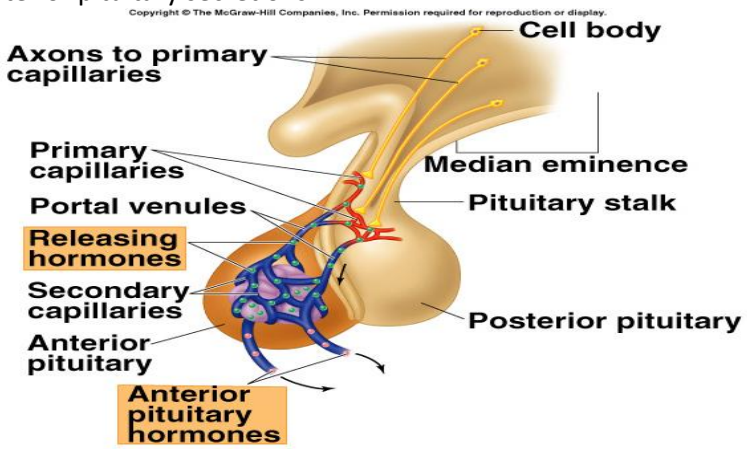
b: Physiological linkage → discovered by Harris in 1947.

- Hypophysectomized (removed pituitary gland) of the animals, & divided them into 2 groups:

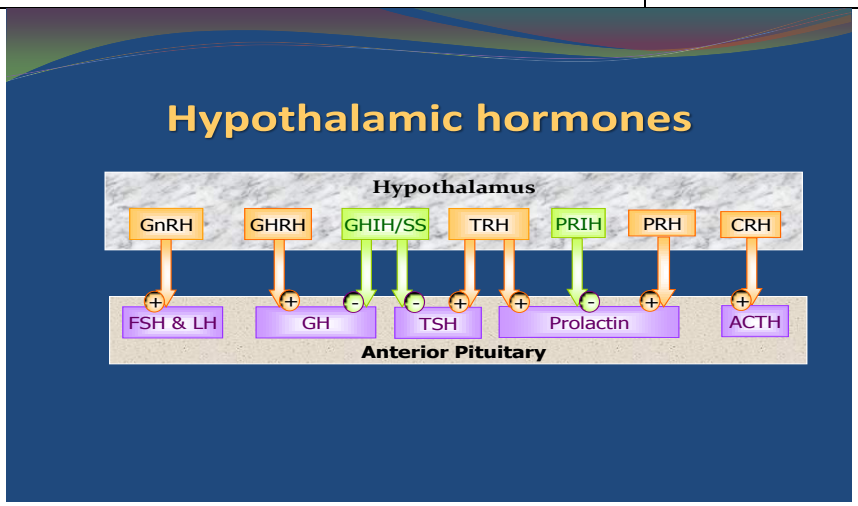
Group 1: Transplanted new pituitary below the hypothalamus (normal position): → a. new blood vessels developed between hypothalamus & new pituitary gland;
b. Pituitary was living & provided its normal functions.

Group 2: Transplanted new pituitary into either kidney or eye:
→ a. Pituitary was living;
b. Does not function normally (since blood from hypothalamus to kidney or eye is not direct & is diluted with blood of other tissues).

- Hypothalamus secrete hormones called "hypothalamic releasing & inhibitory hormones" that regulate the anterior pituitary secretions.

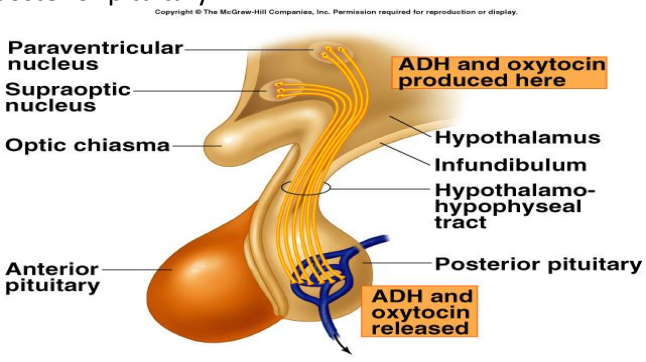


no	Hormones	Effect on Ant Pituitary
1.	Thyrotropin-releasing hormone (TRH)	(+) TSH & Prolactin
2.	Corticotropin-releasing hormone (CRH)	(+) ACTH
3.	Growth hormone releasing hormone (GHRH)	(+) GH
4.	Growth hormone inhibitory hormone (GHIH) "Somatostatin (SS)"	(-) GH (-) TSH
5.	Gonadotropin-releasing hormone (GnRH)	(+) Gonadotropic hormones (LH, & FSH)
6.	Prolactin releasing hormone (PRH)	(+) Prolactin
7.	Prolactin releasing inhibitory hormone (PRIH) "Dopamine"	(-) Prolactin



❖ II: Hypothalamic Control of Posterior Pituitary Gland

- **Relationship with the posterior pituitary gland**
  - Posterior pituitary gland is connected to hypothalamus by "unmylenated" nerve fibers.
  - Cell bodies of the nerves that secrete posterior pituitary hormones are <u>located in</u> supraoptic & paraventricular nuclei of hypothalamus , & <u>NOT</u> in posterior pituitary gland itself.
  - Nerve fibers extend through the infundibulum along with small neuralgia-like cells called pituicytes to the posterior pituitary.



