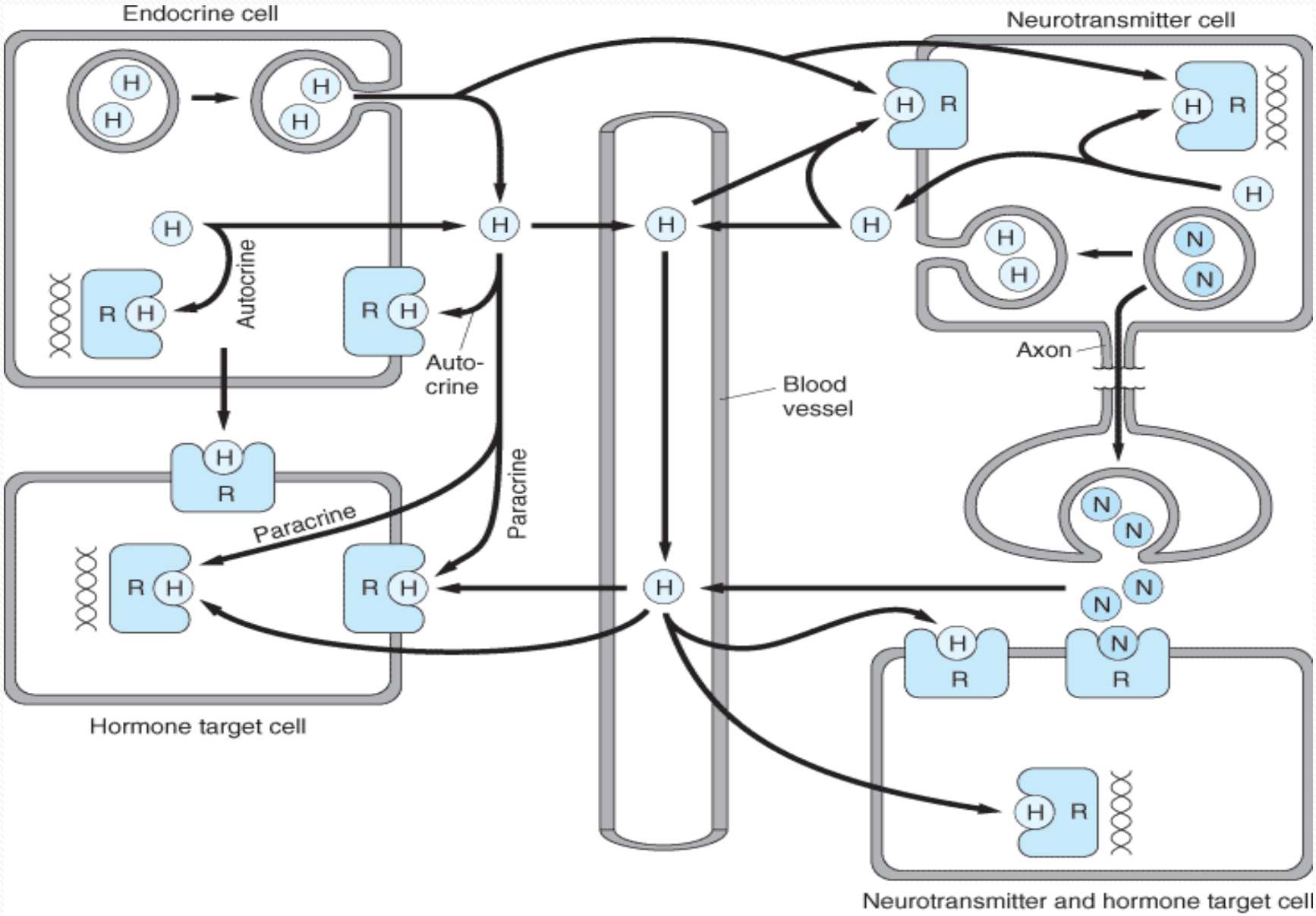
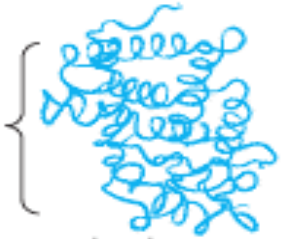
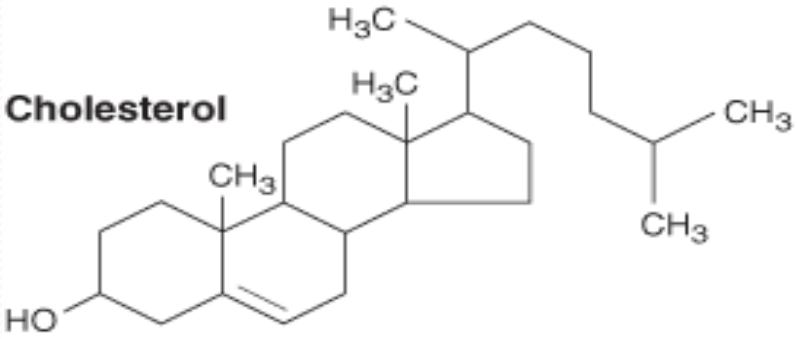
