M.Sc. 4th Semester

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Unit:33

Module: 02

Topics: Hypothalamo-hypophyseal axis and anterior pituitary hormones

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HYPOTHALAMO-HYPOPHYSIAL AXIS

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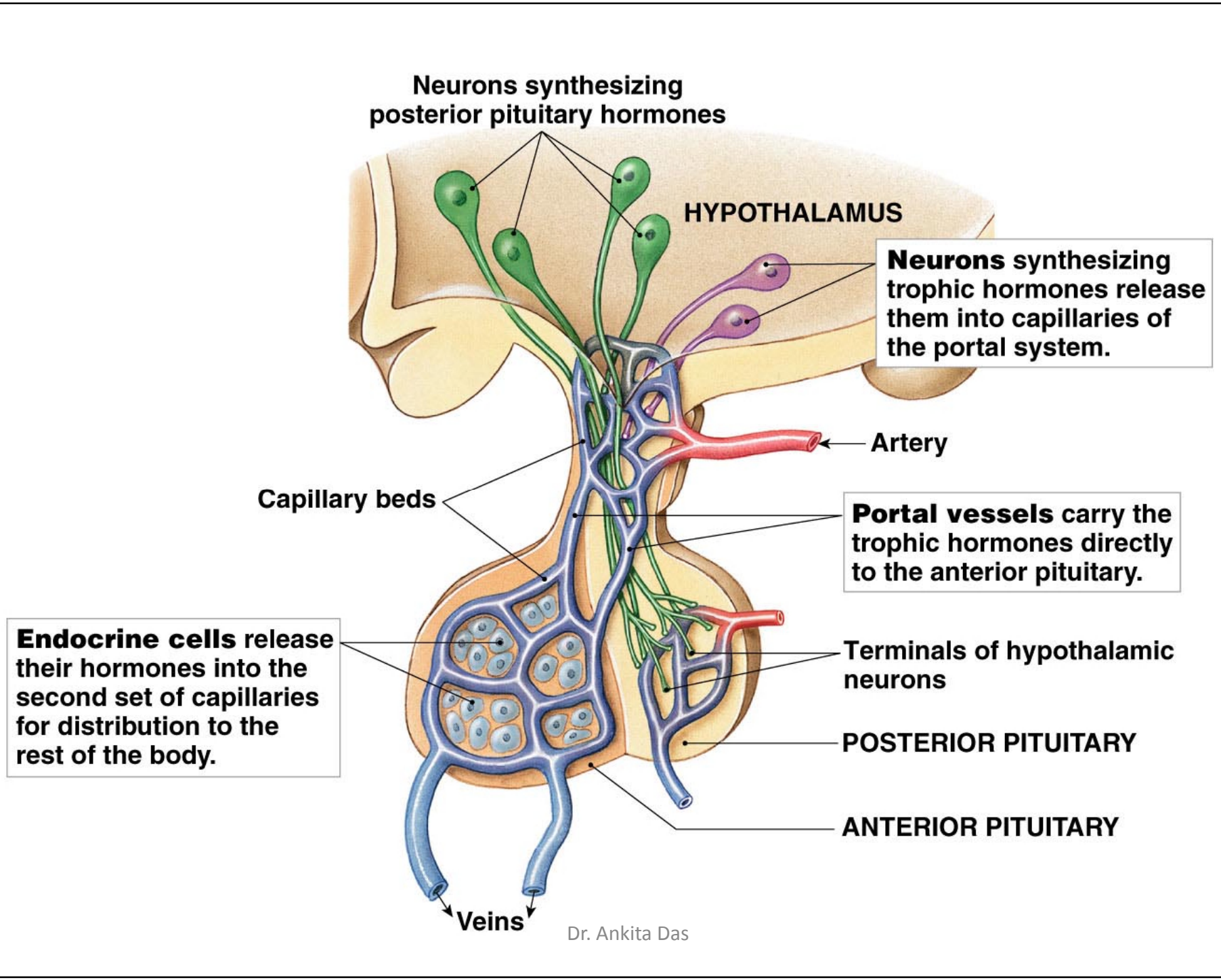
❖ The hypothalamus and pituitary gland form a complex interface between the nervous system and the endocrine system.

❖ The brain can influence the activity of Neurosecretory cells and hormones can influence the release of other hormones.

Pituitary Anatomy

- Also known as the hypophysis.
- Divided into the glandular anterior lobe and the neuronal posterior lobe.
- Anterior lobe is also known as the **adenohypophysis.**
- Posterior lobe is also known as the **neurohypophysis.**
- The pituitary is connected to the hypothalamus via a stalk of tissue called the **infundibulum.**



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Anterior Pituitary

The six major anterior pituitary hormones are peptides.

The Six Major Anterior pituitary hormones are:

1. Thyroid Stimulating Hormone (TSH or thyrotropin)
2. Follicle Stimulating Hormone (FSH, a gonadotropin)
3. Luteinizing Hormone (LH, a gonadotropin)
4. Adrenocorticotropic Hormone (ACTH, or corticotropin)
5. Growth Hormone (GH)
6. Prolactin (PRL)

Targets and Functions of the Anterior Pituitary Hormones

1. **TSH** – target thyroid gland and stimulates secretion of thyroid hormone (TH).
2. **FSH** – targets follicles in the ovaries of females and stimulates growth of follicle and production of estrogen. In males it targets the testes and stimulates sperm cell production.
3. **LH** – targets follicle, triggers ovulation and increases secretion of progesterone. In males it stimulates testosterone production.
4. **ACTH** – targets the adrenal cortex and causes the secretion of glucocorticoids.
5. **GH** - targets most bodily tissues and stimulates metabolism and growth of those tissues.
6. **PRL** - targets the breasts in females. Stimulates breast development and lactation.

Posterior Pituitary

- Is composed primarily of neuronal tissue.
- Is connected to the supraoptic and paraventricular nuclei of the hypothalamus via axons in the infundibulum.

Stores two major neurohormones for later release.

1. **ADH (vasopressin)** – stimulates water reabsorption by kidneys.
2. **Oxytocin** – stimulates labor contractions during birth.

- Release of posterior pituitary and hypothalamic hormones is identical to neurotransmitter release by other neurons.
- Molecules that function as hormones in the hypothalamic-pituitary axis are often neurotransmitters, neuromodulators, or paracrines in other places in the body.

Hypothalamic Hormones

- Are the first in a series of hormones that ultimately leads to the secretion of hormones by specific endocrine glands.

- Several of the hypothalamic hormones stimulate tropic hormones in the anterior pituitary.

- For each hormone series, negative feedback loops control circulating levels of the target gland hormones.

- Negative feedback from the target gland can be directed at the anterior pituitary, the ventral hypothalamus or both.

