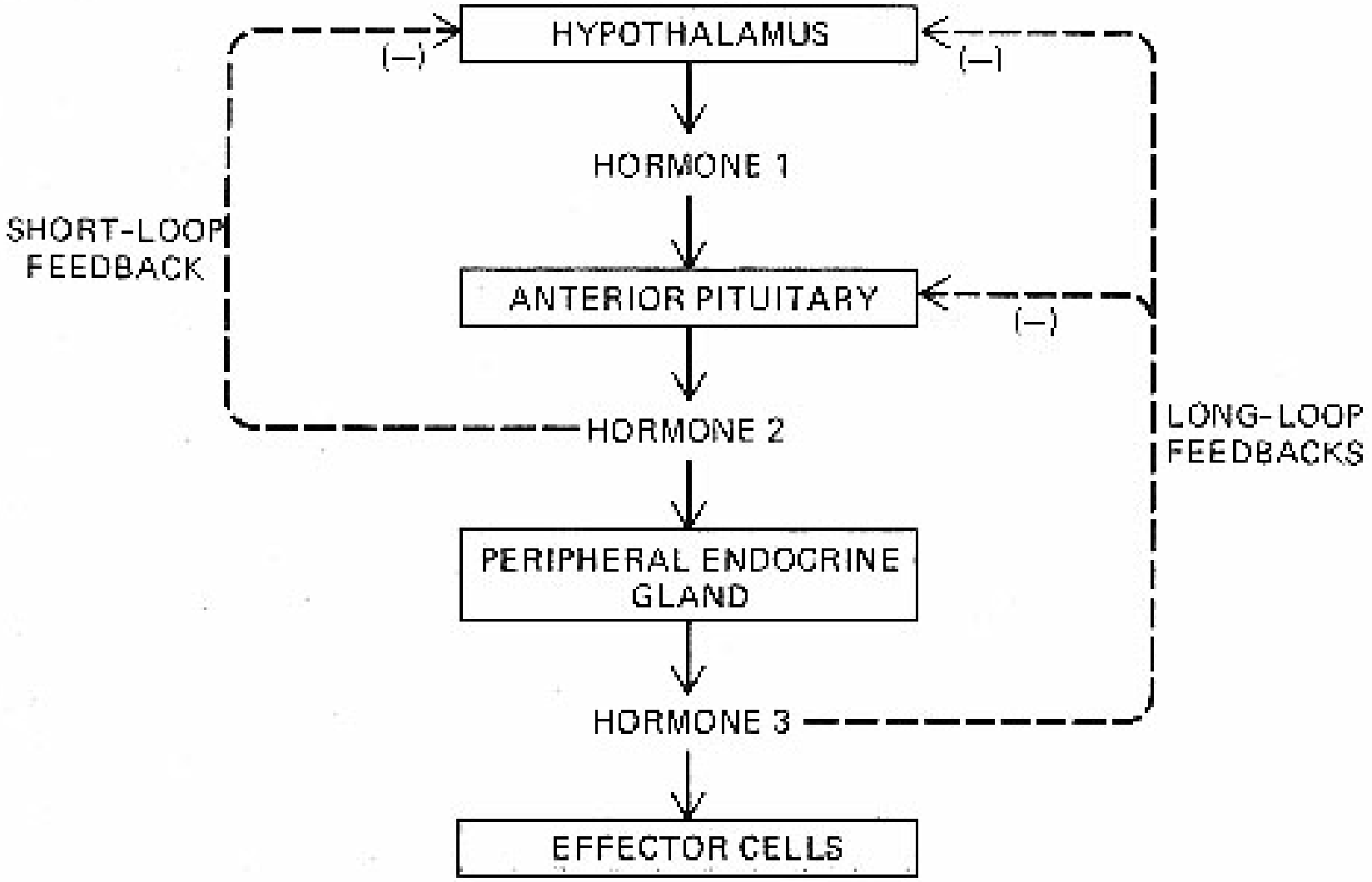
Feedback control



Addison’s Disease

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

he zona fasciculata constitutes the middle zone of the adrenal cortex, sitting directly beneath the zona glomerulosa