- Hormones are then transported to the posterior pituitary gland in the axoplasmic flow of the neuron's nerve fibers passing from hypothalamus to be stored in the posterior pituitary gland.

❖ **Control of Hypothalamic Secretions**

- **Neural signals:** e.g. pain, depression, exciting, smell, etc.
- **Hormonal concentration feedback mechanism:**
- **Chemical stimuli:** such as nutrients, electrolytes, & water concentrations in the blood.

❖ **General Functions of the hypothalamus**

1. Controls body temperature.
2. Controls the cardiovascular system.
3. Controls food intake & body weight.
4. Controls thirst & water balance.
5. Involved in sleep & wakefulness.
6. Involved in emotional reactions.
7. Involved in reactions to stress.
8. Controls ovarian secretions during ovarian cycle.
9. Controls testicular secretions.

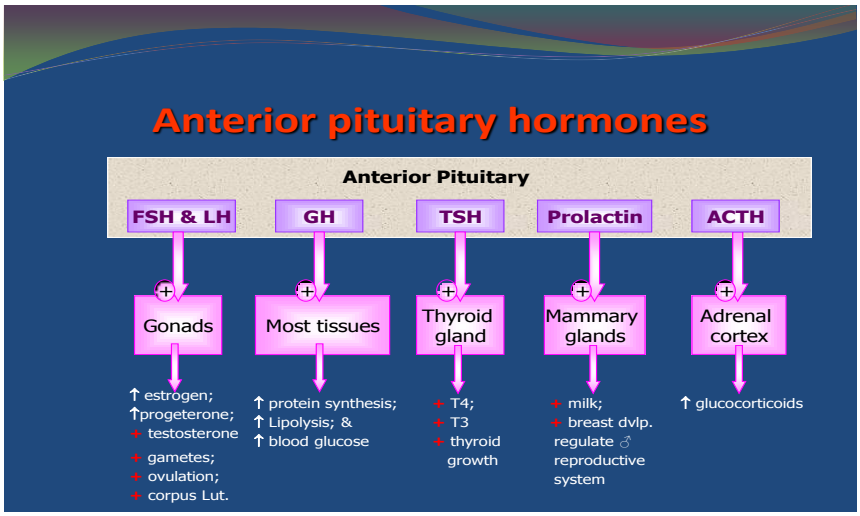
Anterior Pituitary Gland hormones

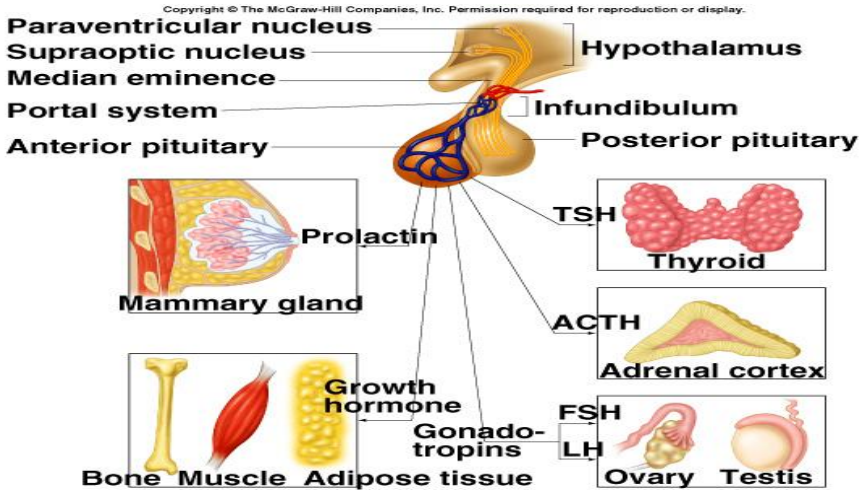
- Called **trophic** hormones; 'trophic' means "feed".
- **High** blood [hormone] causes target organ to hypertrophy.

  Low blood [hormone] causes target organ to atrophy.
- When names applied to the hormones, it is shortened to '**tropic**', meaning "attracted to". That's why APH end with the suffix **–tropin**.

Anterior Pituitary Hormones

Hormones	Target tissue	Principal action
1. Growth hormone (GH, or somatotropin)	**Most tissue**	**(+) protein synthesis & growth; lipolysis;↑ blood glucose**
2. Thyroid-stimulating hormone (TSH, or thyrotropin)	**Thyroid gland**	**(+) thyroid hormones**
3. Adrenocorticotropic hormone (ACTH, or corticotrophins)	**Adrenal cortex**	**(+) glucocorticoids**
4. Follicle-stimulating hormone (FSH, or folliculotropin)	**Gonads**	**(+) gamete production, (+) estrogen in females**
5. Luteinizing hormone (LH, or luteotropin)	**Gonads**	**(+) sex hormones; ovulation & corpus luteum formation in females; (+) testosterone in males**
6. Prolactin (PRL)	**Mammary glands**	**(+) milk in lactating females; regulates male reproductive system**





