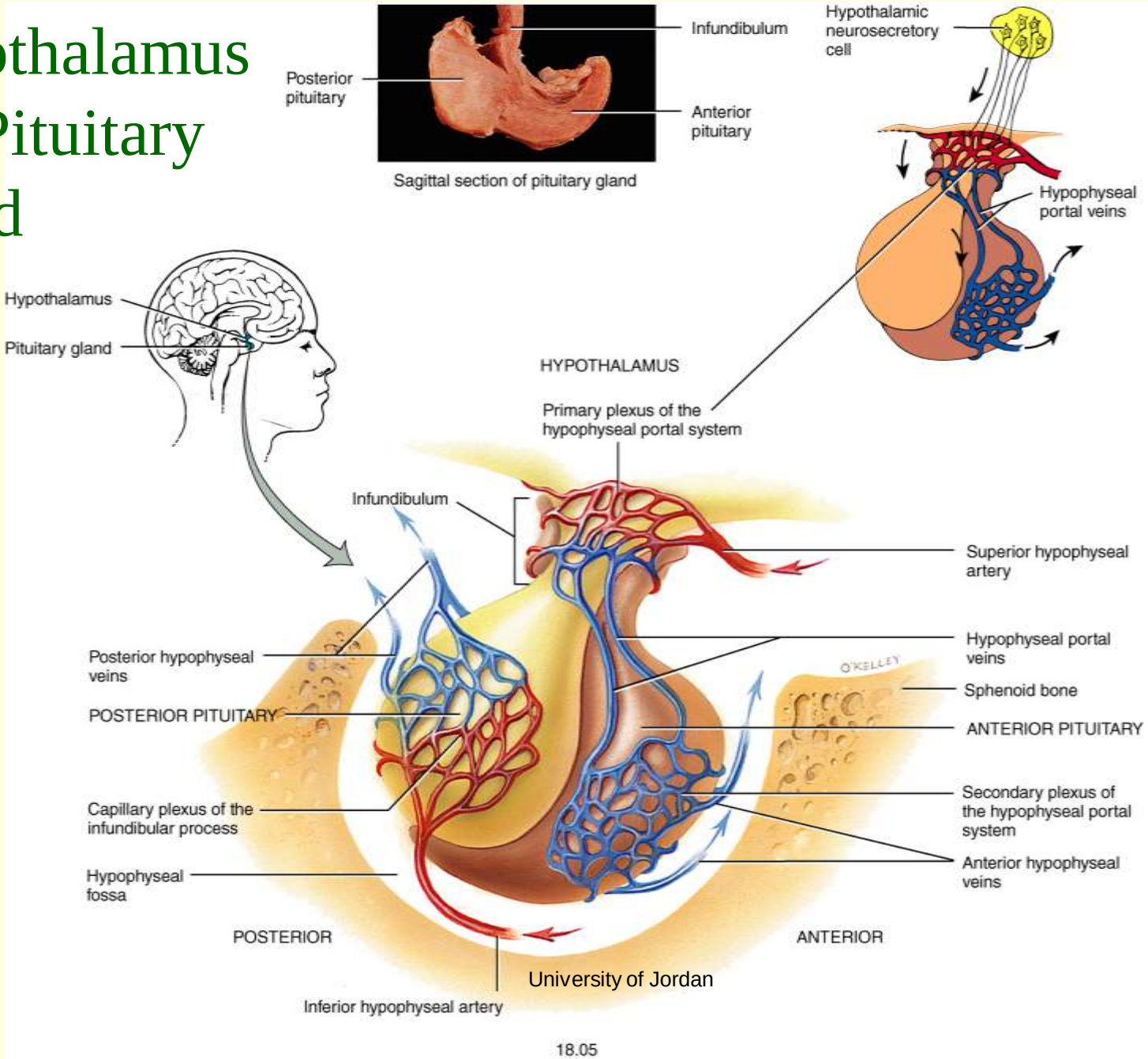
Pituitary Hormones and Their Control by the Hypothalamus

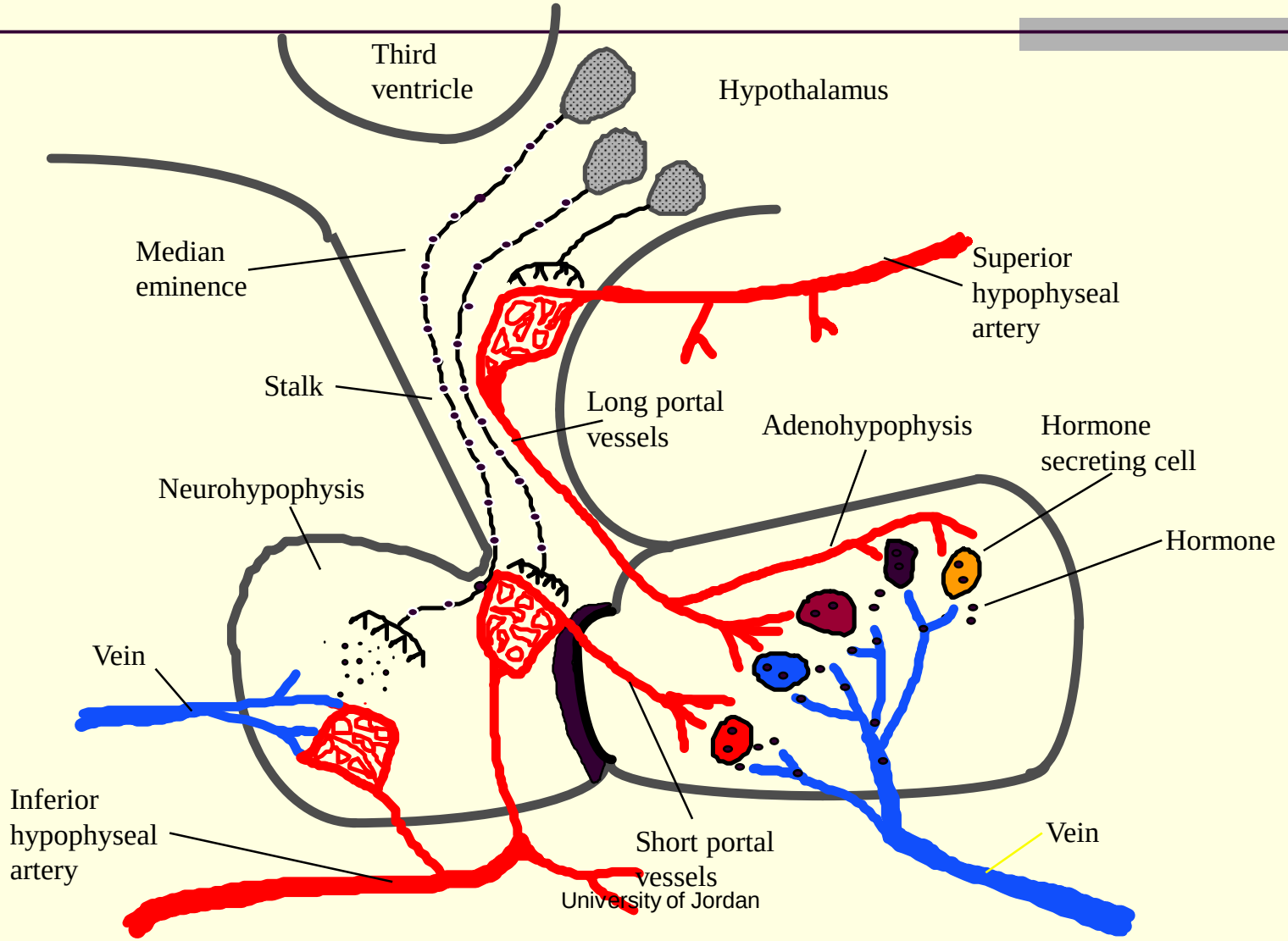
Objectives

- Give an account of the importance of the relationship of the hypothalamus and pituitary
- List anterior pituitary hormones
- Give an account for the action of anterior pituitary hormones
- Follow up the control of anterior pituitary hormones
- Track the abnormalities of anterior pituitary
- List the posterior pituitary hormones
- Give an account of the function of posterior pituitary hormones
- Explain abnormalities of those hormones

Hypothalamus and Pituitary Gland



Endocrine Cells of the Hypothalamohypopyseal Axis & the Portal Circulation



Anterior pituitary

- Release of hormones stimulated by releasing and inhibiting hormones from the hypothalamus
- Also regulated by negative feedback
- Hypothalamic hormones made by neurosecretory cells transported by hypophyseal portal system
- Anterior pituitary hormones that act on other endocrine systems called tropic hormones

Hormones of the Anterior Pituitary

- Human growth hormone (hGH) or somatotropin
  - Stimulates secretion of insulin-like growth factors (IGFs) that promote growth, protein synthesis
- Thyroid-stimulating hormone (TSH) or thyrotropin
  - Stimulates synthesis and secretion of thyroid hormones by thyroid
- Follicle-stimulating hormone (FSH)
  - Ovaries initiates development of oocytes, testes stimulates sperm production
- Luteinizing hormone (LH)
  - Ovaries stimulates ovulation, testes stimulates testosterone production

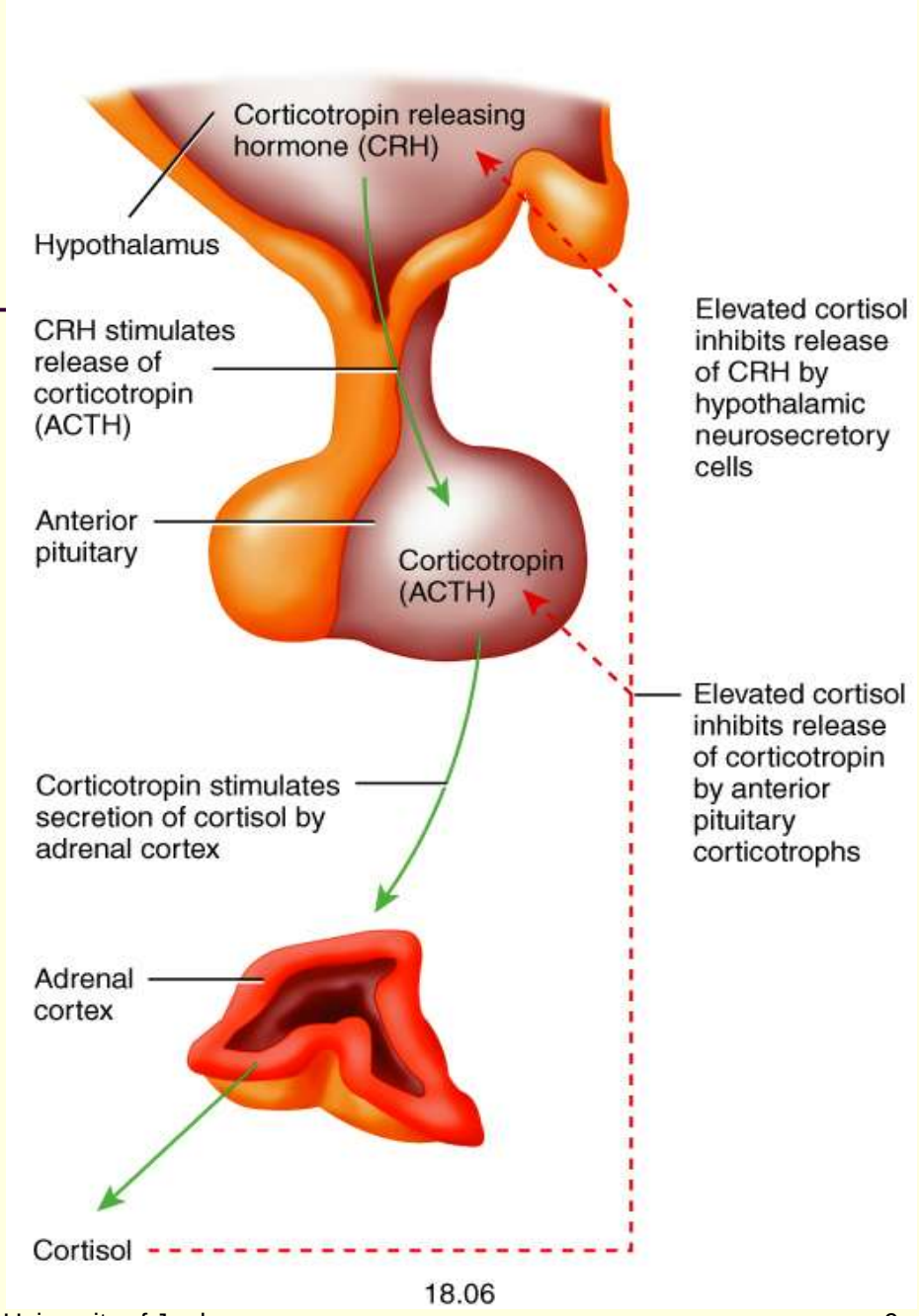
Hormones of the Anterior Pituitary

- Prolactin (PRL)
  - Promotes milk secretion by mammary glands
- Adrenocorticotropic hormone (ACTH) or corticotropin
  - Stimulates glucocorticoid secretion by adrenal cortex
- Melanocyte-stimulating Hormone (MSH)
  - Unknown role in humans

