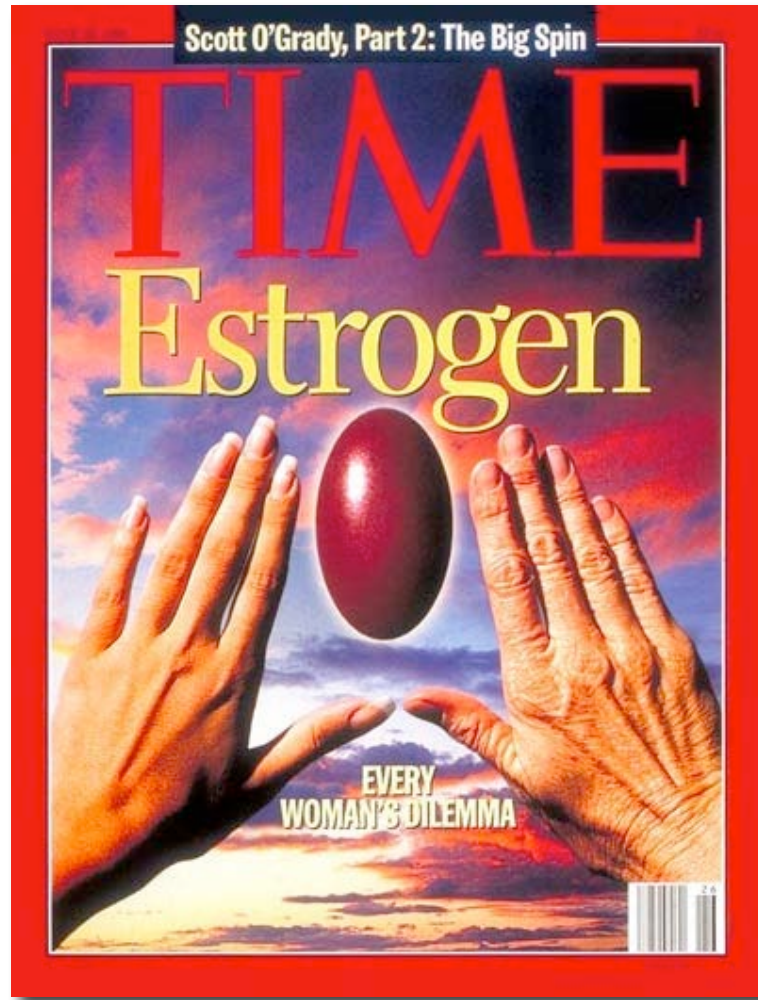
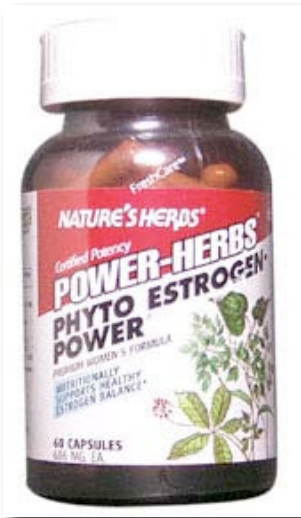


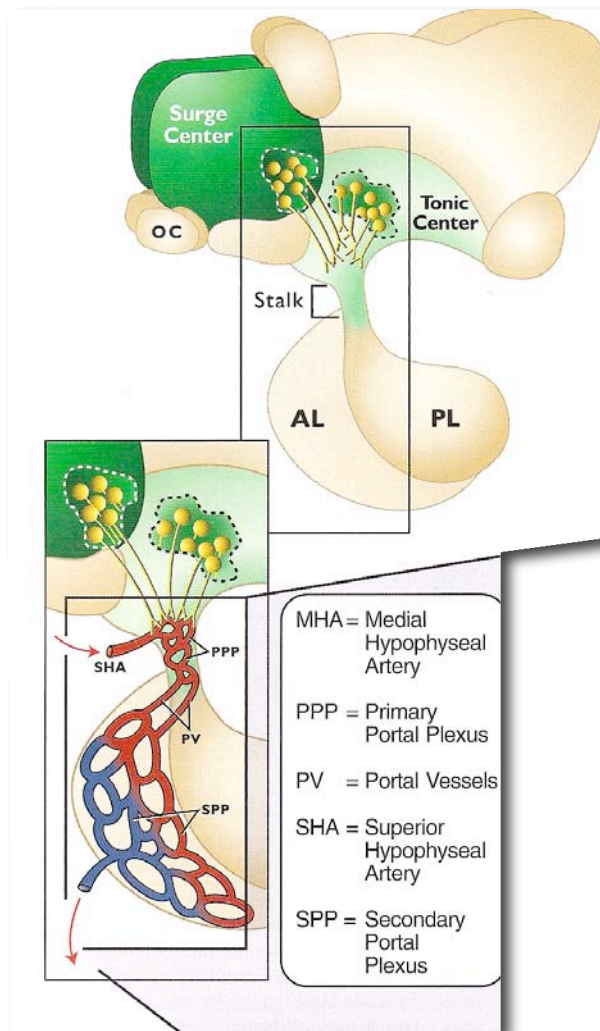
Reproductive Endocrinology



Reproductive Endocrinology

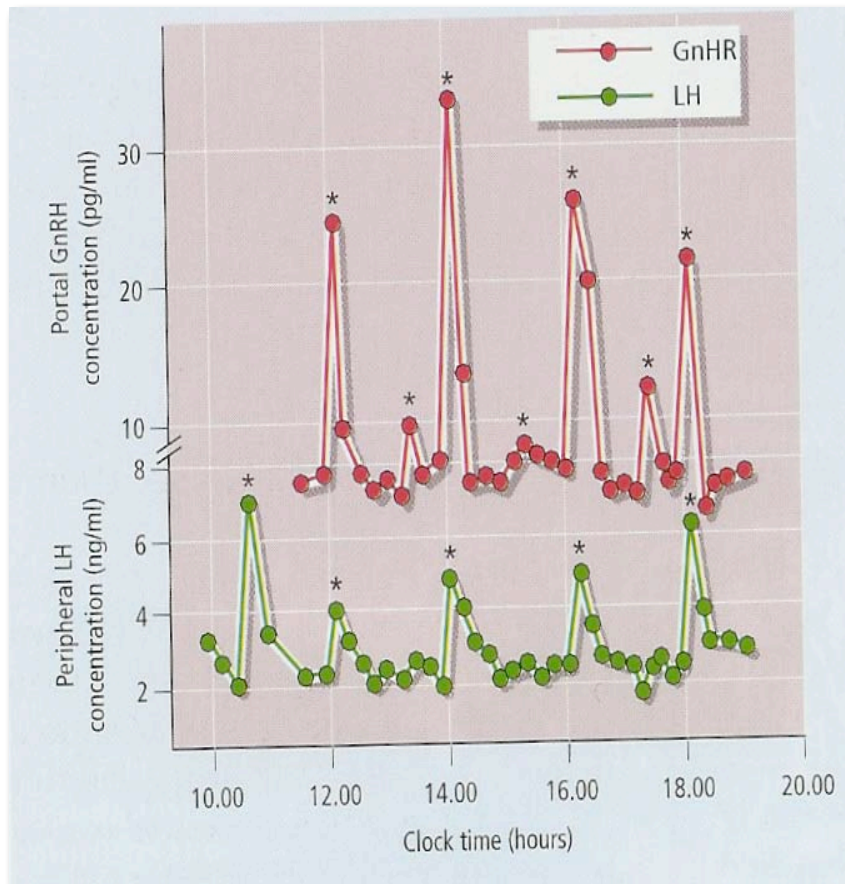
- **Hypothalamic hormones**
 - Gonadotropin releasing hormone (GnRH)
 - stimulate release of
 - FSH = follicle stimulating hormone
 - LH = luteinizing hormone
 - from pituitary
- 'Gonadotropin' = gonad stimulating

Hypothalamic Surge/Tonic Centers



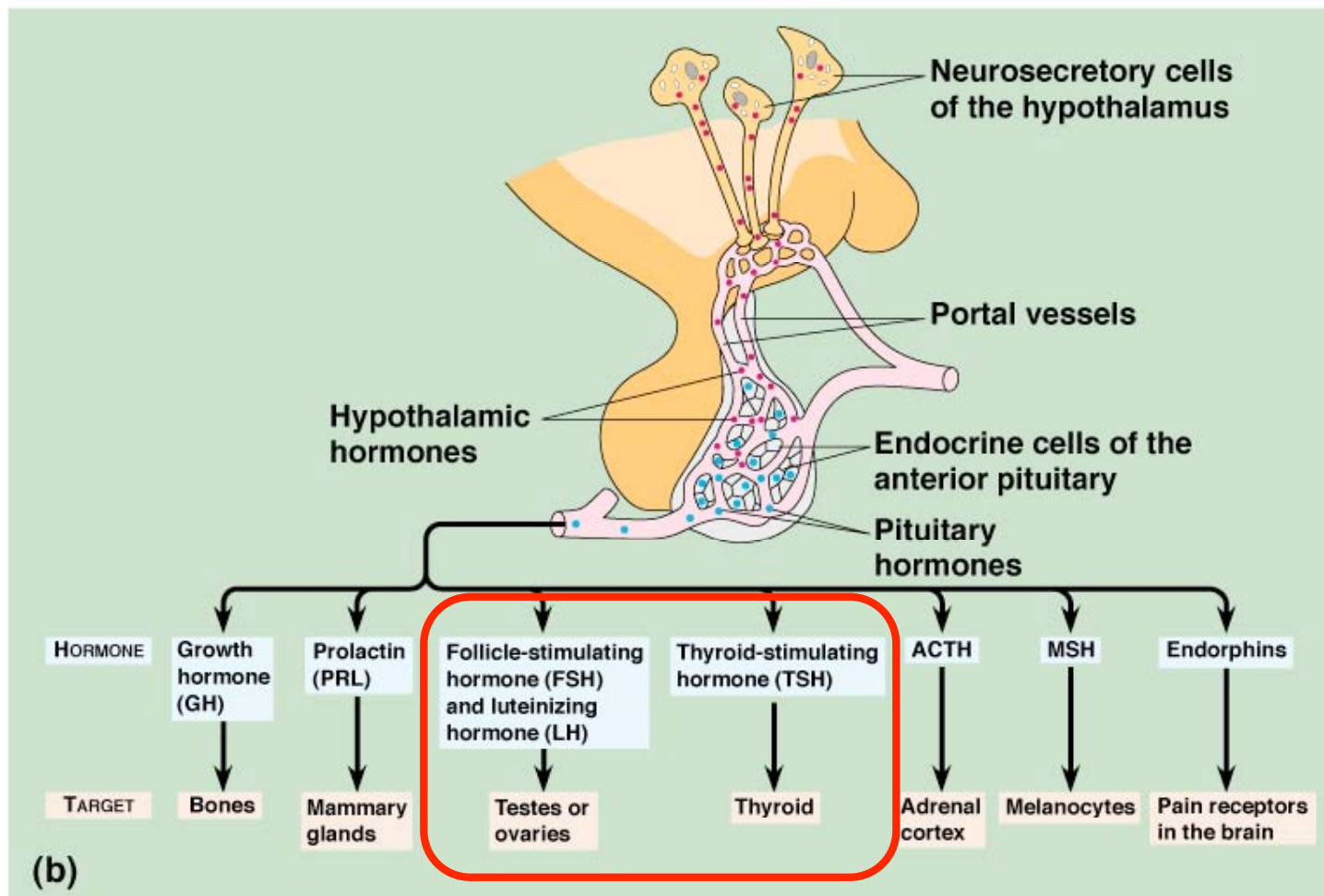
- Neurosecretory neurons from surge and tonic centers deposit neurohormones into portal system
- Portal system delivers these hormones to the adenohypophysis

