

Pharmacology - ES

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Hypothalamus and Pituitary

Hypothalamus and Pituitary

☒ The importance of the hypothalamus and the pituitary gland is due to the fact that they work together as one unit and control the whole endocrine system

- The hypothalamus-pituitary unit is the most dominant portion of the entire endocrine system.
- The output of the hypothalamus-pituitary unit regulates the function of the (endocrine glands) thyroid, adrenal and reproductive glands and also controls somatic growth, lactation, milk secretion and water metabolism. And the glands that do these jobs

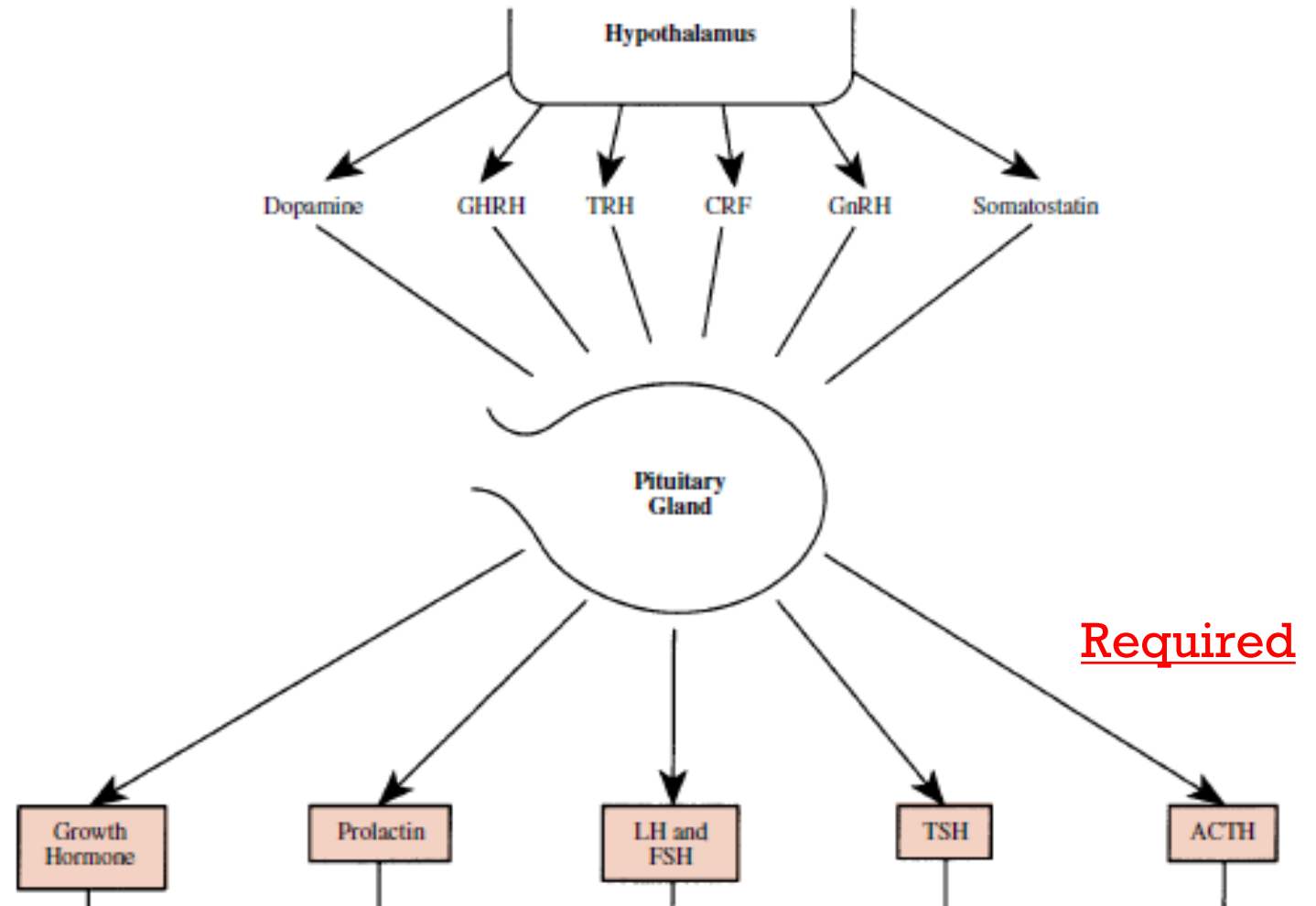
- Pituitary function depends on the hypothalamus and the anatomical organization of the hypothalamus-pituitary unit reflects this relationship.