Hypophysiotropic Hormones

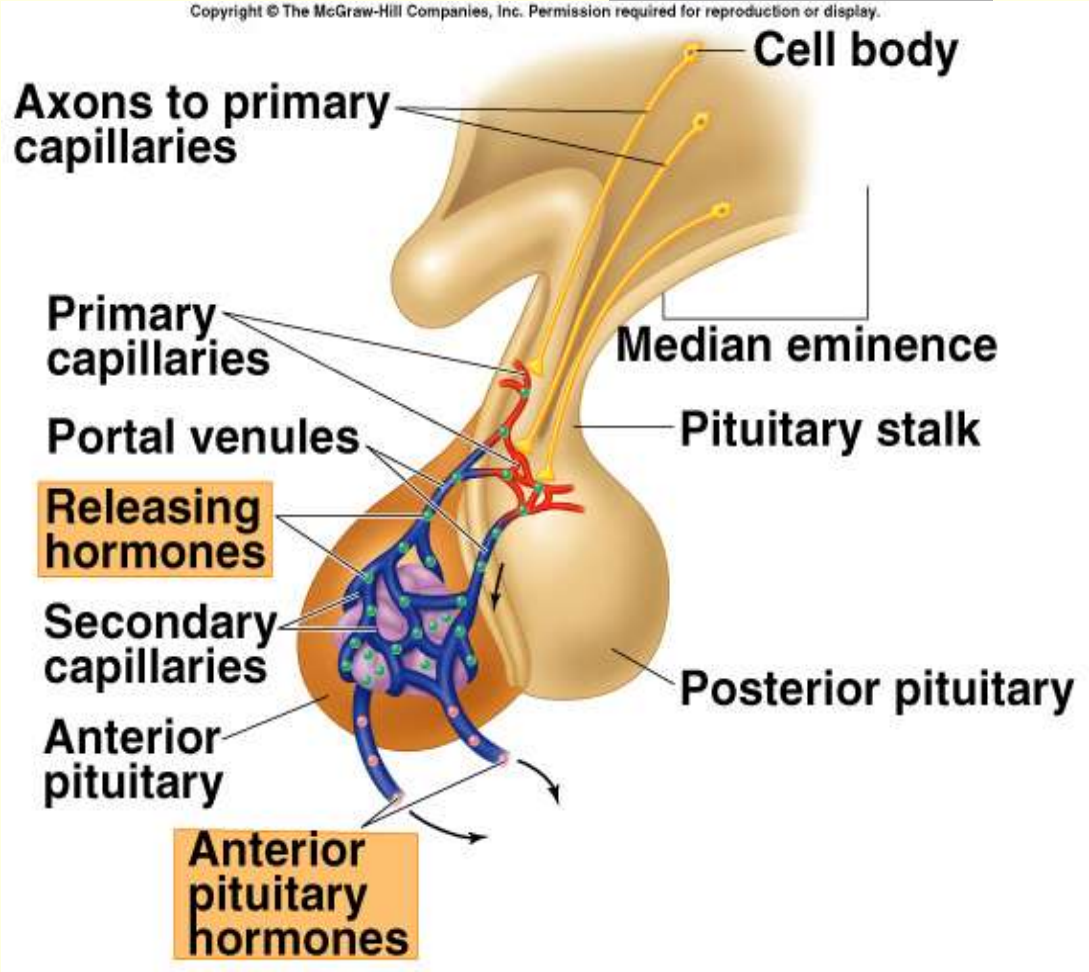
Hormone	Predominant hypothalamic localization	Structure	Actions on Anterior Pituitary
Thyrotropin-releasing hormone (TRH)	Paraventricular	Peptide consisting of 3 amino acids	Stimulates secretion of TSH by thyrotropes; stimulates expression of genes for α and ß subunits of TSH thyrotropes; stimulates synthesis of PRL by lactotropes
Gonadotropin-releasing hormone (GnRH)	Arcuate	Single chain of 10 amino acids	Stimulates secretion of FSH and LH by gonadotropes
Corticotropin-releasing hormone (CRH)	Paraventricular	Single chain of 41 amino acids	Stimulates secretion of ACTH by corticotropes; stimulates expression of gene for POMC in corticotropes
Growth hormone-releasing hormone (GHRH)	Arcuate	Single chain of 44 amino acids	Stimulates secretion of GH by somatotropes; stimulates expression of gene for GH in somatotropes
Growth hormone-inhibiting hormone (somatostatin)	Anterior periventricular	Single chain of 14 amino acids	Inhibits secretion of GH by somatotropes
Prolactin-inhibiting hormone (PIH)	Arcuate	Dopamine	Inhibits biosynthesis and secretion of PRL by lactotropes

Negative Feedback Regulation



Hypothalamic Control of the Anterior Pituitary

- Hormonal control rather than neural.
- Hypothalamus neurons synthesize releasing and inhibiting hormones.
- Hormones are transported to axon endings of median eminence.
- Hormones secreted into the hypothalamo-hypophyseal portal system regulate the secretions of the anterior pituitary

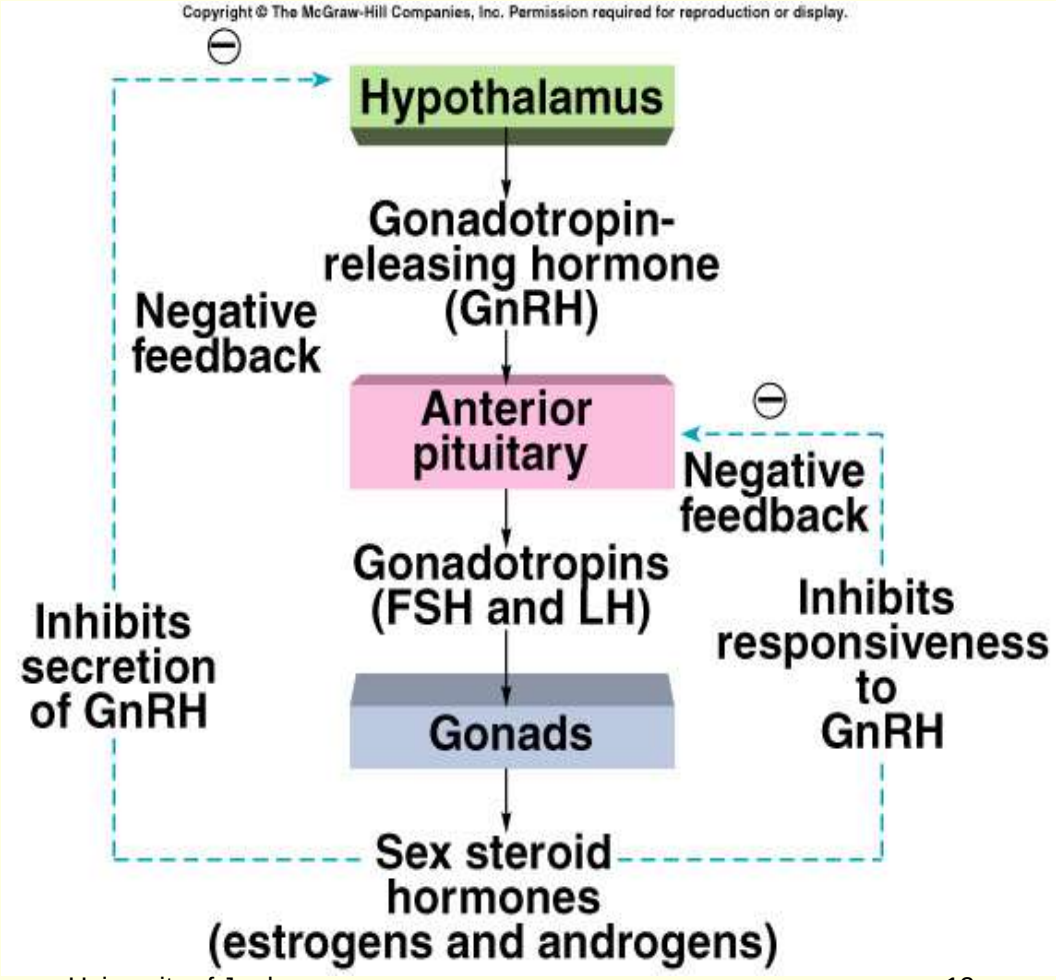


Feedback Control of the Anterior Pituitary

- Anterior pituitary and hypothalamic secretions are controlled by the target organs they regulate.
  - Secretions are controlled by negative feedback inhibition by target gland hormones.
- Negative feedback at 2 levels:
  - The target gland hormone can act on the hypothalamus and inhibit secretion of releasing hormones.
  - The target gland hormone can act on the anterior pituitary and inhibit response to the releasing hormone.

Feedback Control of the Anterior Pituitary (continued)

- 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."

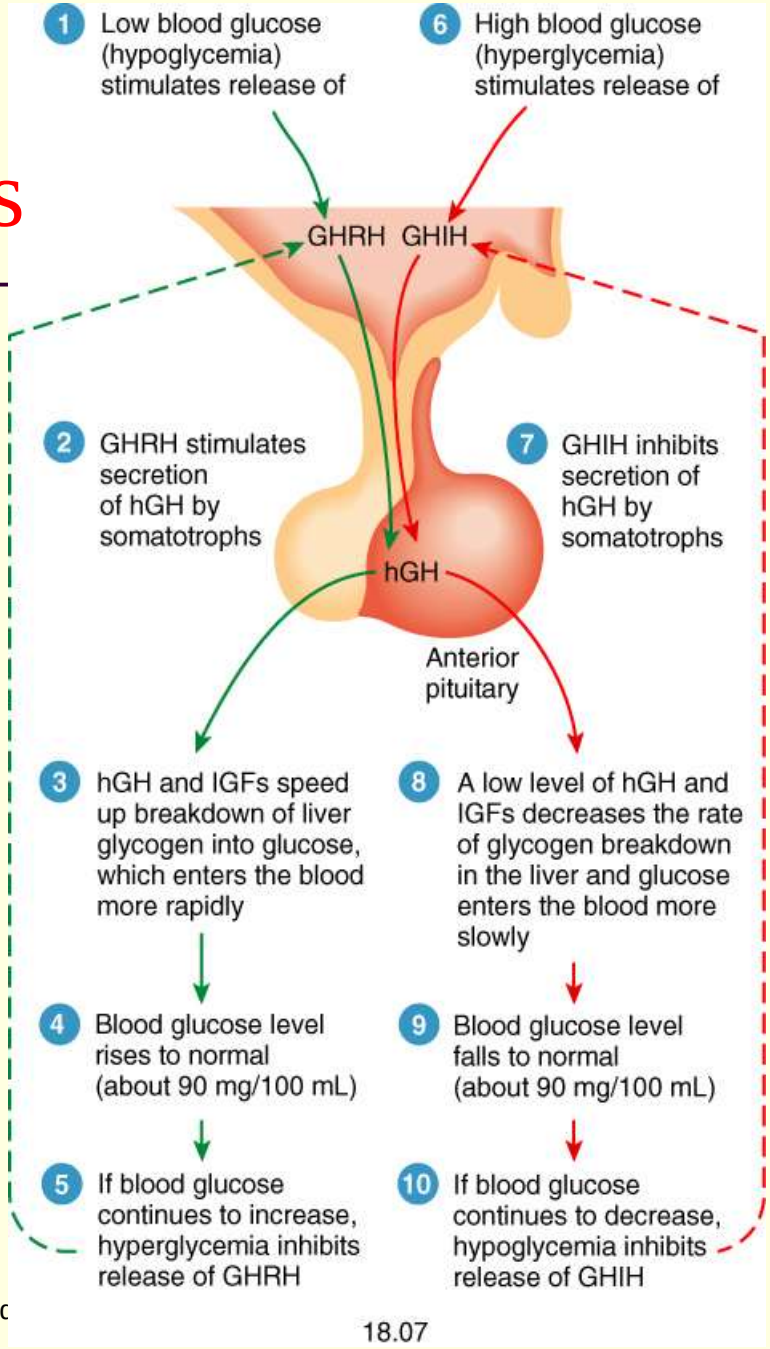


Higher Brain Function and Pituitary Secretion

- 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.