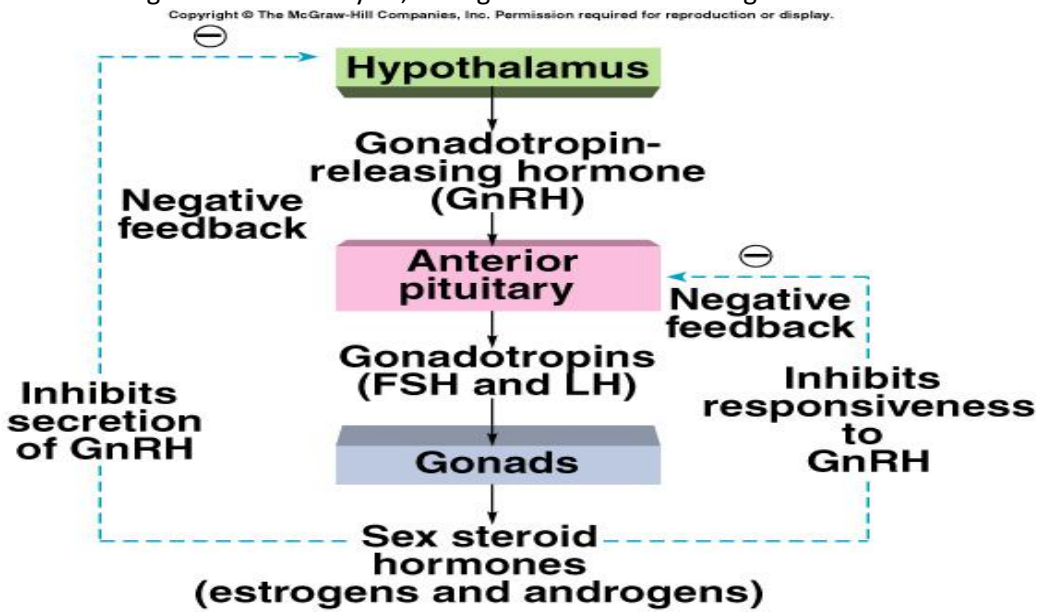
❖ **Pars intermedia:**

- **<u>In fetus & some lower animals</u>,** secretes melanocyte - stimulating hormone (MSH).
- **<u>In adults</u>:** Some cells of adenohypophysis are derived from fetal pars intermedia → a large polypeptide prohormone called pro-opiomelanocortin (POMC), whose major products are β-endorphin, MSH, & ACTH.

♦ **Feedback Control of the Anterior Pituitary**

- Anterior pituitary & hypothalamic secretions are controlled by negative feedback inhibition by their target gland hormones.
- **Negative feedback at 2 levels:**
  - Target gland hormone can act on the hypothalamus & inhibit secretion of its releasing hormones.
  - Target gland hormone can act on the anterior pituitary & inhibit its response to the releasing hormone.
  - **Short feedback loop:**
    - Retrograde transport of blood from anterior pituitary to the hypothalamus.
      - Hormone released by anterior pituitary inhibits secretion of releasing hormone.

- **Positive feedback effect:**
    - During the menstrual cycle, estrogen stimulates "LH surge."



♦ **Higher Brain Function and Pituitary Secretion**

- Axis:
    - Relationship between anterior pituitary and a particular target gland.
        - Pituitary-gonad axis.
- Hypothalamus receives input from higher brain centers.
    - Psychological stress affects:
        - Circadian rhythms.
        - Menstrual cycle.

❖ Growth hormone (GH)

- Also called "Somatotropic hormone" or "Somatotropin".
- A small protein molecule that contains 191 amino acids in a single chain.
- It has great effect in growth & metabolism.
- It acts on muscles, liver & adipose tissue
- It effects will be on all cells of the body throughout life.
- Synthesized in the ER of the glandular cells as preprohormone, & stored in secretory vesicles in its active form until stimulated.
- Dissolve freely in the blood.
- Its receptors are found on or in the cell membrane of the target cells.
- It stimulates the G-proteins in the membrane of target cell, which stimulate (2) second messenger systems:
    1. adenyl cyclase → cAMP.
    2. phospholipase C → IP_3/ Ca^{2+}

Functions of growth hormone:

A) Promotion of growth:

✓ It ↑ cellular sizes & ↑ mitosis (no.)

- ✓ It ↑ tissue growth & organ size.
- ✓ GH does not act directly on bone & cartilage.
- ✓ Depends on somatomedin C (also called 'insulin – like growth factor I' [IGF-I] secreted by the liver. It is responsible for the effect of GH on bone & cartilage growth.

