

Endocrine Pharmacology

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Basic principles

- Endocrine pharmacology vs endocrine physiology
- 2nd in importance to CNS
- **Endocrine System**
 - Uses chemical signals (hormones) for cell to cell communication
 - Coordinates the function of cells
 - Response to an endocrine signal occurs within minutes to hours (ductless glands)

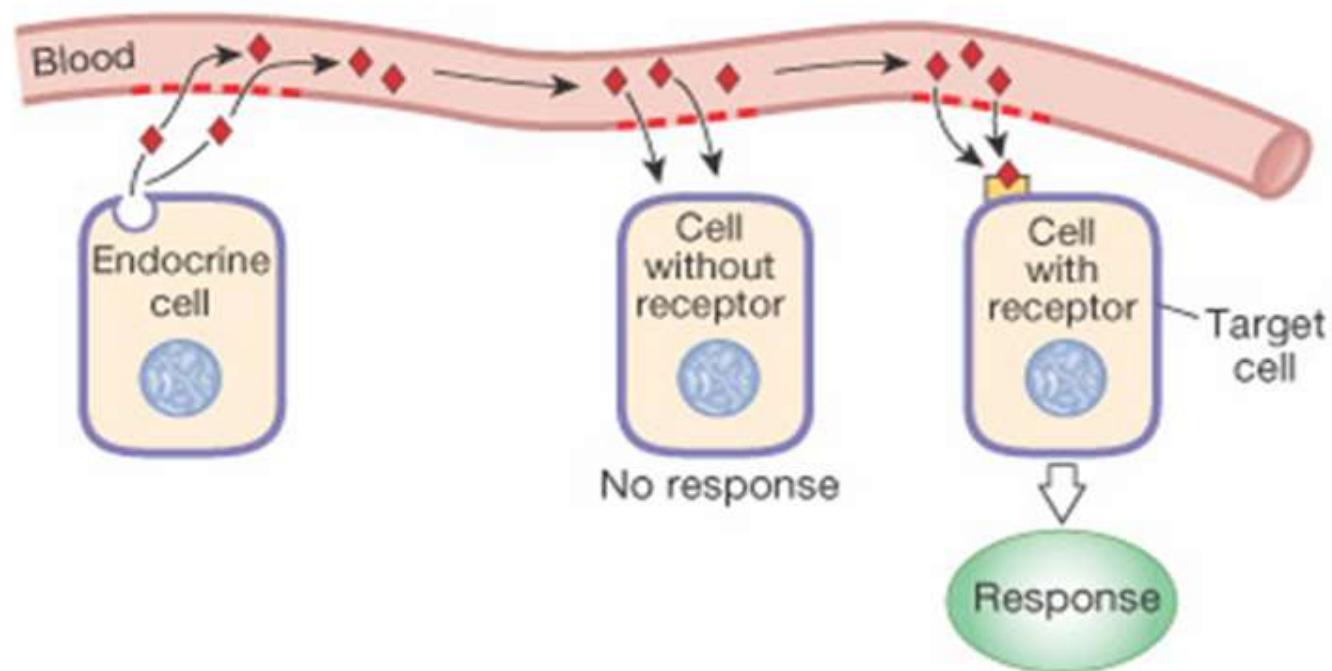
■ Hormonal regulation ↑↓

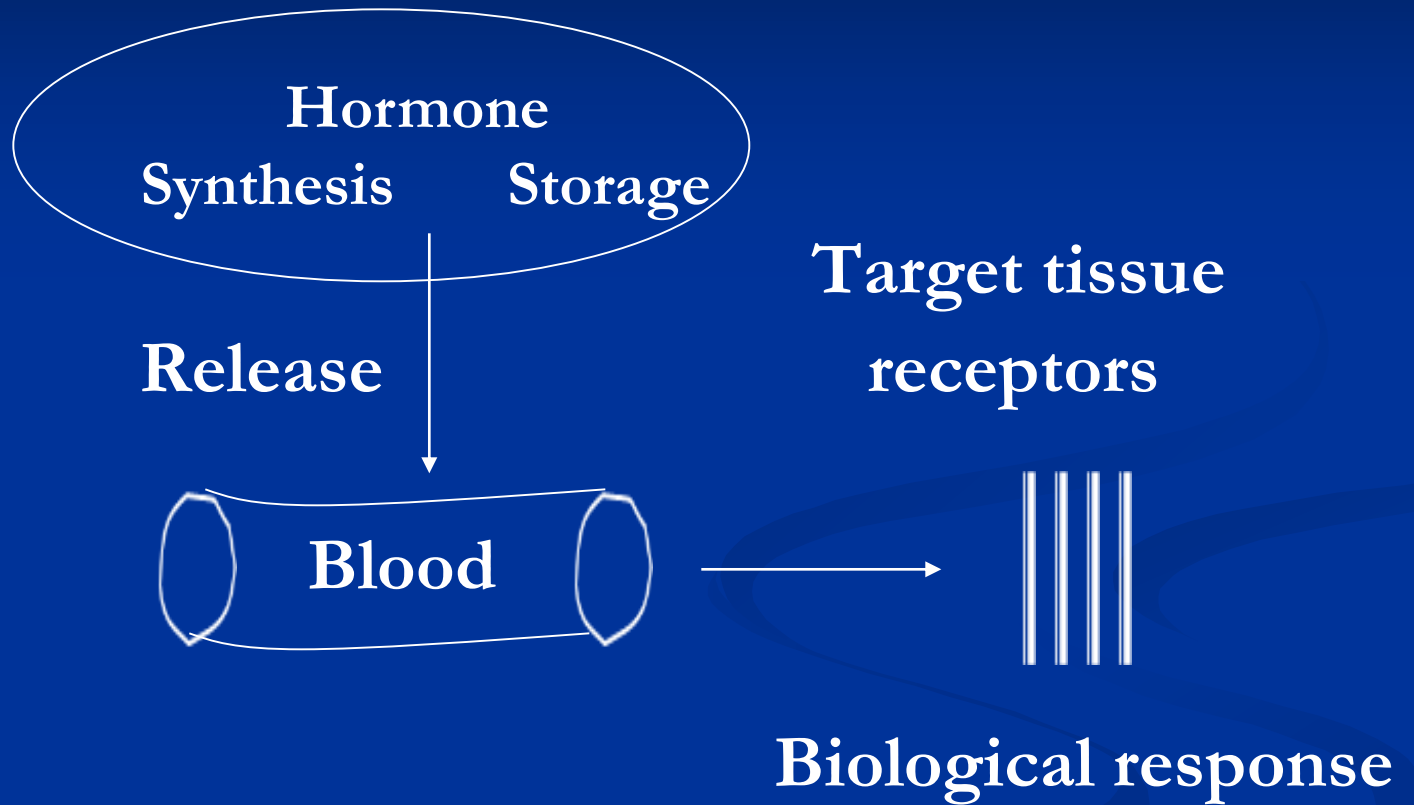
- Growth & development
- Reproduction, fertility, sexual function
- Response to environmental situations
(stress...)
- Maintenance of normal homeostasis

■ Hormones

- Chemical substances synthesized in and released from highly specialized cells collectively known as endocrine glands, immediately secreted into blood stream and act at some other place
- Considered cell to cell communication molecules
- Transported by blood
- Distant or local target tissue receptors
- Activates physiological response

Hormones are secreted by endocrine glands or cells into the blood. Only target cells with receptors for the hormone will respond to the signal.