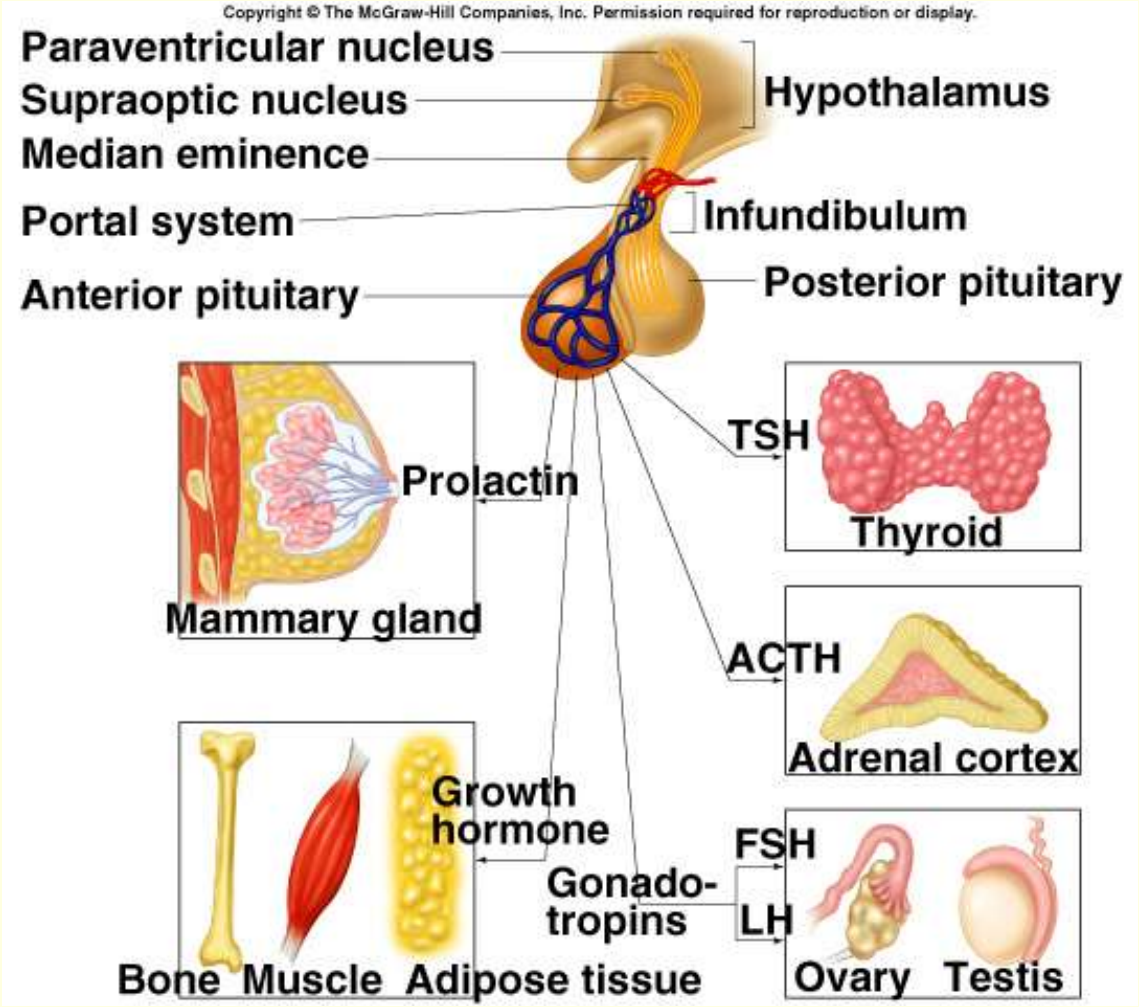
Effects of hGH and IGFs

High levels of GH before puberty causes Gigantism, after puberty causes Acromegaly. Low levels of GH before puberty causes Dwarfism, after puberty leads to some Metabolic effects



Pituitary Hormones

- Anterior Pituitary:
  - Trophic effects:
    - High blood [hormone] causes target organ to hypertrophy.
    - Low blood [hormone] causes target organ to atrophy.



Adenohypophyseal Hormones

- ACTH
- TSH
- FSH
- LH
- PRL
- GH

Adenohypophyseal Cells & Hormones

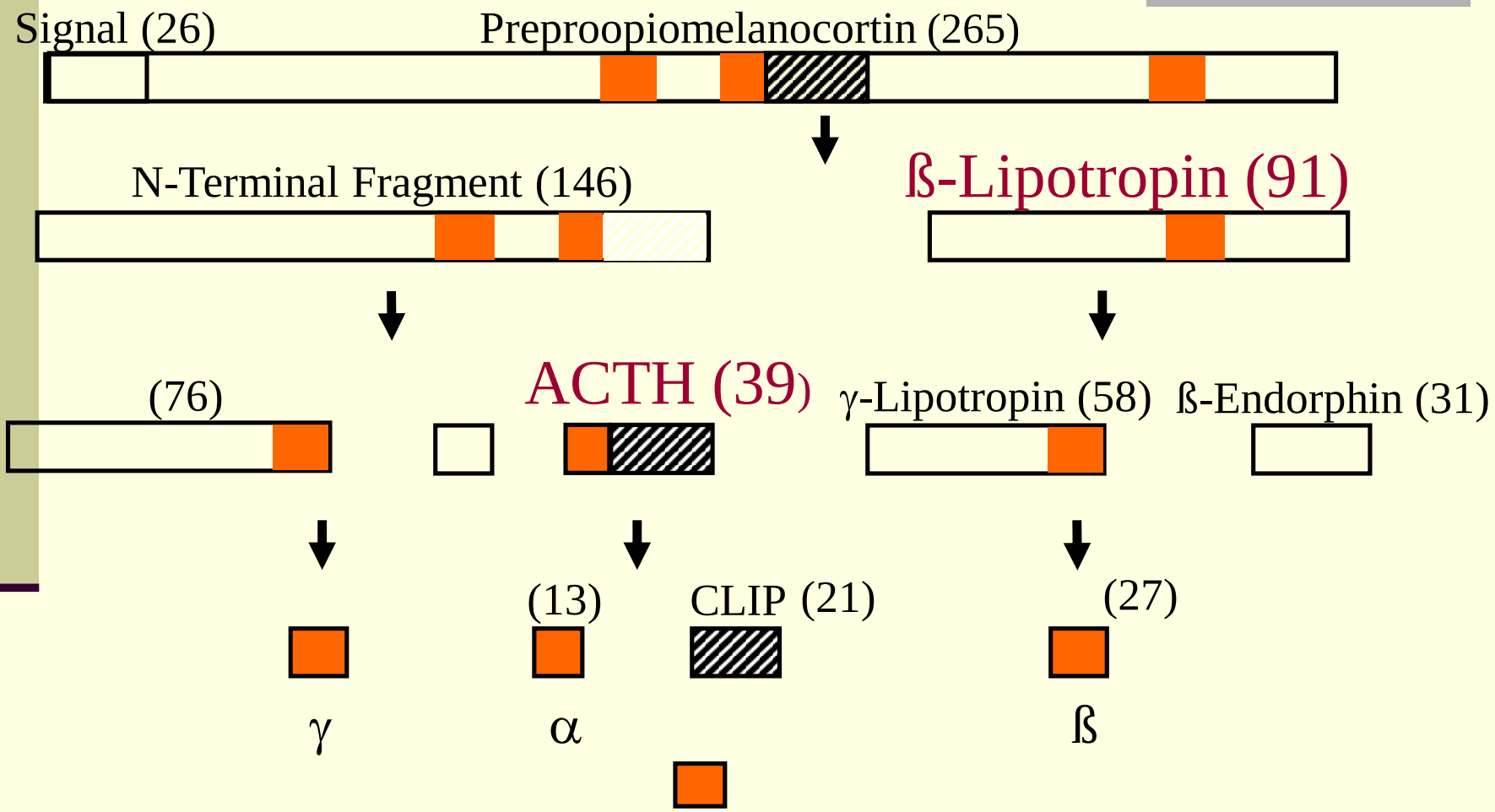
Cell	Hormone	Chemistry	Physiologic Actions
Corticotropes	Adrenocorticotropic hormone (corticotropin; ACTH)	Single chain of 39 amino acids	Stimulates production of glucocorticoids and androgens by the adrenal cortex; maintains size of zona fasciculata and zona reticularis of cortex
Thyrotropes	Thyroid-stimulating hormone (thyrotropin; TSH)	Glycoprotein having two subunits, α (89 amino acids) and ß (112 amino acids)	Stimulates production of thyroid hormones, T4 and T3, by thyroid follicular cells; maintains size of follicular cells
Gonadotropes	Follicle-stimulating hormone (FSH)	Glycoprotein having two subunits, α (89aa) and ß (115aa)	Stimulates development of ovarian follicles; regulates spermatogenesis in the testis
Gonadotropes	Lutenizing hormone (LH)	Glycoprotein having two subunits, α (89aa) and ß (115aa)	Causes ovulation and formation of corpus luteum in the ovary; stimulates production of estrogen and progesterone by the ovary; stimulates testosterone production by the testis
Mammotropes, Lactotropes	Prolactin (PRL)	Single chain of 198 amino acids	Essential for milk production by lactating mammary gland
Somatotropes	Growth hormone (somatotropin; GH)	Single chain of 191 amino acids	Stimulates postnatal body growth; stimulates secretion of IGF-1; stimulates triglyceride lipolysis; inhibits actions of insulin on carbohydrate and lipid metabolism

Examples of Peptide Hormone Families

Insulin Family	Glycoprotein Family	POMC Family
Insulin Insulinlike growth factor I (IGF-1, somatomedin C) Insulinlike growth factor II Relaxin	Lutenizing hormone (LH) Follicle-stimulating hormone (FSH) Thyroid-stimulating hormone (TSH) Chorionic gonadotropin (HCG)	Adrenocorticotropic hormone (ACTH) Melanocyte-stimulating hormone (MSH)

Secretin-Glucagon Family	Growth Hormone Family	Neurohypophyseal Family
Secretin Glucagon Gastrointestinal polypeptide Glicentin Gastric inhibitory polypeptide (GIP) Glucagon-like peptide 1 (GLP-1)	Growth hormone (GH) Prolactin (PRL) Chorionic somatomammotrophin (HCS) or Human placental lactogen (HPL)	Antidiuretic hormone (ADH) Oxytocin

