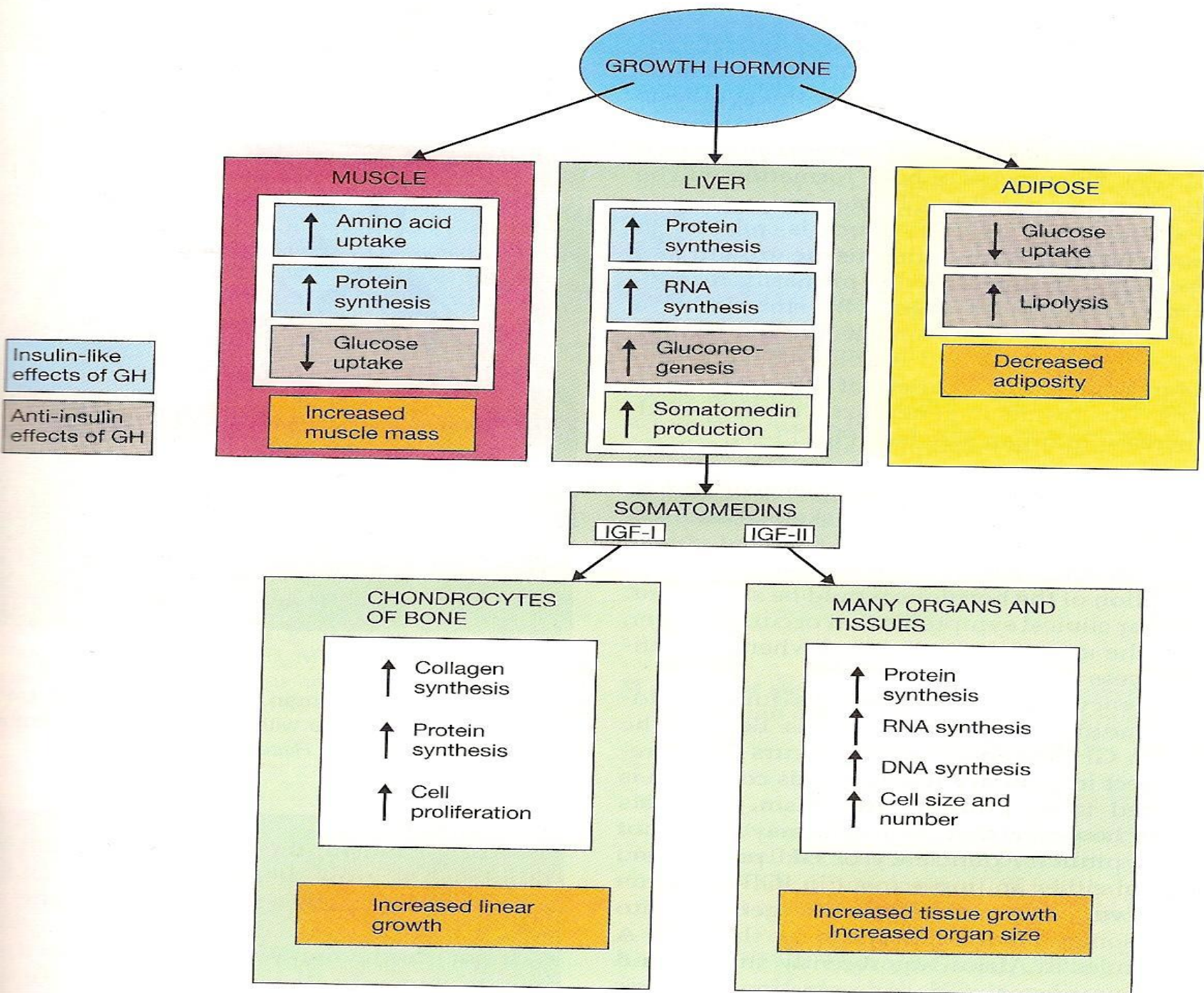
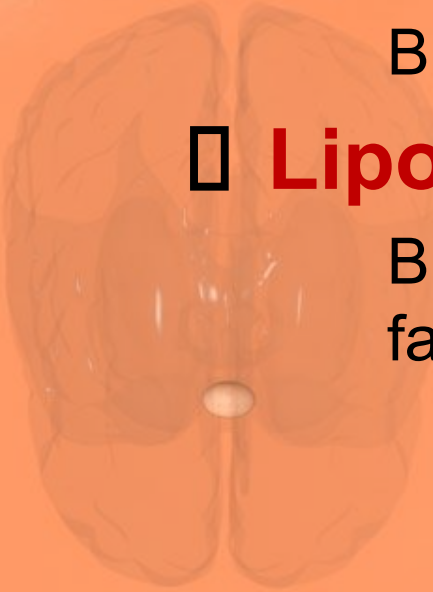