- The hypothalamic hormones also maintain the anterior pituitary and the tropic hormones help to maintain their target endocrine glands.

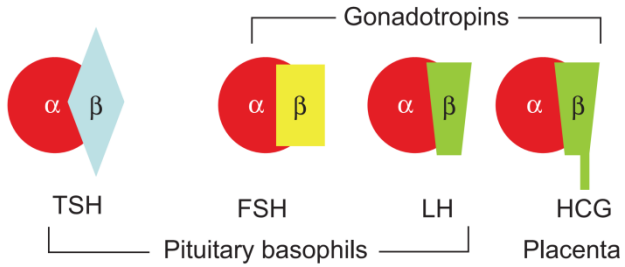
- In some instances hormones of one series will cause the secretion of the hormones of another series (i.e. TH stimulates secretion of GH).

- Prolactin (PRL) is unique because its primary stimulus from the hypothalamus is inhibitory except after birth when milk production begins.

Hormones of the Anterior Pituitary Gland

- All the anterior pituitary hormones are proteins or glycoproteins
- They are divided into 3 categories according to structure similarity:
  - Glycoprotein Hormones
  - Growth hormone and prolactin
  - Adrenocorticotropin family

Glycoprotein Hormones



Hormone	Target	Major actions in humans
Thyroid-stimulating hormone (TSH), also called thyrotropin	Thyroid gland	• Stimulates synthesis and secretion of thyroid hormones
Follicle-stimulating hormone (FSH)	Ovary	• Stimulates growth of follicles and estrogen secretion
	Testis	• Acts on Sertoli cells to promote maturation of sperm
Luteinizing hormone (LH)	Ovary	• Stimulates ovulation of ripe follicle • and formation of corpus luteum; • stimulates estrogen and progesterone synthesis by corpus luteum
	Testis	• Stimulates interstitial cells of Leydig to synthesize and secrete testosterone

Growth Hormone and Prolactin

- Somatotropes (GH producing cells) are by far the most abundant anterior pituitary cells, and account for at least half the cells
- Structurally, prolactin (PRL) is closely related to GH

Hormone	Target	Major actions in humans
Growth hormone (GH), also called somatotropic hormone (STH)	Most tissues	• Promotes growth in stature and mass; • stimulates production of insulin-like growth factor (IGF-I); • stimulates protein synthesis; • usually inhibits glucose utilization and promotes fat utilization
Prolactin	Mammary glands	• Promotes milk secretion and mammary growth

Adrenocorticotropin Family

- The ACTH related peptides constitute a family because:
  - they contain regions of homologous amino acid sequences, which may have arisen through exon duplication,
  - and because they all are encoded in the same gene

Hormone	Target	Major actions in humans
Adrenocorticotropic hormone (ACTH), also known as adreno-corticotropin or corticotropin	Adrenal cortex	• Promotes synthesis and secretion of adrenal cortical hormones
β-Lipotropin	Adipose Tissue	• Physiological role not established

Physiology of the Posterior Pituitary

- The posterior pituitary gland secretes two hormones which are:
  - oxytocin ,
    - increase uterine contractions during parturition
    - Contraction of mammary glands to secret milk
  - and vasopressin or arginine vasopressin (AVP) (or Antidiuretic Hormone 'ADH')
    - contract vascular smooth muscle and thus raise blood pressure
    - promote reabsorption of water by renal tubules

HYPOTHALAMO-HPOPHYSIAL ADRENAL AXIS

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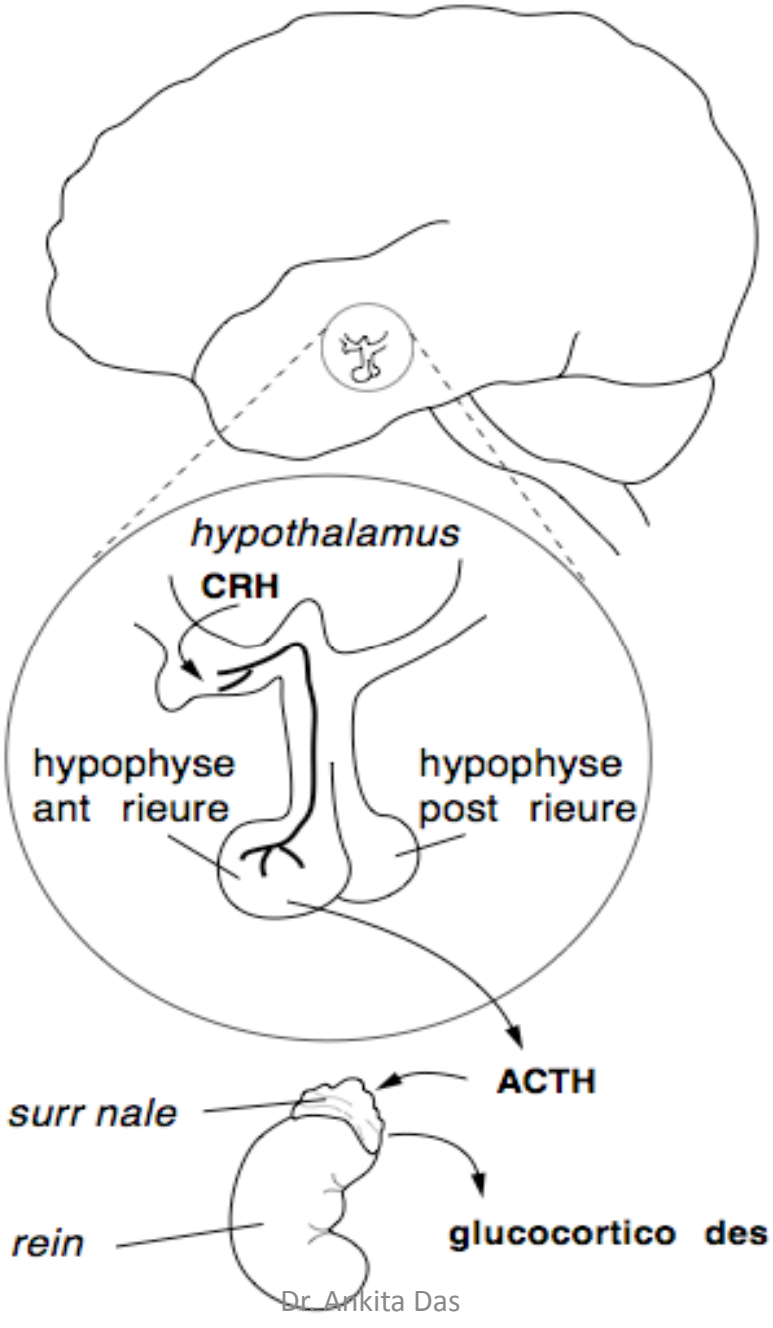