Processing of Preproopiomelanocortin



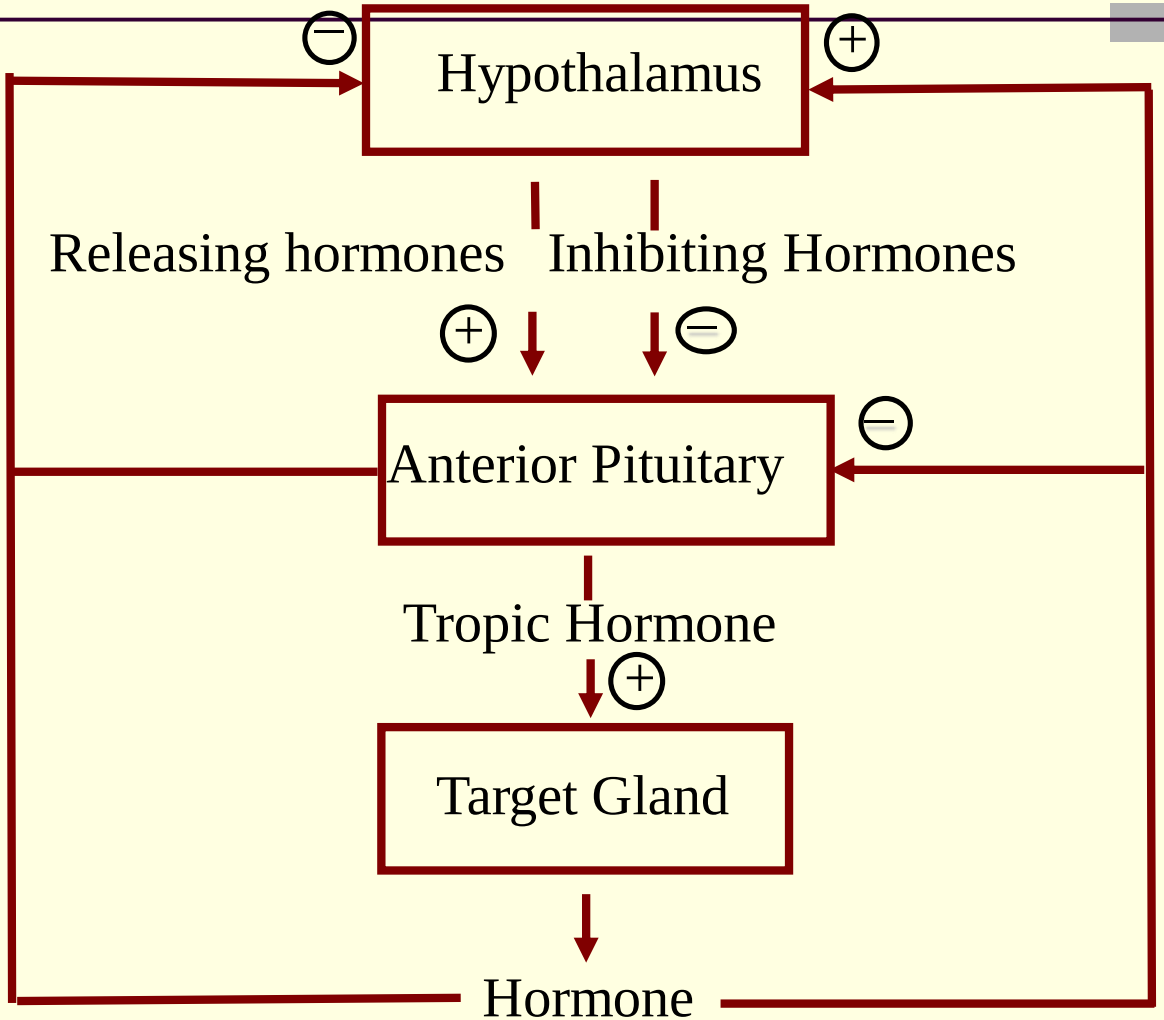
Hypophysiotropic Hormones

- TRH
- GnRH
- CRH
- GHRH
- Somatostatin
- Dopamine

Hypophysiotropic Hormones

Hormone	Predominant hypothalamic localization	Structure	Actions on Anterior Pituitary
Thyrotropin-releasing hormone (TRH)	Paraventricular	Peptide consisting of 3 amino acids	Stimulates secretion of TSH by thyrotropes; stimulates expression of genes for α and ß subunits of TSH thyrotropes; stimulates synthesis of PRL by lactotropes
Gonadotropin-releasing hormone (GnRH)	Arcuate	Single chain of 10 amino acids	Stimulates secretion of FSH and LH by gonadotropes
Corticotropin-releasing hormone (CRH)	Paraventricular	Single chain of 41 amino acids	Stimulates secretion of ACTH by corticotropes; stimulates expression of gene for POMC in corticotropes
Growth hormone-releasing hormone (GHRH)	Arcuate	Single chain of 44 amino acids	Stimulates secretion of GH by somatotropes; stimulates expression of gene for GH in somatotropes
Growth hormone-inhibiting hormone (somatostatin)	Anterior periventricular	Single chain of 14 amino acids	Inhibits secretion of GH by somatotropes
Prolactin-inhibiting hormone (PIH)	Arcuate	Dopamine	Inhibits biosynthesis and secretion of PRL by lactotropes

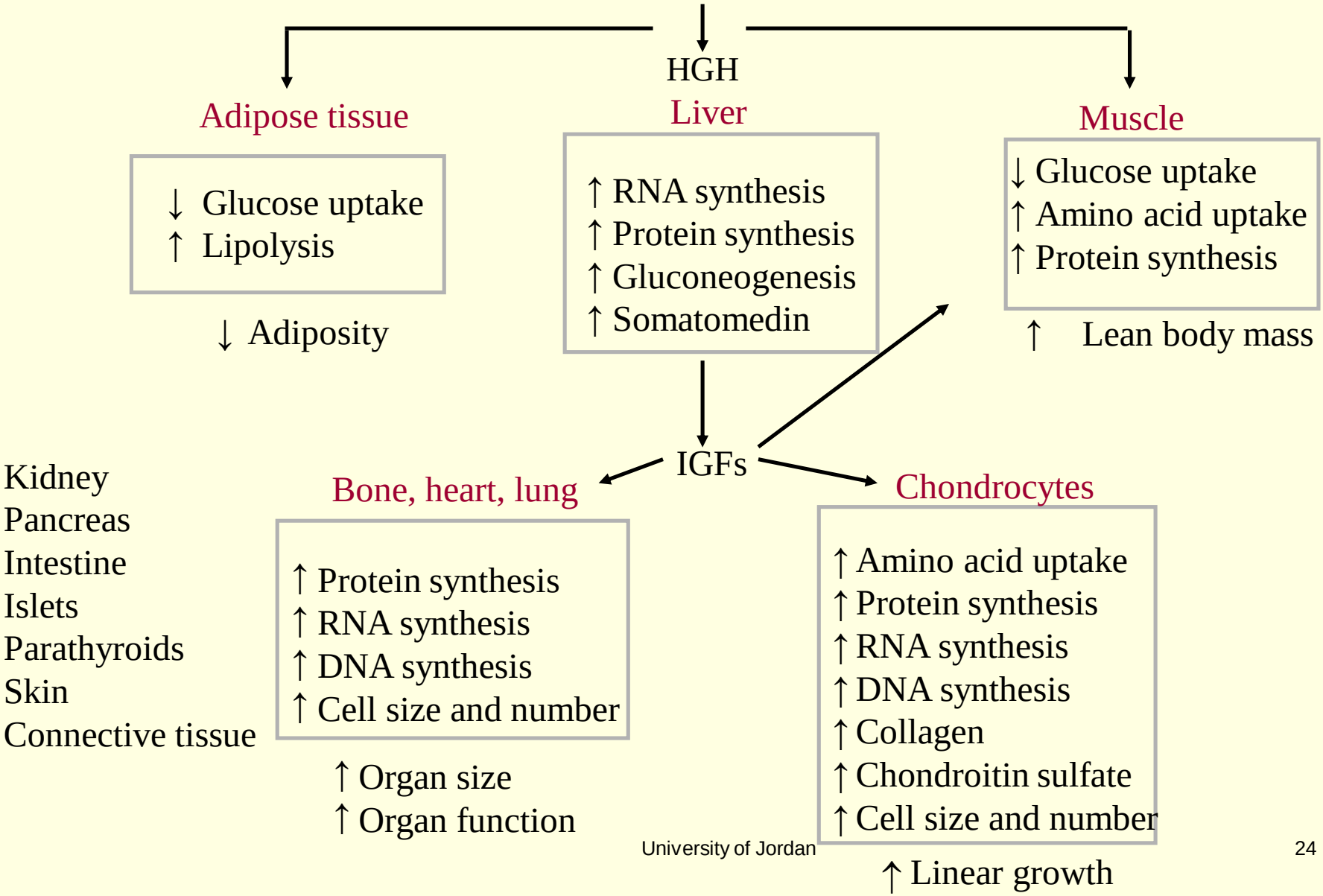
Hypothalamohypophyseal –Target Gland Axis