**** Glands**

Ductless

Hypothalamus

Pituitary

Thyroid

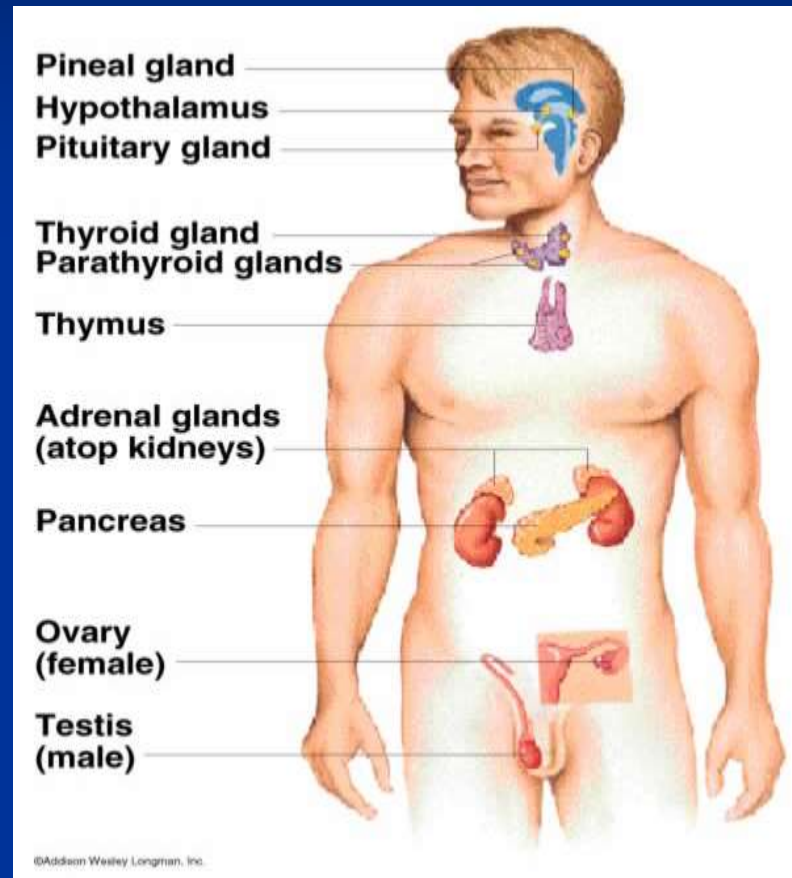
Parathyroid

Pancreas

Adrenals

Ovaries

Testes



■ Chemical nature of hormones

- a. a derivatives:

T3; T4; Dopamine (precursor=Tyrosine)

- Small peptides; polypeptides; large proteins or glycoproteins:

Hypothalamic hormones; GH; PRL; Insulin; Glucagon; LH; FSH; TSH...