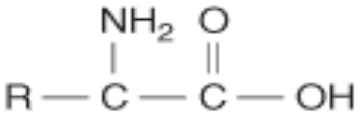
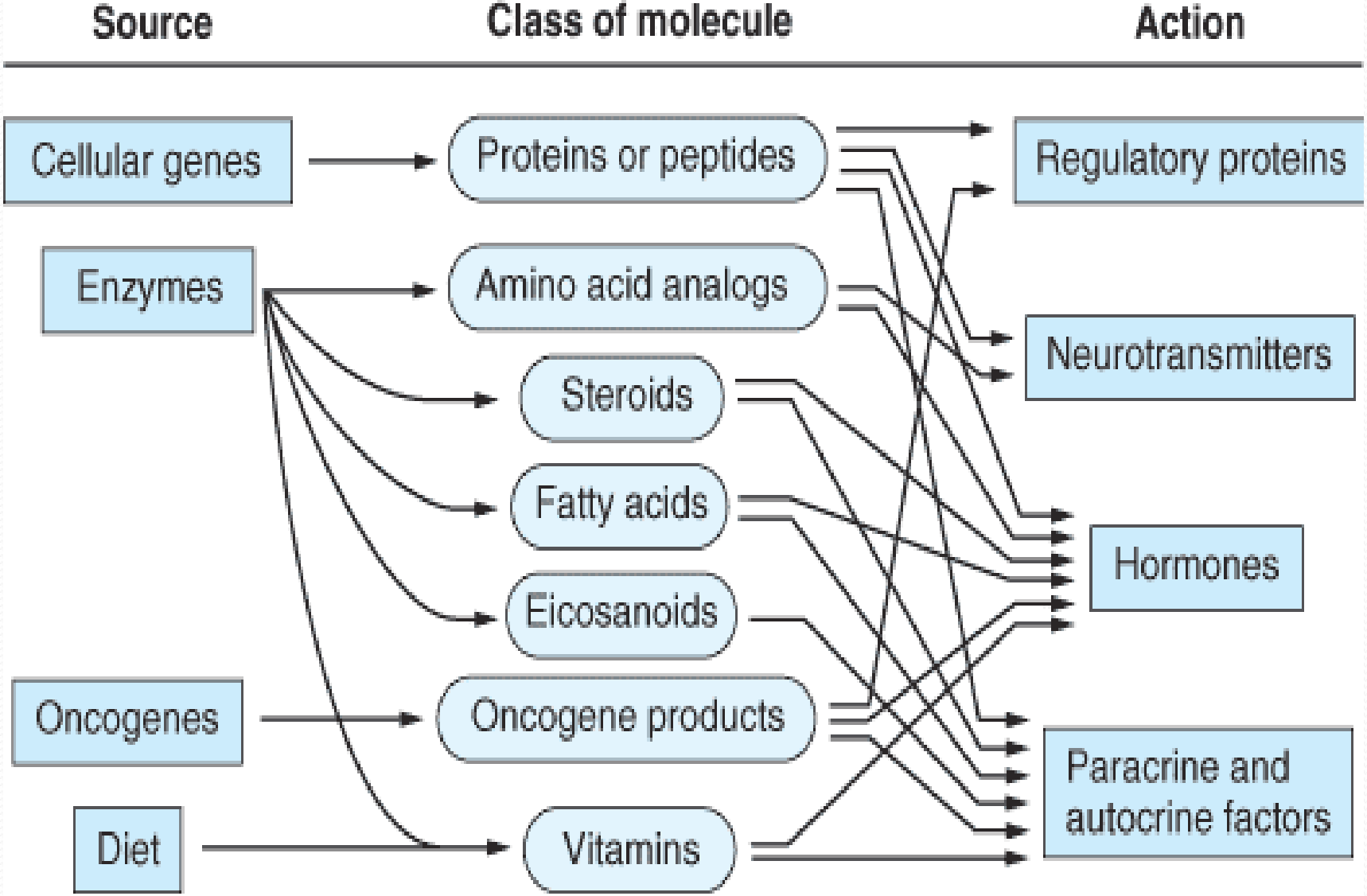
Action of hormones and neurotransmitters