Adenohypophyseal Hormones

- ACTH
- TSH
- FSH
- LH
- PRL
- **GH**

Biological Actions of Growth Hormone



Growth Hormone

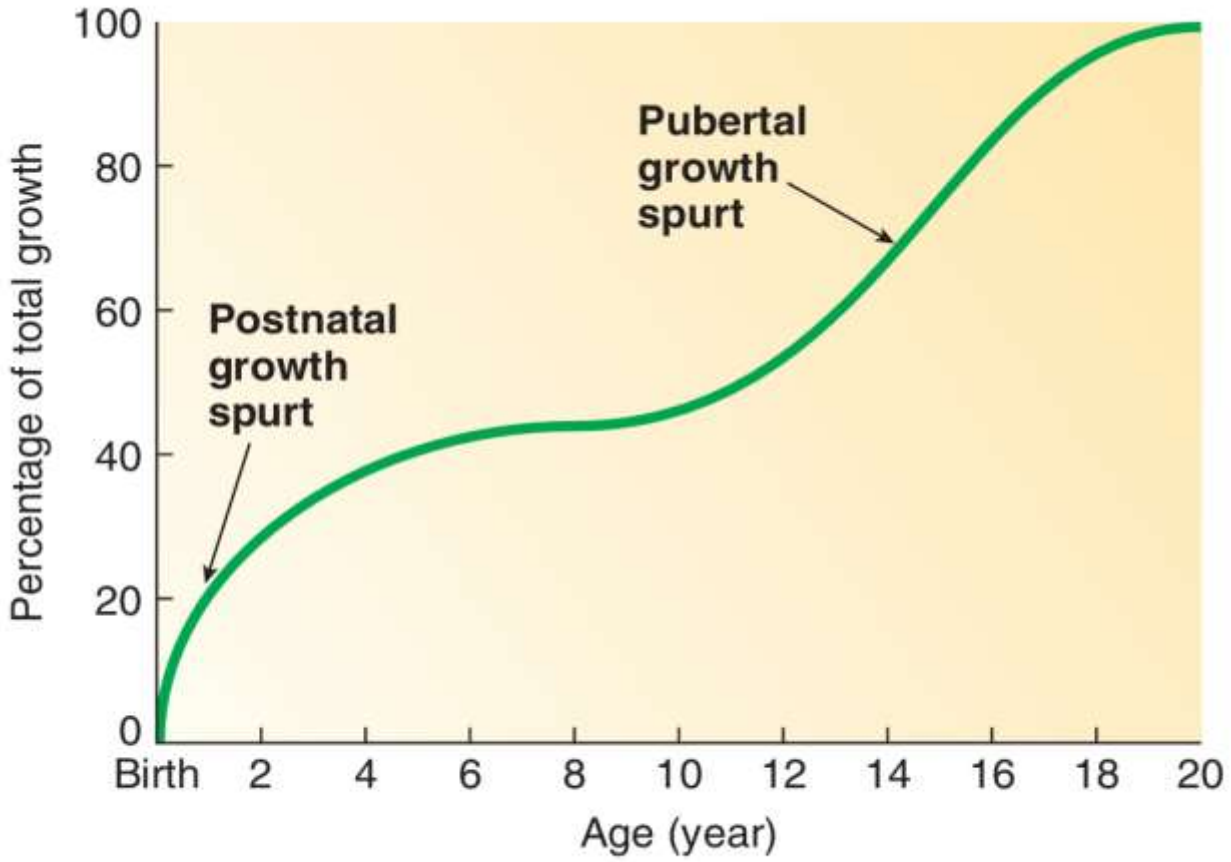
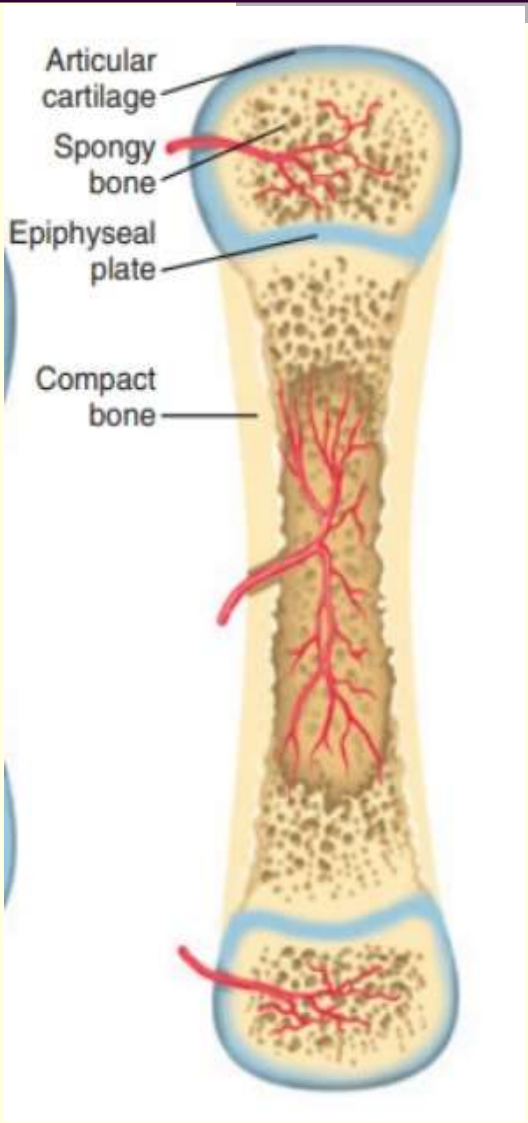
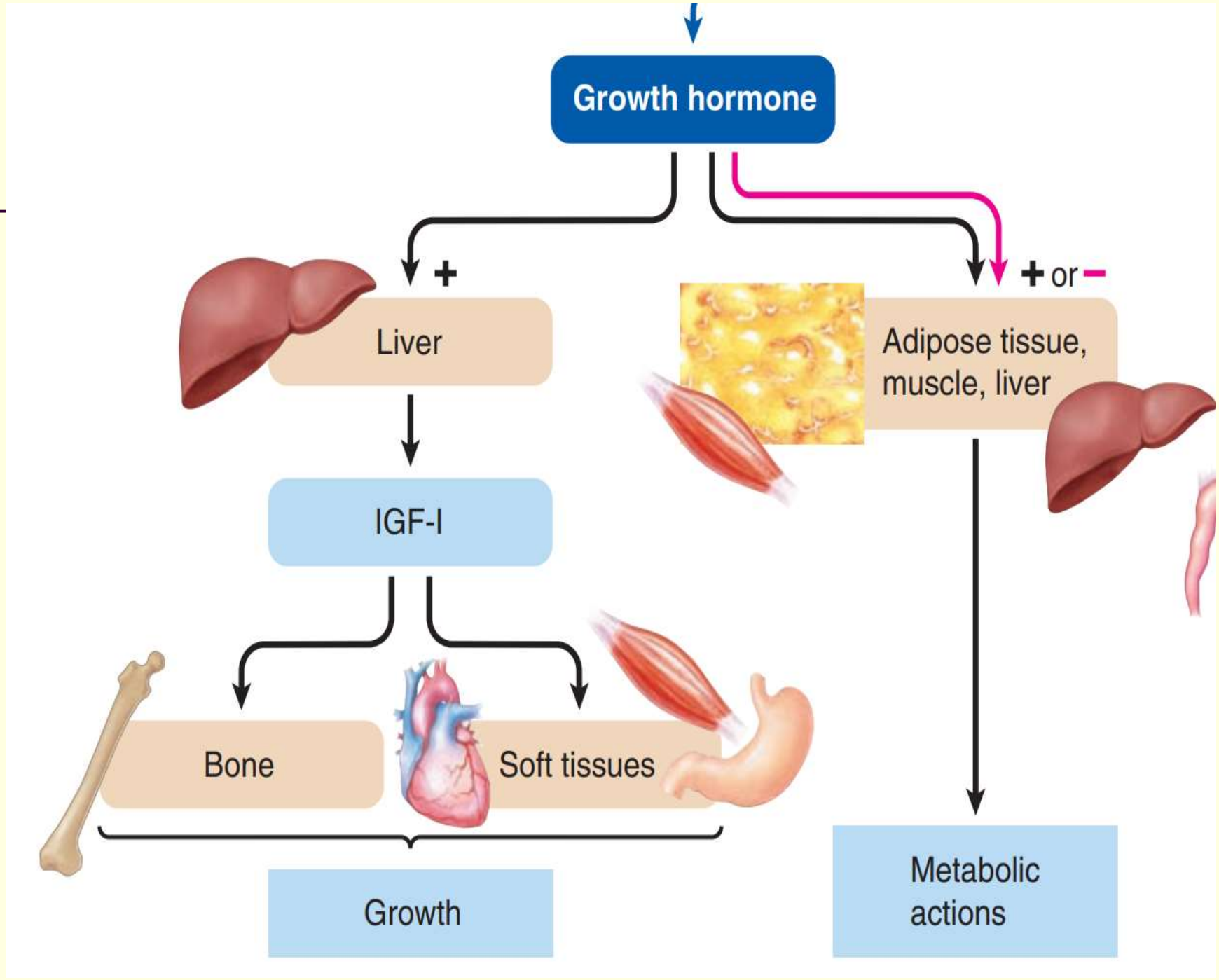


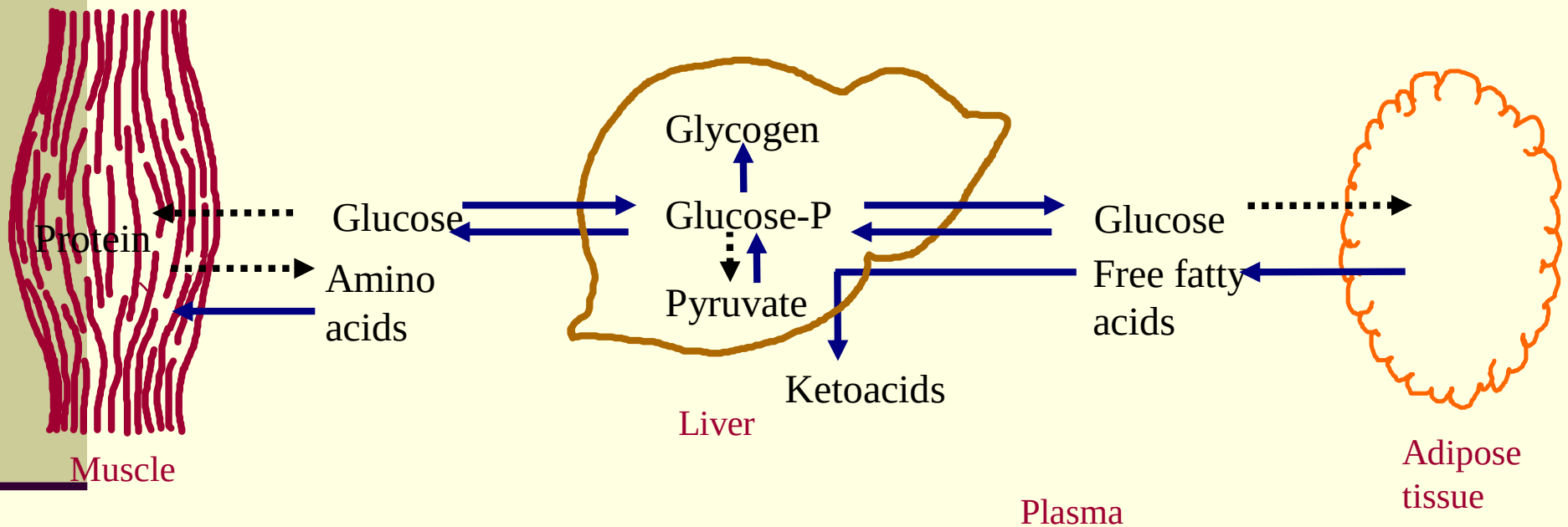
Figure 18-8 Normal growth curve.

- Growth in thickness: Osteoblast > Osteoclast
- Growth in length: chondrocyte proliferation at the epiphyseal plate, ossification.




Growth hormone
+
+ or –
Liver
Adipose tissue, muscle, liver
IGF-I
Bone
Soft tissues
Growth
Metabolic actions

Metabolic Effects of Growth Hormone



Stimulate
Inhibit

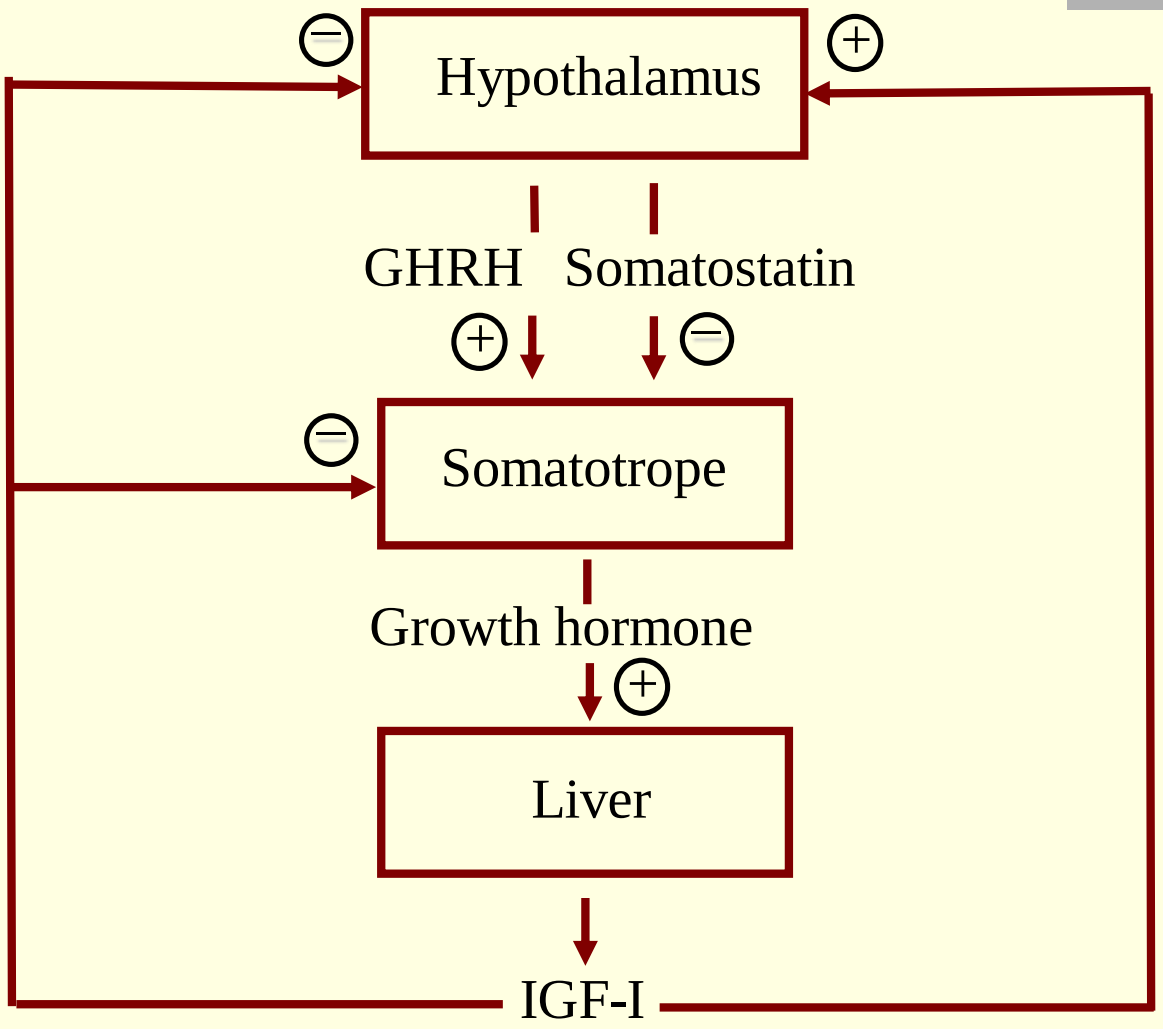
Plasma

↑ Glucose
↑ Free fatty acids
↑ Ketoacids
↓ Amino acids

IGF-I (Somatomedin C)

- Circulating IGF-I produced in liver in response to GH
- Local production in tissues
- Stimulates chondrocytes → ↑ linear growth
- Structure & receptors ~ to those of insulin
- Inhibits GH secretion
- Highly bound to plasma proteins-- $T_{1/2}$: IGF-I > GH

Hypothalamohypophyseal-GH Axis



Factors Affecting GH Secretion

Stimulation	Inhibition
Glucose decrease	Somatostatin
Free fatty acid decrease	Glucose increase
Amino acid increase (arginine)	Free fatty acid increase
Fasting	Somatomedins
Prolonged caloric deprivation	Growth hormone
Stress	Senescence
Exercise	
Puberty	
Androgens and estrogens	
Sleep	