GnRH release is pulsatile



- GnRH pulse generator in hypothalamus called 'circadian clock'
- Circadian pulses
 - One pulse every hour
 - Each LH peak coincides with a GnRH pulse

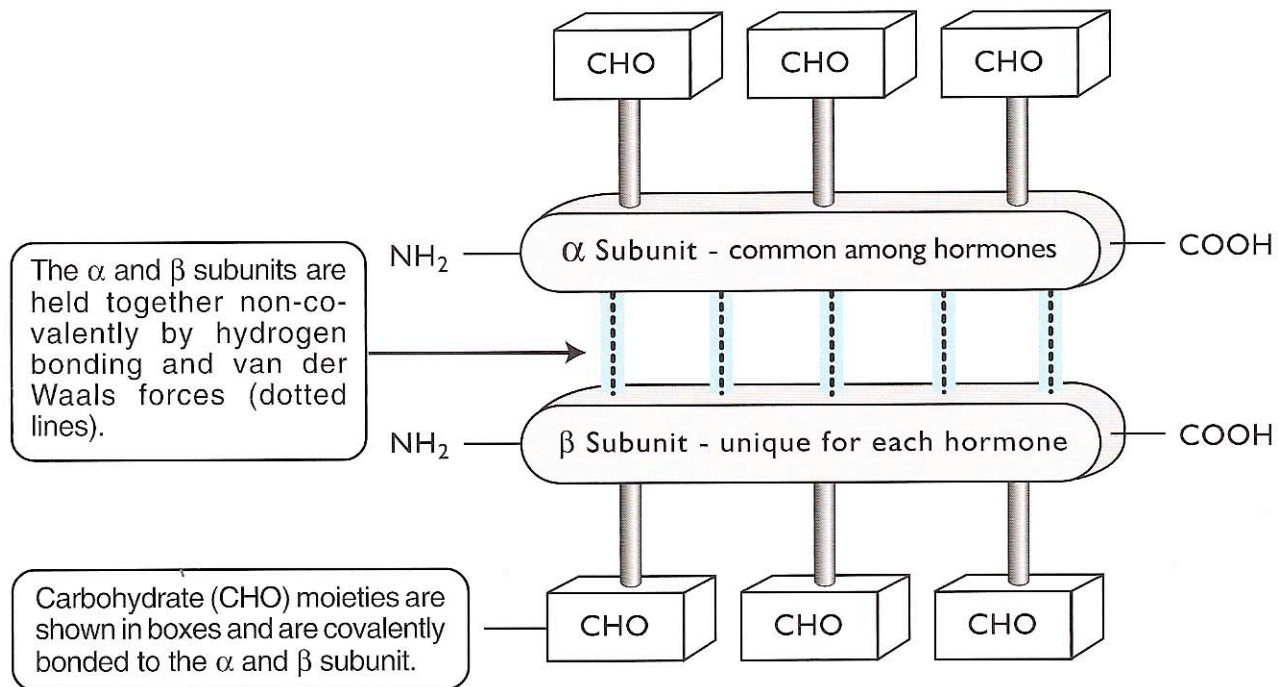
Adenohypophysis



Pituitary Glycoproteins

FSH - LH - TSH

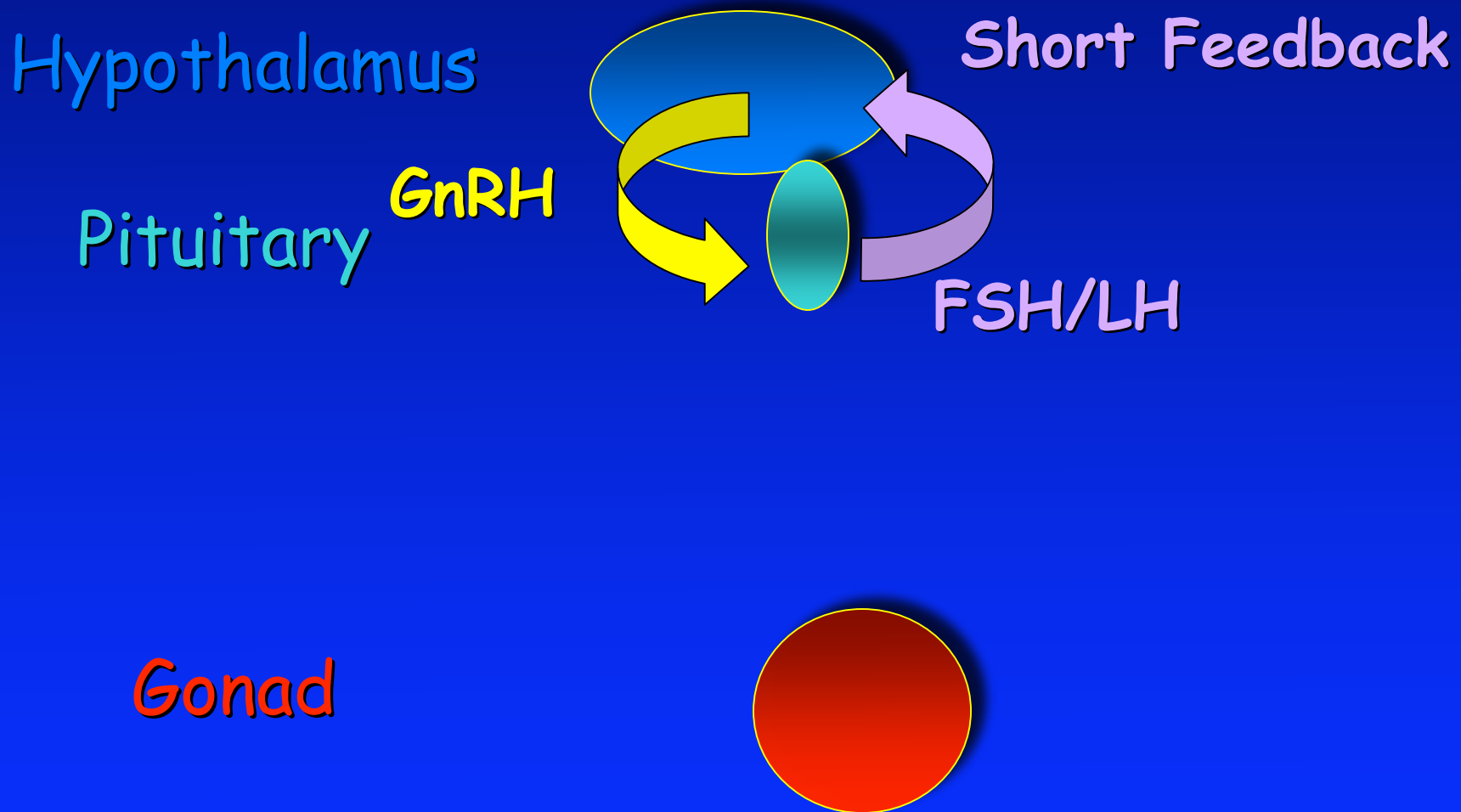
Figure 5-8. Diagram of an Anterior Lobe Glycoprotein Hormone