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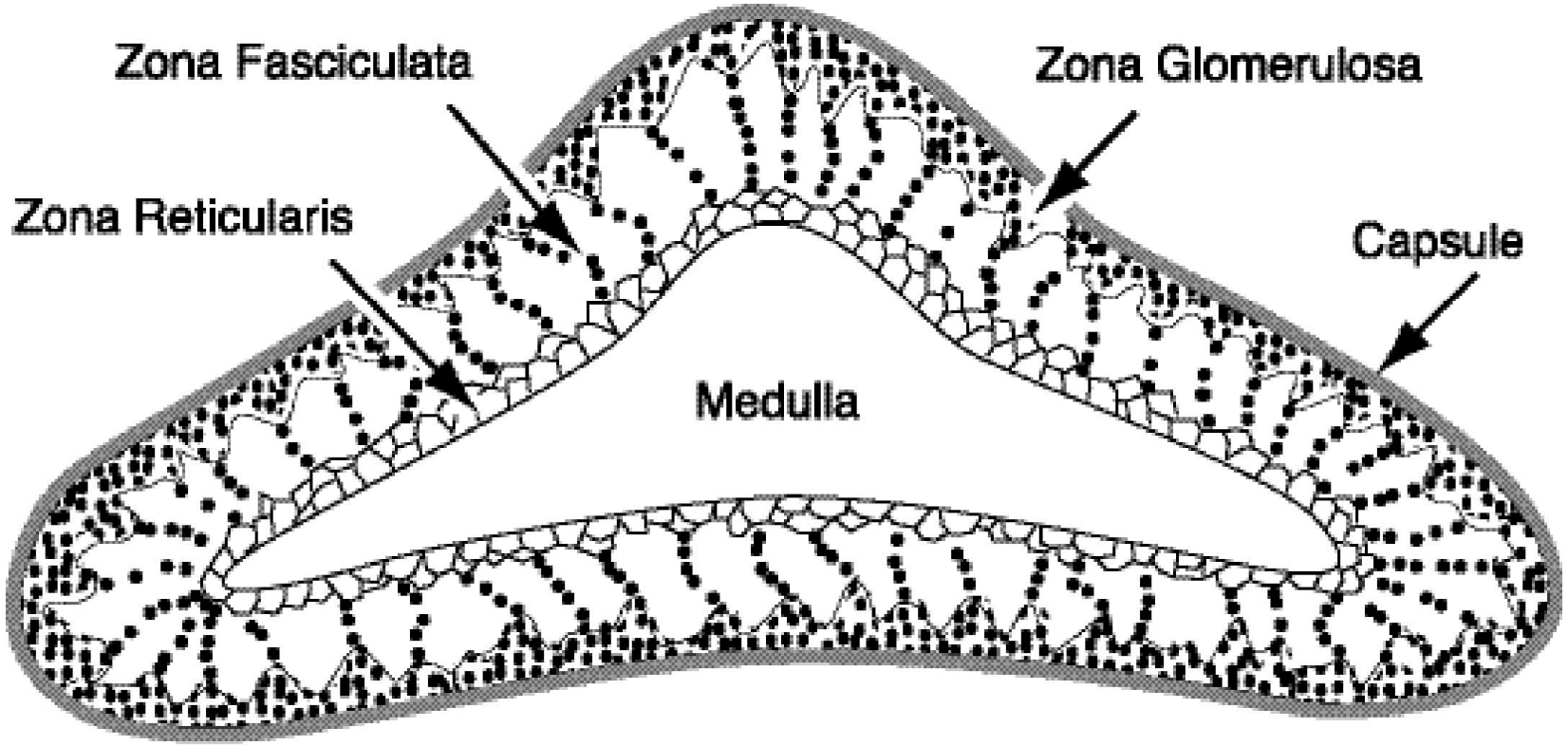
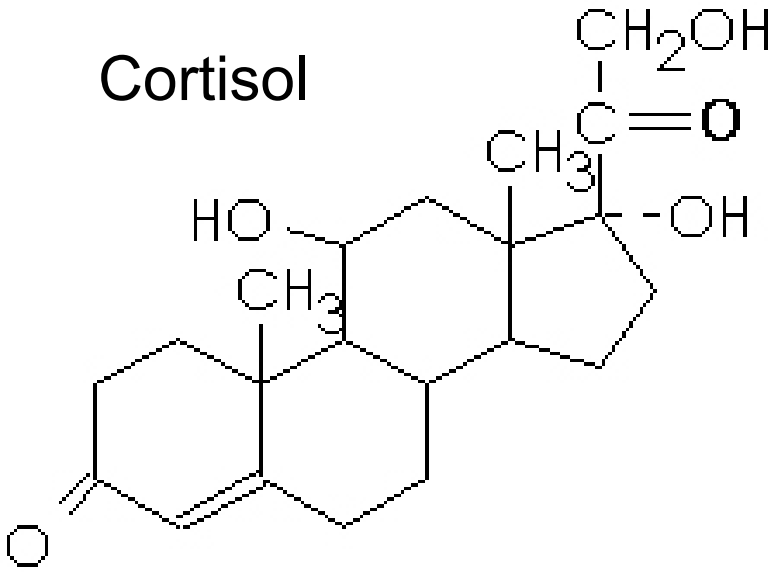


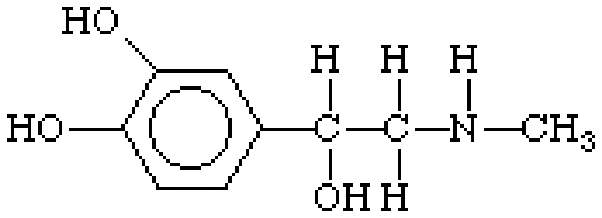
Cortex

- all layers → corticosterone
- z. fasciculata & reticularis → cortisol & sex hormones
- z. glomerulosa → aldosterone