Regulation of ACTH

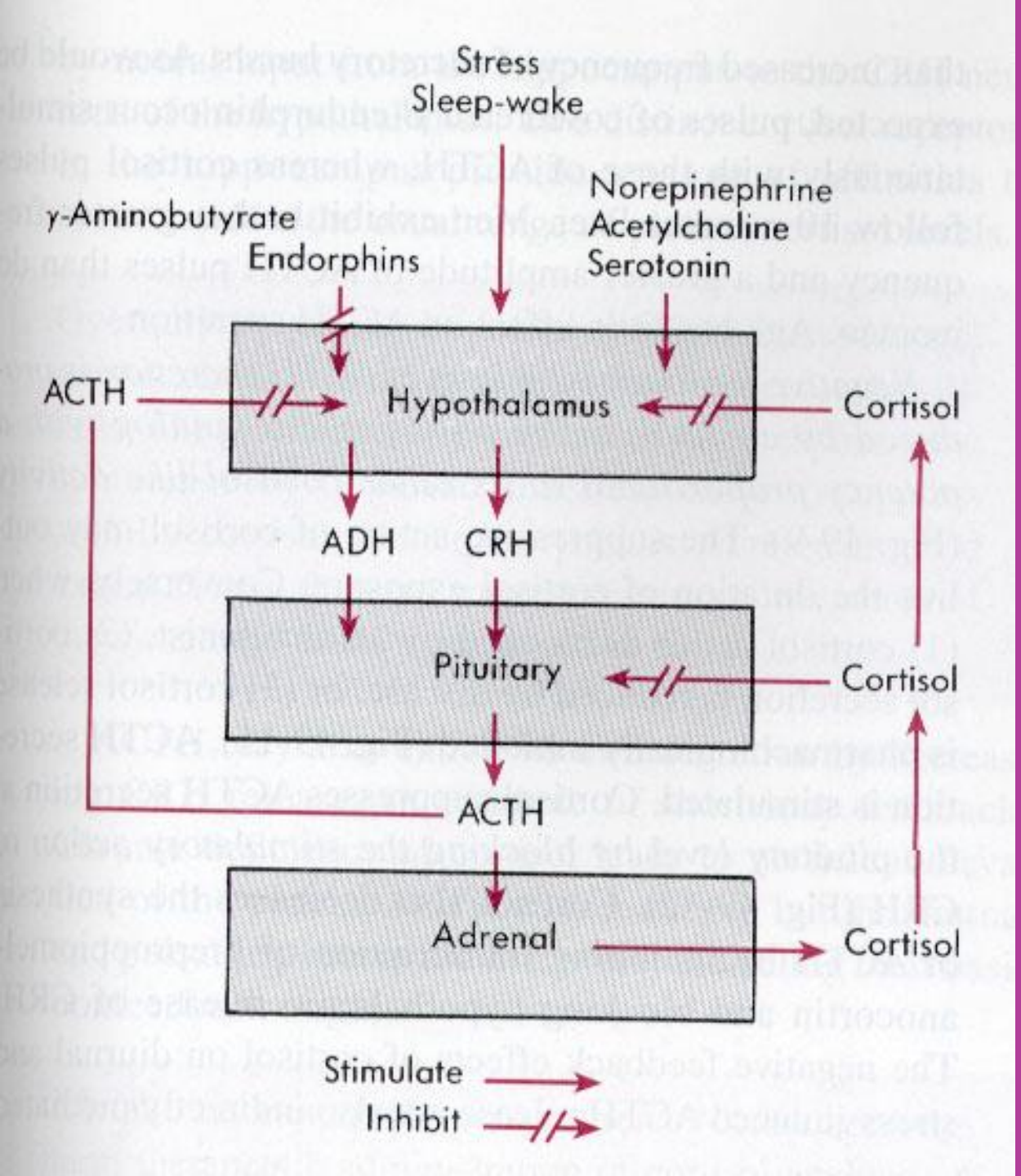
- ACTH stimulates production of glucocorticoids from the adrenal cortex
- Stimulation of release
  - CRH and ADH
  - Stress
  - Hypoglycemia
- CRH and ADH both synthesized in hypothalamus