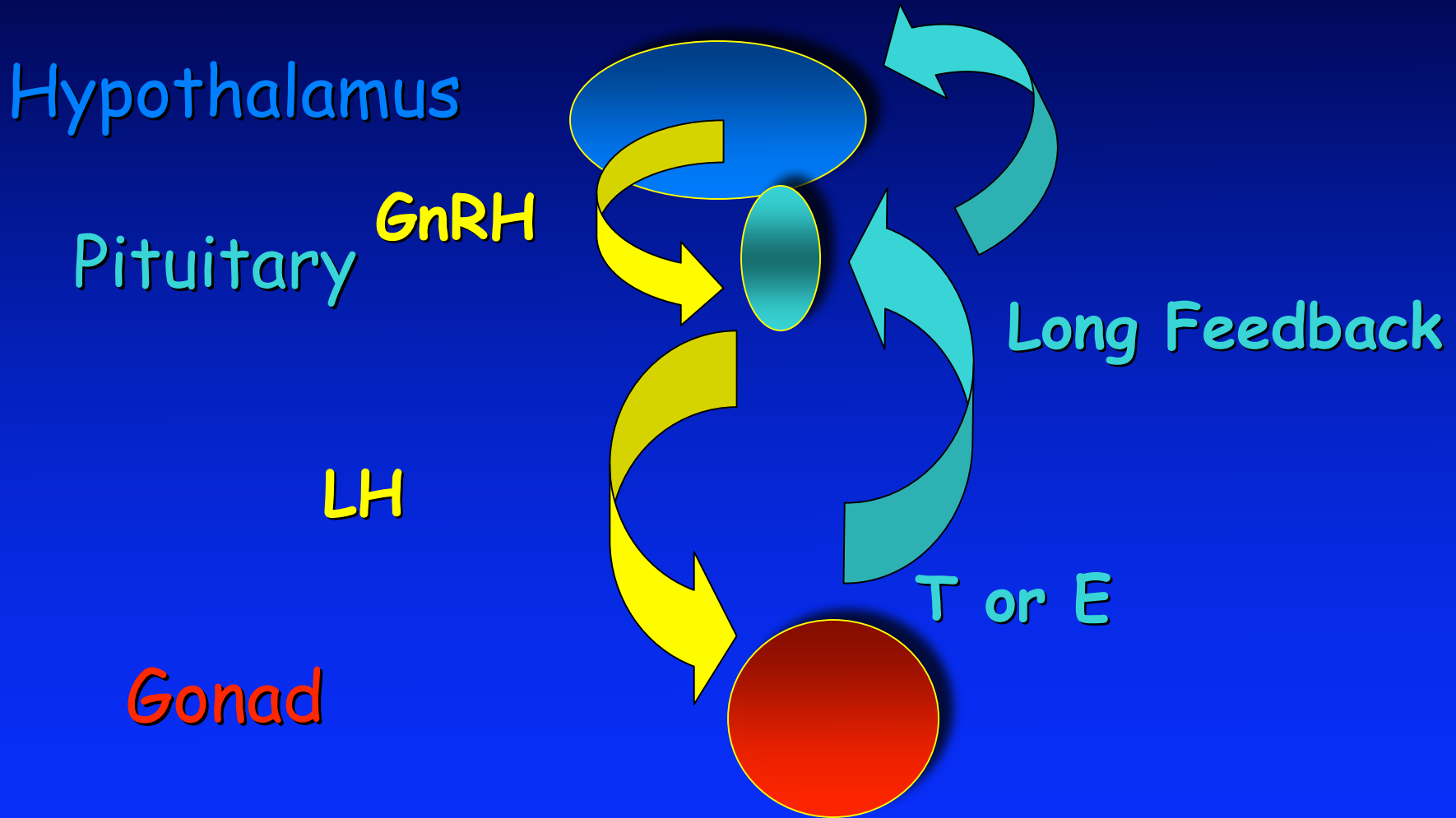
Pituitary Hormones

- Follicle stimulating hormone
 - stimulates gametogenesis in males and females
- Luteinizing Hormone
 - stimulates steroidogenesis in males and females
- Prolactin
 - stimulates the synthesis of milk in mammalian females
 - maternal behavior in some species
- Oxytocin -
 - stimulates smooth muscle contraction
 - associated with birth and milk release

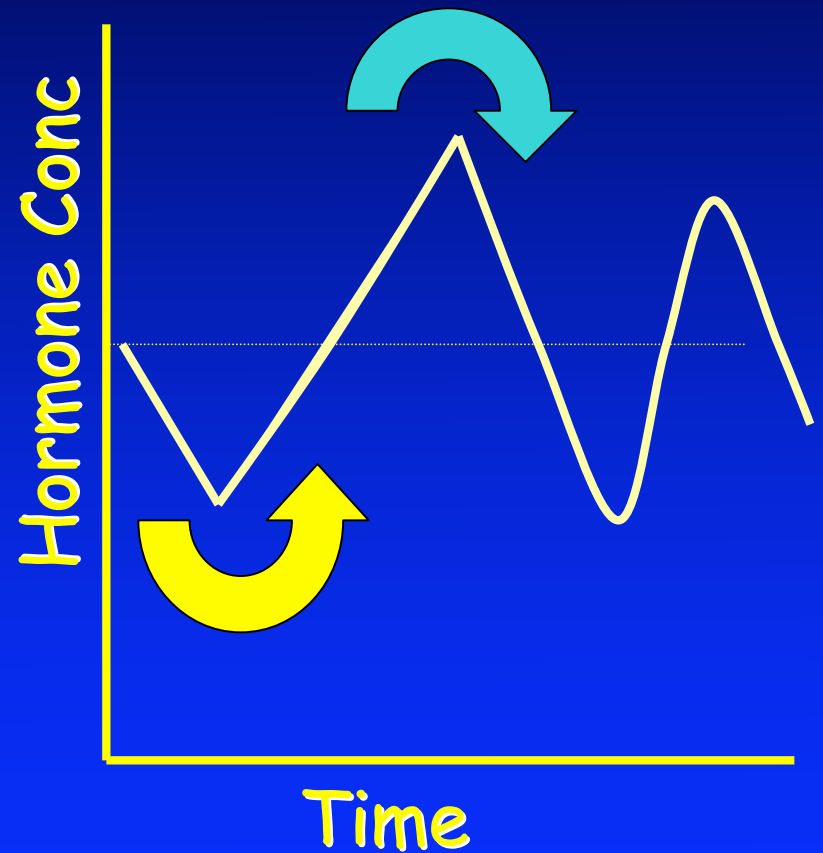
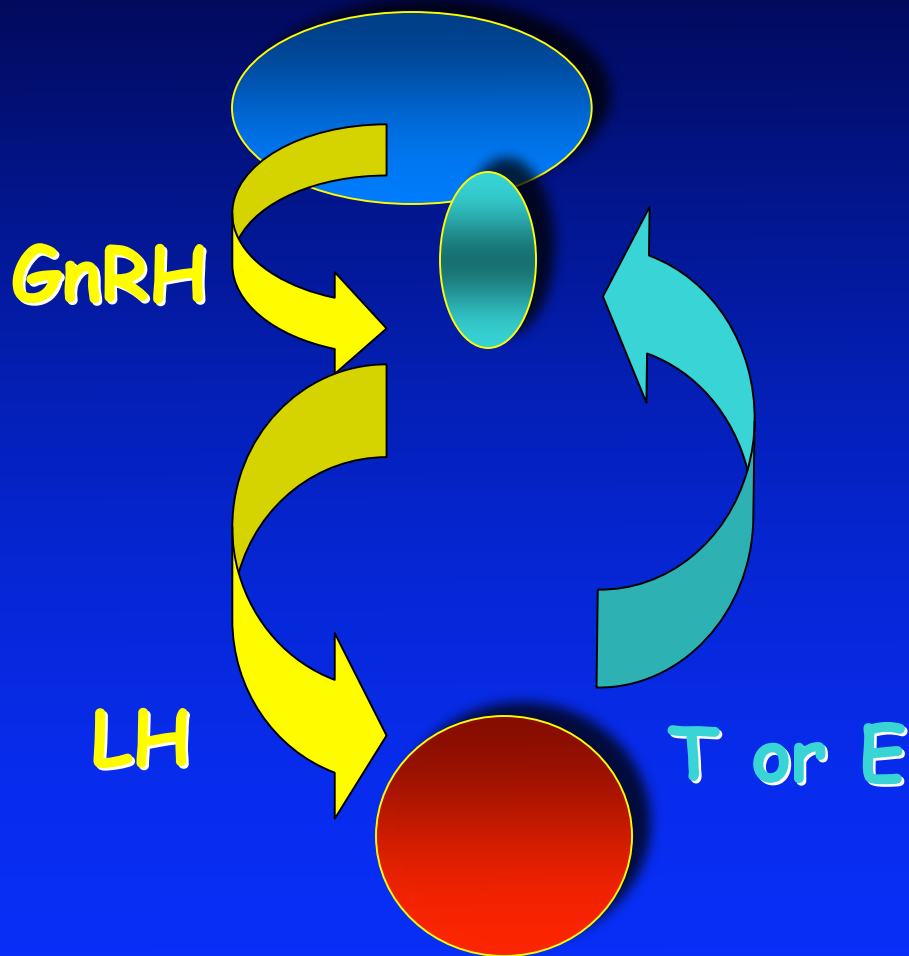
Negative Feedback



Negative Feedback



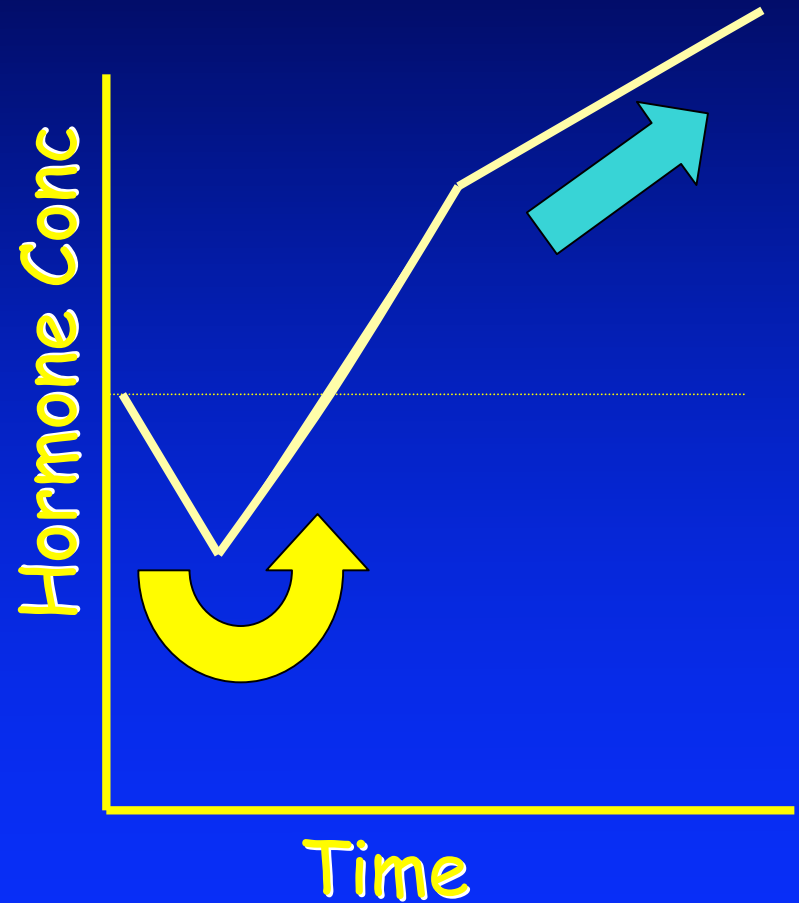
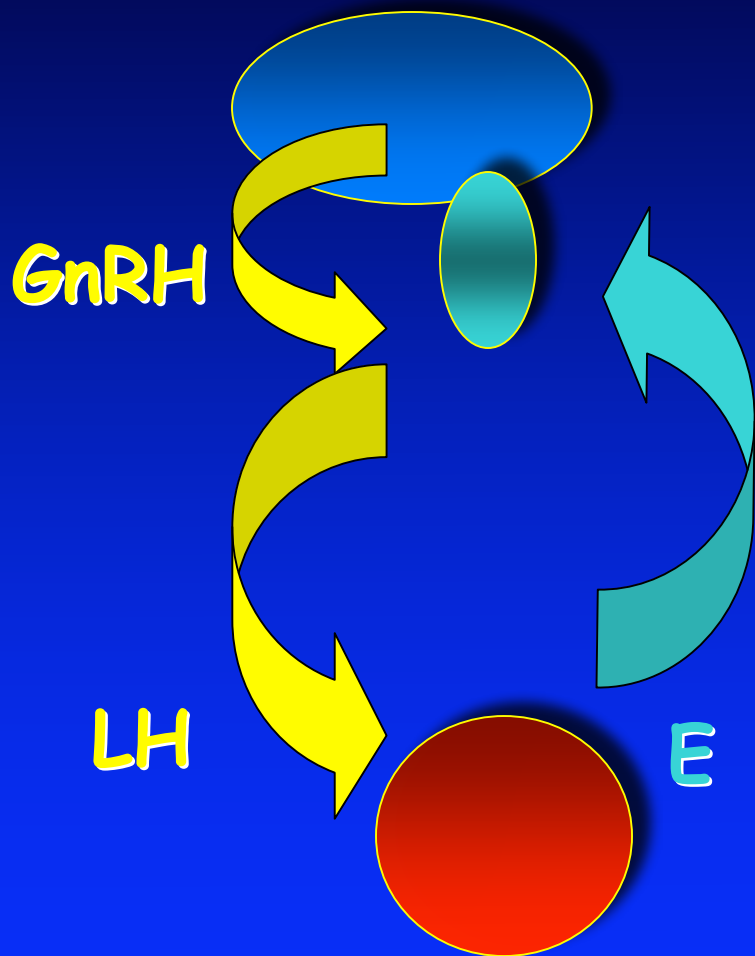
Negative Feedback & Homeostasis