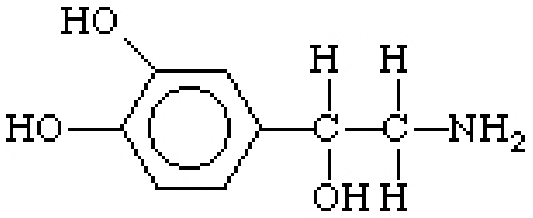
Medulla → epinephrine & norepinephrine

Cortisol





Epinephrine



Norepinephrine

Actions Of Glucocorticoids

Liver

↑ cellular absorption of glucose
glycogenesis

Muscle

↑ celluar absorption of amino acids

White Blood Cells

anti inflammatory action

Brain

↑ excitability (EEG)
behavioral changes

Hypothalamus/Anterior Pituitary

negative feedback of CRH, ACTH, GCs

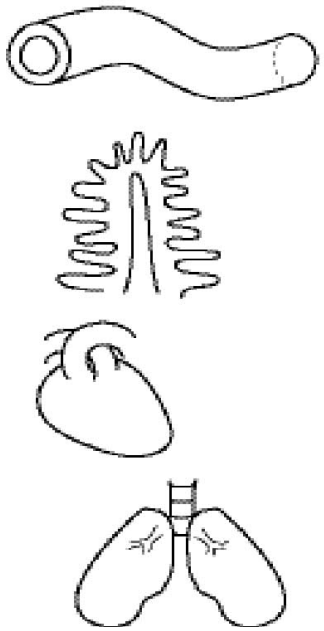
Kidney

Sodium reabsorption (especially by aldosterone)

Bone

↑ bone resorption
osteoporosis

Actions of Adrenaline/Noradrenaline Target

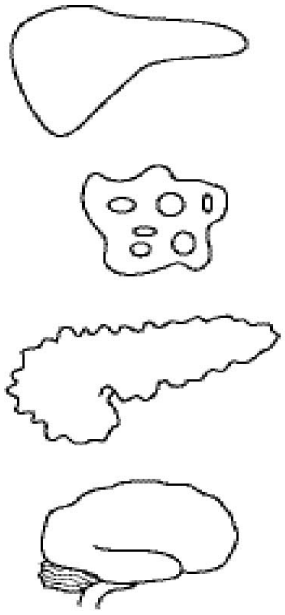


Blood Vessel
vasoconstriction
vasodilatation

Intestine
relaxation of motility
constriction of sphincters of GI tract and bladder

Heart
excitation
contraction

Lungs
brochial dilation



Liver
activation of glycogenolysis
mobilization of metabolic energy

Adipocytes
activation of lipolysis

Pancreas
inhibition of insulin secretion
stimulation of insulin secretion

Brain
vigilance
anxiety, fear, rage
functions of emergency

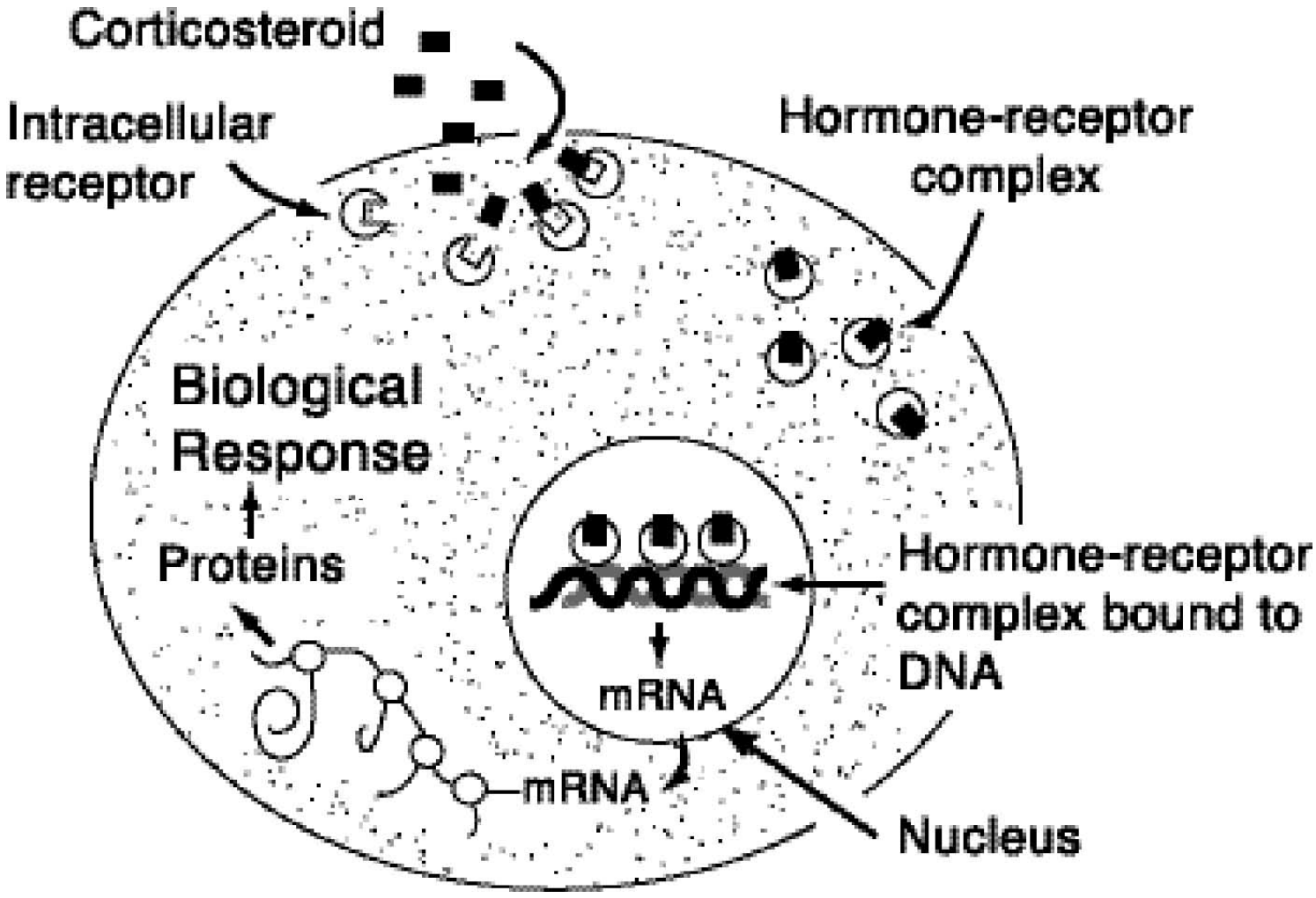
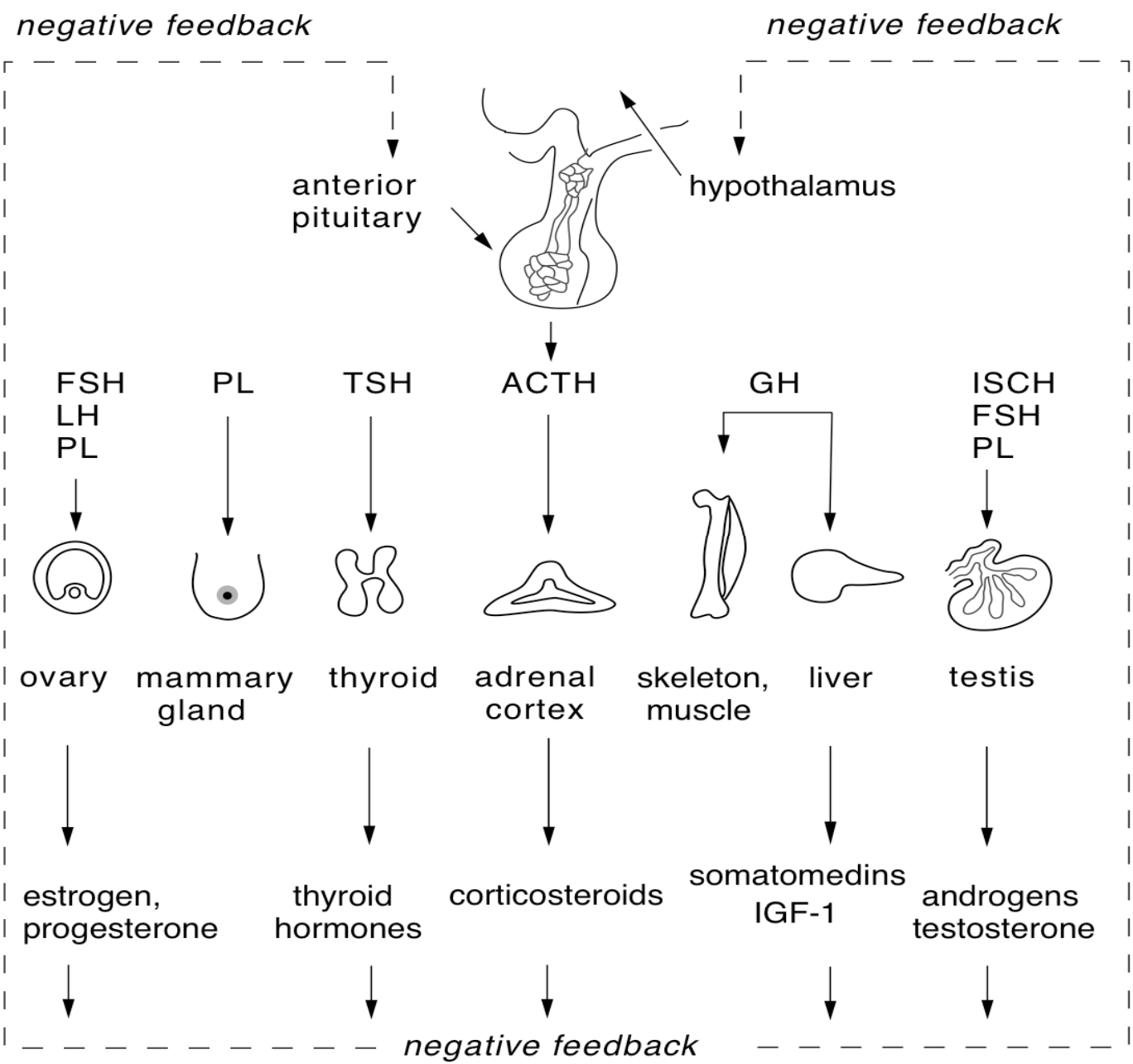