- The pituitary gland lies in a pocket of bone at the base of the brain, just below the hypothalamus to which it is connected by a stalk containing nerve fibers and blood vessels. The pituitary is composed to two lobes-- **anterior** and **posterior (each lobe is responsible for secreting certain types of hormones)**

ANTERIOR PITUITARY HORMONES

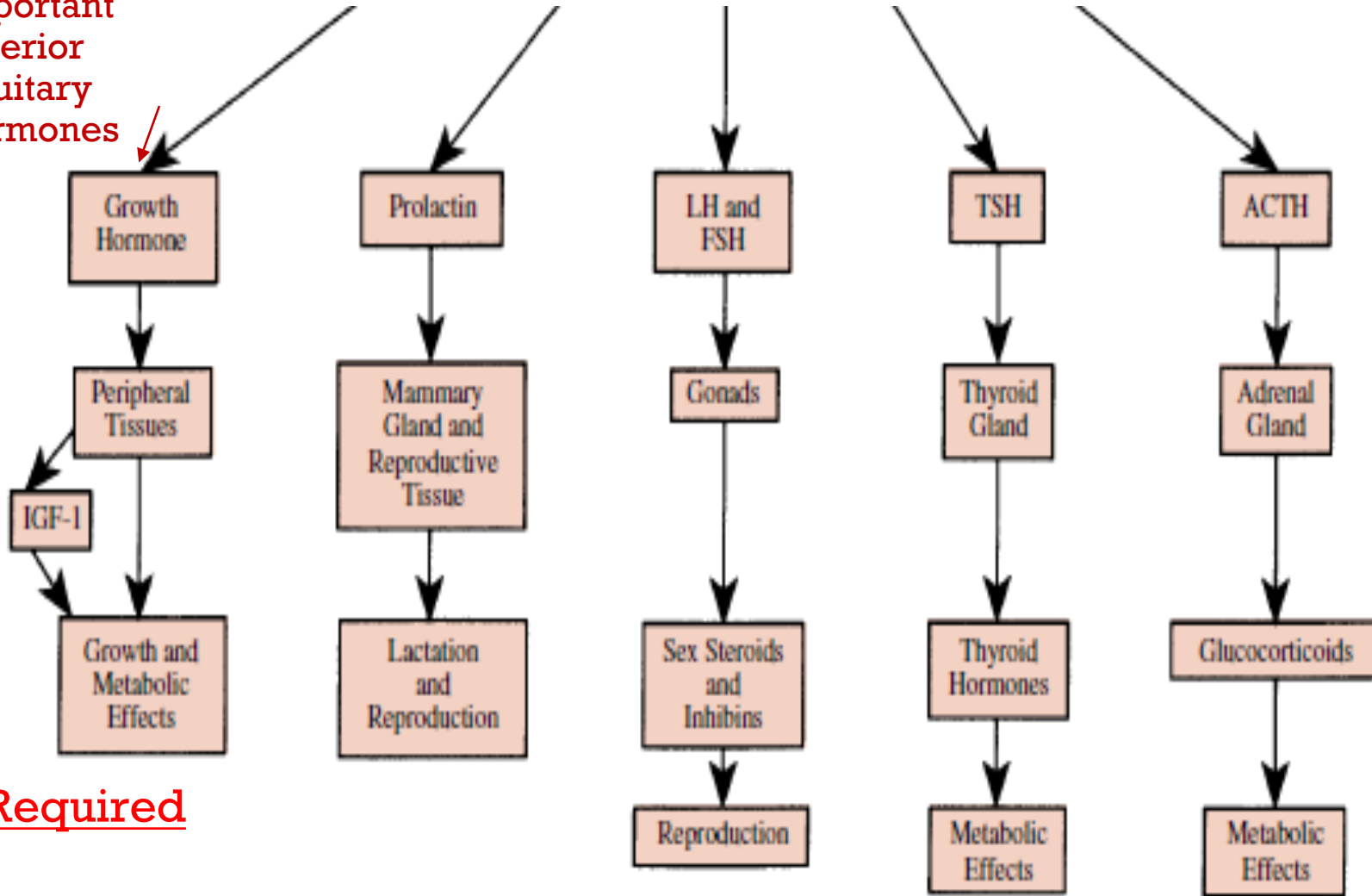
Six major hormones are secreted by the adenohypophysis, or anterior pituitary gland