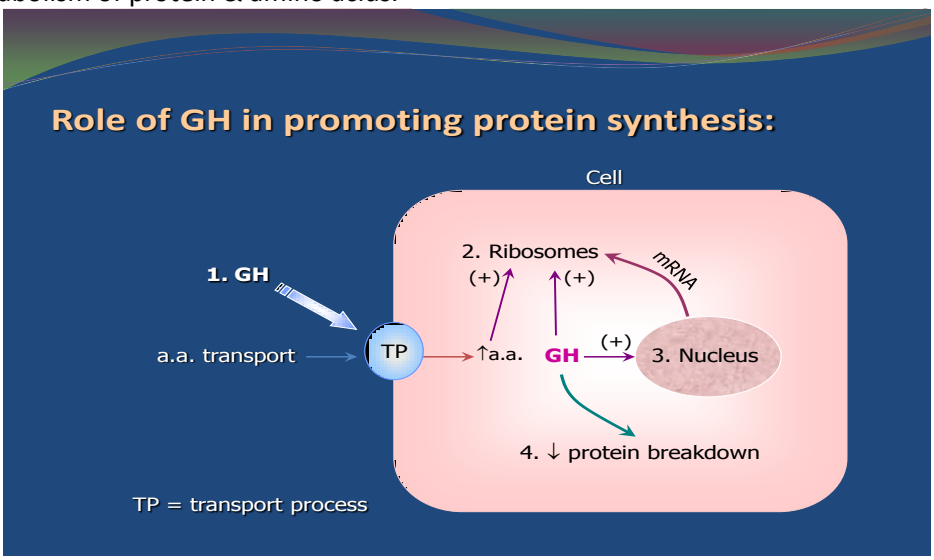
- ***In vivo* experiment:**
  GH → growth & development of cartilage.
- ***In vitro* experiments:**
  GH in tissue culture of cartilage → poor development of bone & cartilage; while adding sulphation factor (growth factor) enhanced the growth.

2 mechanisms of bone growth:

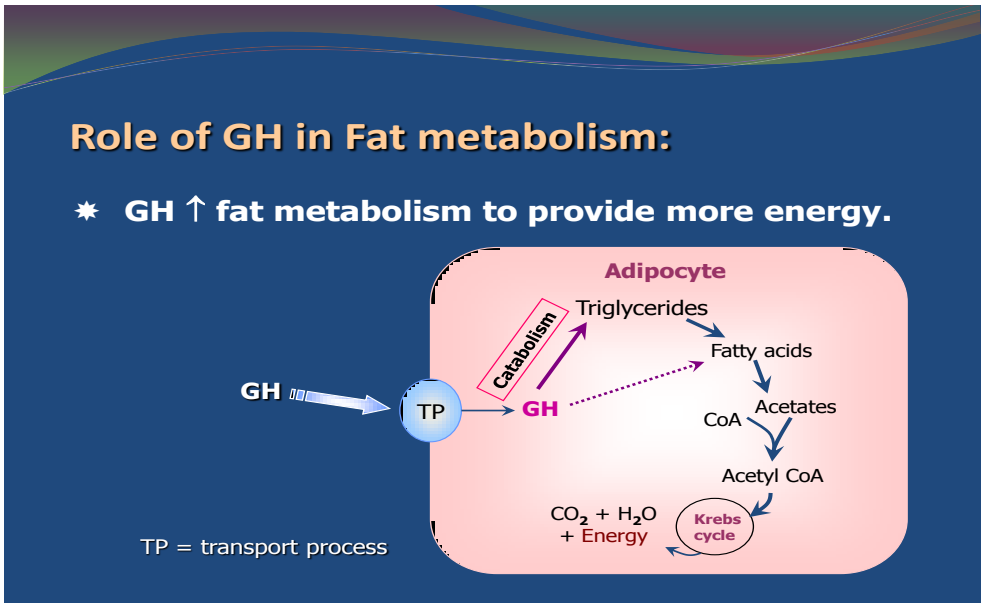
1. Linear growth of long bones:
   - Long bones grow in length at epiphyseal cartilages, causing deposition of **New Cartilage** (↑collagen synthesis) followed by its conversion into bone.
   - When bony fusion occurs between shaft & epiphysis at each end, no further lengthening of long bone occur.
2. Deposition of **New Bone** (↑ cell proliferation) on surface of older bone & in some bone cavities, increasing thickness of bone.
   - Occurs in membranous bones, e.g. jaw, & skull bones.

B) Short- term metabolic effects:

1. Protein metabolism: Anabolic, ↑ rate of protein synthesis in all cells by:
- Enhancement of amino acid transport through the cell membranes.
- Enhancement of RNA translation to cause protein synthesis by the ribosomes.
- ↑ nuclear transcription of DNA to form RNA.
- ↓ catabolism of protein & amino acids.



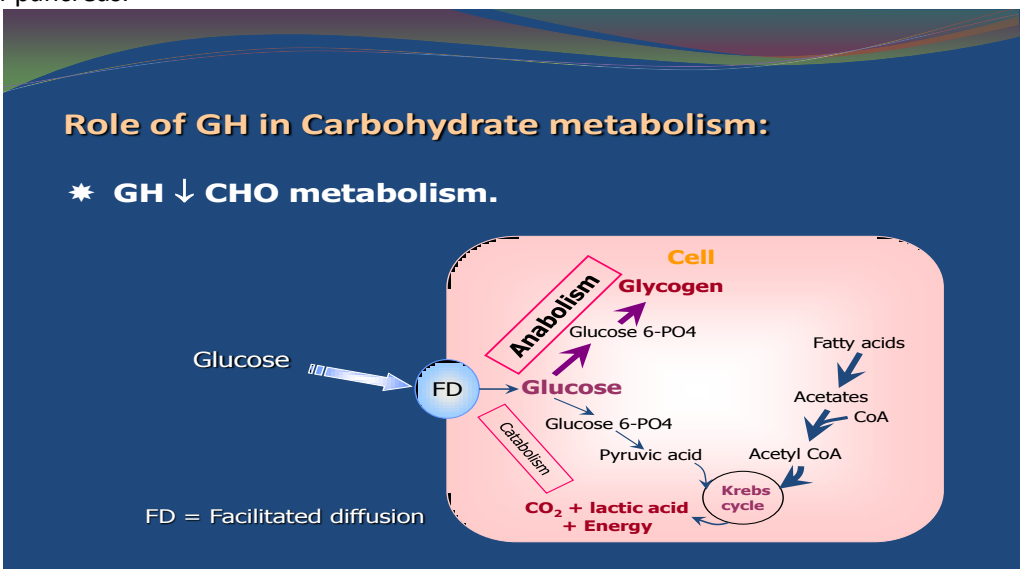
2. Fat metabolism: Catabolic, GH enhances fat utilization for energy.
- Acts on fat cells (adipocytes) to release fatty acids from the triglycerides to the blood.
- Produces several 2 carbon fragments (acetates).
- Formation of acetyl- CoA.
  [acetate + Co-enzyme A (Co-A) → acetyl-CoA].
- Acetyl-CoA enters Krebs cycle to produce CO_2 + H_2O + Energy.