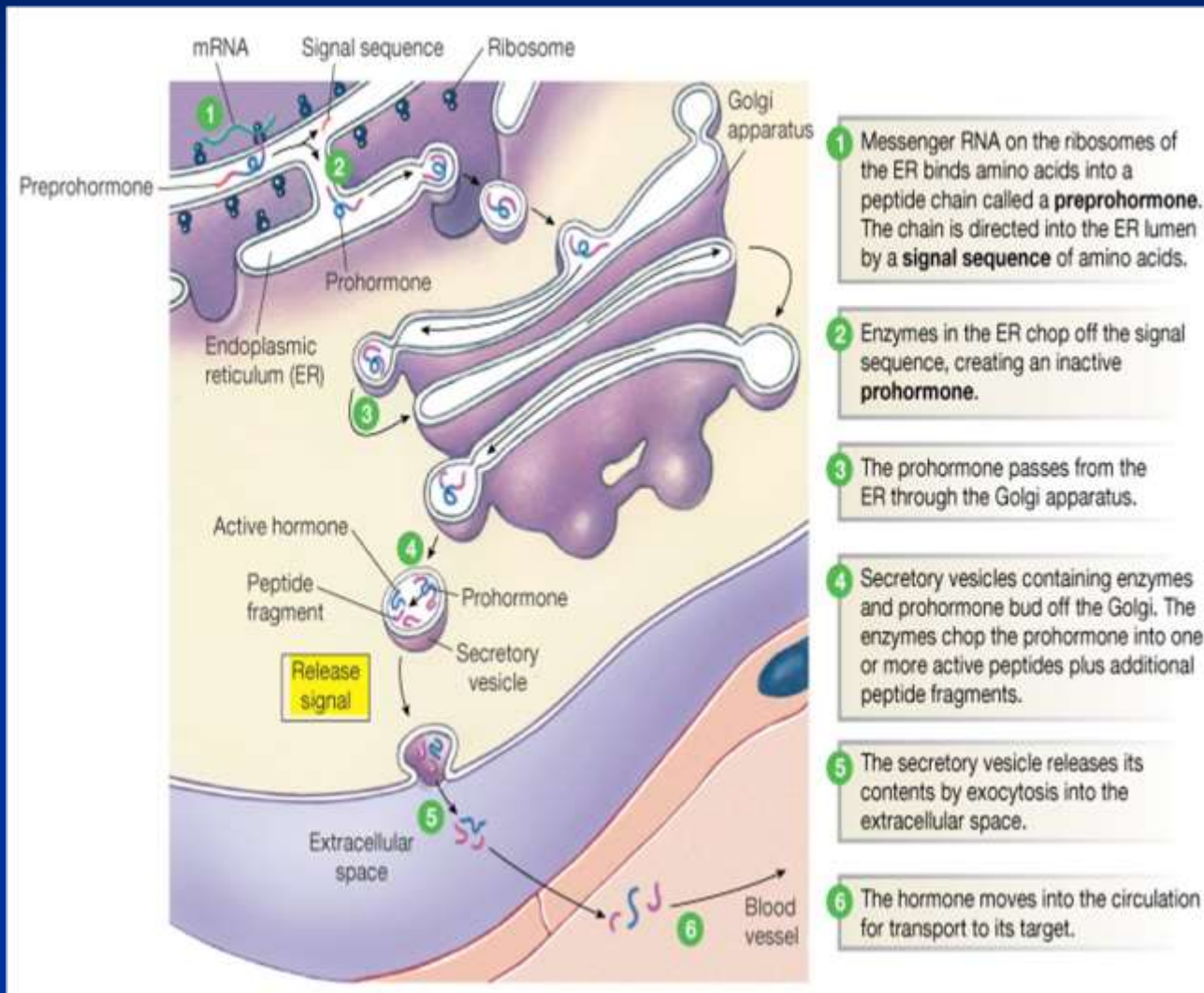
- Steroids

Cortisol; Aldosterone; Estrogen; Progesterone; Androgens

■ Amine Hormones

- Derived from the amino acid tyrosine
- Include the catecholamine dopamine & thyroid hormones
- Stored until secreted
 - * Receptor locations
 - Surface (Dopamine)
 - Intracellular (nuclear; T_3 & T_4)