Pathophysiology of Growth Hormone

- **Gigantism**
- Acromegaly
- Dwarfism

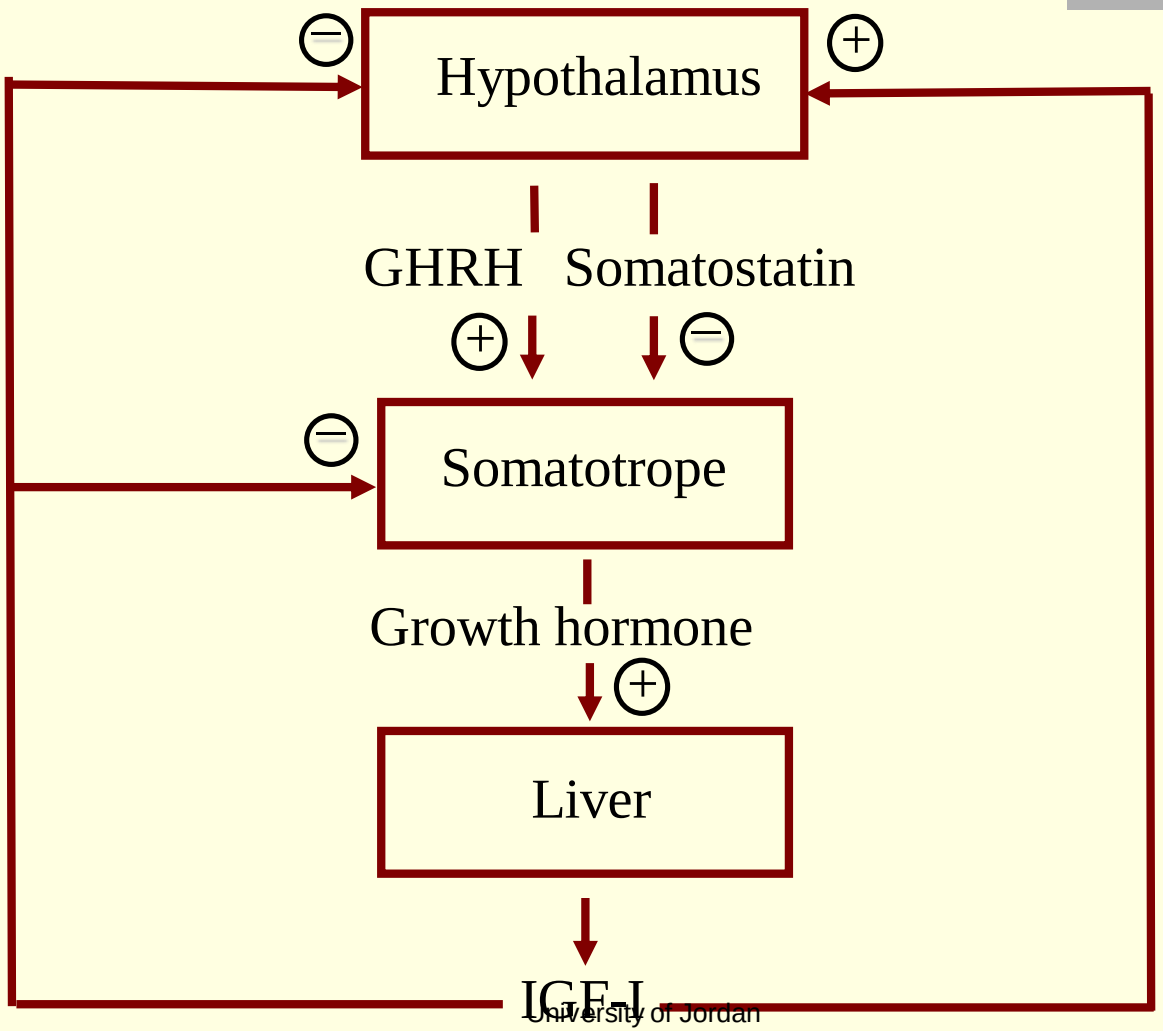
Pathophysiology of Growth Hormone

- Gigantism
- **Acromegaly**
- Dwarfism

Clinical Features of Acromegaly

- **Local tumor effects**
  - ↑ piuitary, visual field defects, headache
- **Somatic systems**
  - Acral enlargement, prognathism, carpal tunnel syndrome
- **CV system**
  - Ventricular hypertrophy, cardiomyopathy, HT, HF
- **Pulmonary system**
  - Sleep disturbances, sleep apnea
- **Visceromegaly**
  - Tongue, thyroid gland, liver, spleen, liver, kidney, prostate
- **Metabolic**
  - Insulin resistance, fasting hyperglycemia

Hypothalamohypophyseal-GH Axis



Therapies for Gigantism-Acromegly

- Hypophysectomy
- Radiation
- Somatostatin analogues (octreotide, lanreotide)
- GH antagonists (pegvisomant)

Pathophysiology of Growth Hormone

- Gigantism
- Acromegaly
- **Dwarfism**

Gigantism and Acromegaly

A: Typical facies.

C: Large fleshy hands.

B: Separation of lower teeth.

D: Widening of the feet.

@Macleod's clinical examination

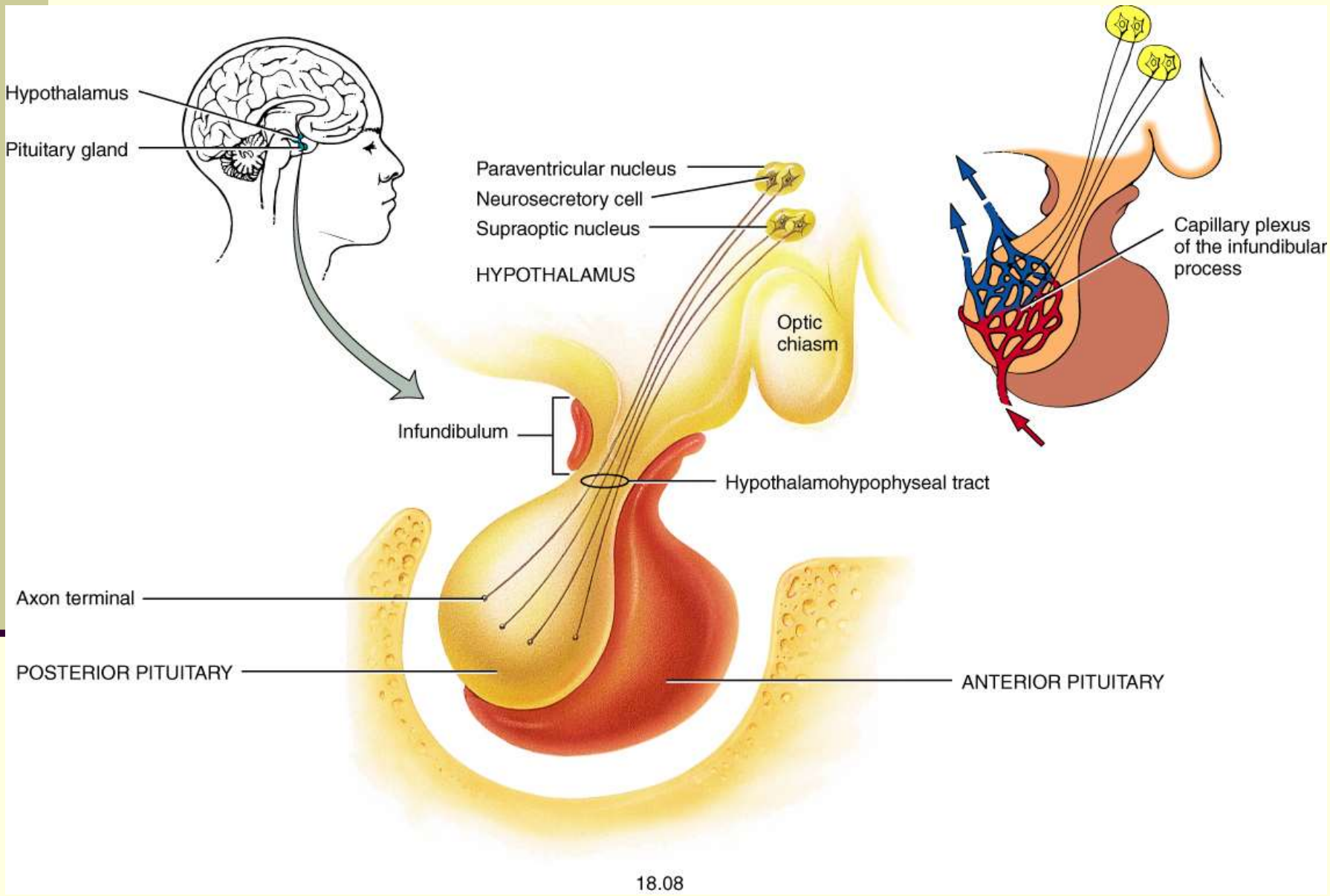
Posterior pituitary

- Does not synthesize hormones
- Stores and releases hormones made by the hypothalamus
  - Transported along hypothalamohypophyseal tract
- Oxytocin (OT)
- Antidiuretic hormone (ADH) or vasopressin

Posterior Pituitary Hormones

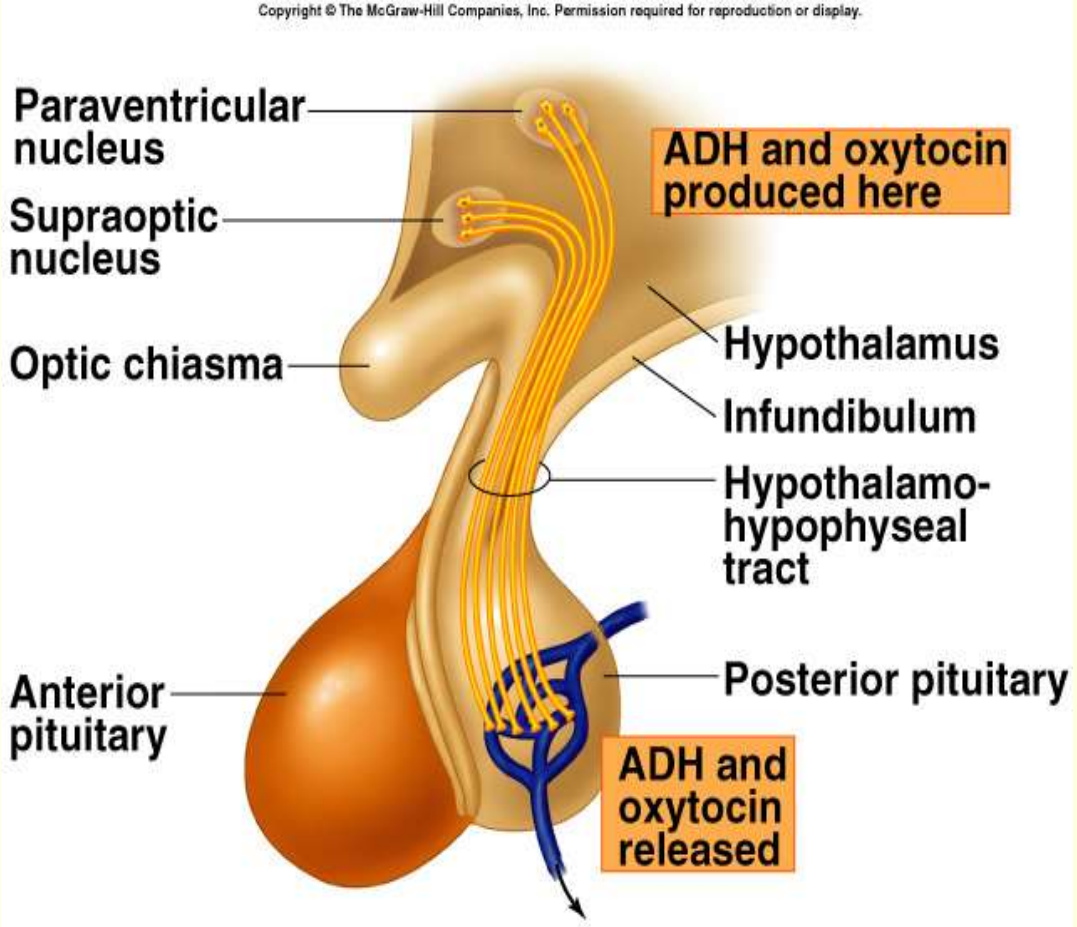
- Posterior pituitary:
  - Stores and releases 2 hormones that are produced in the hypothalamus:
    - Antidiuretic hormone (ADH/vasopressin):
      - Promotes the retention of H_20 by the kidneys.
        - Less H_20 is excreted in the urine.
    - Oxytocin:
      - Stimulates contractions of the uterus during parturition.
      - Stimulates contractions of the mammary gland alveoli.
        - Milk-ejection reflex.