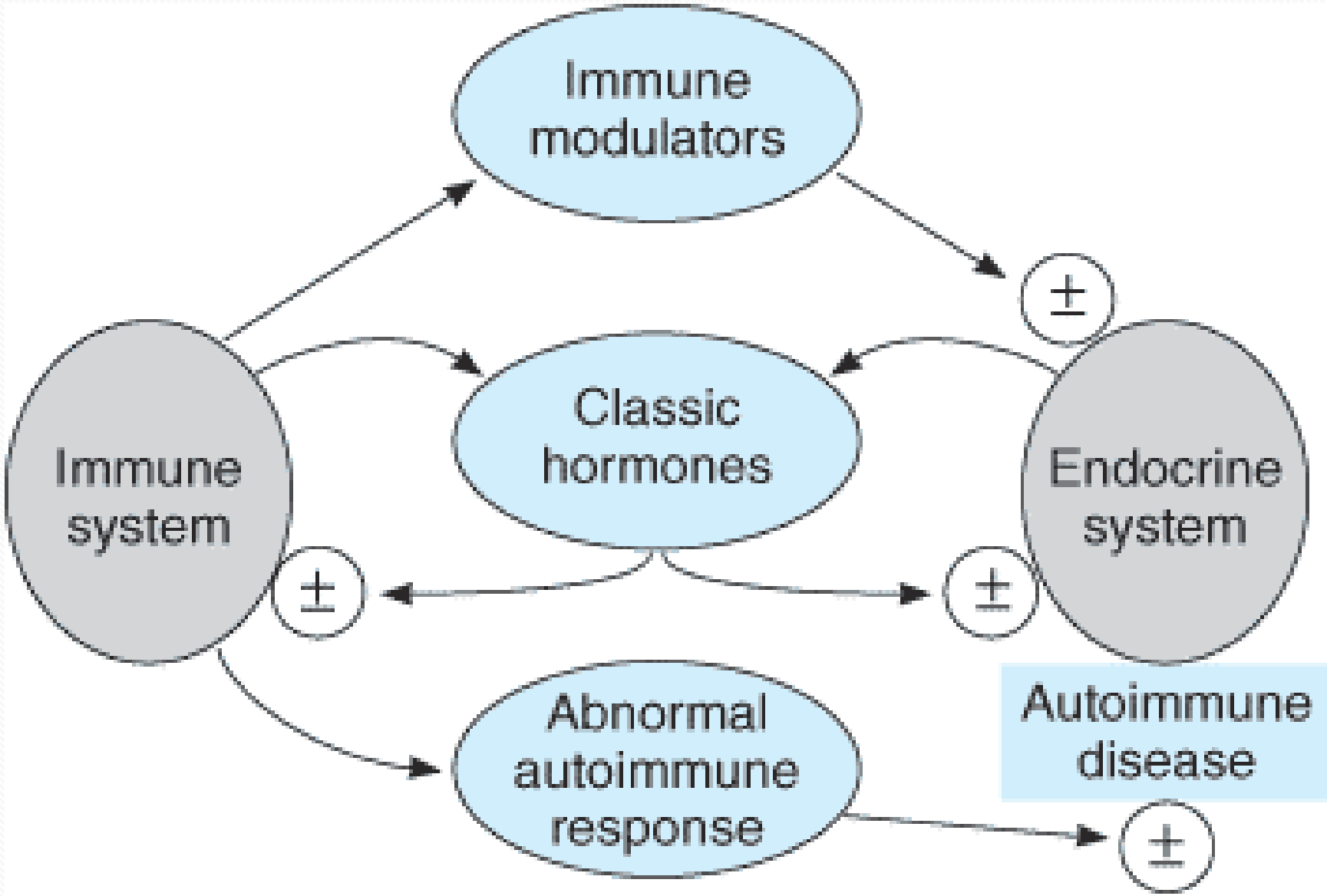
Precursors of hormones

Precursor		Type of compound	Example of hormone
Protein		Protein	Growth hormone
	Cleavage of peptide	Peptide	ACTH
	Cleavage of amino acid	Thyronine	Thyroxine
Cholesterol		Steroid	Cortisol
		Steroid	1,25 OHD_3
Amino acid		Modified amino acid	Epinephrine
		Tripeptide	TRH
Fatty acid		Retinoid	Retinoic acid
		Eicosanoid	Prostaglandin E_1

Source, class, and actions of various molecules in the endocrine system



Endocrine and the immune system



Hormone Synthesis and Release

Overview

- **Compartmentation**
- **Hormones stored in vesicles:**
  polypeptide hormones, neurotransmitters.
- **Hormones not stored in vesicles:**
  steroids, eicosanoids.

Vesicle-Mediated Hormone Export

Targeting and Translocation Across ER

- **Signal sequence (targeting):**
- **Translocation**
- **Modification**

Modulation of Hormone Levels (1)

Hormone Synthesis

Regulation of Hormone Production

- Transcription
- Translation
- Release

Modulation of Hormone Levels (2)

Hormone Transport

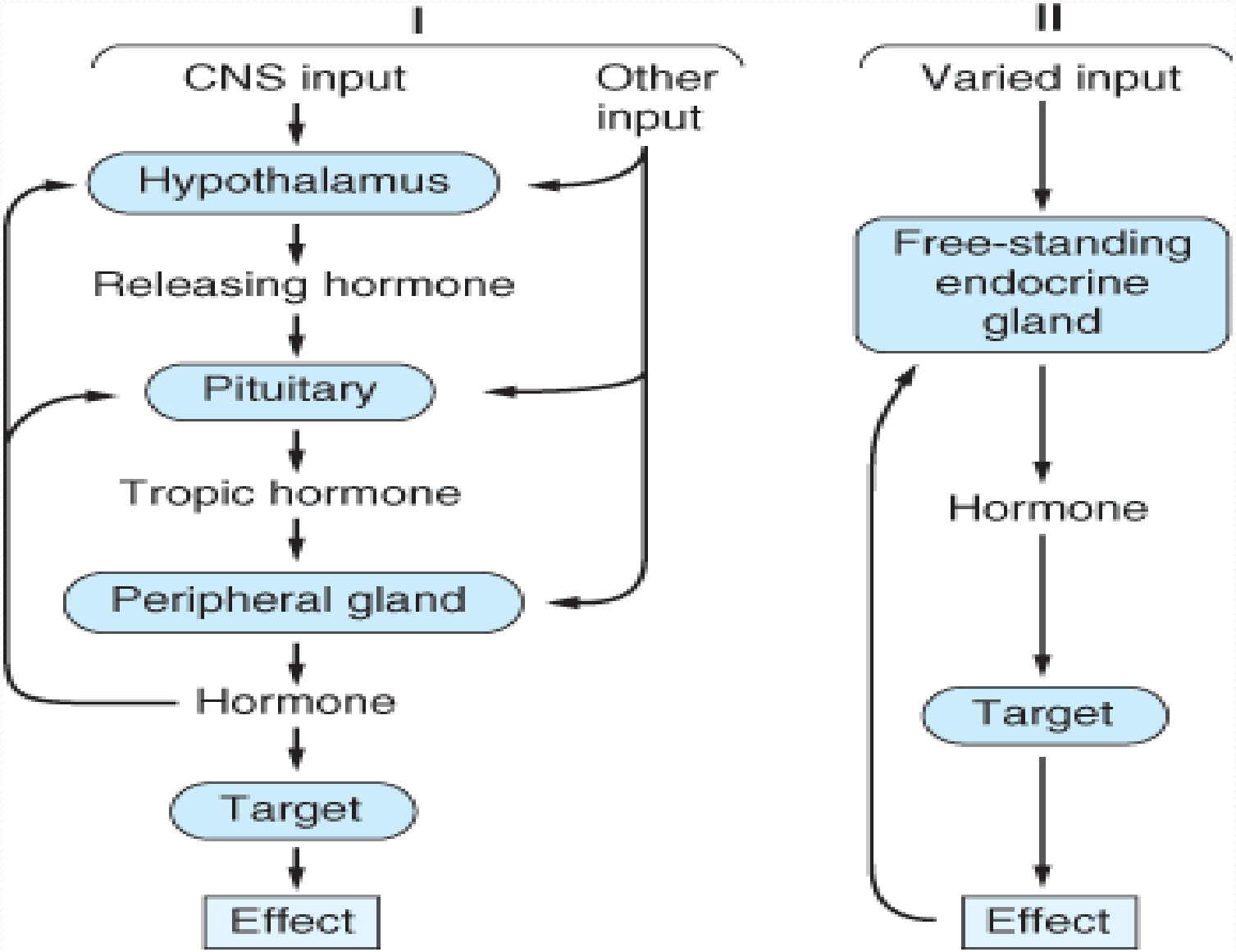
- In the circulation: free-bound (CBG, SHBG, TBG,…)
- Across the membrane.