The diagram shows the connection between the hypothalamus and the pituitary gland, the anterior pituitary gland, to be exact. The connection is through hormones secreted from the hypothalamus. These hormones affect/regulate the pituitary gland and induce the release of pituitary hormones. With regards to the anterior pituitary gland, there are 6 hormones which control and regulate the endocrine glands



Hormones of the hypothalamus and the anterior pituitary gland

One of the most important anterior pituitary hormones



Required

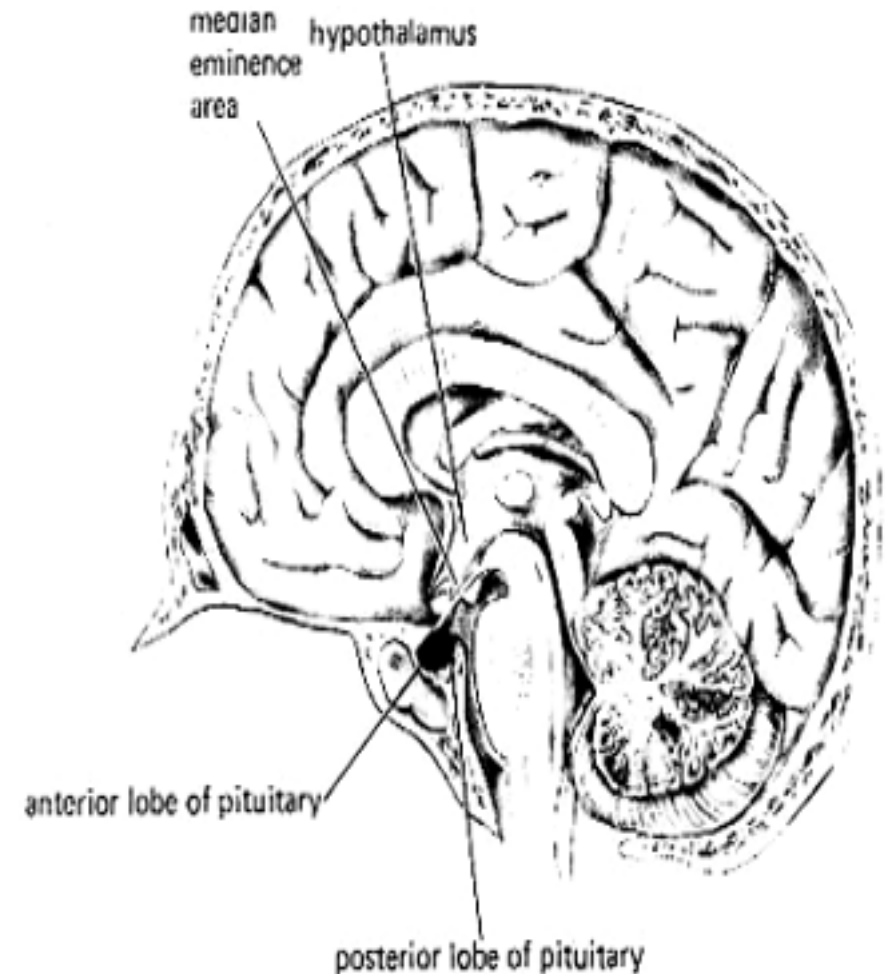
The diagram illustrates what we've said before. There are six hormones secreted by the anterior pituitary gland. (You'll have to refer back to this diagram every time we talk about a specific hormone)..Throughout this lecture, we'll be talking about the hormones that are shown in this diagram, further explaining the relationship between the pituitary gland hormones and the glands that are controlled by these hormones.