Negative feedback

- 1. peptide hormones
 - alter G protein response
- 2. steroid hormones
 - E_2 and P_4 decrease transcription of β FSH-mRNA and levels of β FSH-mRNA
 - P_4 causes decrease in GnRH release

Positive Feedback & Homeostasis

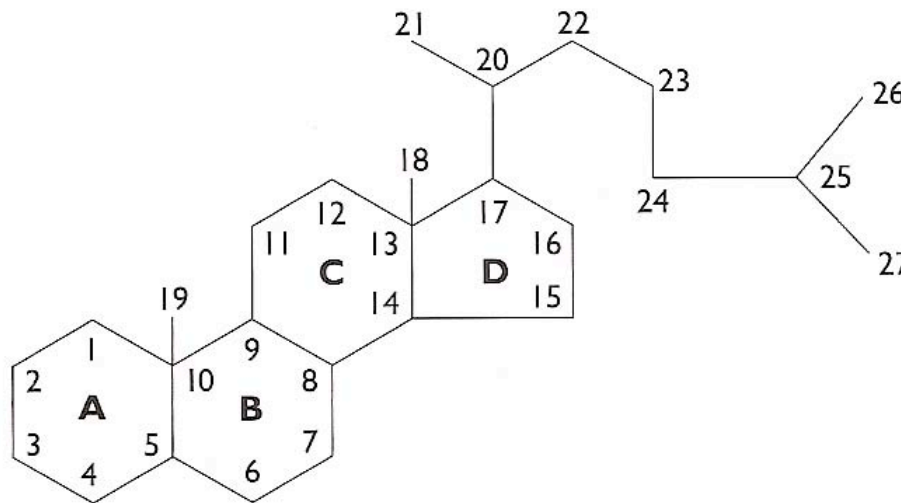


Permissive action of hormones

- steroid hormones may act as permissive agents by
 - increase number of receptors
 - increase protein kinases
 - increase inhibitors of cyclic nucleotides

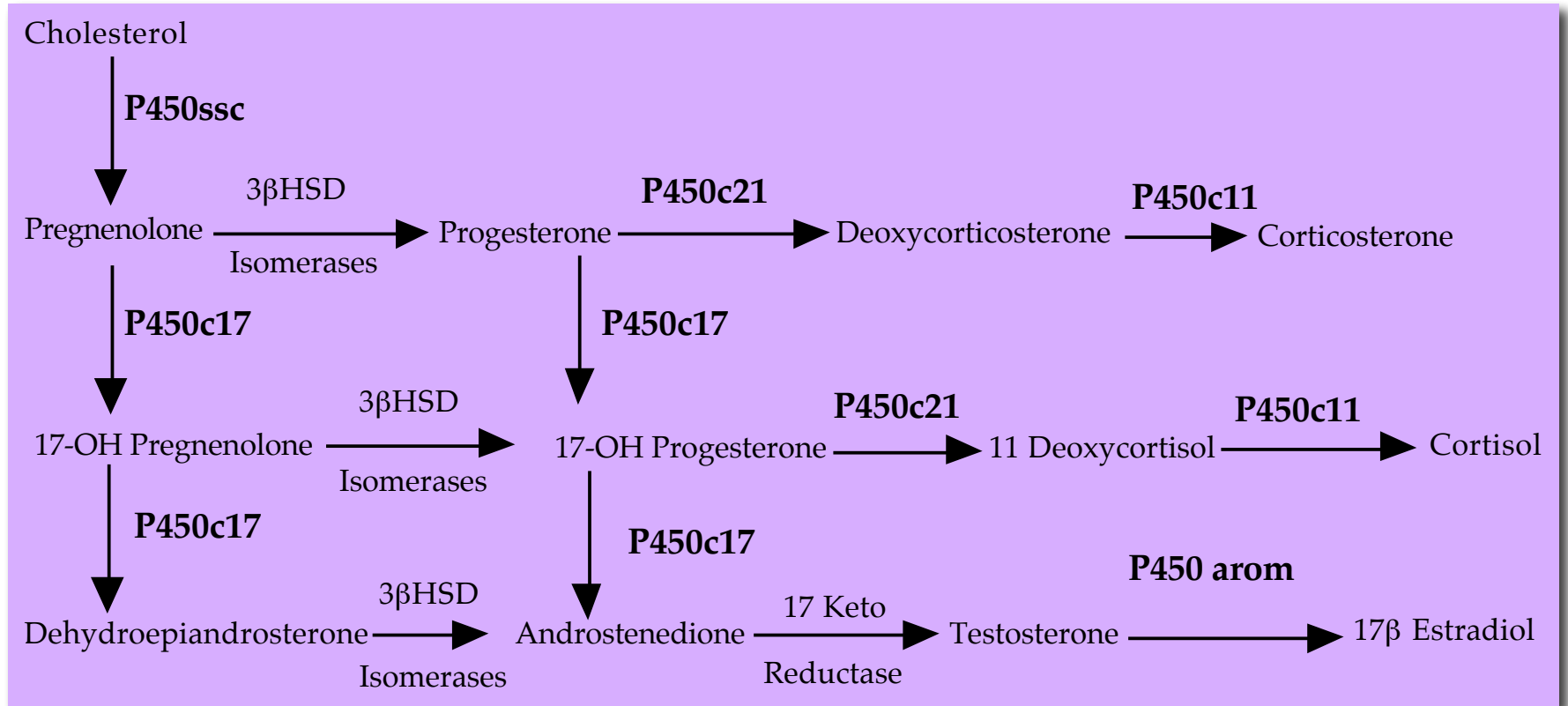
Other Endocrine Organs

- gonads
 - steroids
 - synthesis stimulated by LH
 - derived from cholesterol

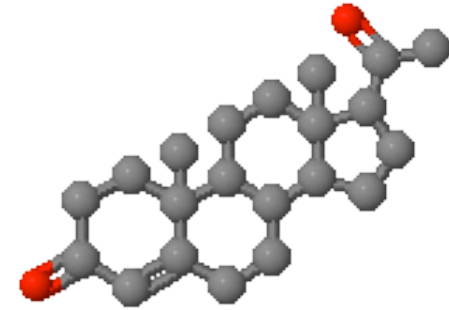


A, B, C and D designate specific rings.
Numbers designate specific carbons.

Steroidogenesis



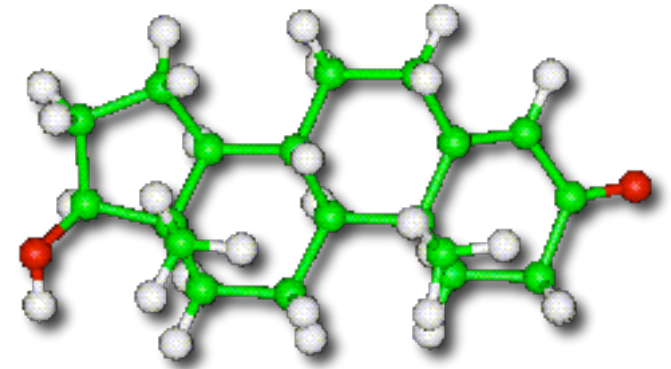
Progestagens



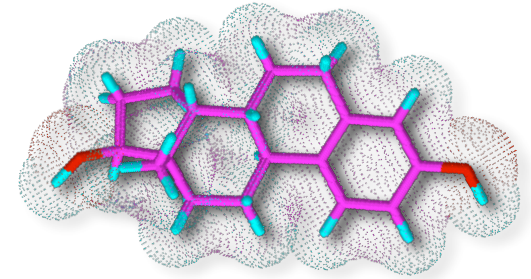
- Primary progestagen
 - Progesterone
- Secondary progestagens
 - 17α -Hydroxyprogesterone (17α -OHP)
 - 20α -Hydroxyprogesterone (20α -OHP)
 - Aka 20α -dihydroxyprogesterone
- Three nuclear receptors
 - PR-A; PR-B and new PR-C (humans to date)
- Membrane receptors (two distinct classes)
 - progesterone membrane receptor component
 - (PGMRC; subtypes 1 and 2)
 - membrane progestin receptors
 - (mPR; subtypes alpha, beta and gamma)