□ Gluconeogenesis

Breakdown of proteins and lipids and conversion of amino acids and fatty acids into glucose

□ Glycogenolysis

Breakdown of liver glycogen into glucose

□ Lipolysis

Breakdown of adipose tissue into non-esterified fatty acids (NEFA)

Diabetogenic Effect of Human Growth Hormone

- Excess of growth hormone
 - ✓ raises blood glucose concentration
 - ✓ pancreas releases insulin continually
 - ✓ beta-cell burnout
- Diabetogenic effect
 - ✓ causes diabetes mellitus if no insulin activity can occur eventually



Role of GH in growth of bone & cartilage

▣ 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 surfaces of older bone & in some bone cavities, ↑ thickness of bone.

- Occurs in membranous bones, e.g. jaw, & skull bones.

Control of GH secretion

□ **The hypothalamus:**

- ✓ GHRH $\rightarrow$ $\uparrow$ GH secretion.
- ✓ GHIRH (somatostatin) $\rightarrow$ $\downarrow$ GH secretion.
- ✓ Estrogens and androgens

□ **Hypoglycemia** $\rightarrow$ $\uparrow$ GH secretion.

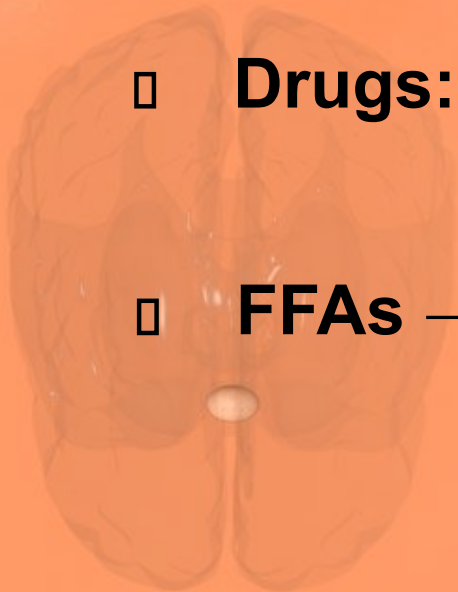
(N.B. glucose intake $\rightarrow$ $\downarrow$ GH secretion).

□ **Muscular exercise** $\rightarrow$ $\uparrow$ GH secretion.

□ **Intake of protein or amino acids** $\rightarrow$ $\uparrow$ GH secretion.

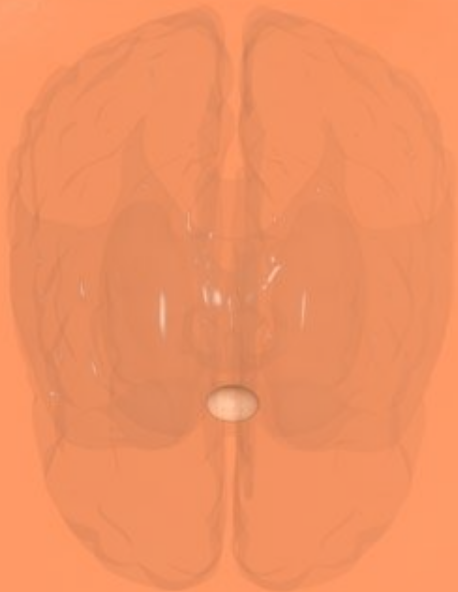
Control of GH secretion

- **During sleep** → ↑ more in children. The first 2 hrs of deep sleep (non-REM)
- **Stress conditions**, e.g. trauma or emotions →
↑ GH secretion.
- **Drugs**: glucagon, lysine-vasopressin & L-Dopa →
↑ GH secretion.
- **FFAs** → ↓ GH secretion.