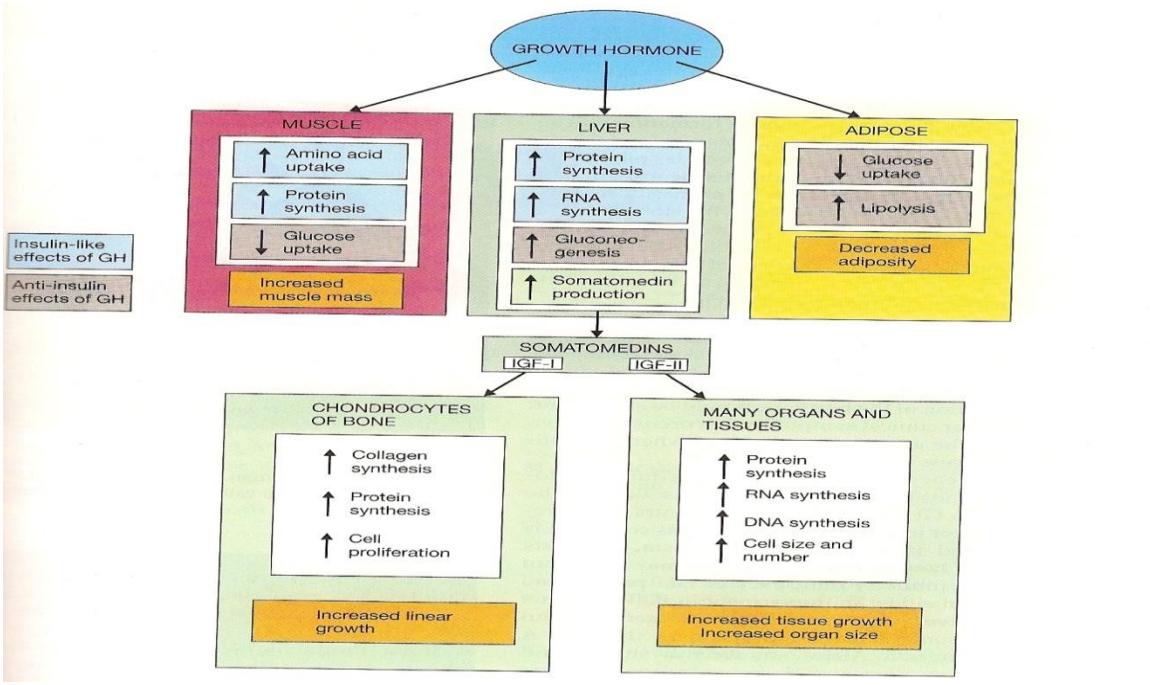


3. **<u>CHO metabolism</u>:** Hyperglycemic, ↓ rate of glucose utilization throughout the body:
   - Enhancement of glycogen deposition in the cell.
   - Diminished uptake of glucose by the cells & ↑ blood glucose concentration – " Pituitary Diabetes".
   - ↓ use of glucose for energy.
   - ↑ secretion of insulin – Diabetogenic effect of growth hormone.

N.B.

- ✓ Usage of fat by Kreb's cycle reduces glucose breakdown.
- ✓ Cells build up glycogen up to certain limit.
- ✓ Glucose concentration ↑ intracellularly until equilibrium with ECF.
- ✓ This block glucose entry into the cell.
- ✓ Blood glucose will ↑ with next meal, which promotes insulin secretion till exhaustion of β cells of pancreas.





Control of GH secretion:

1. The hypothalamus:
   a. GHRH → ↑ GH secretion.
   b. GHIRH (somatostatin) → ↓ GH secretion.
2. Hypoglycemia → ↑ GH secretion.
   (N.B. glucose intake → ↓ GH secretion).
3. Muscular exercise → ↑ GH secretion.
4. Intake of protein or amino acids → ↑ GH secretion.
5. During sleep → ↑ more in children.
6. Stress conditions, e.g. trauma or emotions → ↑ GH secretion.
7. Drugs: glucagon, lysine-vasopressin & L-Dopa → ↑ GH secretion.
8. FFAs → ↓ GH secretion.