Androgens

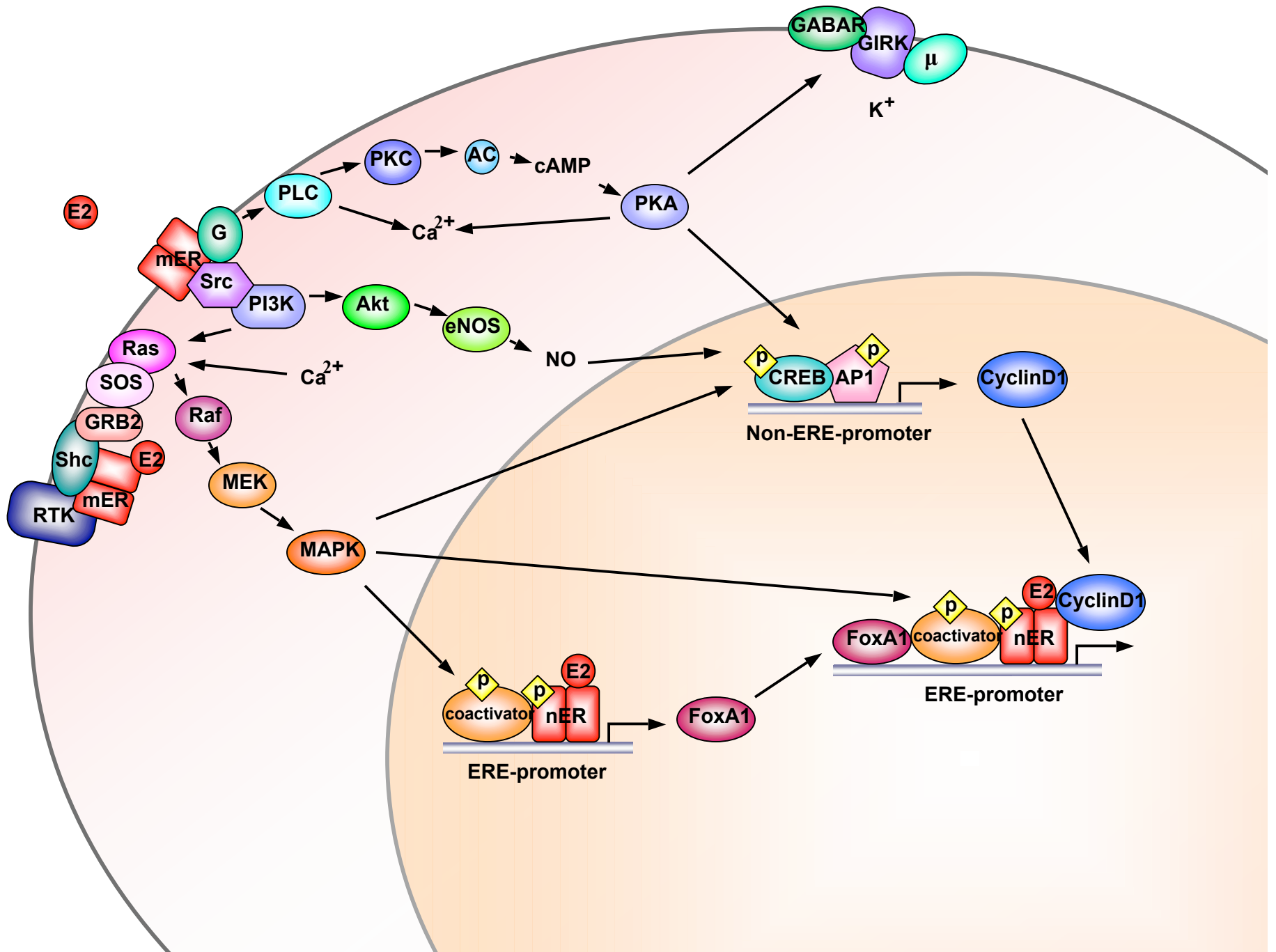
- Androgens
 - two 1° androgens
 - Testosterone (T)
 - dehydrotestosterone (DHT)
 - two 2° androgens
 - Androstenedione (A4)
 - Dehydroepiandrosterone (DHEA)
 - One nuclear receptor
 - AR
 - One membrane receptor?
 - Characterization/no cloning and sequence to date

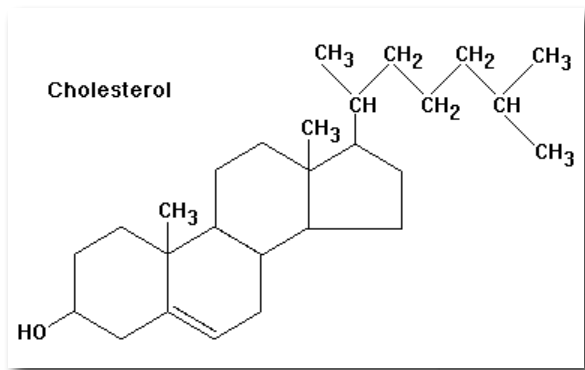


Estrogens

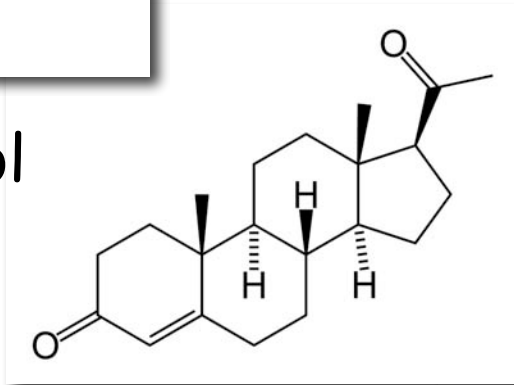


- in vertebrates -
 - three 1° estrogens (Oestrogens)
 - Estradiol-17 β (E2)
 - Estriol
 - Estrone
 - Two nuclear receptors
 - ER α
 - ER β
 - One membrane receptor
 - GPR30



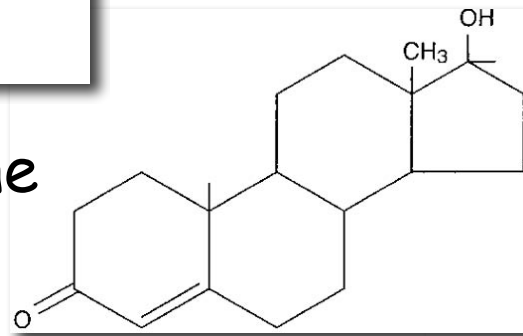


Cholesterol



Gain carbonyl groups
Loss carbon tail

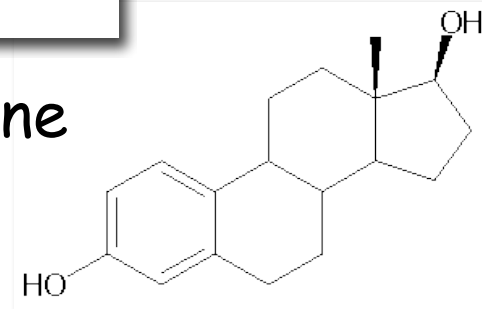
Progesterone



Testosterone



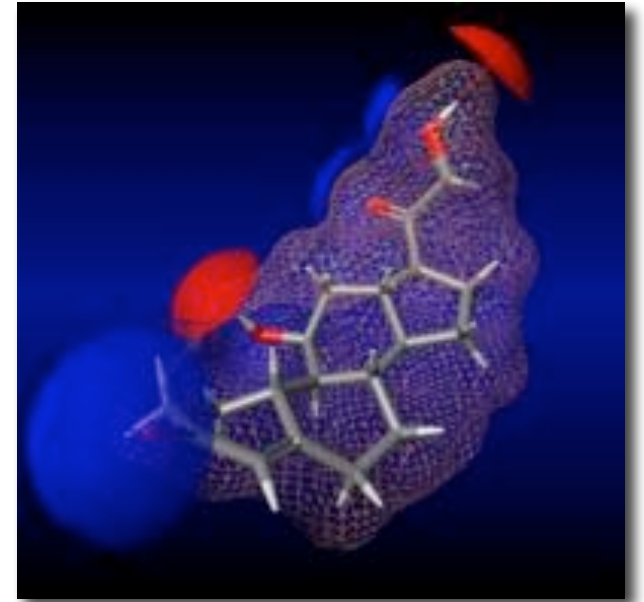
Gain hydroxyl
Loss carbonyl &
methyl



Estradiol-17β

Adrenal

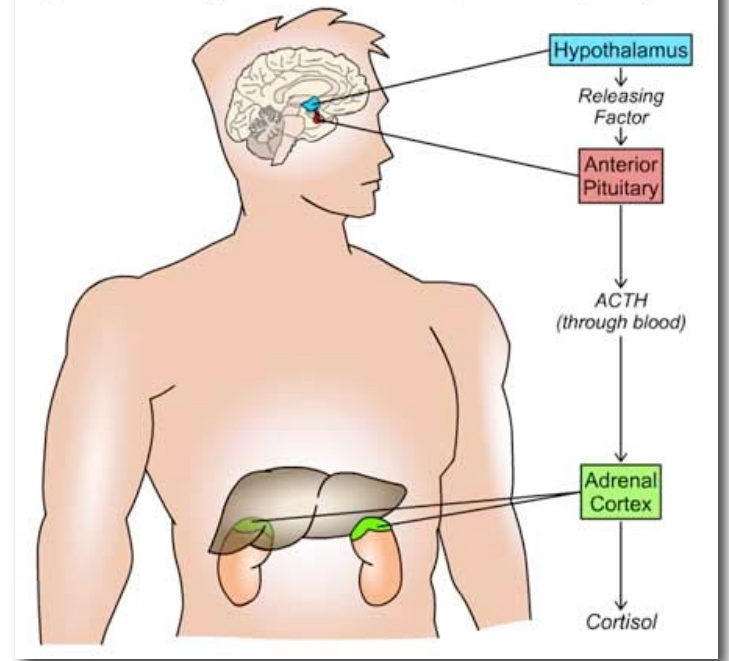
- Mineralocorticoids
 - aldosterone
- Glucocorticoids
 - cortisol or corticosterone
- Weak Androgens
 - Dehydroepiandrosterone (DHEA)
- All derived from progesterone