Regulation of Growth Hormone Secretion

- β -adrenergic receptors stimulate somatostatin release and inhibit GH
- β -adrenergic receptors inhibit hypothalamic release of GHRH



Regulation of hGH secretion (inhibition)

□ **Factors inhibiting secretion:**

- ✓ Hyperglycemia
- ✓ High fatty acids in the blood
- ✓ Aging
- ✓ Obesity

□ **REM sleep**

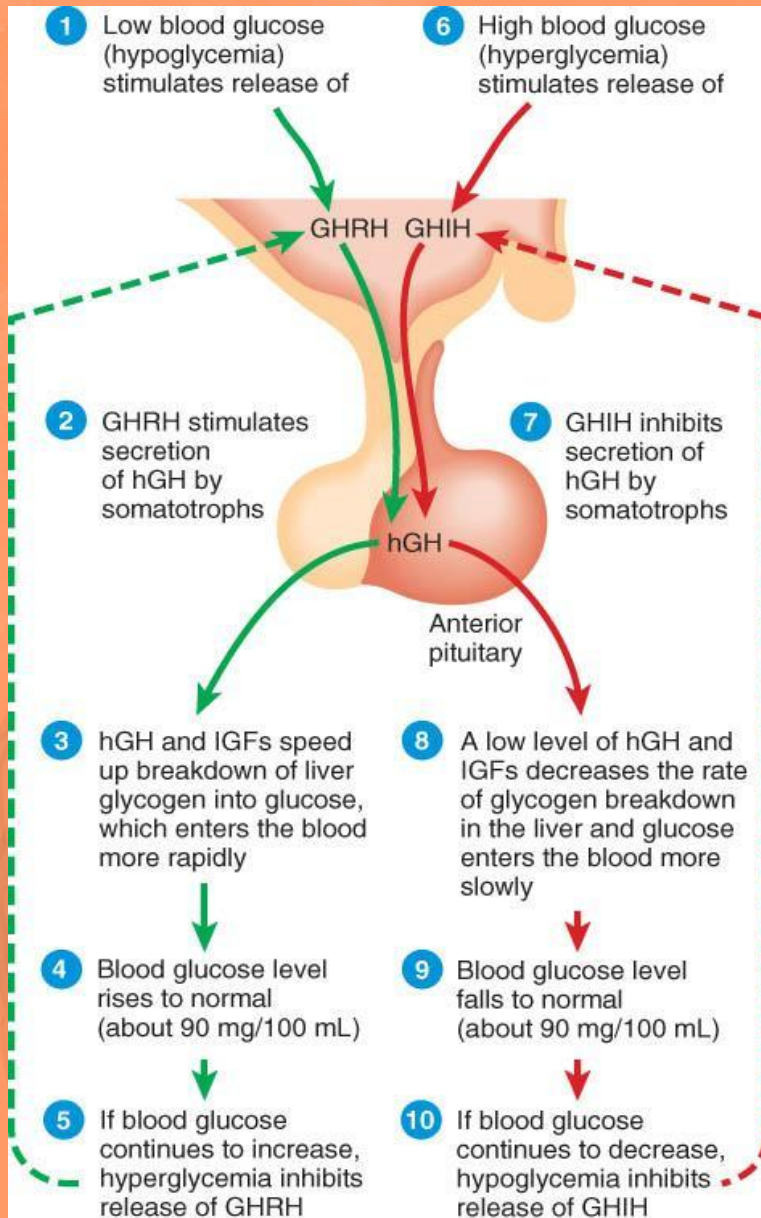
□ **Hormones:**

- ✓ GHIH = Growth hormone inhibitory hormone (Somatostatin)
- ✓ Exogenous growth hormones
- ✓ Somatomedins (IGF)

Human Growth Hormone and Insulin-like Growth Factors

- *Human growth hormone (hGH)* is the most plentiful anterior pituitary hormone.
- It acts indirectly on tissues by promoting the synthesis and secretion of small protein hormones called *insulin-like growth factors (IGFs)*.
 - ✓ IGFs stimulate general body growth and regulate various aspects of metabolism.
 - ✓ Various stimuli promote and inhibit hGH production
 - ✓ One symptom of excess hGH is hyperglycemia.
(Clinical Application)

Regulation of Human Growth Hormone



- Low blood sugar stimulates release of GHRH from hypothalamus
 - ✓ anterior pituitary releases more hGH, more glycogen broken down into glucose by liver cells
- High blood sugar stimulates release of GHIH from hypothalamus
 - ✓ less hGH from anterior pituitary, glycogen does not breakdown into glucose

Actions of growth hormone

- In the liver, growth hormone generates the production of **somatomedins [insulin-like growth factors (IGF)]**, which serve as the intermediaries of several physiologic actions.
- The **IGF receptor** has **tyrosine kinase activity** similar to the insulin receptor.
- **Actions of growth hormone via IGF**
 - (a) ↑ protein synthesis in chondrocytes and ↑ linear growth (pubertal growth spurt)
 - (b) ↑ protein synthesis in muscle and ↑ lean body mass
 - (c) ↑ protein synthesis in most organs and ↑ organ size

Abnormalities of hGH secretion (hypofunction)

□ **Panhypopituitarism** = decrease of secretion of all anterior pituitary hormones