Modulation of Hormone Levels (3)

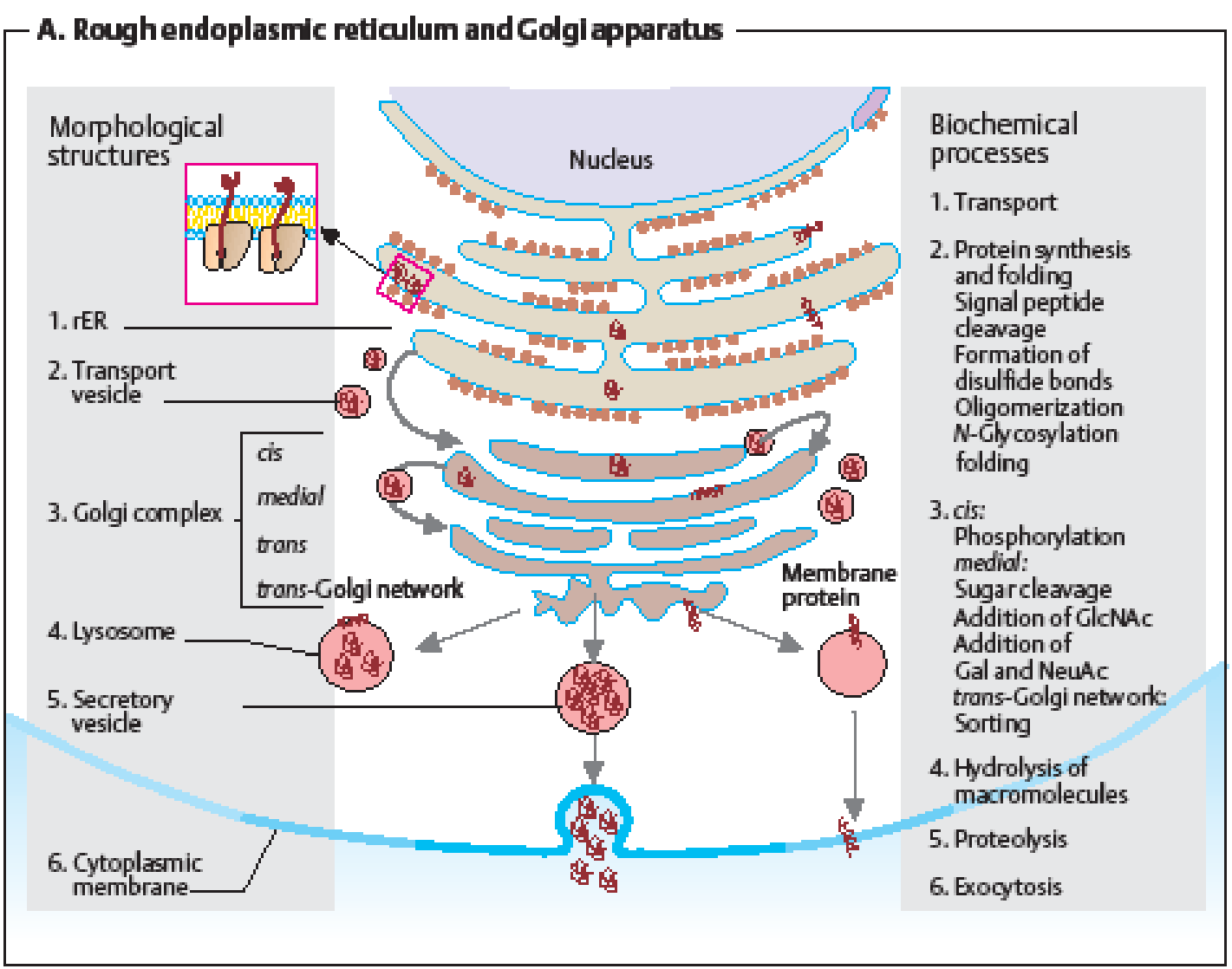
Hormone Metabolism

- Peptide hormones: glycosylation, internalization.
- Steroid, thyroid hormone, vit. D: conjugation, Activation (T4 → T3 ; T → DHT)
- Catecholamines and Eicosanoids.