Hypothalamohypophyseal tract



Hypothalamic Control of Posterior Pituitary

- Hypothalamus neuron cell bodies produce:
  - ADH: supraoptic nuclei.
  - Oxytocin: paraventricular nuclei.
- Transported along the hypothalamo-hypophyseal tract.
- Stored in posterior pituitary.
- Release controlled by neuroendocrine reflexes.

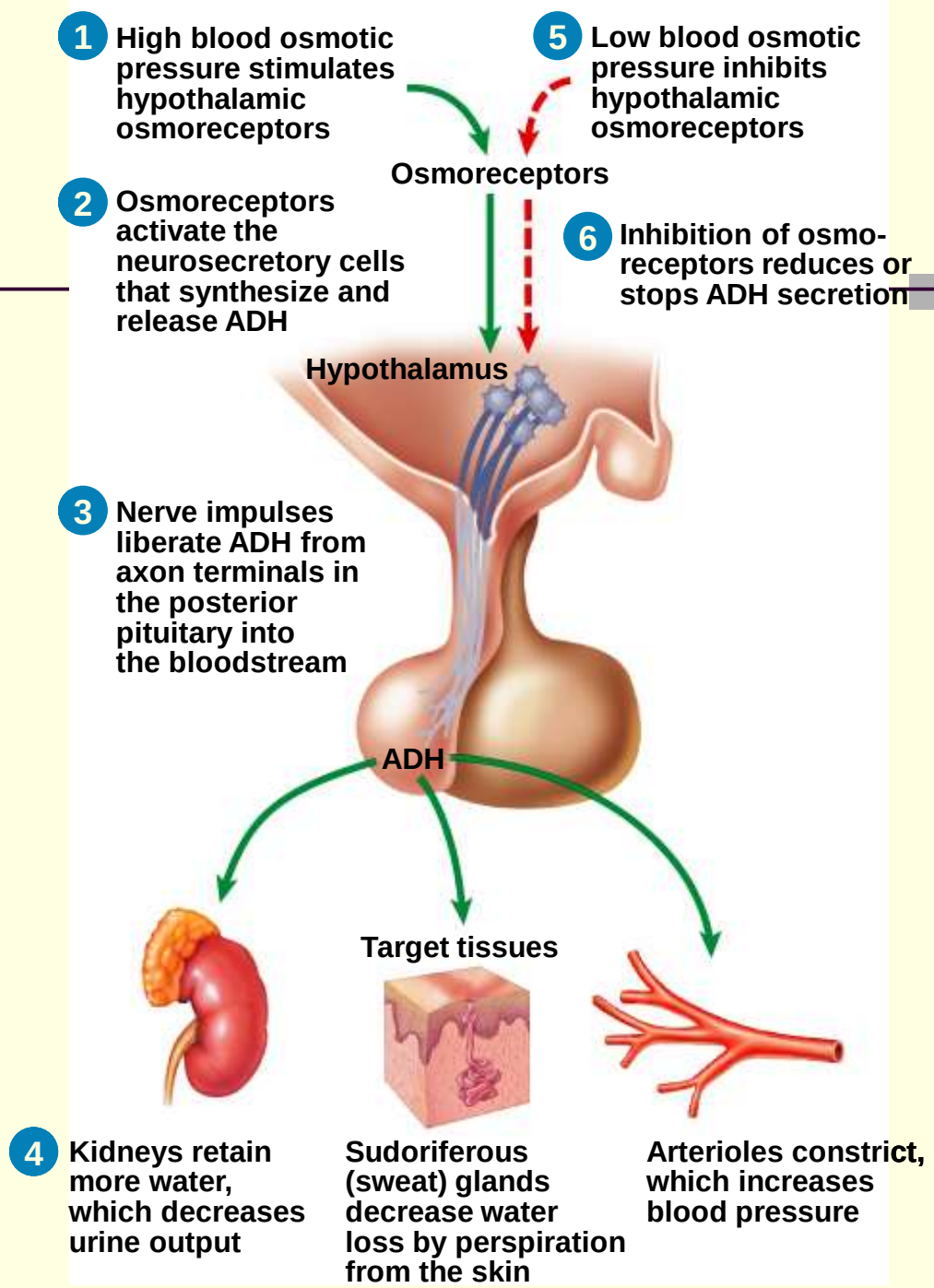


Oxytocin (OT)

- During and after delivery of baby affects uterus and breasts
- Enhances smooth muscle contraction in wall of uterus
- Stimulates milk ejection from mammary glands

Antidiuretic Hormone (ADH)

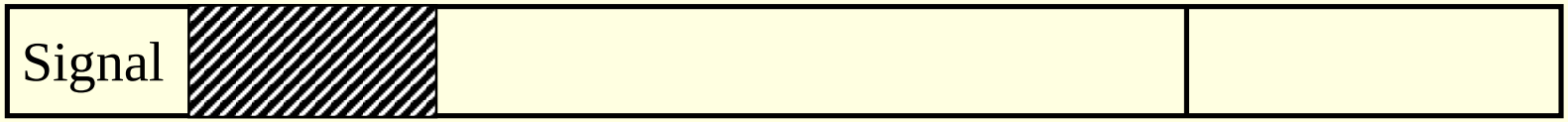
- Decreases urine production by causing the kindeys to return more water to the blood
  - Also decreases water lost through sweating and constriction of arterioles which increases blood pressure (vasopressin)


1 High blood osmotic pressure stimulates hypothalamic osmoreceptors
5 Low blood osmotic pressure inhibits hypothalamic osmoreceptors
Osmoreceptors
2 Osmoreceptors activate the neurosecretory cells that synthesize and release ADH
6 Inhibition of osmo-receptors reduces or stops ADH secretion
Hypothalamus
3 Nerve impulses liberate ADH from axon terminals in the posterior pituitary into the bloodstream
ADH
Target tissues
4 Kidneys retain more water, which decreases urine output
Sudoriferous (sweat) glands decrease water loss by perspiration from the skin
Arterioles constrict, which increases blood pressure

Neurohypophyseal Hormones

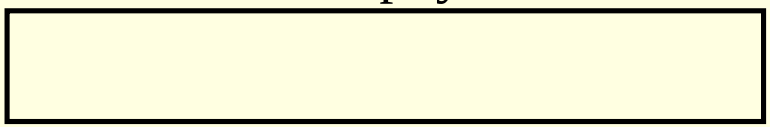
- **ADH**
- Oxytocin

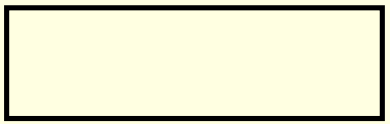
Processing of Prepro-oxyphysin & Prepropressophysin



Hormone

Neurophysin





oxytocin (9)
AVP (9)

neurophysin I
neurophysin II

Structure-Activity Relationships for Neurohypophyseal Hormones

Peptide	Oxytocic (O)	Milk Ejection (ME)	Vasopessor (P)	Antidiuretic (A)	Activity Ratios O/A	O/P	A/P
Oxytocin	520	475	4	4	130	130	----
Arginine Vasopressin (AVP)	14	70	370	320	----	----	1
Desmopressin (dDAVP)			0.5	955	----	----	2000