Protein and Polypeptide Hormones: Synthesis and Release



LH

FSH

TSH

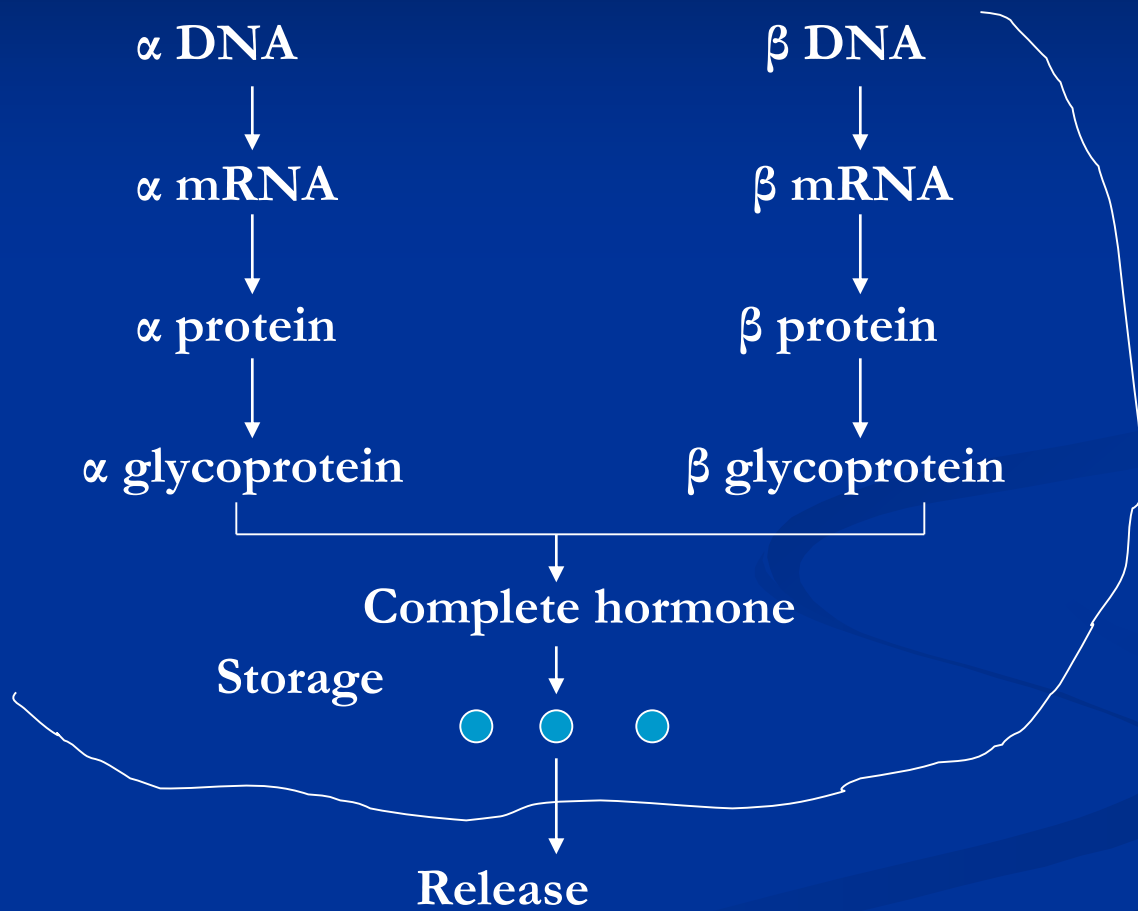
hCG

α



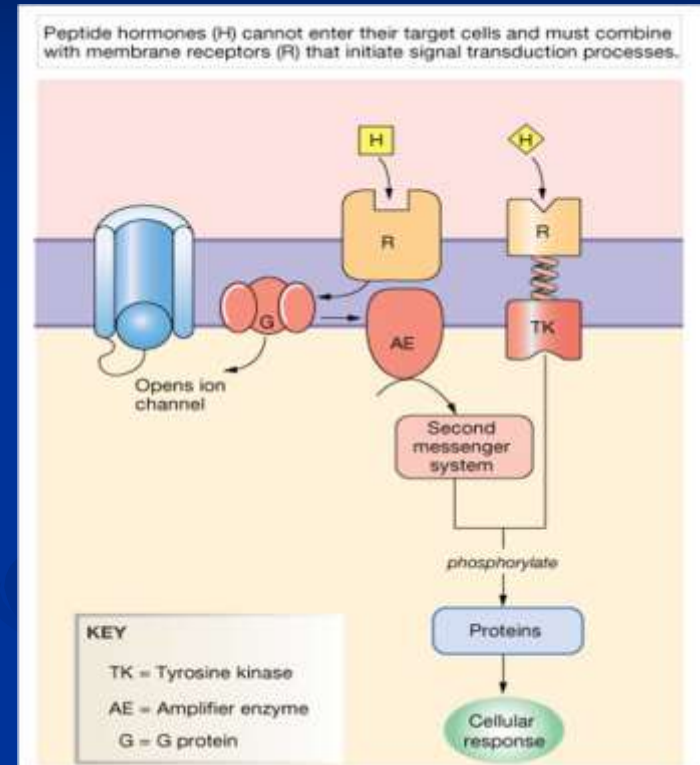
β



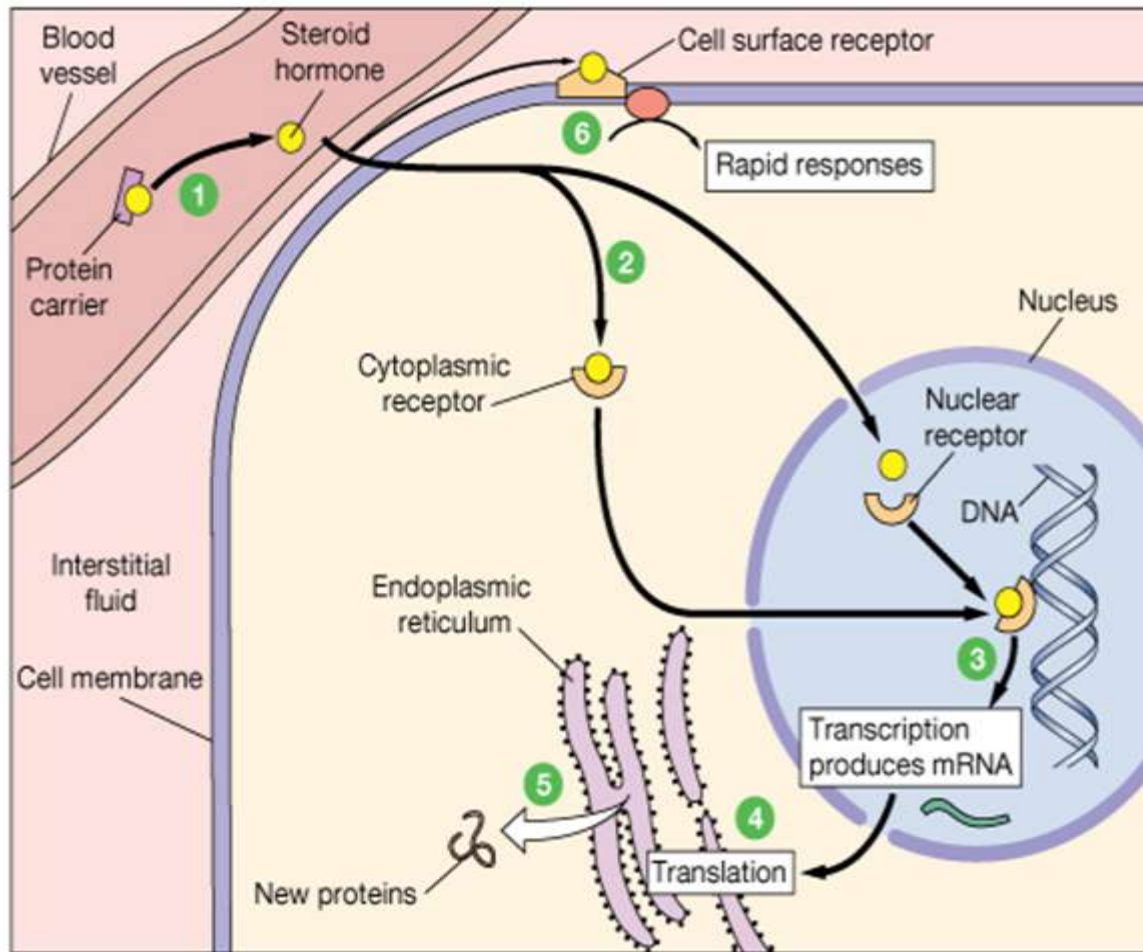


Protein and Polypeptide Hormone Receptors

- Bind to surface receptor
- Transduction
 - System activation
 - Open ion channel
 - Enzyme activation
 - Second messenger systems
 - Protein synthesis