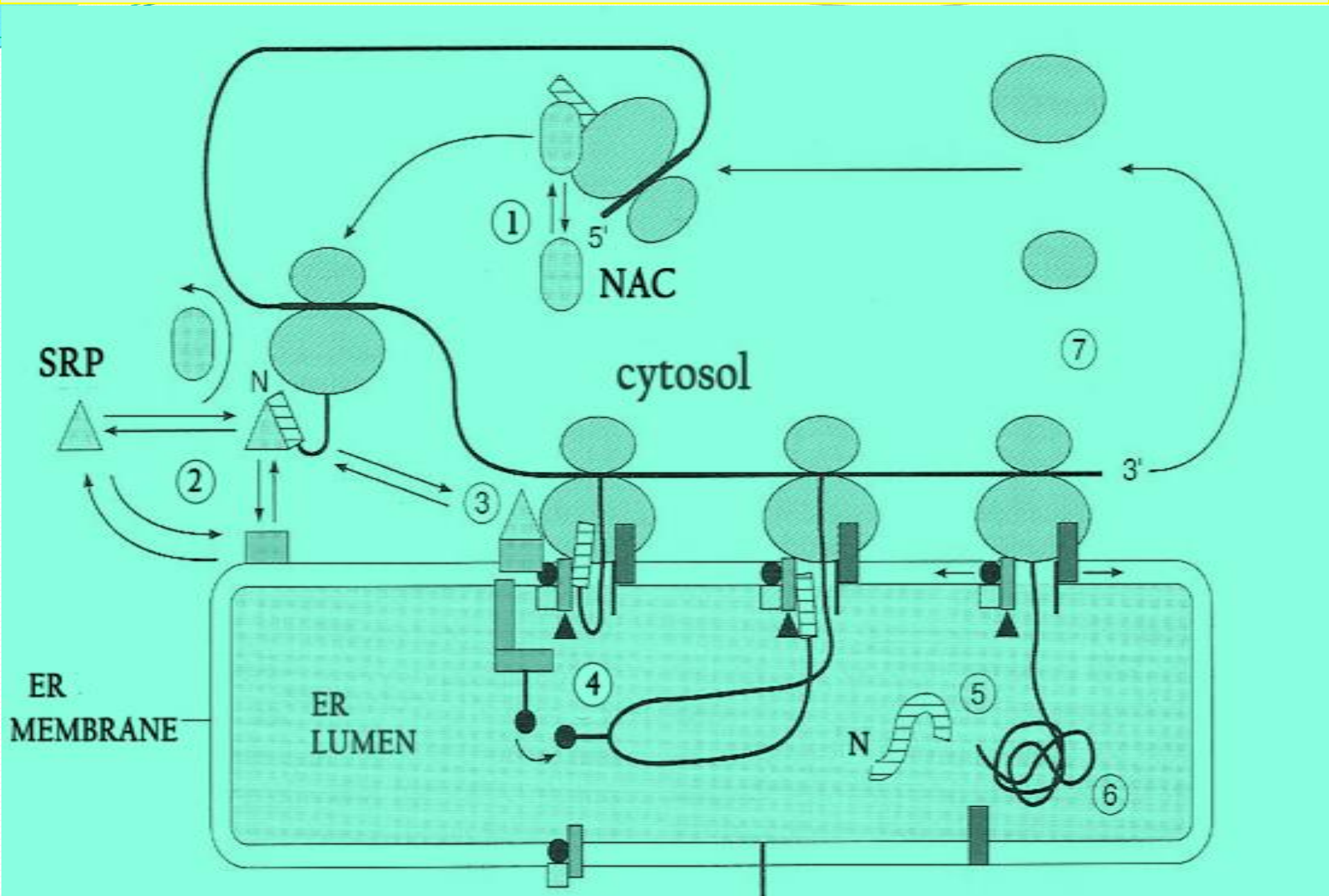
Control of endocrine gland function