Oxytocin

1 2 3 4 5 6 7 8 9

Cy-Tyr-Ile-Gln-Asn-Cy-Pro-Leu-Gly-NH_2

S ——————— S

AVP

1 2 3 4 5 6 7 8 9

Cy-Tyr-Phe-Gln-Asn-Cy-Pro-L-Arg-Gly-NH_2

S ——————— S

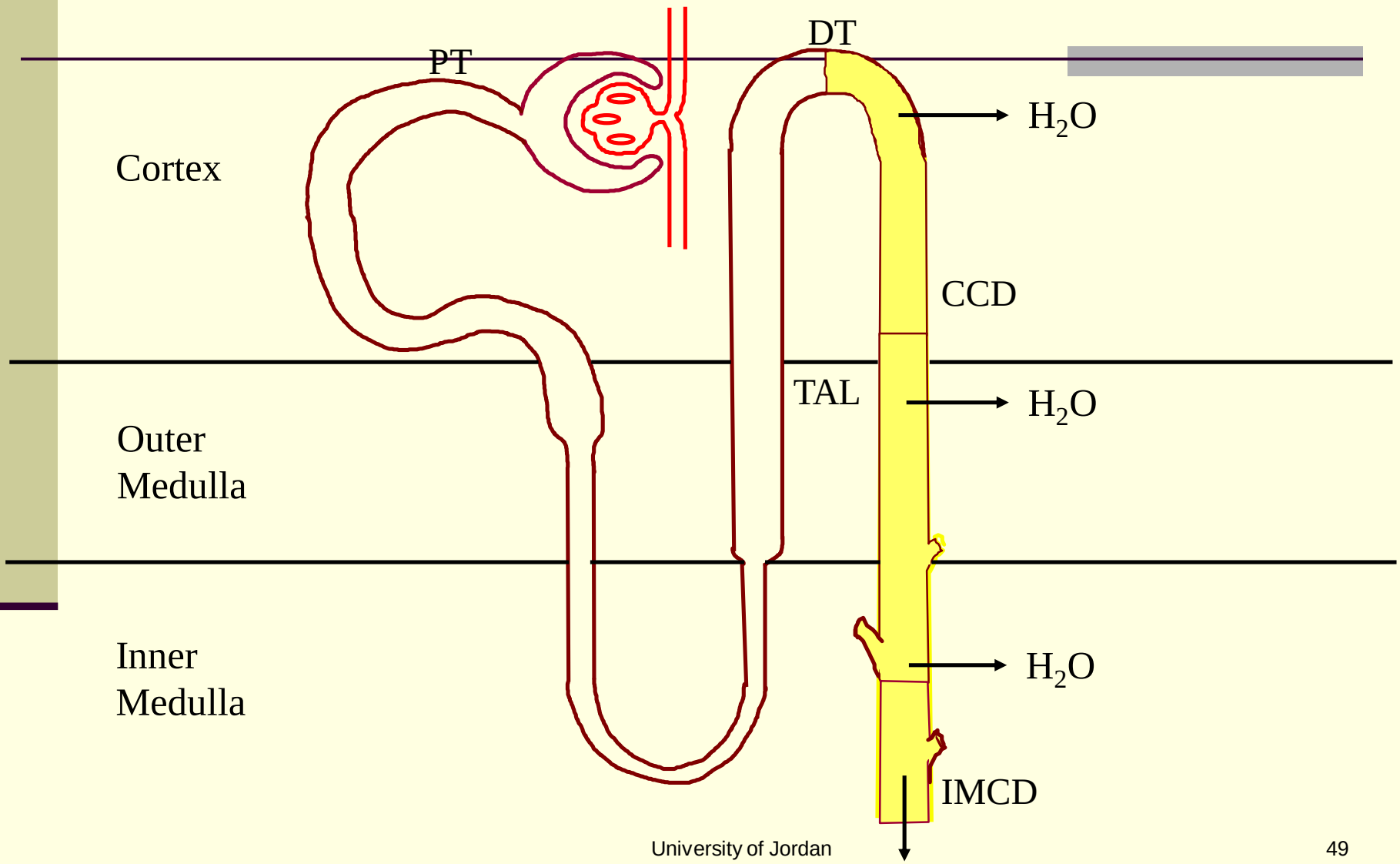
dDAVP

1 2 3 4 5 6 7 8 9

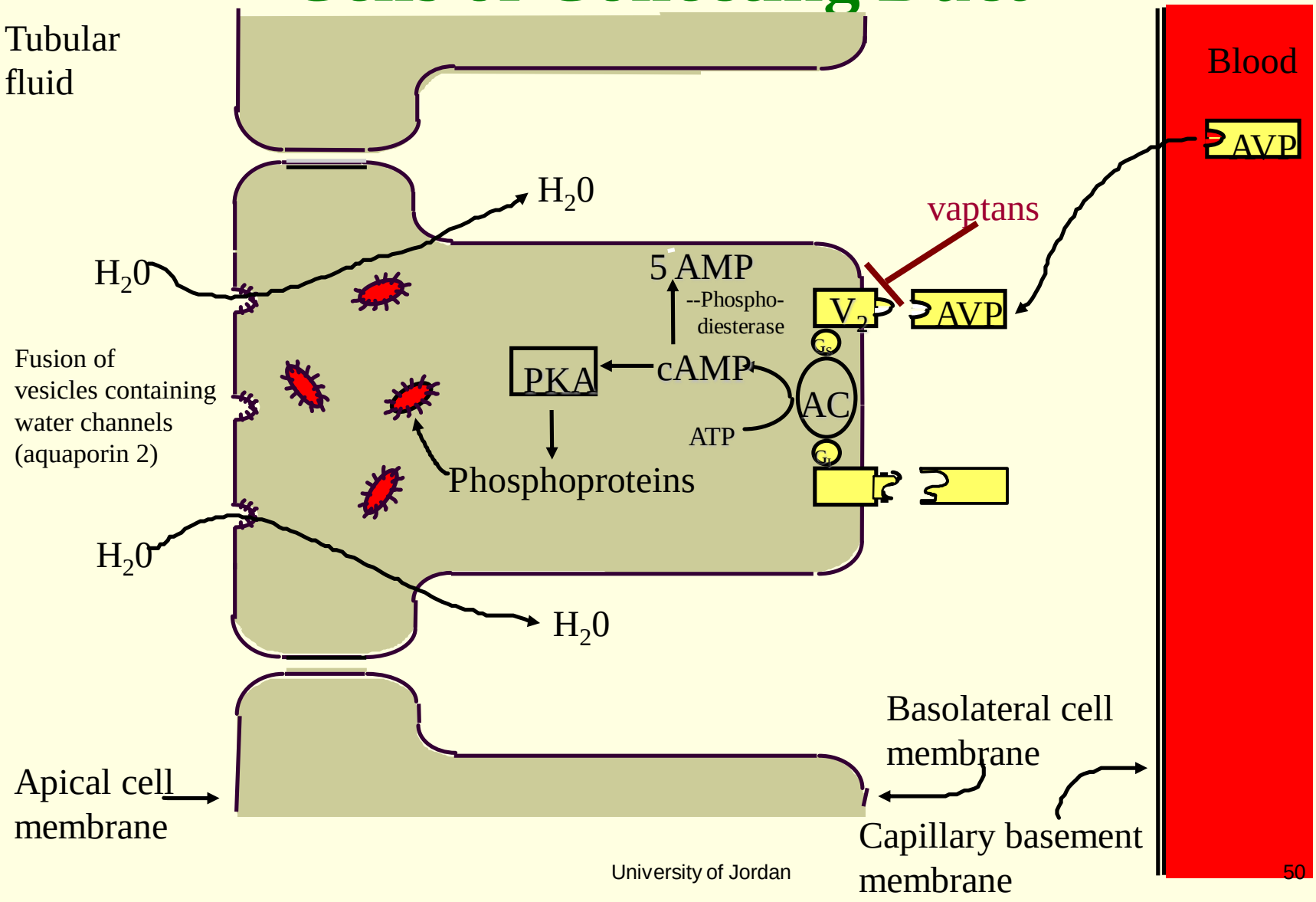
$(CH_2)_2$-CO-Tyr-Phe-Gln-Asn-Cy-Pro-D-Arg-Gly-NH_2

S ——————— S

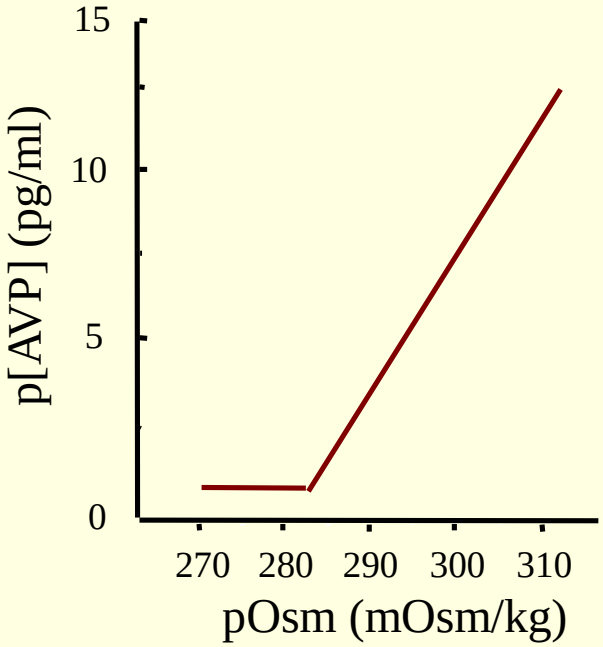
Tubular Effects of AVP

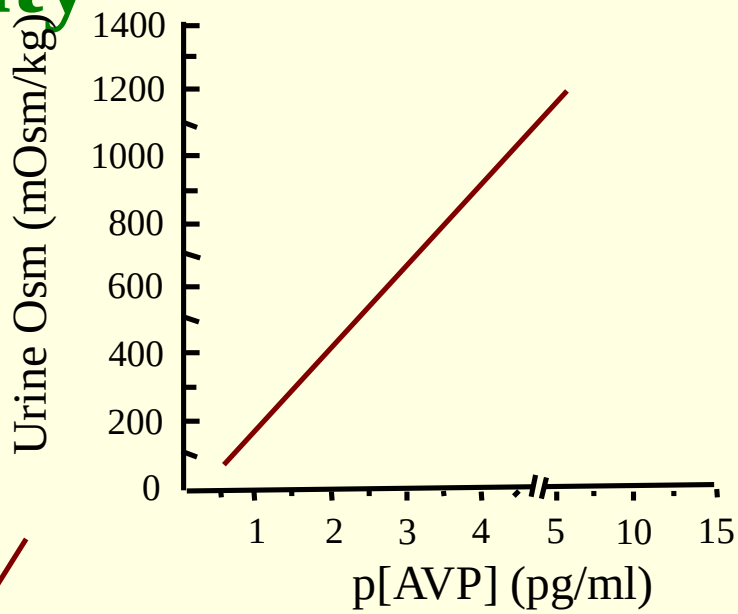


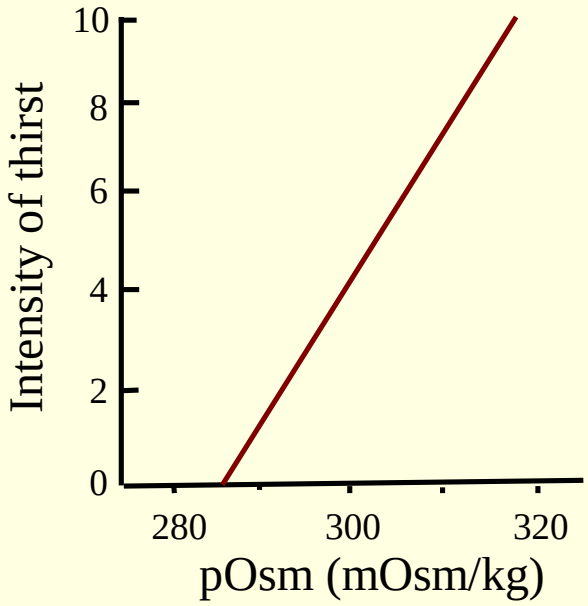
Cellular Actions of AVP on Principal Cells of Collecting Duct



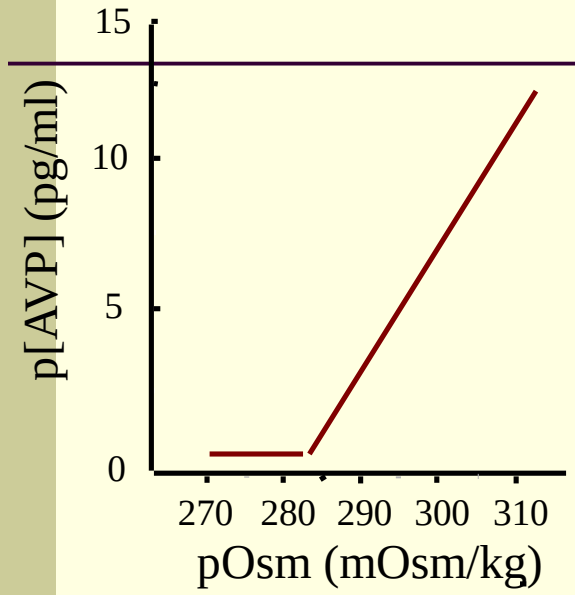
AVP Responses to Changes in Plasma Osmolality

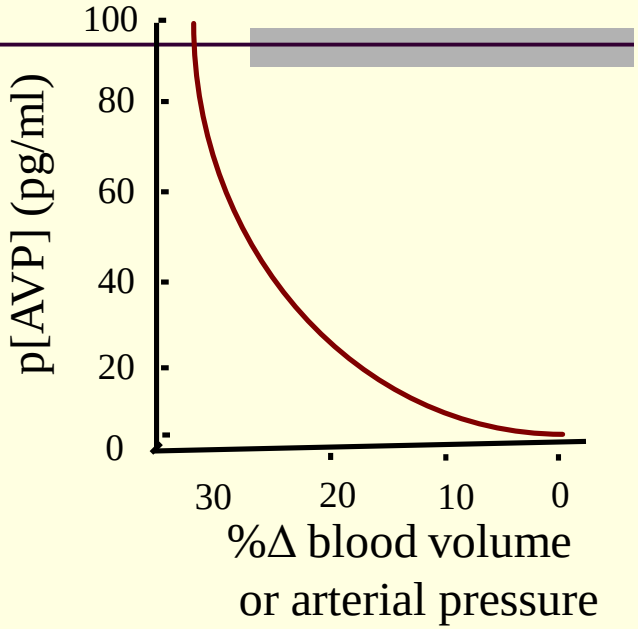


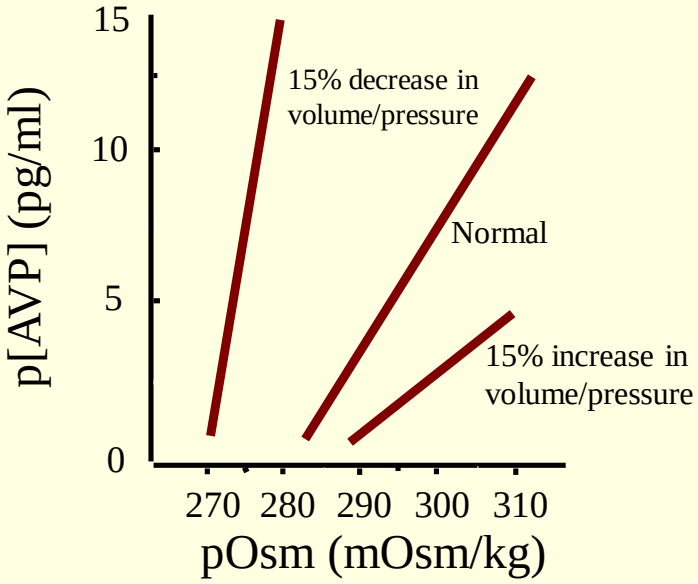




Osmolar and Volume Control of AVP Secretion







Factors Affecting AVP Secretion

Stimulation	Inhibition
Extracellular fluid osmolality increase	Extracellular fluid osmolality decrease
Volume decrease	Volume increase
Pressure decrease	Ethanol
Pain	
Nausea and vomiting	
Stress	
Drugs	
Nicotine	
Morphine	
Barbituates	

Pathophysiology of ADH

- SIADH (syndrome of Inappropriate ADH secretion)
  - Central DI

- Diabetes insipidus
  - Nephrogenic DI

Treatment of SIADH

- Water restriction
- Demeclocyline
- Nonpeptide vasopressin antagonists (vaptans)
  - Conivaptan
  - Tolvaptan

Pathophysiology of ADH

- SIADH (**Syndrome of Inappropriate Antidiuretic Hormone secretion)**
- **Diabetes insipidus**
  - Central DI
  - Nephrogenic DI

Treatment of Diabetes Insipidus

- Central diabetes insipidus

  -DDAVP (desmopressin- (1-desamino-8-D-arginine vasopressin) synthetic vasopressin

Nephrogenic diabetes insipidus

(Treatment for **nephrogenic diabetes insipidus (NDI)** focuses on symptom management and preventing dehydration, as the kidneys cannot respond to antidiuretic hormone)

Thank You