TRH, thyrotropin releasing hormone; CRF, corticotropin releasing hormone; GnRH, gonadotropin releasing hormone; LH, luteinizing hormone; FSH, follicle-stimulating hormone; TSH, thyroid-stimulating hormone; ACTH, adrenocorticotrophic hormone; IGF-1, insulinlike growth factor 1.

Anterior pituitary: adenohypophysis

- **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).**

This is a cross section of the brain, which shows the hypothalamus and the pituitary gland (ant. and post. parts). It shows the median eminence, the area of connection between the hypothalamus and pituitary gland



Posterior Pituitary: neurohypophysis

- **Posterior pituitary:** an outgrowth **or protrusion** of the hypothalamus composed of neural tissue.
- Hypothalamic neurons pass through the neural stalk and end in the posterior pituitary.
- The upper portion of the neural stalk extends into the hypothalamus and is called the **median eminence**. **the area that connects the hypothalamus to the pituitary gland.**

Hypothalamic releasing hormones Travel to specific cells in anterior pituitary to stimulate synthesis and secretion of trophic hormones

Specific hormones are secreted from the hypothalamus (hypothalamic releasing hormones) induce the production and The release of hormones from the pituitary gland

Hypothalamic releasing hormone	Effect on pituitary
Corticotropin releasing hormone (CRH)	Stimulates ACTH secretion
Thyrotropin releasing hormone (TRH)	Stimulates TSH and Prolactin secretion
Growth hormone releasing hormone (GHRH)	Stimulates GH secretion
Somatostatin	Inhibits GH (and other hormone) secretion
Gonadotropin releasing hormone (GnRH)	Stimulates LH and FSH secretion
Prolactin releasing hormone (PRH)	Stimulates PRL secretion
Prolactin inhibiting hormone (dopamine)	Inhibits PRL secretion

Required

ANTERIOR PITUITARY HORMONES

Anterior pituitary hormones

ANTERIOR PITUITARY GLAND CELL TYPE	STIMULATORY HYPOTHALAMIC FACTORS	INHIBITORY HYPOTHALAMIC FACTORS	PITUITARY HORMONES RELEASED	MAJOR TARGET ORGAN	TARGET GLAND HORMONES
Somatotroph	GHRH, Ghrelin	Somatostatin	GH	Liver	Insulin-like growth factors
Lactotroph	TRH	Dopamine, Somatostatin	Prolactin	Mammary gland	None
Gonadotroph	GnRH	None known	LH and FSH	Gonads	Estrogen, progesterone, and testosterone
Thyrotroph	TRH	Somatostatin	TSH	Thyroid gland	Thyroxine and triiodothyronine
Corticotroph	CRH	None known	ACTH	Adrenal cortex	Cortisol, adrenal androgens

The table gives us information about :

- 1) Anterior pituitary gland cell types
- 2) The hormones that are released from each type of cell
- 3) The hypothalamic factors (stimulatory/inhibitory hormones) which regulate the release of these anterior pituitary hormones.
- 4) The major target organ
- 5) target gland hormones (hormones released from the affected /stimulated target organ [which is affected by ant. Pituitary hormones])

Examples from the table:

✓ Ex1:

- **GHRH** (Growth hormone Releasing hormone), is released from the **hypothalamus**. It stimulates the release of **GH** from the anterior pituitary gland (from **Somatotrophs**).
- On the other hand, **Somatostatin** is released from the hypothalamus, inhibiting **GH** release.
- The GH targets the **LIVER** and affects the release of **Insulin-like growth factors**.

✓ Ex2:

- **Prolactin** is released from the **Lactotrophs** of the anterior pituitary gland in response to stimulation by hypothalamic TRH (Thyroid Releasing Hormone). It is inhibited by **Somatostatin and Dopamine**.