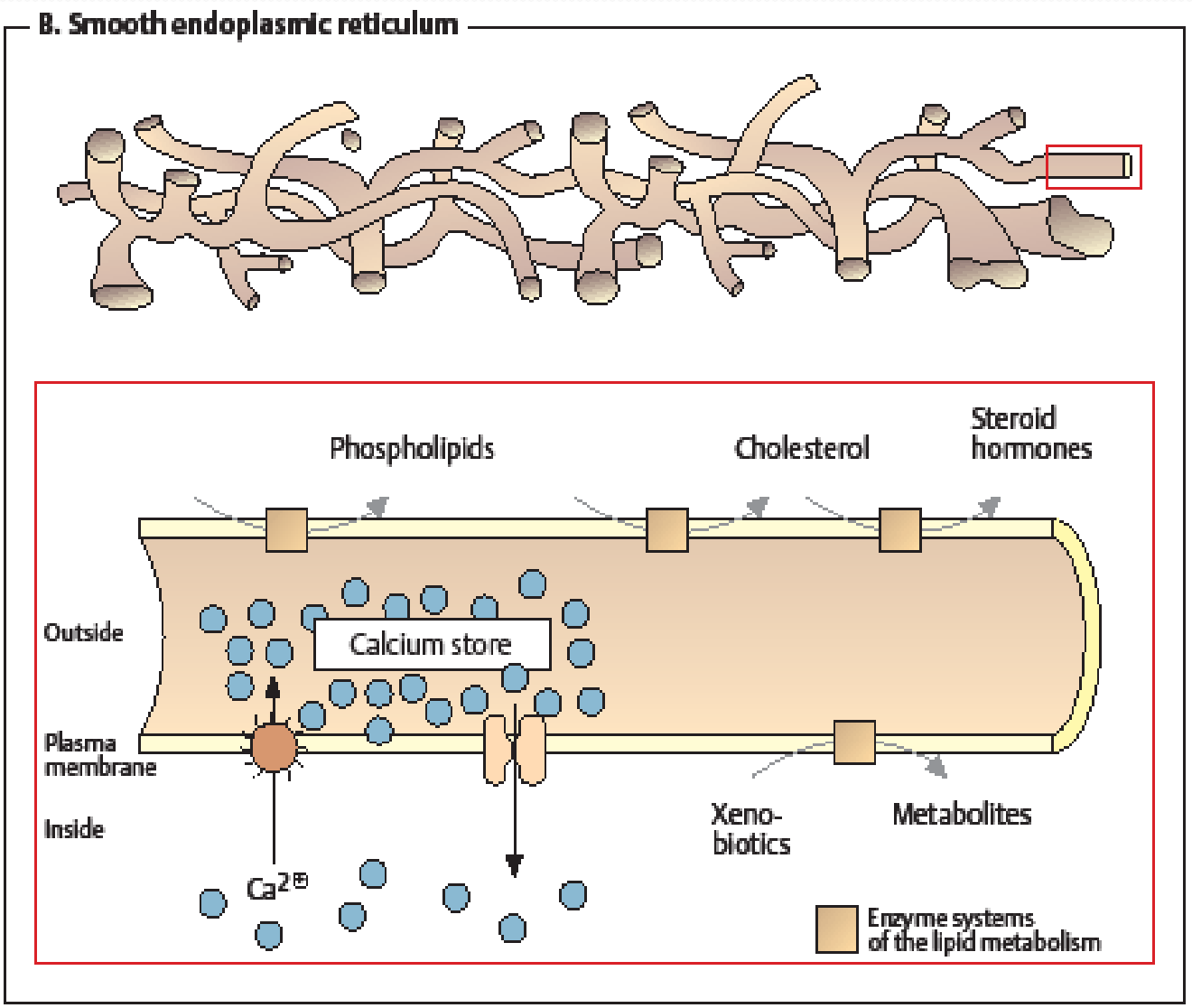
Hormone synthesis



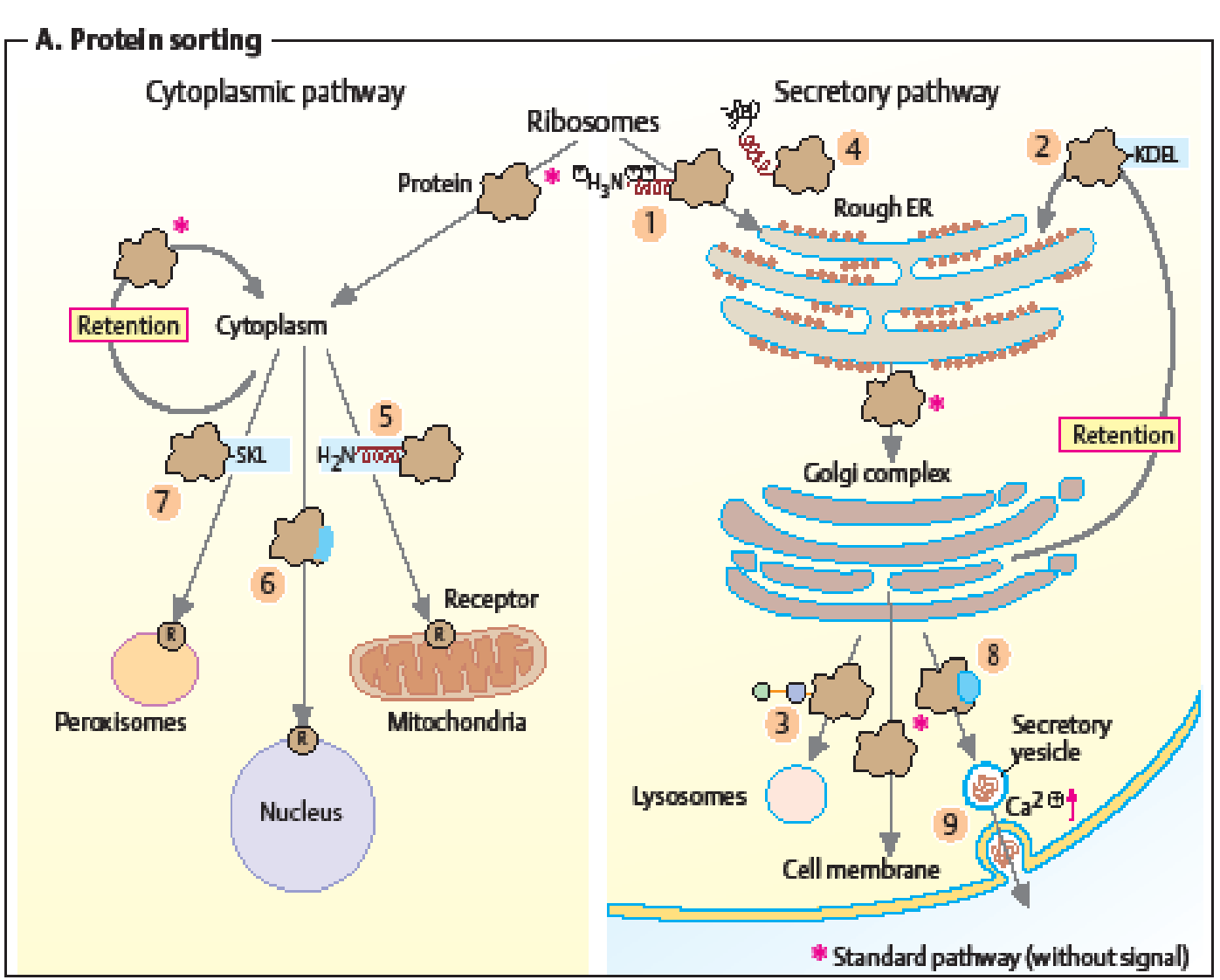