Fig: Schematic diagram of corticosteroid action in target cell


negative feedback
negative feedback
anterior pituitary
hypothalamus
FSH
LH
PL
PL
TSH
ACTH
GH
ISCH
FSH
PL
ovary
mammary gland
thyroid
adrenal cortex
skeleton, muscle
liver
testis
estrogen, progesterone
thyroid hormones
corticosteroids
somatomedins IGF-1
androgens testosterone
negative feedback

Changes with Aging in the Hypothalamo-Pituitary-Adrenal Axis

No significant changes in healthy, non-stressed, elderly

The few changes that occur are rapidly compensated for (e.g. decreased secretion of GCs from the adrenal cortex)

but also

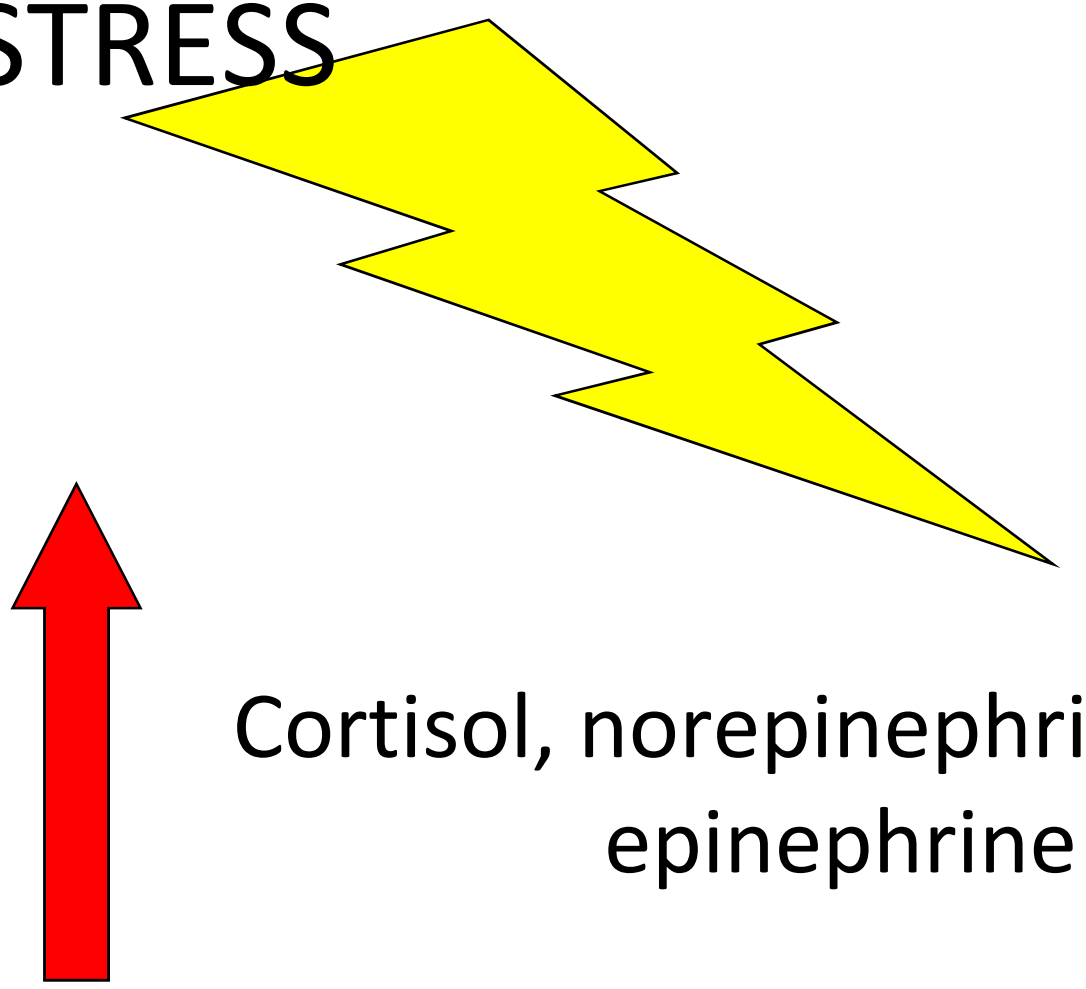
<u>less rapid metabolism</u> in the liver & <u>less urine excretion</u>