Growth Hormone

- Growth hormone, or somatotropin, is a protein that stimulates linear body growth in children and regulates cellular metabolism in both adults and children

2 Major effects

- stimulates lipolysis, enhances production of free fatty acids, elevates blood glucose

- Enhance production of an insulinlike growth factor (IGF-1)
Has an effect on linear body growth in children and regulates cellular metabolism in adults and children.

- Growth hormone

is released during sleep, with maximum release (peak) occurring an hour after the onset of sleep. (that's why we stress on the importance of sleep for children, in order to keep their growth patterns within the appropriate limits).

Prolactin

- In women, prolactin acts with other hormones on the mammary gland during pregnancy to develop lactation and after birth to maintain it.
- Hyperprolactinemia (**increase prolactin levels**) causes impotence in men and amenorrhea and infertility in women
- Prolactin serum levels increase during pregnancy and breast-feeding, at least immediately after the birth.
- Increases markedly during stress

- There is no known therapeutic use for prolactin, but serum levels are measured to diagnose hyperprolactinemia
- Approximately one-third of women who need treatment for infertility have high serum prolactin levels. In some cases the only reason for infertility is hyperprolactinemia, so the treatment will be lowering the hormone level
- Hyperprolactinemia has been traditionally treated by the dopaminergic agonist bromocriptine (*Parodel*) If you refer to the table, you will notice that Dopamine (released from the hypothalamus) INHIBITS the release of Prolactin. So, a dopaminergic agonist would be effective in lowering prolactin levels.

Lactotrophs

- Site of production of prolactin
- Lactogenesis (milk synthesis) requires prolactin
- Dopamine inhibits prolactin production → **Dopaminergic agonists are used to treat hyperprolactinemia**
- Prolactin releasing hormone is TRH
 - Oxytocin also stimulates prolactin release
 - Estradiol enhances prolactin synthesis

ACTH: adrenocorticotrophic hormone: synthesis and regulation of secretion

- Produced in corticotrophs (anterior pituitary gland cells)
- 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). (Their levels increase with increased ACTH level)
- ACTH is a key regulator of the stress response (used to measure stress)

Over stress is also reflected by an increase in MSH \rightarrow overproduction of melanin \rightarrow skin pigmentation

ACTH

- Adrenocorticotrophic hormone (ACTH), or corticotropin
 - ACTH is made up of 39 amino acids
 - Regulates adrenal cortex and synthesis of adrenocorticosteroids
 - Overproduction of ACTH may accompany increased pigmentation due to α -MSH. **Overproduction may lead to increased pigmentation of areas of the skin.**
- ACTH stimulates