Targeting and Translocation Across ER



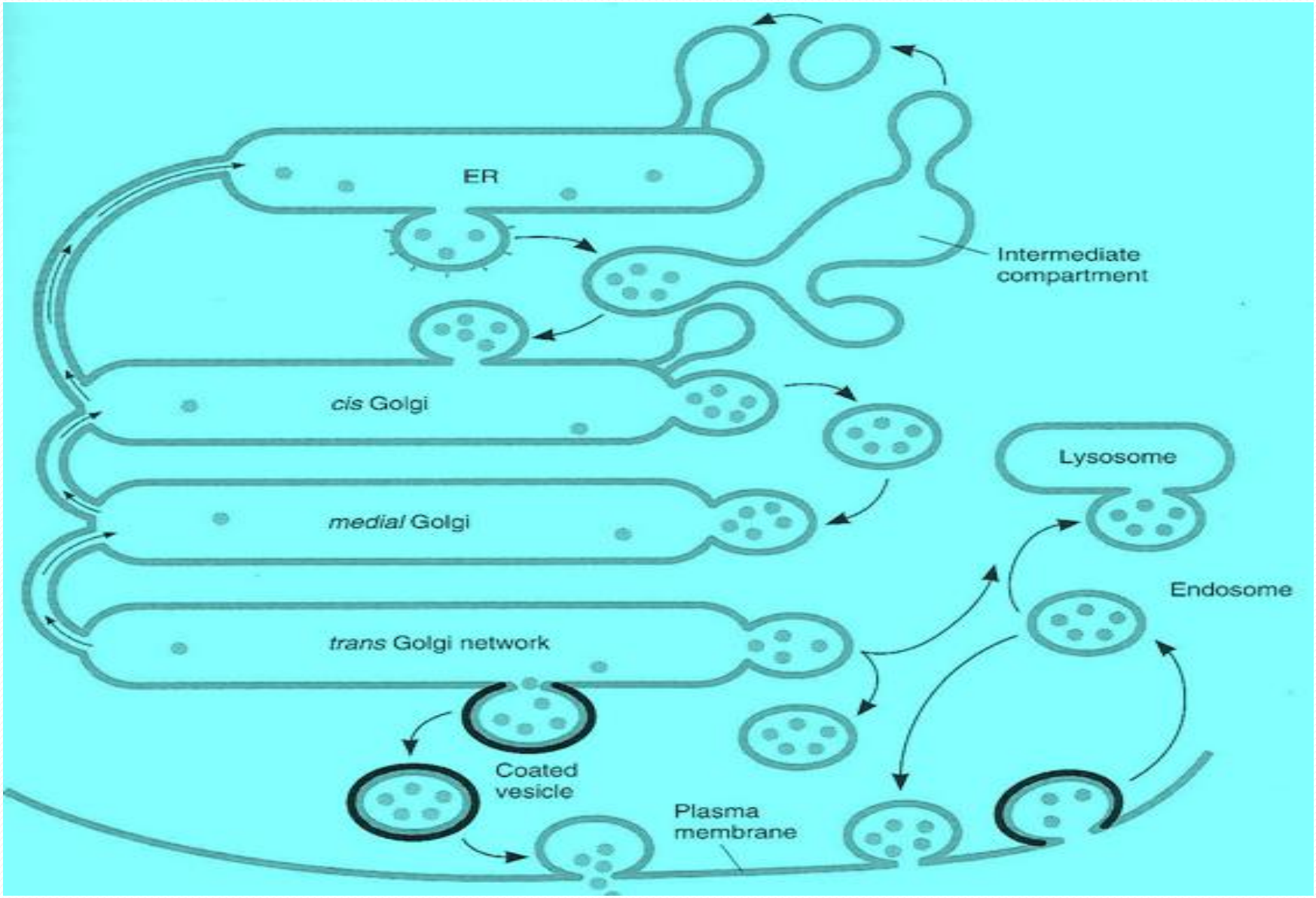
Hormone synthesis ...