- ✓ Congenital
- ✓ Induced by tumor that destroys the gland

□ **Dwarfism**

- ✓ Decrease of all or more than 1 hormone of anterior pituitary (the person does not reach sexual maturation = missing gonadal hormones)
- ✓ Decrease just in hGH – only smaller person, but can mature

□ **Panhypopituitarism in the adulthood**

- ✓ **Due to:** tumor or thrombosis of the pituitary blood vessels
- ✓ **Results in:** hypothyroidism, decrease in glucocorticoids, suppression of gonadotropic hormones

Abnormalities of hGH secretion (hyperfunction)

- **Gigantism** – increased growing (randomly) = giants
 - ✓ Due to: increased activity of somatotropes or tumor during development
- **Acromegaly** – increased growing of acral parts of the body
 - ✓ Due to: increased activity of somatotropes or tumor after puberty (after closure the epiphysal slits)
 - ✓ Bones grow only to thickness (enlargement of hands and feet, membranous bones such as cranium, nose, supraorbital ridges, chin etc.

Symptoms

- Swelling of the hands and feet
- Facial features become coarse as bones grow
- Body hair becomes coarse as the skin thickens and/or darkens
- Increased perspiration accompanied with body odor
- Protruding jaw
- Voice deepening
- Enlarged lip, nose, and tongue
- Degenerative arthritis
- Thickened ribs (creating a barrel chest)
- Joint pain
- Enlarged heart

Acromegaly

High blood - [Growth Hormone]

Pituitary adenoma
(CT scan or MRI)

Hypertrophy of
sweat & sebaceous glands

Galactorrhoea
(prolactin)

Cardiomegaly
Hypertension

Sexual dysfunction

Peripheral
neuropathy

Visual field defects

Prominent supraorbital ridge

Large nose and jaw
Teeth are separated or lacking

Abnormal glucose
tolerance test
Glucosuria/polyuria

Spade-shaped
hands and feet

Arthrosis



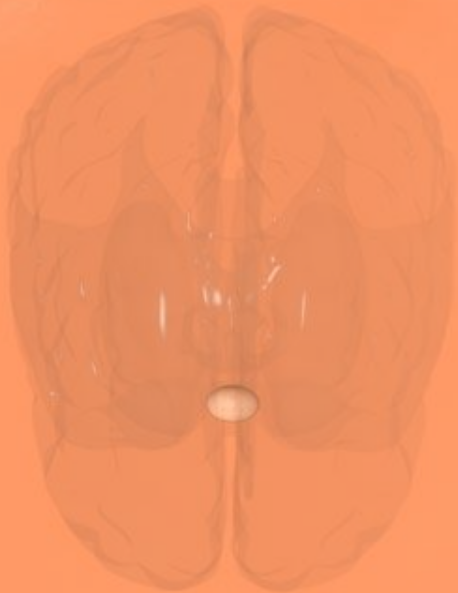




Wide spacing of the teeth

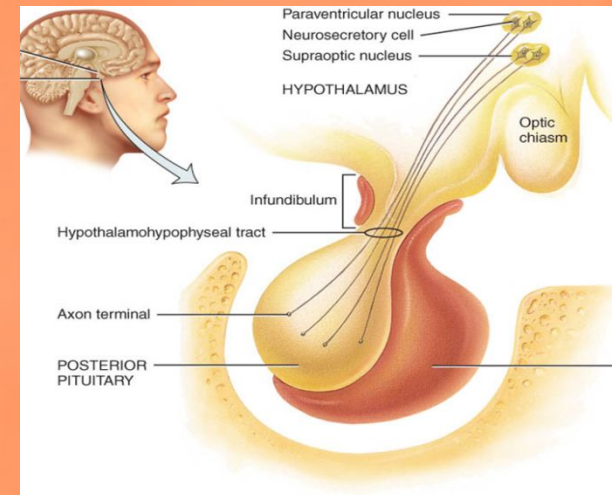


Posterior Pituitary (neurohypophysis)



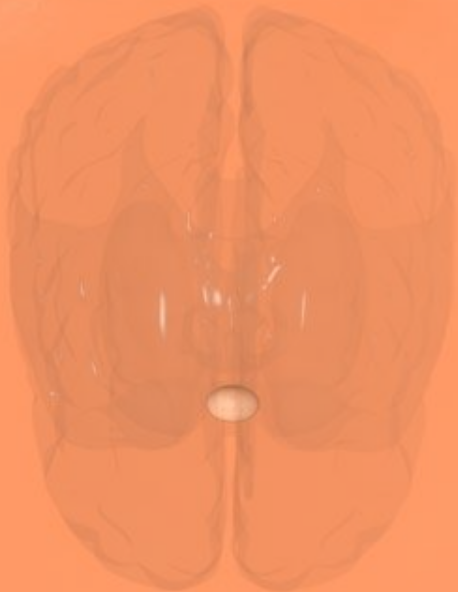
Posterior Pituitary Gland (Neurohypophysis)