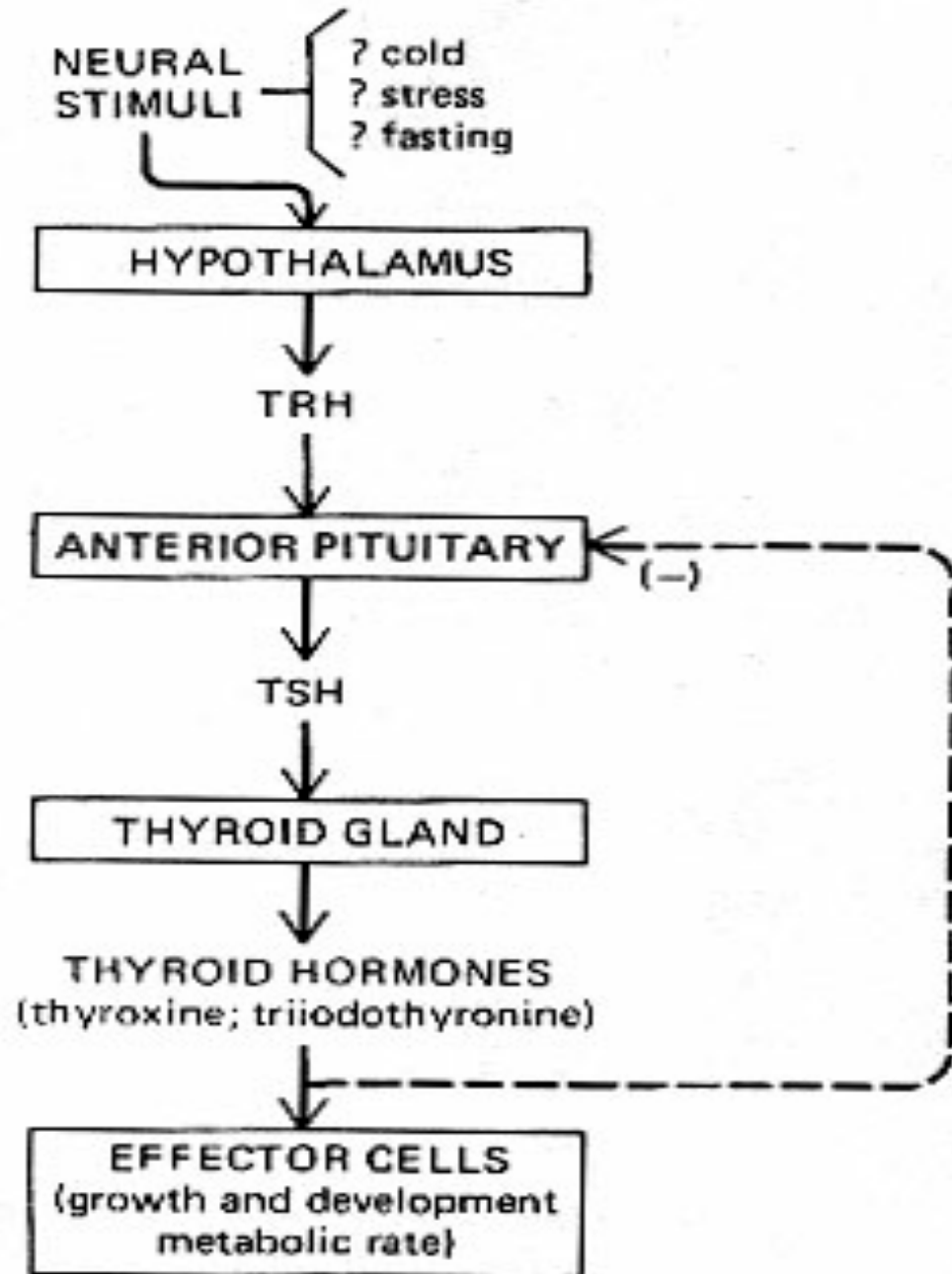
Thyroid-Stimulating Hormone

- TSH, or thyrotropin, is a glycosylated protein of two subunits, and .
- TSH stimulates the thyroid gland to produce thyroid hormones.
- Deficiencies (**including hypothyroidism**) are treated by giving thyroxine itself rather than TSH, (**the last product**)
- but TSH is available for diagnostic purposes to differentiate between pituitary and thyroid gland failure as causes of hypothyroidism

Thyrotrophs

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

Feedback control of thyroid function



The diagram shows how the hypothalamus stimulates the anterior pituitary gland by **TRH** → Anterior pituitary gland releases **TSH** → Stimulates the thyroid gland → The thyroid gland secretes **thyroid hormones** (Such as Thyroxine and Triiodothyronine). The accumulation of thyroid hormones will exert **negative feedback** → This stops the anterior pituitary gland from releasing TSH → Thyroid gland isn't stimulated → **No** production of thyroid hormones (THIS PREVENTS THE ACCUMULATION OF THYROID HORMONES).

Feedback regulation of hypothalamus/pituitary

This diagram shows the feedback regulation of the hypothalamus and the pituitary gland by the final product/hormone (in this ex >> hormone 3)

- A prominent feature of each of the hormonal sequences initiated by the hypothalamic releasing hormones is negative feedback exerted upon the hypothalamic-pituitary system by the hormones whose production are stimulated in the sequence.

The hypothalamus releases HORMONE 1, which stimulates the release of HORMONE 2 from the anterior pituitary → HORMONE 2 then stimulates the release of the final product HORMONE 3 from the Peripheral endocrine gland that is stimulated. → HORMONE 3 accumulates → Inhibits the anterior pituitary gland (negative feedback) → This stops/inhibits the anterior pituitary gland from further stimulating the peripheral endocrine gland.

