

Anterior pituitary

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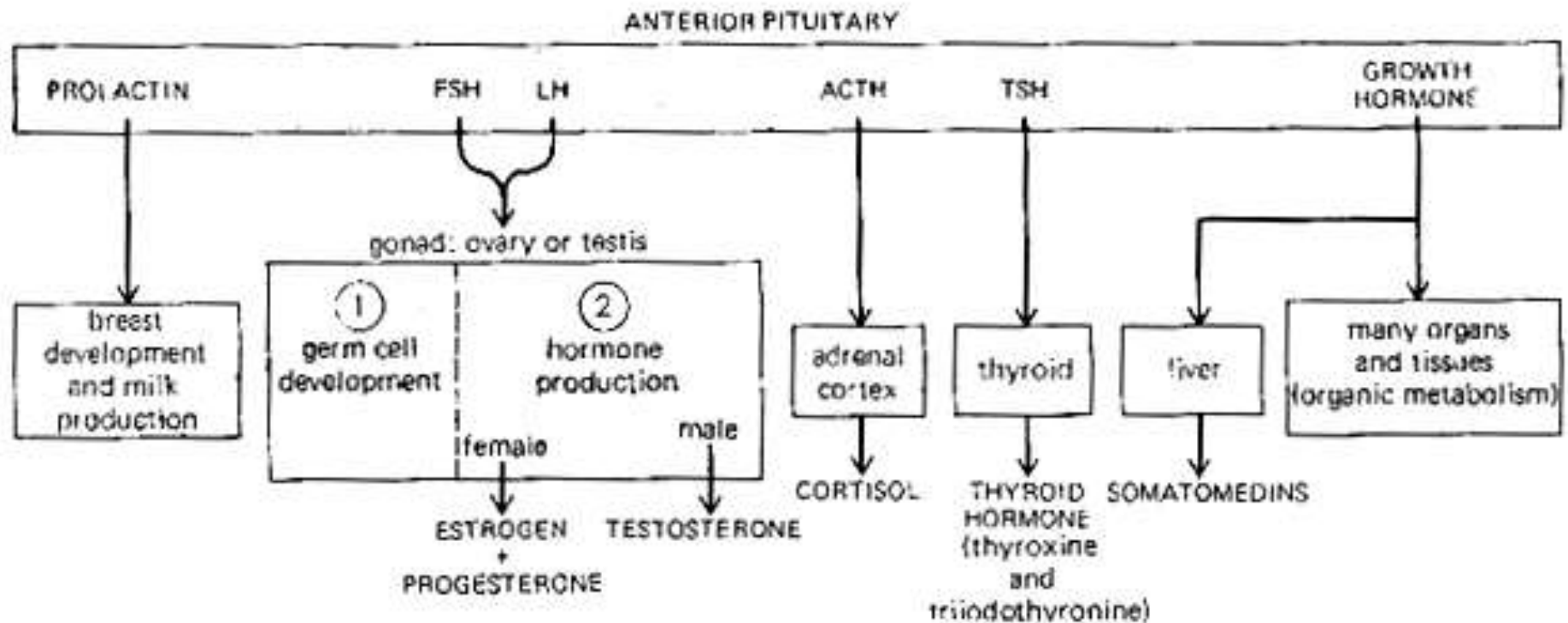
Anterior pituitary

- **Anterior pituitary:** connected to the hypothalamus by hypothalamoanterior pituitary portal vessels.
- The anterior pituitary produces six peptide hormones:
 - prolactin, growth hormone (GH),
 - thyroid stimulating hormone (TSH),
 - adrenocorticotrophic hormone (ACTH),
 - follicle-stimulating hormone (FSH),
 - luteinizing hormone (LH).

Anterior pituitary cells and hormones

Cell type	Pituitary population	Product	Target
Corticotroph	15-20%	ACTH β -lipotropin	Adrenal gland Adipocytes Melanocytes
Thyrotroph	3-5%	TSH	Thyroid gland
Gonadotroph	10-15%	LH, FSH	Gonads
Somatotroph	40-50%	GH	All tissues, liver
Lactotroph	10-15%	PRL	Breasts gonads

Anterior pituitary hormones



Regulation of Growth Hormone Secretion

- GH secretion controlled primarily by hypothalamic GHRH stimulation and somatostatin inhibition
- Neurotransmitters involved in control of GH secretion— via regulation of GHRH and somatostatin
- Neurotransmitter systems that stimulate GHRH and/or inhibit somatostatin
 - Catecholamines acting via α 2-adrenergic receptors
 - Dopamine acting via D1 or D2 receptors
 - Excitatory amino acids acting via both NMDA (N-methyl D-Aspartic acid) and non-NMDA receptors

Growth hormone vs. metabolic state

- During protein intake GH and insulin promote anabolic reactions. They convert amino acids to protein and stimulate growth.
- During carbohydrate intake, GH antagonizes insulin effects-- blocks glucose uptake to prevent hypoglycemia.
- When there is adequate glucose as during absorptive phase, and glucose uptake is required, then GH secretion is inhibited so it won't counter act insulin action.
- During fasting, GH antagonizes insulin action and helps mediate glucose sparing, ie stimulates gluconeogenesis
- In general, during anabolic or absorptive phase, GH facilitates insulin action, to promote growth.
- During fasting or post-absorptive phase, GH opposes insulin action, to promote catabolism or glucose sparing.