- Although the posterior pituitary gland does not synthesize hormones, it does store and release two hormones.
- ✓ Hormones made by the hypothalamus and stored in the posterior pituitary are *oxytocin (OT)* and *antidiuretic hormone (ADH)*
- ✓ The neural connection between the hypothalamus and the neurohypophysis is via the *hypothalamohypophyseal tract*
- paraventricular nucleus - oxytocin
- supraoptical nucleus - vasopresin

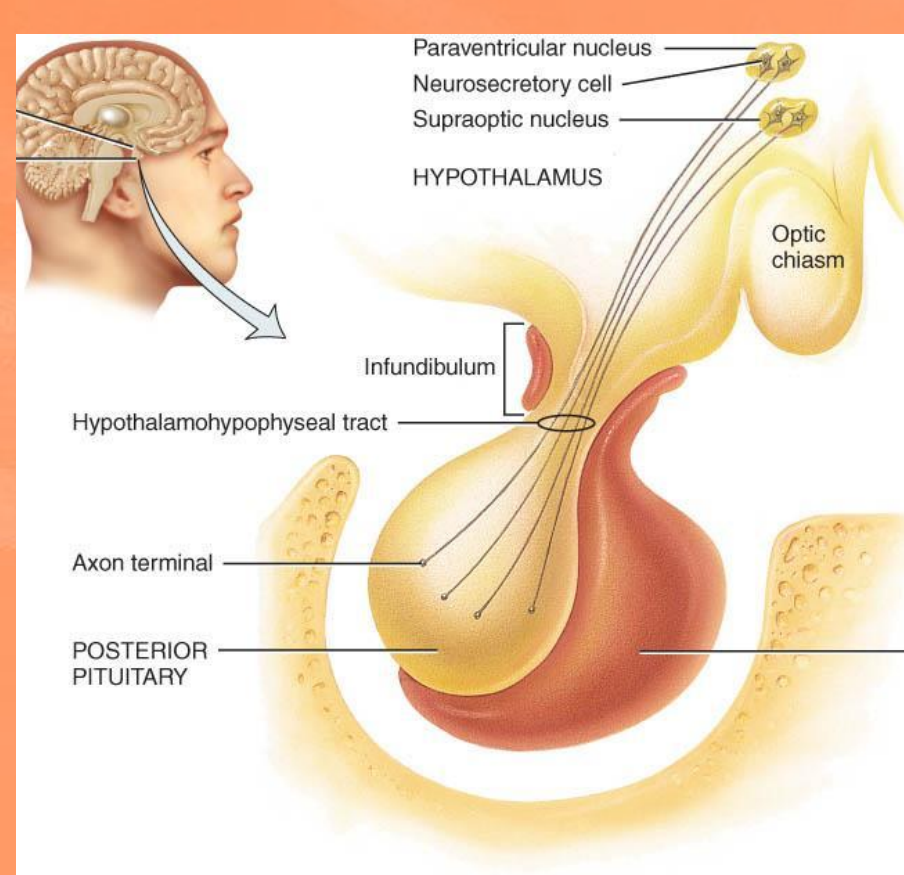


Hormones of the neurohypophysis

- **supraoptic** and **paraventricular nuclei** of the hypothalamus – axoplasm transport of hormones from the hypothalamus to the posterior pituitary
- Similar structure, similar action



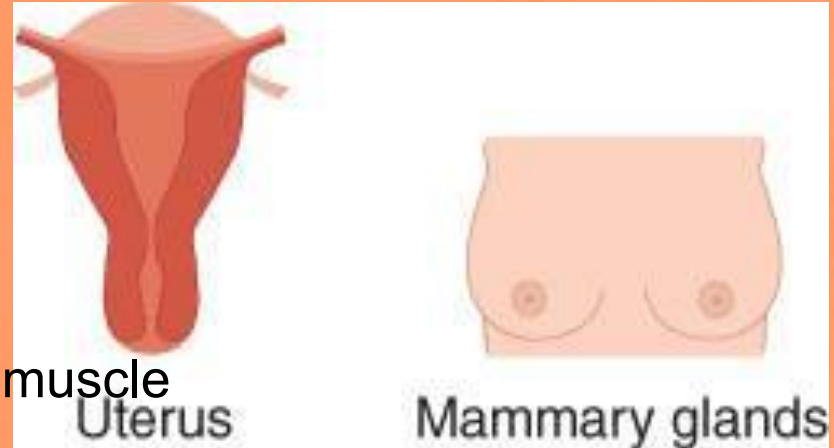
Posterior Pituitary Gland (Neurohypophysis)