Requirement for GH promoting actions:

1. Normal thyroid function.
2. Normal insulin.
3. Sex hormones → necessary for growth during adolescence.

Abnormalities of GH secretion

1. <u>Panhypopituitarism</u>:

= ↓ secretion of all anterior pituitary hormones.

Causes:

a. <u>'in children'</u>:

- ? congenital 'from birth'; or
- ? occur suddenly, or slowly at any time during life.

b. <u>'in adults'</u>:

- ? tumorous conditions, e.g. pituitary adenoma, craniopharyngioma, chromophobe tumors, or shpenoid meningioma; or
- ? thrombosis of pituitary vessels; or
- "Sheehan's syndrome", where pituitary necrosis occurs following post-partum hge. → ↓ THs & prolactin → Mother can't lactate.
- ? hypophysectomy, or pituitary irradiation.

➢ **Signs & symptoms 'in children':**

- Dwarfism (stunted growth), results mostly from panpituitarism.
- Sexual immaturity … (child will not pass through puberty); due to ↓ gonadotropic hormones (LH & FSH).
- Mental development will not be affected.

▪ **<u>Treatment</u>:** human growth hormone.

➢ **Signs & symptoms 'in adults':**

- Lethargic, as a result of ↓ THs.
- Gaining weight due to lack of fat mobilization, as a result of ↓ GH, ↓ ACTH, & ↓ THs.
- Gonadal dysgenesis.
- Loss of all sexual fxs.
- Bone & metabolic diseases.
- Constitutional delayed growth.
- Achondroplasia.

▪ **<u>Treatment</u>:** Except for abnormal sexual fxs, Pt can be treated by ACTH & THs in order to compensate metabolism.

✸ **Abnormalities of GH secretion**

2. <u>↑ GH secretion</u>:

➢ **Causes:**

Occurs as a result of ↑ activity of the acidophilic GH- producing cells of anterior pituitary gland; or due to acidophilic tumors in the gland.

➢ **Signs & symptoms 'in childhood':**

- **Gigantism,** as all body tissues grow rapidly, including bones. Height ↑ as it occurs before epiphyseal fusion of long bones w their shafts.
- **Hyperglycemia (Pituitary diabetes).**

▪ **Treatment:** Microsurgical removal of pituitary gland tumor; or irradiation of the gland.

➢ **Signs & symptoms 'in adults':**

- **Acromegally**,
  - if acidophilic tumor occurs after adolescence, person can't grow taller, BUT soft tissue continue to grow in thickness (skin, tongue, liver, kidney, …)
- Enlargement of bones of hands & feet.
- Enlargement of membranous bones including cranium, nose, forehead bones, supraorbital ridges.

- Protrusion of lower jaw.
- Hunched back (kyphosis) (enlargement of vertebrae).

Prolactin hormone (PRL):

- Hormone secreted from anterior pituitary gland, in both males & females.
- PRL is protein in structure that contains 199 amino acid residues & 3 disulfide bridges.
- Its half life is like GH, which is ≈ 20 min.
- PRL receptors are found in or on the cell membrane & resemble that of GH.
- PRL acts by activating intracellular enzyme cascades which involves increased action of mRNA, that ↑ production of casein & lactalbumin.
- Normal plasma concentration of PRL: ≈ 5 ng/mL … in men, ≈ 8 ng/mL … in females.

➢ **Action of Prolactin**

1. PRL promotes mammary glands & ducts growth & development.
2. PRL promotes milk production.
3. PRL inhibits the effects of gonadotropins (GnRH), which are secreted by the hypothalamus. Possibly by an action at the level of the ovary. Accordingly, it suppresses the female ovarian cycle by inhibiting ovulation.
4. PRL plays a supporting role in regulation of male reproductive system by gonadotropins.
5. PRL acts on kidneys to help regulating water & electrolyte balance.

➢ **Control of Prolactin secretion**

1. The hypothalamus:
a. PRH → ↑ PRL secretion.
b. PIH (Dopamine) → ↓ PRL secretion.

2. Hormones: e.g.
a. estrogen → ↓ PRL; as a result of direct action on lactotropes, in addition to + PIH & block mammary glands stimulation by prolactin.
b. progesterone → ↓ PRL; by + PIH & ↓ milk secretion.
c. Cortisol → ↑ PRL.
d. TRH, & TSH → ↑ PRL secretion.

3. Pregnancy → ↑PRL; fell down to normal level 8 days after delivery.
4. Suckling reflex → ↑ PRL secretion.
5. Stress conditions, e.g. emotions, surgery, trauma, pain → ↑ prolactin.
6. Exercise → ↑ PRL.
7. Sleep → ↑ PRL.
8. Drugs, e.g. L-Dopa → ↓ PRL, by ↑ formation of dopamine.

✸ **Abnormalities of Prolactin secretions**
decreased prolactin secretion:

- **↓ prolactin, as in "Sheehan's syndrome"** → failure of lactation.
- **Treatment:** 'Chlorpromazine' & related drugs, block dopamine receptors & cause ↑ PRL secretion.