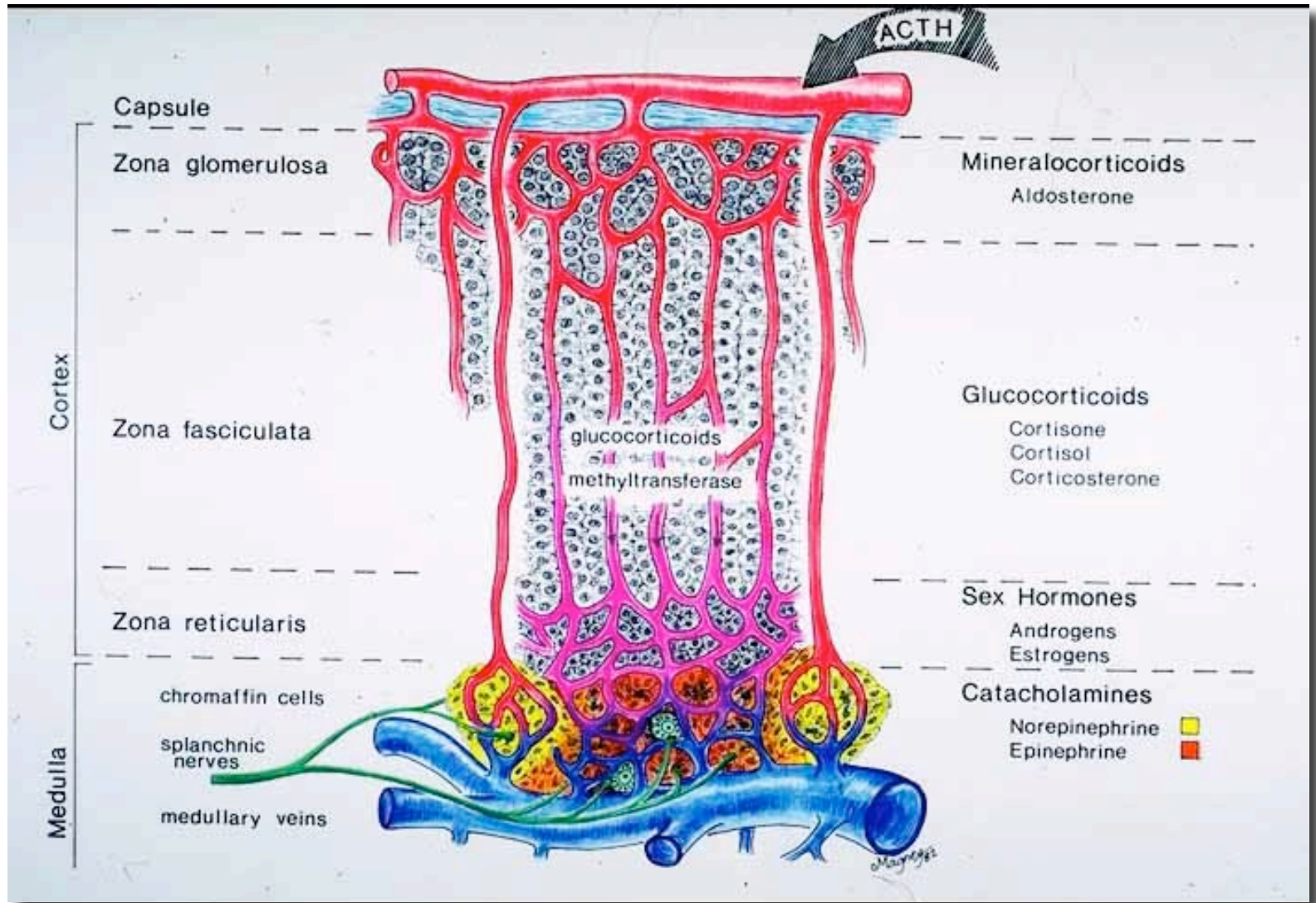
Adrenal

- Mineralocorticoids
 - aldosterone
- Glucocorticoids
 - cortisol or corticosterone
- Weak Androgens
 - Dehydroepiandrosterone (DHEA)
- All derived from progesterone
- Major role in stress response

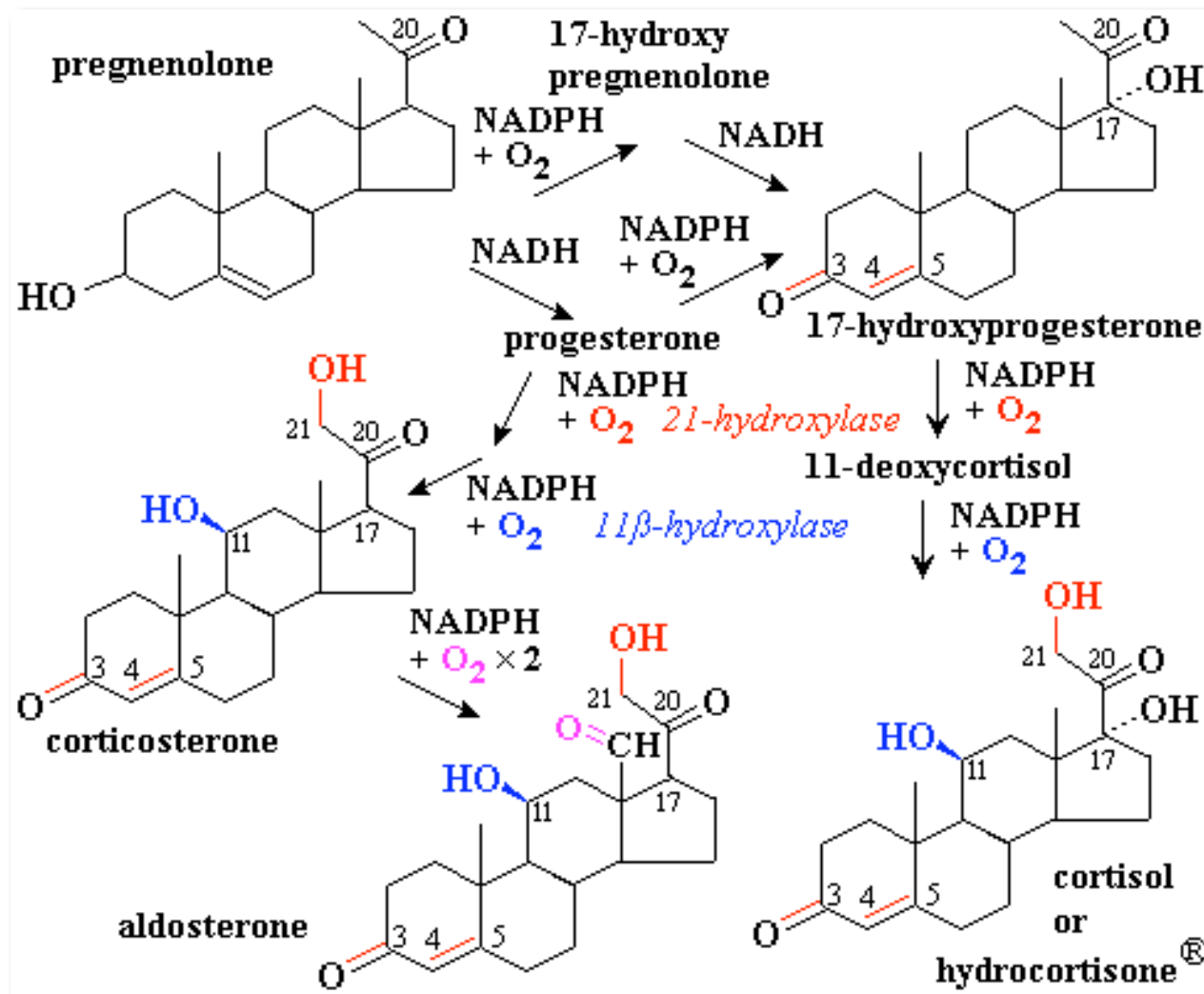
Figure AN-1: Hypothalamic-Pituitary-Adrenal (HPA) Axis



Adrenal Function



Steroidogenesis



Lipid based Hormones

Figure 5-10. Gonadal Steroid Synthetic Pathway

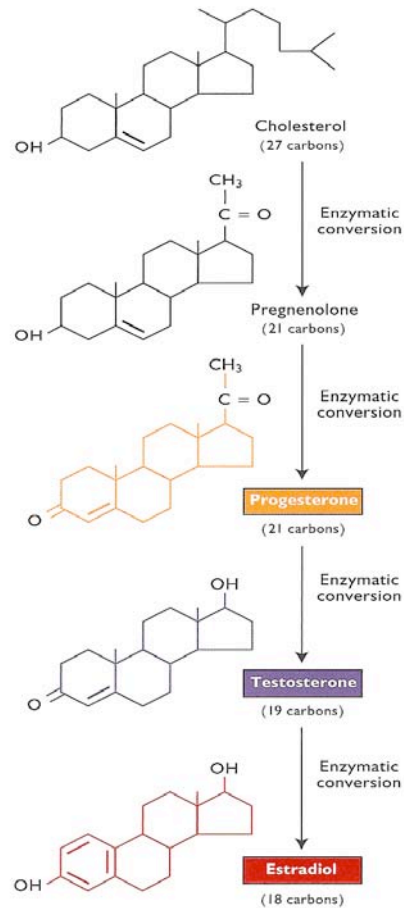
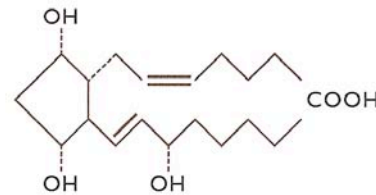


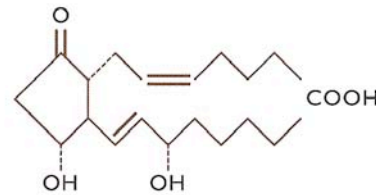
Figure 5-11. Structure of $\text{PGF}_{2\alpha}$ and PGE_2

(The dashed lines represent bonds that extend into the plane of the page)

Prostaglandin $\text{F}_{2\alpha}$ ($\text{PGF}_{2\alpha}$)



Prostaglandin E_2 (PGE_2)