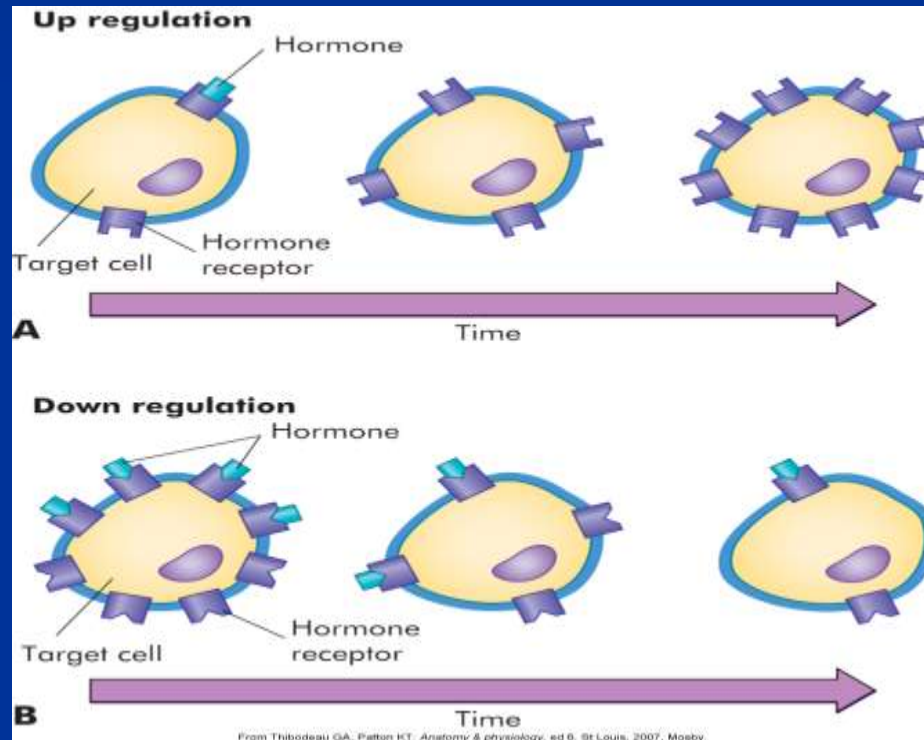


Steroid Hormones Receptors



- 1 Most hydrophobic steroids are bound to plasma protein carriers. Only unbound hormones can diffuse into the target cell.
- 2 Steroid hormone receptors are in the cytoplasm or nucleus.
- 3 The receptor-hormone complex binds to DNA and activates or represses one or more genes.
- 4 Activated genes create new mRNA that moves back to the cytoplasm.
- 5 Translation produces new proteins for cell processes.
- 6 Some steroid hormones also bind to membrane receptors that use second messenger systems to create rapid cellular responses.

Hormone receptors are subject to 2 important phenomena



■ **Basal conditions**...minimal release

■ **Stimuli:**

- Nerve impulse

- Change in composition of ECF

- Another hormone (trophic hormone)

↳ blood → target cells → receptors → initial change → cascade of reactions → recognizable change...

- Change in cell permeability
- Stimulation or inhibition of protein synthesis
 - ** Transcription or translation
- Stimulation or inhibition of mediator release
(second messenger)
 - ** cAMP; DAG; Ca⁺⁺ ; ITP (IP₃)...