✸ **Abnormalities of Prolactin secretions**

Hyperprolactinemia:

- ↑ **prolactin,** 70% of patients have 'chromophobe adenoma', which is an adenoma of pituitary gland:

*** Female:** - Galactorrhea (↑ milk production)
- hypogonadism.
- 2ry Amenorrhea (No menestruation) … 15-20%

*** Male:** - Gynacomastia (breasts like females)
- hypogonadism.
- infertility (as prolactin ↓ GnRH)
- impotence

- **Treatment:** Dopamine agonists, e.g. 'bromocriptine', which binds to dopamine receptors & promotes dopamine action (since ↑ dopamine secretion in hypothalamus will ↓ prolactin secretion.)

The posterior pituitary gland

- Terminal organ of CNS neurosecretary system.
- Cell bodies are in the hypothalamus SON & PVN, where hormones are produced.
- Hormones are transported by Non-myelinated axons of neurosecretary cells.
- Hormones are stored in 'Herring's bodies' in posterior pituitary, which are swelling of neurosecretary fibers, into the close capillaries.
- Hormones are released by exocytosis in response to membrane depolarization.
- Composed mainly of cells called 'Pituicytes', which are similar to neuroglia, & act as packing & supporting cells.

❖ **Blood supply to the posterior pituitary gland**

- Arteries: inferior hypophysial arteries derived from internal carotid arteries.
- Veins: posterior hypophysial veins.

❖ **The posterior pituitary gland hormones**

- **Posterior pituitary gland releases 2 hormones:**
  1. Antidiuretic hormone (ADH), or arginine vasopressin (AVP).
  2. Oxytocin
- Both are polypeptides containing 9 aa, differ by only 2 aa.
- Both have ring structure.
- Both hormones are produced in hypothalamic nuclei:
  - Supraoptic nucleus → (ADH + 1/6 oxytocin)
  - Paraventricular nucleus → (Oxytocin + 1/6 ADH)
- Each is a product of a prohormone.
- After cleavage:
  - Oxyphysin → oxytocin & neurophysin I
  - Pressophysin → vasopressin, neurophysin II & glycopeptide

- Both are transported slowly along the 'hypothalamo-hypophyseal tract' in combination with carrier protein called 'Neurophysin', to the nerve endings in the posterior pituitary gland where they are stored.
- Both travel in blood unbound.
- Both have a t1/2 ≈ 2-3 min.
- Genes are on the same chromosome (Chromosome 20).

1. ADH (vasopressin):

- Is produced mainly in **SON** of hypothalamus.
- Extra-neurak sources of vasopressin:
  - Gonads.
  - Adrenal cortex.
  - Platelets.

➢ **Action of ADH**

- Stimulated in response to increased plasma osmolality.
- Other factors stimulate ADH secretion:
  1. Decreased arterial blood pressure, due to decreased blood volume.
  2. Age → water retension & hyponatremia.
  3. Pain, emotional stress & physical trauma → increase endogenous opioids.
  4. Postural changes.
  5. Angiotensin II induces thirst.
  6. Drugs, e.g. morphine, barbiturates & nicotine
  7. Estrogen & progesterone
  8. Increased body temperature
  9. Alcohol → decrease ADH secretion.

➢ **Mechanism of Action**

- Four subtypes of receptors identified.
- All G protein-coupled.
- V1 – smooth muscle in vascular tissue; V1a (liver), V1b, V3 (anterior pituitary).
- V2 – renal collecting ducts.
- Activates (2) second messenger systems:
  1. cAMP,…(kidneys)
  2. IP_3/Ca^{2+}, …(vessels)

➢ **Action of ADH (Effect)**

1. Osmoregullation:
   By promoting water re-absorption (retention) by distal tubules & collecting ducts of the kidneys → decrease osmotic pressure of the blood.
   ***** This effect is regulated by V_2 receptors, through the action of cAMP.
2. Regulation of blood volume-blood pressure:
   By inducing contraction of certain types of vascular smooth muscles → generalized vasoconstriction.
   ***** This effect is regulated by V_1 receptors, through the action of IP_3/Ca^{2+}.
3. Effects on anterior pituitary:

- ❑ ADH present in median eminence
- ❑ Enhances CRH-stimulated ACTH secretion
- ❑ ↑ cortisol secretion → ↑ sympathetic activity → ↑ BP
- ❑ Equipotent with TRH in stimulating TSH secretion

4. ADH as a neurotransmitter in the brain:

- ❑ Antipyresis
- ❑ Memory consolidation & learning
- ❑ Analgesia
- ❑ Increases paternal behavior, territorial aggression & partner preference
- ❑ Activation of V1-a receptor in the brain was shown to be responsible for a variety of "aggressive" behaviors in rodents.

➢ **Control of ADH release**

1. ↑ in osmotic pressure of the ECF (↑ in plasma osmolality), as in dehydration which will stimulate osmoreceptors in the hypothalamus → ↑ ADH.
2. ↓ blood volume (≥ 8-10%) → stimulate mechanoreceptors in the great arteries (aorta & carotids) & right atrium → ↑ ADH.
3. ↓ arterial blood pressure, due to ↓ blood volume → ↑ ADH.
4. Age: → ↑ ADH secretion → water retention & hyponatremia.
5. Pain, emotional stress & physical trauma → ↑ ADH secretion.
6. Drugs, e.g. morphine, barbiturates, & nicotine → ↑ ADH secretion.
7. Alcohol → ↓ ADH secretion.