Therefore the circulating levels remain constant

Also, *normal* ACTH & cortisol responses to CRH administration

Some alterations of the circadian rhythm

STRESS



Cortisol, norepinephrine, and epinephrine

Symptoms Of Corticosteroid Excess

1. K+ loss, hypokalaemia
2. Na+ retention, increased ECF volume
3. Increased blood pressure

4. Muscle atrophy & fat redistribution
5. Mood changes, euphoria/depression
6. Increased appetite, hyperglycaemia

7. Reduced inflammation
8. Poor wound healing, easy bruising, osteoporosis
9. Reduced Immune responses
10. Increased susceptibility to infection

Symptoms Of Corticosteroid Deficiency

1. K+ retention, hyperkalaemia
2. Na+ loss, decreased ECF volume
3. Decreased blood pressure
4. Muscular weakness
5. Depression, anorexia
6. Hypoglycaemia
7. Increased inflammatory & immune responses

Inability to cope with physical "stress"…

DEATH

HYPOTHALAMO-HPOPHYSIAL GONADAL AXIS

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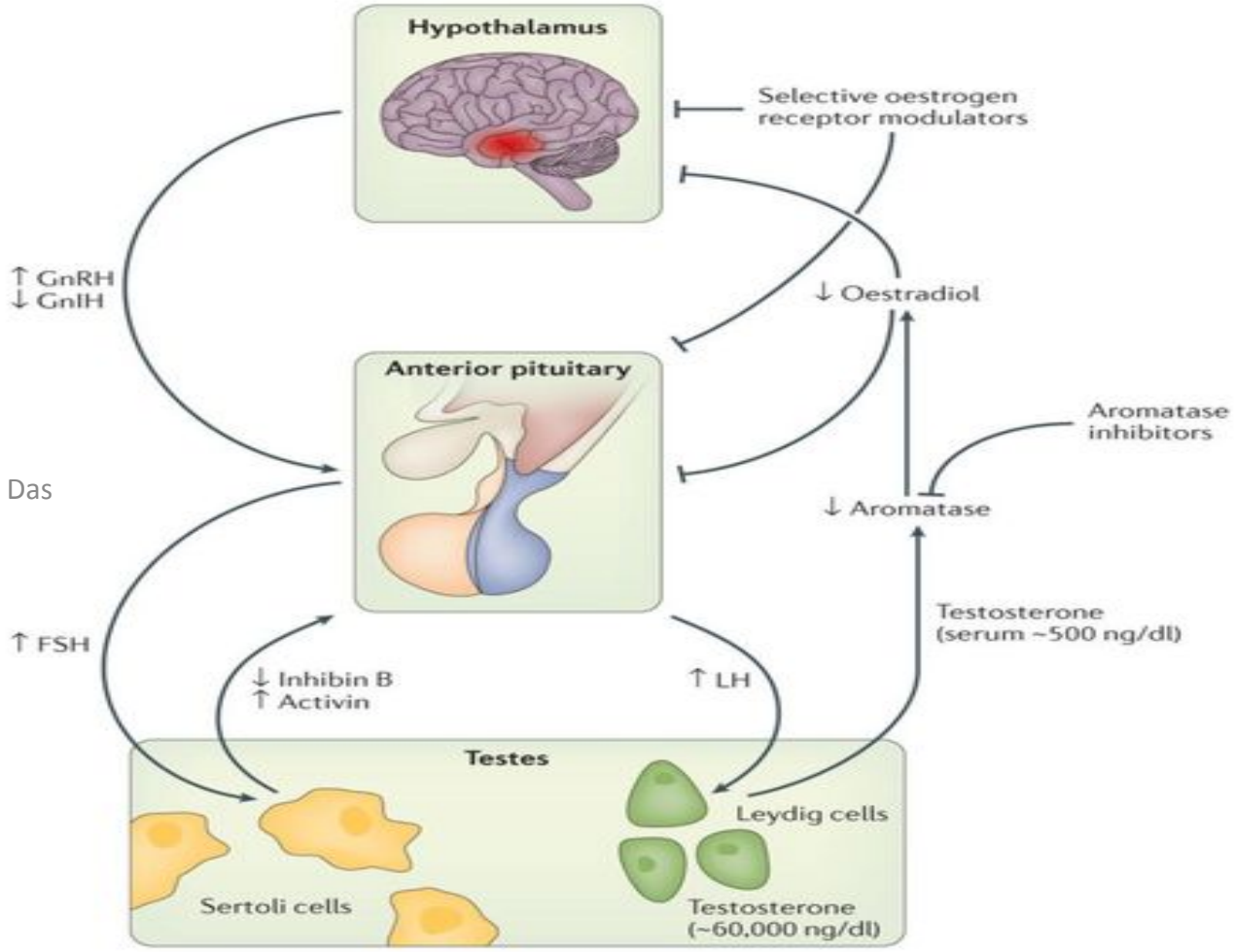
Figure 1 The hypothalamic–pituitary–gonadal axis