Acromegaly and Gigantism

- Caused by eosinophilic adenomas of somatotrophs
- Excess GH leads to development of **gigantism** if hypersecretion is present during early life— a rare condition
 - Symmetrical enlargement of body resulting in true giant with overgrowth of long bones, connective tissue and visceral organs.
- Excess GH leads to **acromegaly** if hypersecretion occurs after body growth has stopped.
 - Elongation of long bones not possible so there is over growth of cancellous bones (*spongy bone*)— protruding jaw, thickening of phalanges, and over growth of visceral organs (interior organs).

ACTH: adrenocorticotrophic hormone: synthesis and regulation of secretion

- Produced in corticotrophs
- ACTH is produced in the anterior pituitary by proteolytic processing of Prepro-opiomelanocortin (POMC).
- Other neuropeptide products include β and γ lipotropin, β -endorphin, and α -melanocyte-stimulating hormone (α -MSH).
- ACTH is a key regulator of the stress response

Addison's Disease

- Disease in which patients lack cortisol from zona fasciculata, and thus lacks negative feedback that suppresses ACTH production
- Result: overproduction of ACTH
- Skin color will darken

β -endorphin

- An endogenous **opioid peptide neurotransmitter** found in the neurons of both the **central** and **peripheral nervous system**.
- It is an agonist of the opioid receptors.
- It is used as an analgesic in the body to numb or dull pains.
- β -endorphin has approximately 80 times the analgesic potency of morphine.
- β -endorphin is believed to have a number of other benefits, including:
 - Slowing the growth of cancer cells
 - Promoting feeling of well-being
 - Increasing relaxation

Melanocyte-stimulating hormone (MSH)

- MSH peptides derived by proteolytic cleavage of POMC
- α -MSH has antipyretic and anti-inflammatory effects
 - Also inhibits CRH and LHRH secretion
- Four MSH receptors identified
- May inhibit feeding behavior
- ACTH has MSH-like activity
- However– MSH has NO ACTH like activity

Glycoprotein hormones

- LH, FSH, TSH and hCG
 - α and β subunits
 - Each subunit encoded by different gene
- α subunit is identical for all hormones
- β subunit are unique and provide biological specificity

Gonadotrophs

- Cells in anterior pituitary that produce LH and FSH
- Synthesis and secretion stimulated by GnRH—major effect on LH
- FSH secretion controlled by inhibin
- Pulsatile secretion of GnRH and inhibin cause distinct patterns of LH and FSH secretion

LH/FSH

- Pulsatile pattern of secretion
 - LH pulses are biphasic (every 1 minute, then large pulse at 1 hour)
 - FSH pulses are uniphasic
- Diurnal– LH/FSH more pronounced during puberty
- Cyclic in females– ovarian cycle with LH surge at time of ovulation
- Males are not cyclic, but constant pulses of LH cause pulses of testosterone to be produced

Thyrotrophs

- Site of TSH synthesis
- Pattern of secretion is relatively steady
- TSH secretion stimulated by TRH
- Feedback control by T3 (thyroid hormone)

Grave's disease

- Hyperthyroidism caused by circulating antibodies to the TSH receptor.
- Associated with diffuse goiter.
- Autoantibodies bind to TSH receptor and mimic the action of TSH itself leads to persistent stimulation of thyroid and elevated levels of thyroid hormones.

Lactotrophs

- Site of production of prolactin
- Lactogenesis (milk synthesis) requires prolactin
- Tonically inhibited
 - Of the anterior pituitary hormones, the only one
 - Multifactoral control, balance favors inhibition
- Dopamine inhibits prolactin
- Prolactin releasing hormone is TRH
 - Oxytocin also stimulates prolactin release
 - Estradiol enhances prolactin synthesis

Prolactin

- Stimulates breast development and lactogenesis
- May be involved in development of Leydig cells in pre-pubertal males
- Immunomodulatory effects– stimulates T cell functions
 - Prolactin receptors in thymus

Antidiuretic Hormone: ADH

ADH is also known as arginine vasopressin (AVP = ADH) because of its vasopressive activity, but its major effect is on the kidney in preventing water loss.

conserve body water and regulate tonicity of body fluids

➤ **Regulated by osmotic and volume stimuli**

➤ **Water deprivation increases osmolality of plasma which activates hypothalamic osmoreceptors to stimulate ADH release**

Actions of ADH

The major action of ADH is on renal cells that are responsible for reabsorbing free (osmotically unencumbered) water from the glomerular filtrate.

ADH responsive cells line the distal convoluted tubules and collecting ducts of the renal medulla.

ADH increases the permeability of these cells to water.

The increase in membrane permeability to water permits back diffusion of water along an osmotic gradient.

ADH significantly reduces free-water clearance by the kidney

Oxytocin

- In uterus during parturition
- In mammary gland during lactation
- suckling is major stimulus for release.
- sensory receptors in nipple connect with nerve fibers to the spine, then impulses are relayed through brain to PVN where cholinergic synapses fire on oxytocin neurons and stimulate release.