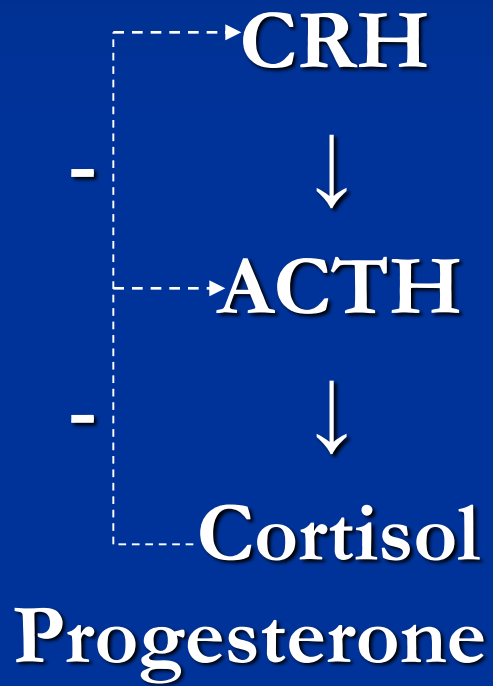
■ How long a hormone stays high in blood?

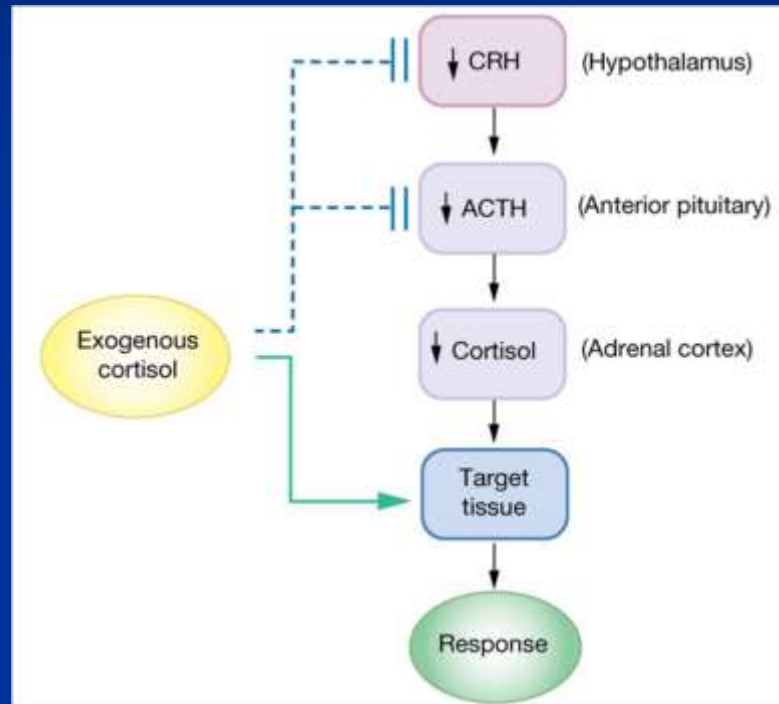
Depends on:

- Extent of protein binding
- Efficiency of degradable enzymes & clearance

Metabolism & excretion

- Efficiency of negative feedback mechanisms





■ Sources of hormones:

- Natural

Human (LH & FSH; hCG); Animal (T_3 & T_4)

- Synthetic

Most hormones and their antagonists

■ Disorders affecting endocrine glands:

- Deficiency states

- . HRT

- . Drugs ↑ synthesis and/or release, or drugs ↑ affinity or sensitivity or number of receptors to hormone

- Excess production of a specific hormone

Inhibitors to the synthetic machinery or
Release inhibitors or
Specific antagonists or
Surgery

■ Clinical pharmacology of hormones:

- Major clinical use of hormones

HRT (physiological doses)

- Supra-physiological doses (pharmacological doses)

Anti-inflammatory effects (non-endocrine-related diseases)...

- Use as diagnostic tool (TRH test ...)

- The use of some drugs which are not hormones, but used in the management of diseases of endocrine origin

Antithyroid drugs, oral hypoglycemic agents...

- Some drugs are used to treat diseases not related to the endocrine system but affecting it

Anticancerous drugs → ♂ & ♀ infertility

- The use of hormones as contraceptives???