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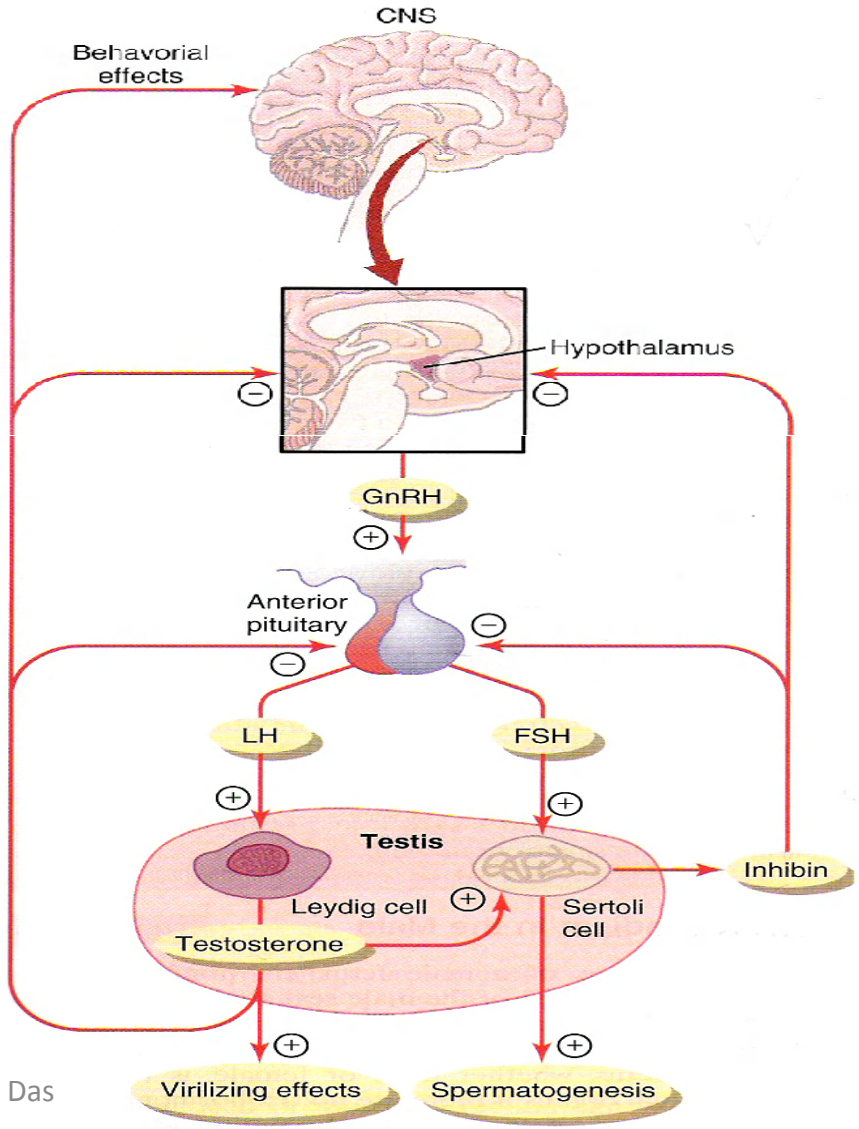
Kathrins, M. & Niederberger, C. (2016) Diagnosis and treatment of infertility-related male hormonal dysfun
Nat. Rev. Urol. doi:10.1038/nrurol.2016.62

Control of **male sexual functions** by hormones from the hypothalamus and anterior pituitary gland

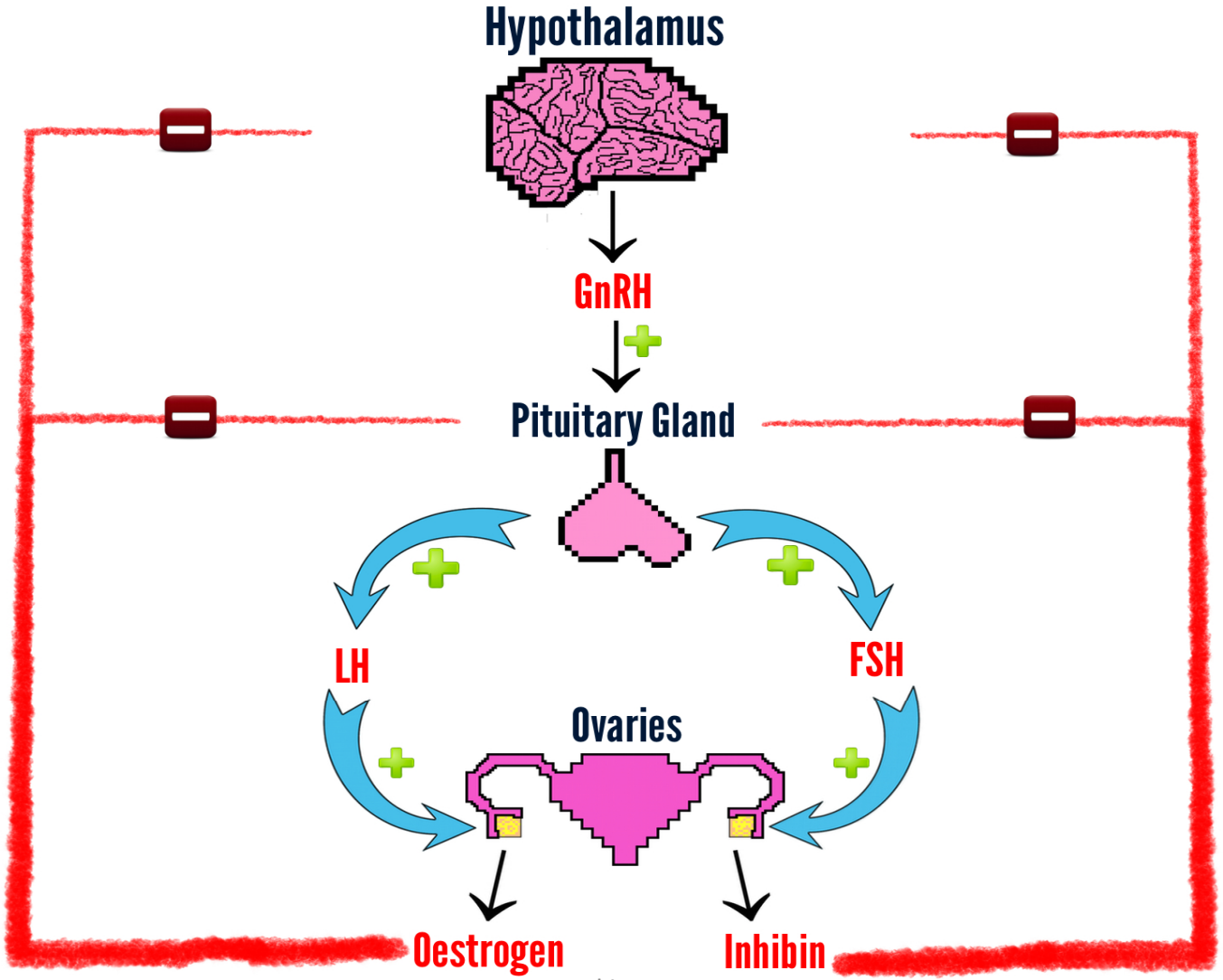
GnRH is secreted intermittently for few minutes every 1 to 3 hrs.