✸ **Abnormalities of ADH release**
Hyposecretion:

Lack of ADH → **Diabetes insipidus.**

2 types of DI: a. Neurogenic (central, or cranial) …
Problem in Hypothalamus or Post pituitary gland; could be 1ry or 2ry.
R/: ADH.
b. Nephrogenic …resistance of V_2 receptors in collecting ducts of the kidneys.
- No ADH is needed as treatment.

➢ **Symptoms:** Polyurea ≈ 20 L/day (N ≈ 1.5 L/d), Polydepsia, ↓ specific gravity of urine (diluted urine), ↑ plasma osmolality.

✸ **Abnormalities of ADH release**
Hypersecretion:

↑ ADH**, 'Schwartz-Bartter Syndrome':**

➢ **Causes**

- occurs after surgery.
- adenoma, ectopic kidney.
- Bronchial carcinoma.

➢ **Signs & Symptoms:**

Hyponatremia, i.e. [Na+] ↓ extracellularly to 110 mM (N = 140 mM); resulting in:

- Mental confusion.
- Coma.
- Death, due to ventricular fibrillation.

✸ **Abnormalities of ADH release**

Syndrome of "Inappropriate Vasopressin Secretion (SIADH)":

- ❑ Vasopressin hypersecretion in the absence of adequate osmotic or volume stimuli
- ❑ **Etiology:** diverse, ectopic production of vasopressin, e.g., chronic lung diseases
- ❑ **Symptoms:**
  - ❑ Water retention↑↑
  - ❑ weight gain and swelling
  - ❑ Urine is inappropriately concentrated
  - ❑ Dilutional hyponatremia (plasma sodium concentration ↓ because of retained water)
  - ❑ Due to low sodium levels in blood, one may experience nausea, vomiting, confusion, seizing, & even coma
  - ❑ "Water intoxication" (cells swell)
- ❑ **Treatment:**
  - ❑ Reduction in H2O intake
  - ❑ NaCl injection if blood Na+ gets too low

2. Oxytocin:

- Oxy = rapid; tocos = labour
- In both sexes, well recognized physiological effects only in women.
- A nonapeptide with a disulfide bridge joining aa 1 to aa 6.
- Is the most abundant peptide in the brain.
- Synthesized in the cell bodies of hypothalamus, mainly in the PVN.
- Extra-hypothalamic sites:
  - ❑ Gonads
  - ❑ Adrenal cortex
  - ❑ Thymus
  - ❑ Uterus
  - ❑ Various brain structures
  - ❑ (neurotransmitter/neuromodulator).

➢ **Mechanism of action**

- One receptor identified on myometrium, & myoepithelial cells of the breast
- Gq, PLC, Ca2+ signaling pathway
- Most effects through intracellular calcium release
- Transitory roles in females
- No clearly established function in males.

➢ **Action of oxytocin**

- Milk release & ejection; by contraction of mammary gland myoepithelial cells of the alveoli & the ducts.
- Uterine smooth muscles contraction → enhance labour.
- Maternal & mating behaviors.

- In non-pregnant female: ? play a role in the physiological contractions of uterine & vaginal smooth muscles. It ? also enhance egg transport.
- In male: ? enhance sperm transport → ↑ ejaculation.
- Other targets of oxytocin:
    - Vascular smooth muscles:
        - Can cause vasoconstriction or vasodilation, depending on species & vascular bed
        - OT causes vasoconstriction of human umbilical arteries & veins
    - Can inhibit CRF-stimulated ACTH secretion in human males
    - Can stimulate prolactin release from cultured rat anterior pituitary cells

➢ **Stimuli of oxytocin release**

1. Uterine distension & Cervical Dilatation during delivery: → ↑ oxytocin
2. Suckling reflex: → ↑ oxytocin
    - Sensory nerve endings localized in nipple & areola of breast are stimulated by suckling
    - Sensory neurons in nipple > spinal cord > mesencephalon > magnocellular neurons
3. Visual &/or auditory stimuli from the baby: → ↑ oxytocin
4. During Coitus: → ↑ oxytocin
5. Psychological & emotional factors, e.g. fear, anxiety & pain: → ↓ oxytocin
6. Alcohol: → ↓ oxytocin
7. Hormones:
    - Note that oxytocin is present in circulation throughout pregnancy
    - Oxytocin levels increase only during final stages of labor (not pregnancy)
    - Prostaglandins & estrogens facilitate the responsiveness of uterus (↑ sensitivity to oxytocin)
    - Progesterone inhibits the responsiveness of uterus (↓ sensitivity to oxytocin)

➢ **Control of oxytocin release**

- Feedback mostly through higher brain centers

1. Stimulation of nipple (suckling reflex) → ↑ oxytocin.
2. Visual or auditory stimuli from the baby → ↑ oxytocin secretion.
3. Distension of uterus & stretching of cervix during delivery → ↑ oxytocin release.
4. During coitus → oxytocin secretion.
5. Psychological & emotional factors, e.g. Fear, anxiety & pain → ↓ oxytocin.
6. Alcohol → ↓ oxytocin secretion.
7. Hormones: a. progesterone → ↓ uterine sensitivity to oxytocin.
   b. estrogen → ↑ uterine sensitivity to oxytocin.