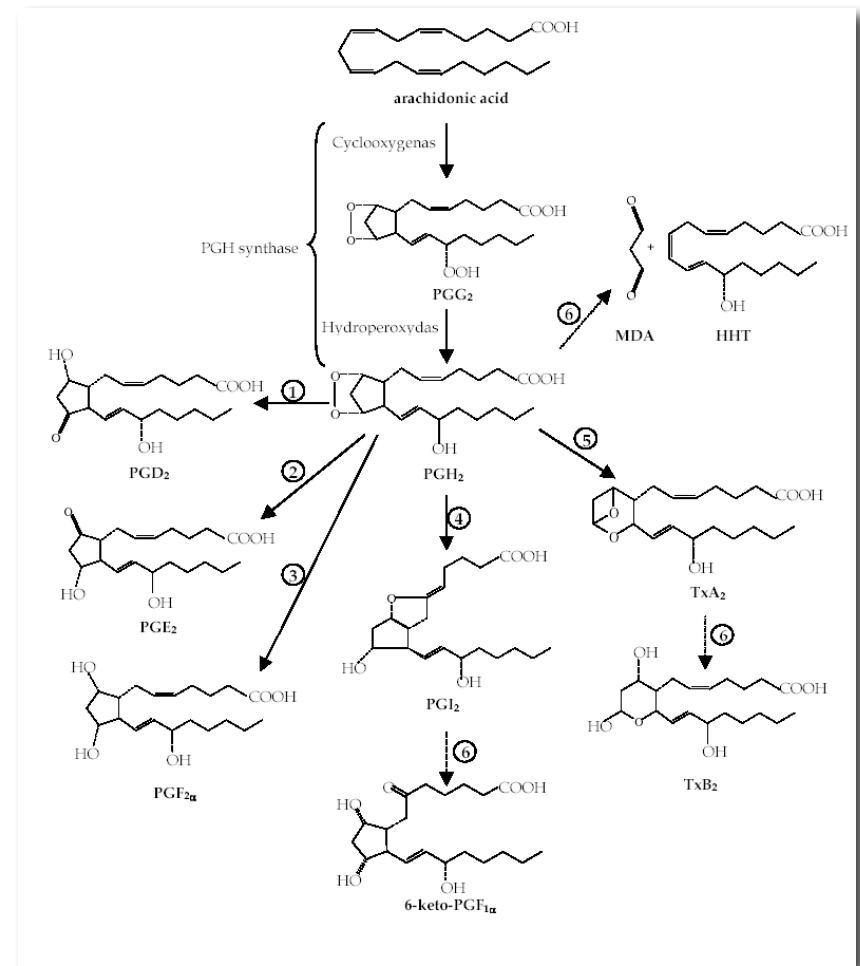
Biochemical classifications include:

- peptides
- glycoproteins
- steroids
- prostaglandins

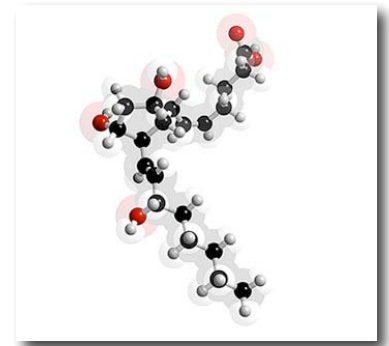
Steroid hormones have a common molecular nucleus called the **cyclopentanoperhydrophenanthrene nucleus**. The molecule is composed of four rings designated A, B, C and D. Each carbon in the ring has a number, as shown in Figure 5-9.

Prostaglandins

- Eicosanoids
 - Along with thromboxanes and prostacyclins
- Lipid based hormones
 - 20 carbon atoms,
 - 5-carbon ring
- Derived from arachidonic acid

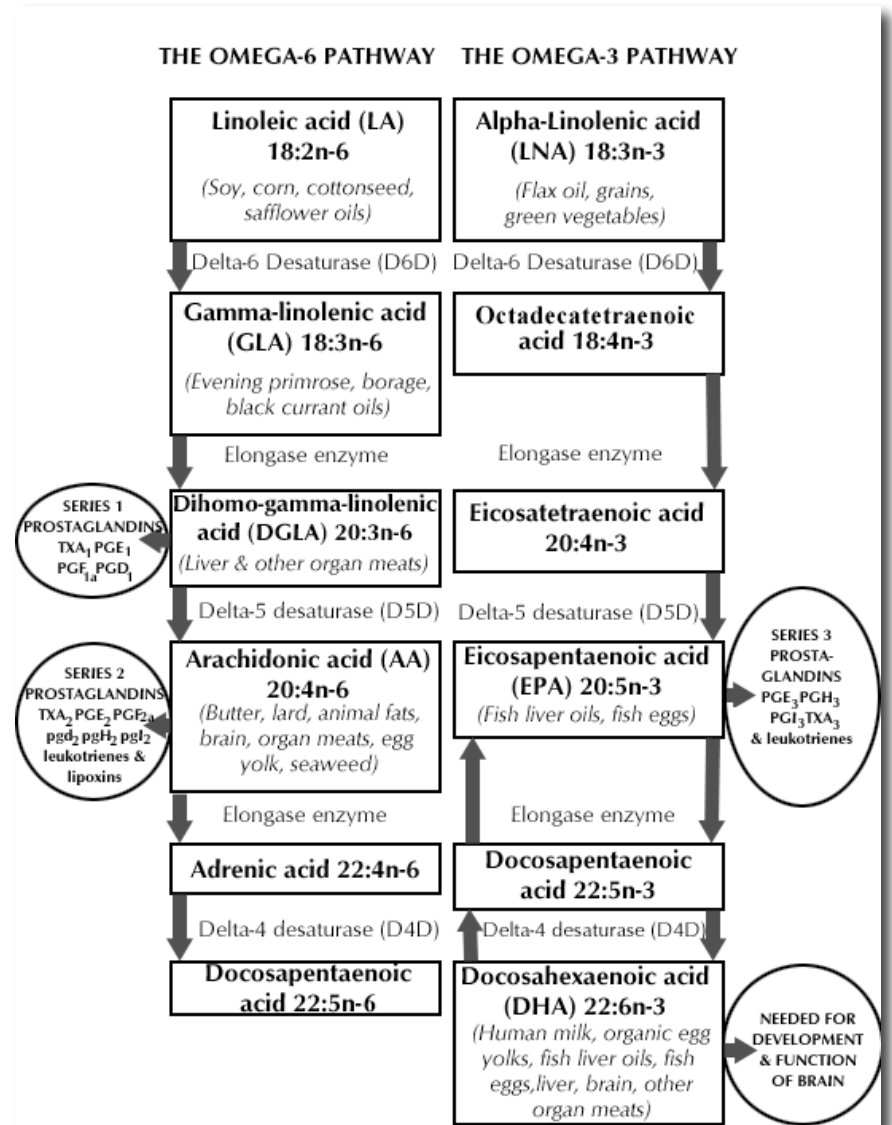
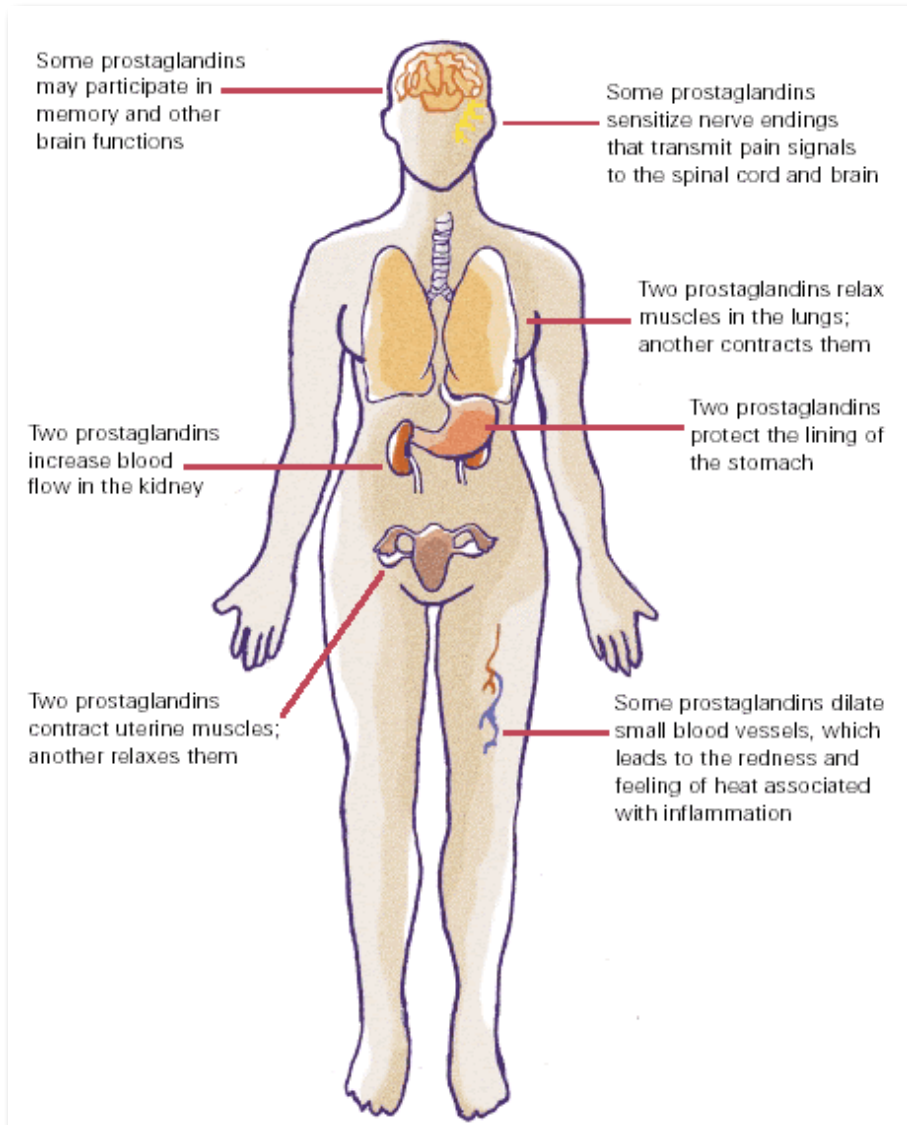