Vasopressin, also known as **antidiuretic hormone** (**ADH**)

Corticotropin-releasing hormone (**CRH**)

ACTH

- Circadian pattern of release
  - Highest levels of cortisol are in early AM following ACTH release
  - Depends on sleep-wake cycle, jet-lag can result in alteration of pattern
- Opposes the circadian pattern of growth hormone secretion



Regulation of ACTH

It
is easier and less expensive to treat patients having adrenocortical insufficiency with glucocorticoid replacement
therapy than it is to use ACTH
Therefore,
use of ACTH (*Acthar) is restricted to diagnosis;*

ACTH

- Acts on adrenal cortex
  - stimulates growth of cortex (trophic action)
  - Stimulates steroid hormone synthesis

- Lack of negative feedback from cortisol results in aberrantly high ACTH, elevated levels of other adrenal corticosteroids– adrenal androgens

Gonadotropins

- Follicle-stimulating hormone (FSH),
- luteinizing hormone(LH),
- human chorionic gonadotropin (hCG)
- TSH

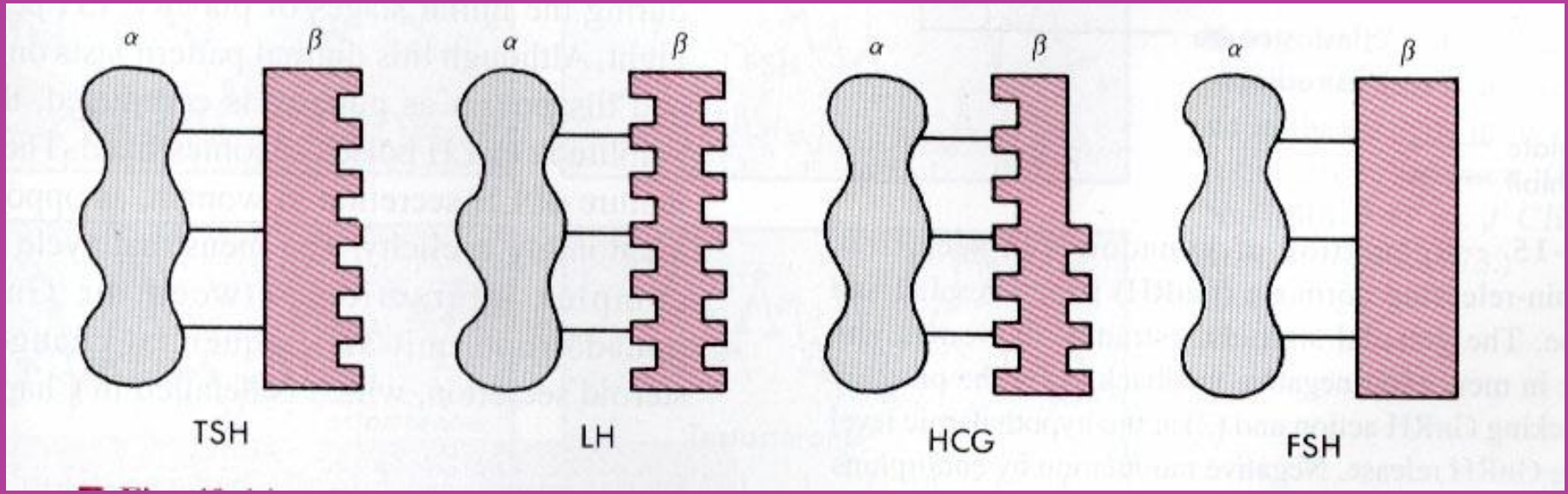
they have

- 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

Glycoprotein hormones

Glycoprotein hormones contain two subunits, a common α subunit and a distinct β subunit: TSH, LH, FSH and hCG.