- ❑ Does not synthesize hormones
- ❑ Consists of axon terminals of hypothalamic neurons
- ❑ Neurons release two neurotransmitters into capillaries
 - ❑ antidiuretic hormone
 - ❑ oxytocin

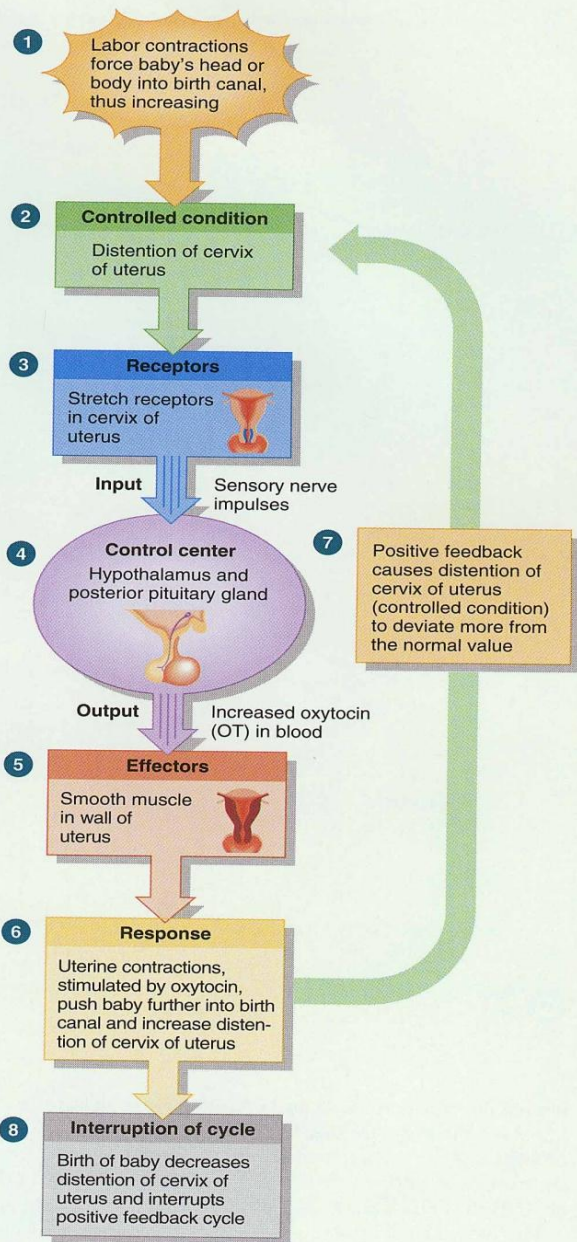
Physiologic effects of oxytocin

- Two target tissues both involved in neuroendocrine reflexes
- During delivery
 - ✓ baby's head stretches cervix
 - ✓ hormone release enhances uterine muscle contraction
 - ✓ baby & placenta are delivered
- After delivery
 - ✓ *Oxytocin* stimulates contraction of the uterus and ejection (let-down) of milk from the breasts.
 - ❖ Nursing a baby after delivery stimulates oxytocin release, promoting uterine contractions and the expulsion of the placenta (Clinical Application).
 - ❖ suckling & hearing baby's cry stimulates milk ejection



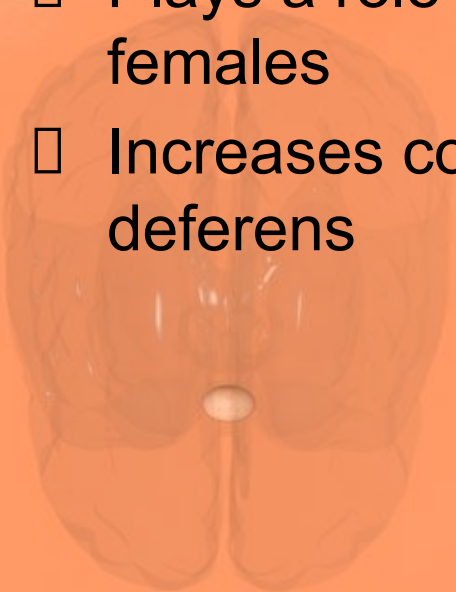
Oxytocin during Labor

- Stimulation of uterus by baby
- Hormone release from posterior pituitary
- Uterine smooth muscle contracts until birth of baby
- Baby pushed into cervix, increase hormone release
- More muscle contraction occurs
- When baby is born, positive feedback ceases