Prostaglandins

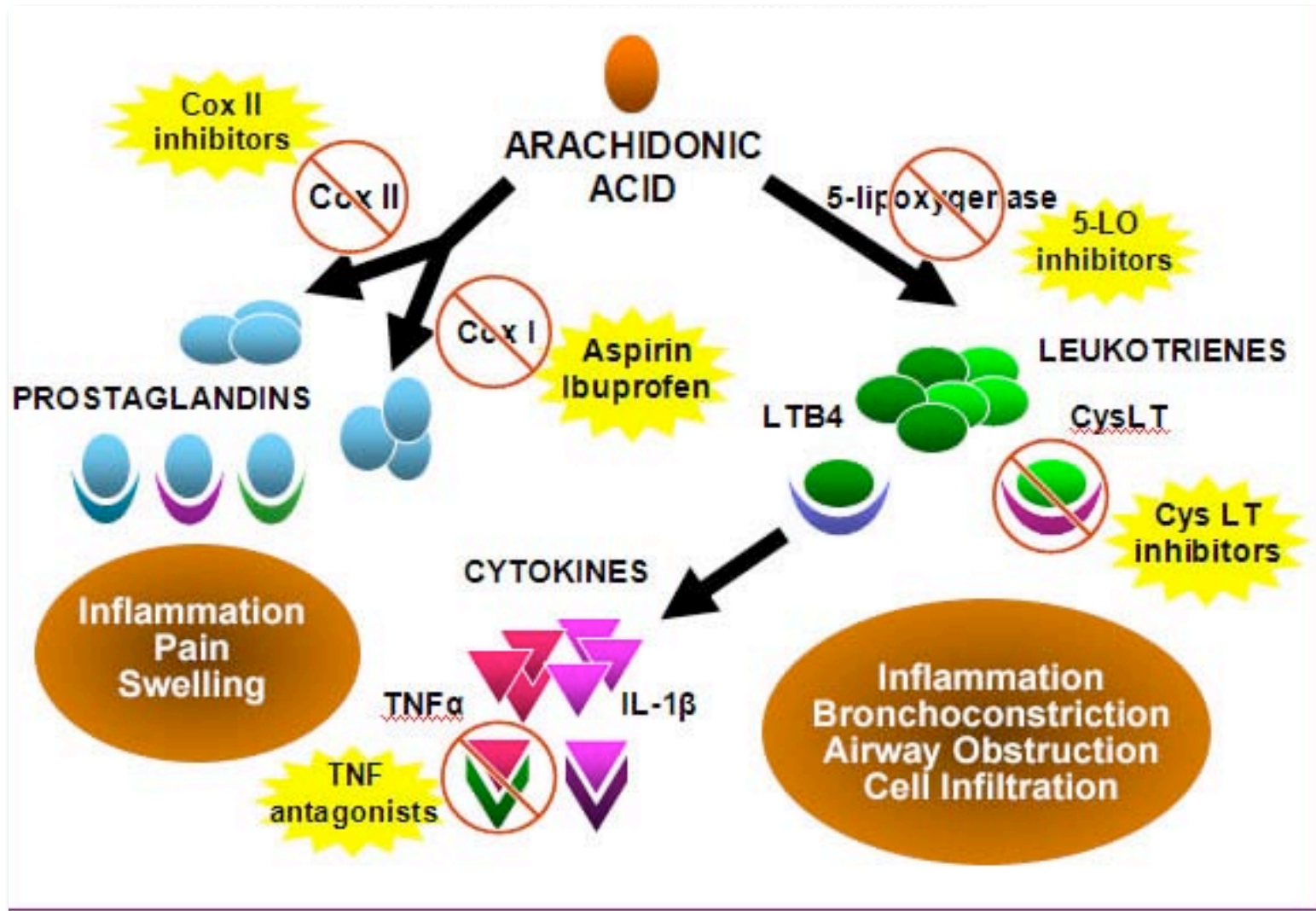


- First isolated from seminal fluid in 1935
 - by the Swedish physiologist Ulf von Euler
 - and independently by M.W. Goldblatt
- believed to be from prostate
 - Actually produced by the seminal vesicles
- Produced in virtually all tissues and organs
 - autocrine and paracrine mediators
 - act upon multiple cell types
 - platelets, endothelium, uterine and mast cells
- Non-Steroidal Anti-Inflammatory Drug (NSAID)
 - Target COX and other aspects of PGs pathways

Prostaglandins

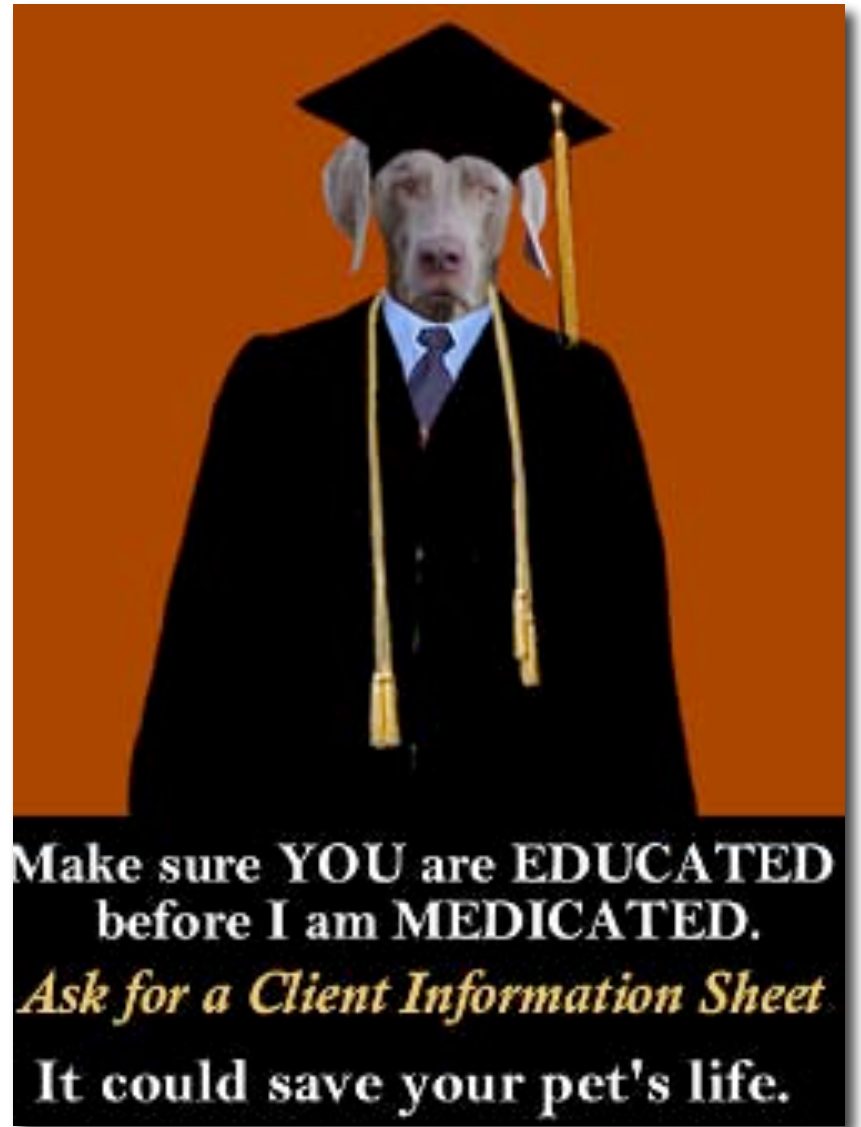


Prostaglandin blockers - NSAIDs



Unintended Consequences

- FDA
 - more than 22,000 dogs have gotten sick
 - some have died after taking non-steroidal anti-inflammatory drugs
 - including Metacam, Deramaxx, Previcox and Rimadyl.



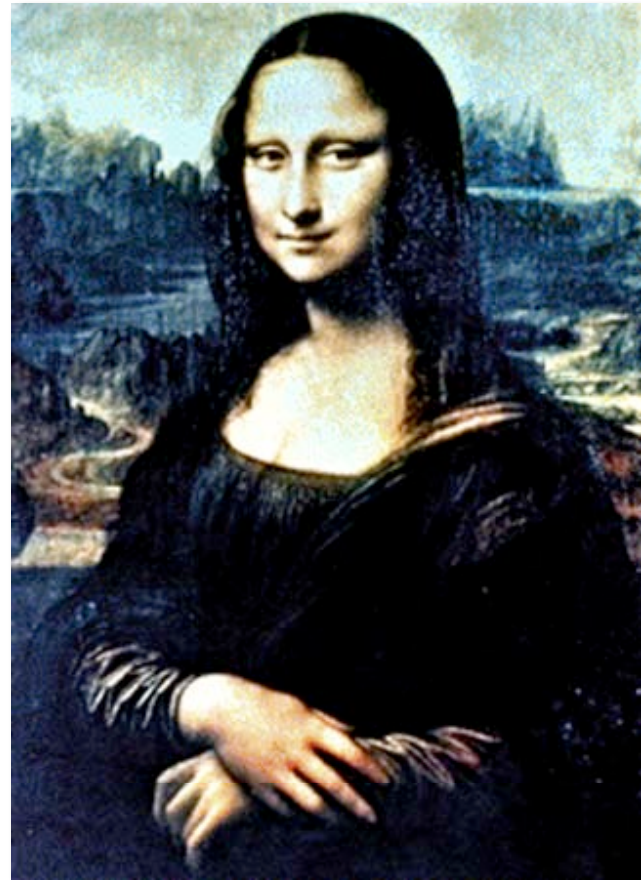
Diclofenac (NSAID) and Vultures

- Unintended consequences
 - Not all species the same
- Diclofenac
 - Non-Steroidal Anti-Inflammatory Drug (NSAID)
- cause gout and renal failure in vultures of the *Gyps* genus
- In India 3 *Gyps* species
 - lost over 99 percent of population in a decade
- Still sold in Africa
 - Used for cattle



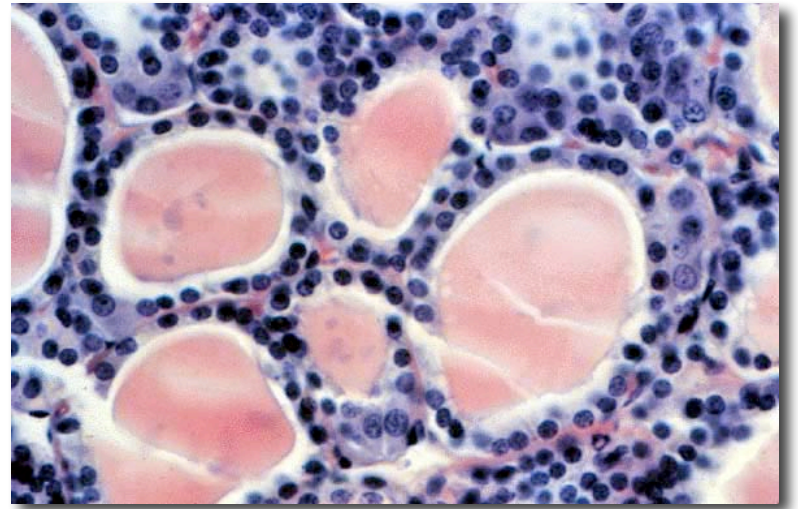
Thyroid

- thyroxin (T_4) or triiodothyronine (T_3)
- iodine as a central component
- alters metabolism
- nuclear receptor in mitochondria



Thyroid

- Two lobes in the neck
- Two hormones
 - Thyroxine (T4)
 - Triiodothyronine (T3)
 - Require iodide for synthesis
- Major role in development and control of metabolism



Thyroid follicle