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
- Pulsitile secretion of GnRH and inhibin cause distinct patterns of LH and FSH secretion

LH/FSH

- LH and FSH are pituitary hormones secreted in pulsatile
- fashion approximately every 2 hours.
- In women before menopause, this pattern is superimposed on much larger changes that occur during the normal menstrual cycle
- FSH is released in substantial amounts during the follicular phase of the menstrual cycle
- Required for proper development of ovarian follicles and for estrogen synthesis from granulosa cells of the ovary

Regulation of LH/FSH

- Negative feed-back
  - Testosterone from Leydig cells– synthesis stimulated by LH, feedsback to inhibit GnRH production from hypothalamus and down-regulates GnRH receptors
  - Progesterone– suppresses ovulation, basis for oral contraceptives. Works at both the level of pituitary and hypothalamus.
- Dopamine, endorphin, and prolactin inhibit GnRH release.
  - Prolactin inhibition affords post-partum contraceptive effect
- Overproduction of prolactin via pituitary tumor can cause amenorrhea– shuts off GnRH
  - Treated with bromocryptine (dopamine agonist)
  - Surgical removal of pituitary tumor

Regulation of LH/FSH

- Positive feedback
  - Estradiol at high plasma concentrations in late follicular phase of ovarian cycle stimulates GnRH and LH surge– triggers ovulation

HYPOTHALAMIC REGULATORY HORMONES

Five peptides isolated from the hypothalamus regulate release of one or more pituitary hormones. In addition, dopamine released from the hypothalamus inhibits prolactin production.

Somatostatin

- Somatostatin (or somatotropin release–inhibiting factor [SRIF]) occurs primarily as a 14–amino acid peptide, although a 28–amino acid form also exists
- Somatostatin inhibits the secretion of many substances in addition to growth hormone
- not useful clinically
- Inhibition of secretion of

Growth hormone, Thyroid-stimulating hormone, Prolactin
ACTH, Insulin, Glucagon, Pancreatic polypeptide
Gastrin

Thyrotropin-Releasing Hormone

•Thyrotropin-releasing hormone, or protirelin, consists of three amino acids.

•TRH (*Relefact TRH) is used for* tests to distinguish primary from secondary hypothyroidism

Gonadotropin-Releasing Hormone

GnRH (gonadorelin, luteinizing hormone–releasing hormone)

•is a decapeptide that stimulates production of LH and FSH. It is released in bursts from the hypothalamus at regular intervals, about every 2 hours,

•The pituitary gland responds to these regular pulses by producing LH and FSH

Posterior pituitary hormones: ADH (AVP) and Oxytocin

- Both are synthesized in the cell bodies of hypothalamic neurons
- ADH: supraoptic nucleus
- Oxytocin: paraventricular nucleus
- Both are synthesized as preprohormones and processed into nonapeptides (nine amino acids**).**
- They are released from the termini in response to an action potential which travels from the axon body in the hypothalamus

Oxytocin:

- stimulates myoepithelial contractions
- In uterus during parturition
- In mammary gland during lactation
- milk ejection from lactating mammary gland
- 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.
- uterine contractions
- Reflexes originating in the cervical, vaginal and uterus stimulate oxytocin synthesis and release via neural input to hypothalamus
- Increases in plasma at time of ovulation

ADH: conserve body water and regulate tonicity of body fluids

- **Also known as vasopressin**
- **Regulated by osmotic and volume stimuli**
- **Water deprivation increases osmolality of plasma which activates hypothalmic osmoreceptors to stimulate ADH release**