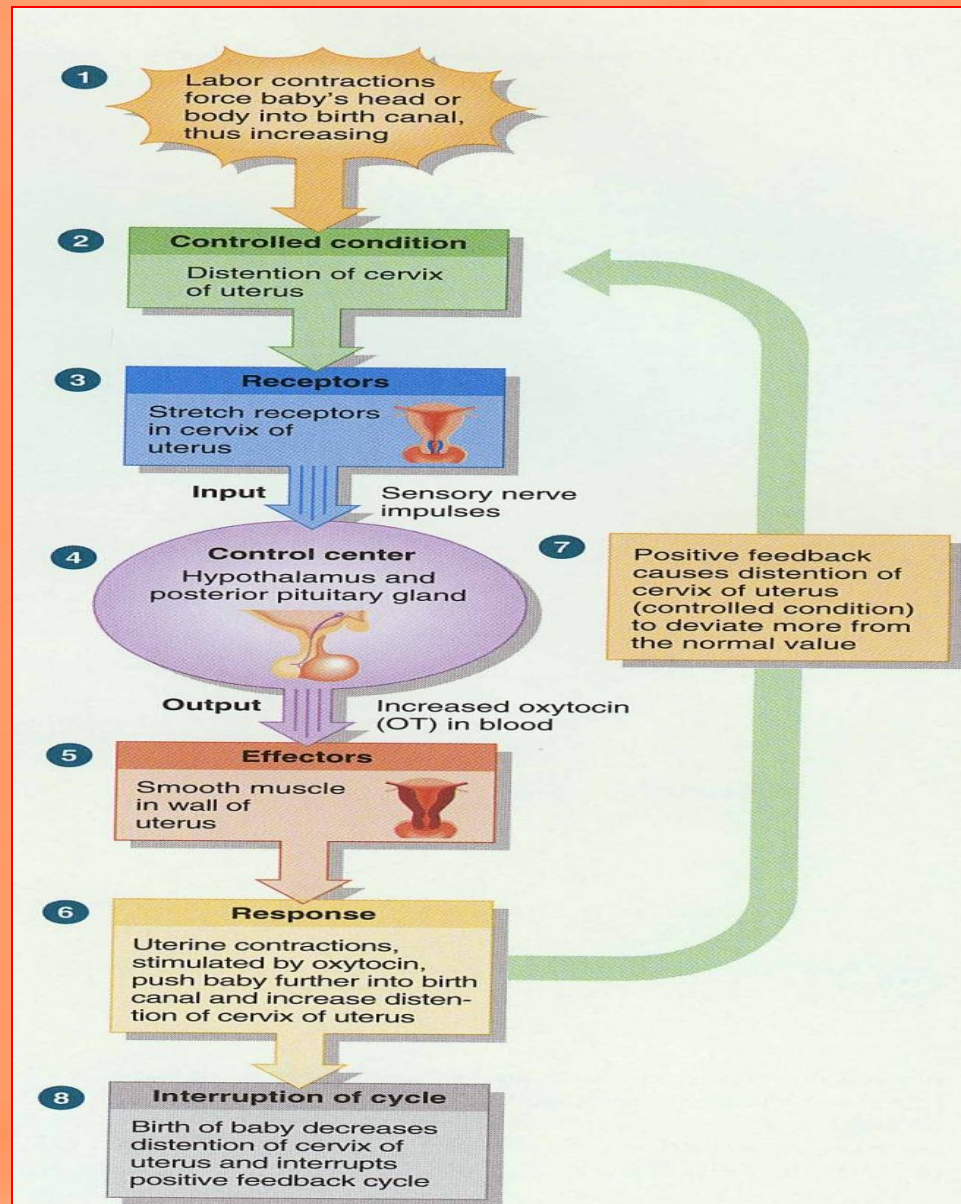
Physiologic effects of oxytocin

- Stimulates uterine contractions during childbirth by mobilizing Ca^{2+} through a PIP_2 (phosphatidylinositol 4,5-diphosphate) - Ca^{2+} second-messenger system
- Also triggers milk ejection (“letdown” reflex) in women producing milk
- Plays a role in sexual arousal and orgasm in males and females
- Increases contraction of smooth muscle of the vas deferens



Positive Feedback

- Oxytocin stimulates uterine contractions
- Uterine contractions stimulate oxytocin release



Physiologic effects of oxytocin

- Stimulates contraction of the smooth muscle (myometrium) of the lactating mammary gland (**milk ejection**) and myometrium of the uterus.
- The sensitivity of the myometrium to exogenous oxytocin during pregnancy increases as pregnancy advances.
- Oxytocin plays a role in **labor** and has been shown to be a useful therapeutic agent in the induction of labor.