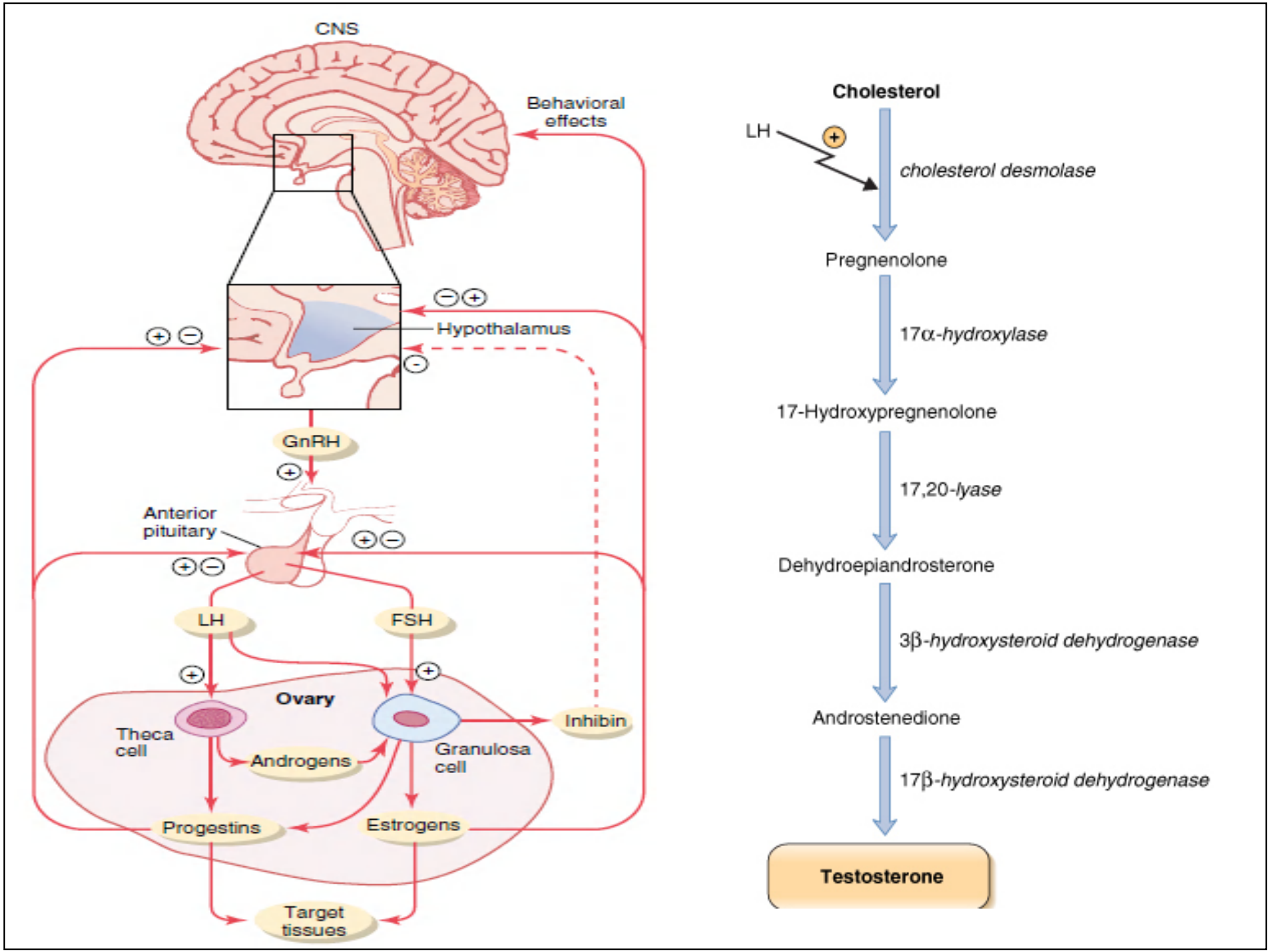
– The secretion of **LH** by the anterior pituitary is also cyclical following the pulsatile release of GnRH. Conversely, **FSH** secretion increases and decreases only slightly with each fluctuation of GnRH secretion

- **Testosterone**
- **Spermatogenesis**



Negative feedback effects of estrogen and progesterone in decreasing both **LH** and **FSH** secretion




CNS
Behavioral effects
Hypothalamus
GnRH
Anterior pituitary
LH
FSH
Ovary
Theca cell
Androgens
Granulosa cell
Inhibin
Progestins
Estrogens
Target tissues
Cholesterol
LH
cholesterol desmolase
Pregnenolone
17α-hydroxylase
17-Hydroxypregnenolone
17,20-lyase
Dehydroepiandrosterone
3β-hydroxysteroid dehydrogenase
Androstenedione
17β-hydroxysteroid dehydrogenase
Testosterone

The HPO axis

DEFINITION
INTRODUCTION

- The hypothalamo-pituitary-ovarian axis is essentially a complex but necessary interplay between the hypothalamus, the pituitary and the ovaries in such a way that they behave like one neuroendocrine organ.
- The axis is functionally involved in the development of primary and secondary sexual characteristics, the control of oogenesis and by extension reproduction.

- The female reproductive system is coordinated normally with influences from within the classical model which has the GnRH pulse generator located within the hypothalamus as the primary structure that drives the axis.

- It releases the decapeptide gonadotrophin-releasing hormone GnRH that stimulates the gonadotropes in the anterior pituitary to produce luteinising hormone (LH) and follicle stimulating hormone (FSH).

The gonadotropins, LH and FSH, are synthesized within the gonadotrophs in the anterior pituitary gland located in the sella turcica of the sphenoid bone.

They are both glycoprotein hormones comprising α and β subunits. The β subunit confers hormone specificity and function while the α subunit is common to LH, FSH, human chorionic gonadotropin (HCG) and thyroid-stimulating hormone (TSH).

Functional activity of these hormones require the presence of both subunits.

- Morphologic effects can be grouped into effects that comprise the ovarian cycle/ folliculogenesis i.e., the cyclical recruitment of follicles from the ovarian reserve.

- Which under the phasic concentrations of LH and FSH will lead to the production of one dominant mature follicle ready for ovulation and the formation of a corpus luteum after ovulation.

INTEGRATION

- Control and communication between the hypothalamic-pituitary unit and the ovaries is essential for the normal physiology of the reproductive cycle and the functions required of it.

- It is important for the higher components of the axis (hypothalamus and pituitary) to modulate their secretions in response to the secretions and activity the ovary.

Books to refer:

1.Medical Physiology, Guyton and Hall

2.Medical Physiology, Ganong

3.General Physiology, A.K. Jain

Practice Questions:

1. Draw the anatomy of pituitary gland.
2. Name the major anterior pituitary hormones.
3. Why GH is also known as somatotropic hormone or STH?
4. Draw and briefly describe the hypothalamo-hypophysial-adrenal axis.
5. What are the functions glucocorticoids?
6. Briefly describe the feedback control mechanism of hypothalamo-hypophysial-adrenal axis.
7. Describe the hypothalamo-hypophysial-gonadal axis.
8. Discuss the negative feedback control of LH and FSH.
9. What is HPO axis?