Control of oxytocin secretion

Stimuli

- Stimulation of the “touch receptor” around the nipples
- Milk let-down or “milk ejection reflex” (latent period: 30-60 seconds)
- Genital tract stimulation

Inhibition

- Milk let-down can be inhibited by emotional stress and psychic factors such as fright
 - ✓ NE & Epi inhibit its secretion
 - ✓ Ethanol
 - ✓ enkephalins

Vasopressin (ADH)

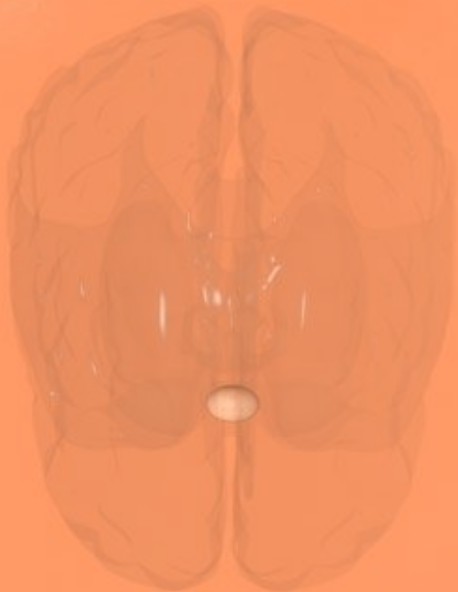
Is also known as antidiuretic hormone (ADH)

Participates in body water regulation (Water is lost from lungs, sweat, feces and urine on a daily basis)



Synthesis of ADH

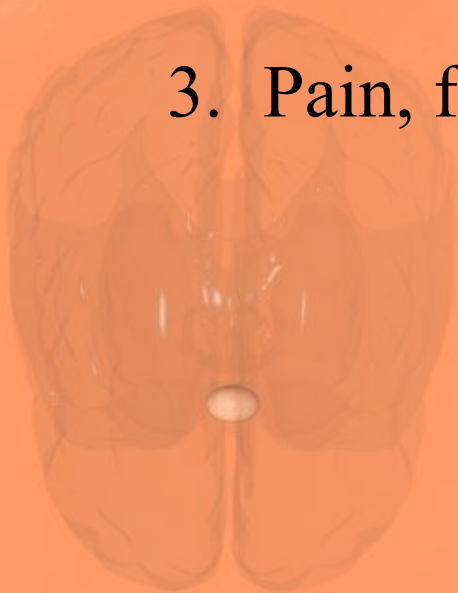
- ADH synthesized in the cell bodies of hypothalamic neurons in the supraoptic nucleus
- ADH is stored in the neurohypophysis (posterior pituitary)—forms the most readily released ADH pool



Vasopressin (ADH) Secretion

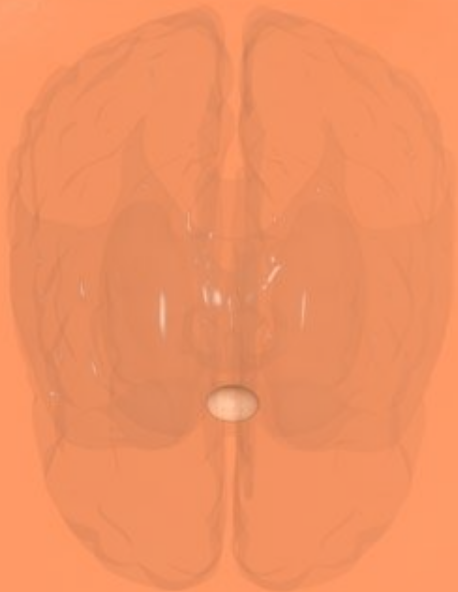
Secretion is Stimulated by:

1. Large decreases in blood volume
2. Decreases in blood pressure
3. Pain, fear, trauma, and stress



Vasopressin

- Antidiuretic hormone V_2 -receptor: collecting duct
and distal convoluted tubule
- Vasopressor hormone V_1 -receptor: vascular
smooth muscle



Vasopressin

Decreases water excretion by kidneys (V_2 receptors)

Constricts blood vessels (V_1 receptors)- arteriolar smooth muscle