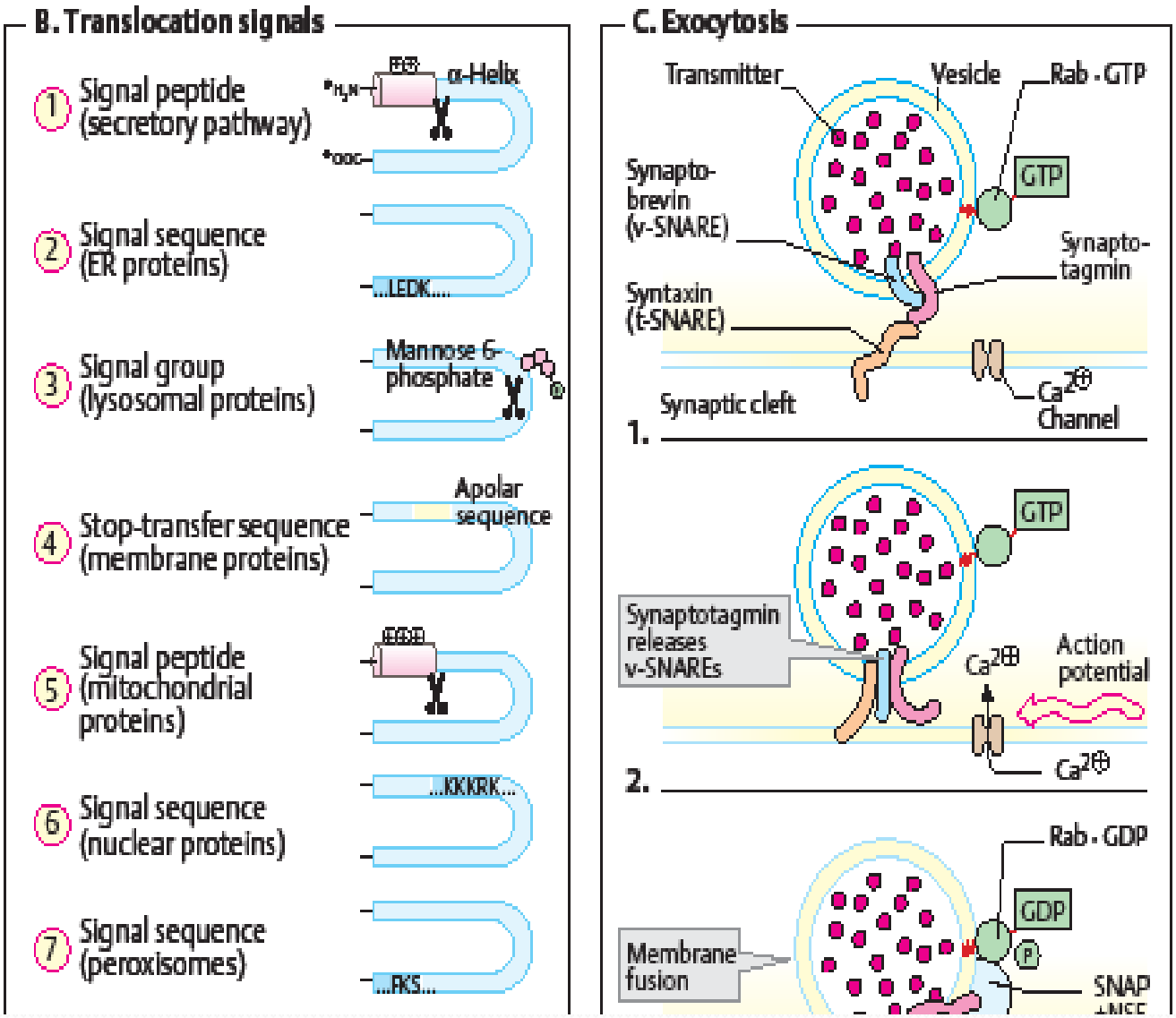
Protein sorting



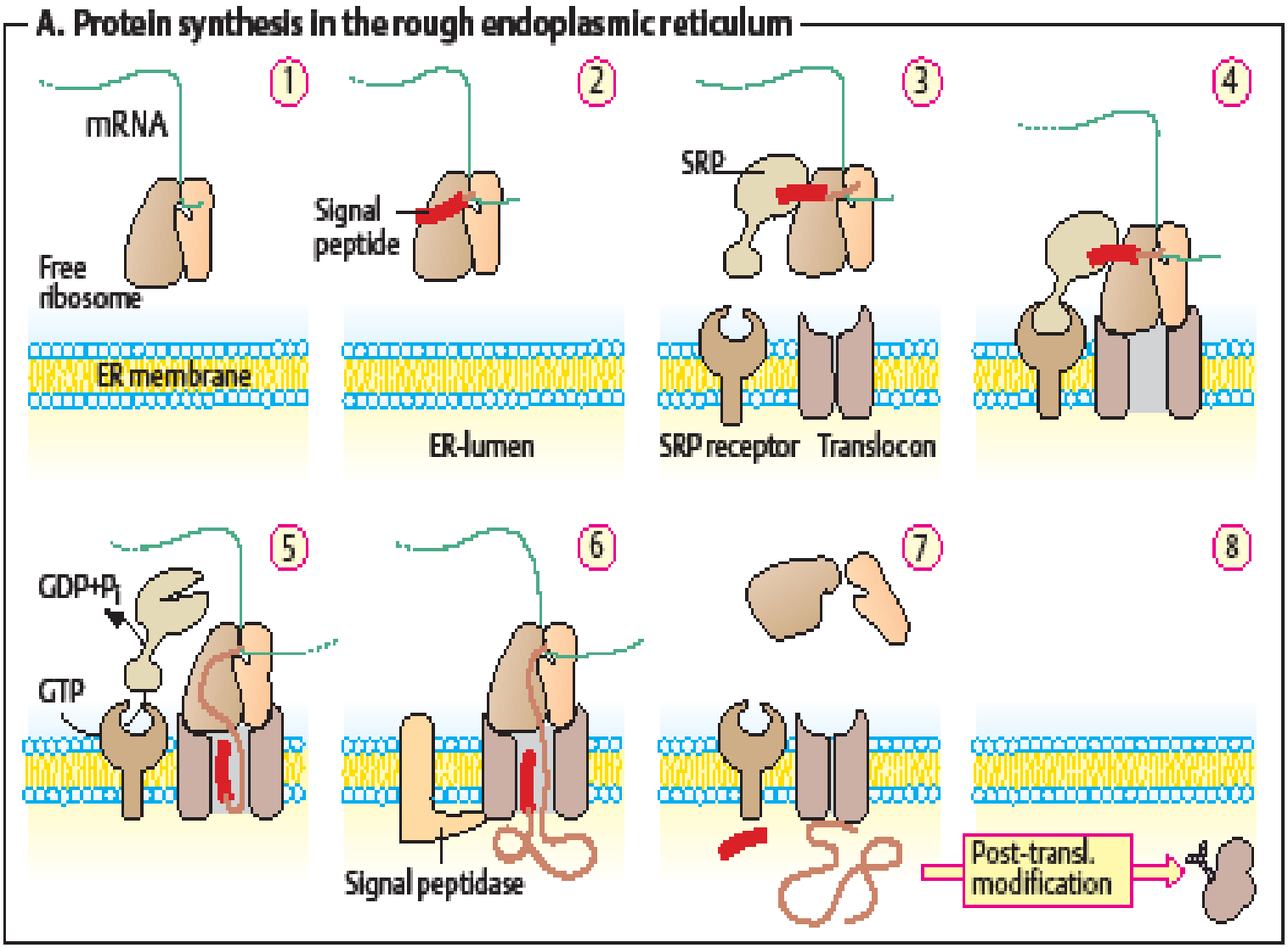
Vesicular Traffic: Exocytosis or Lysosomes



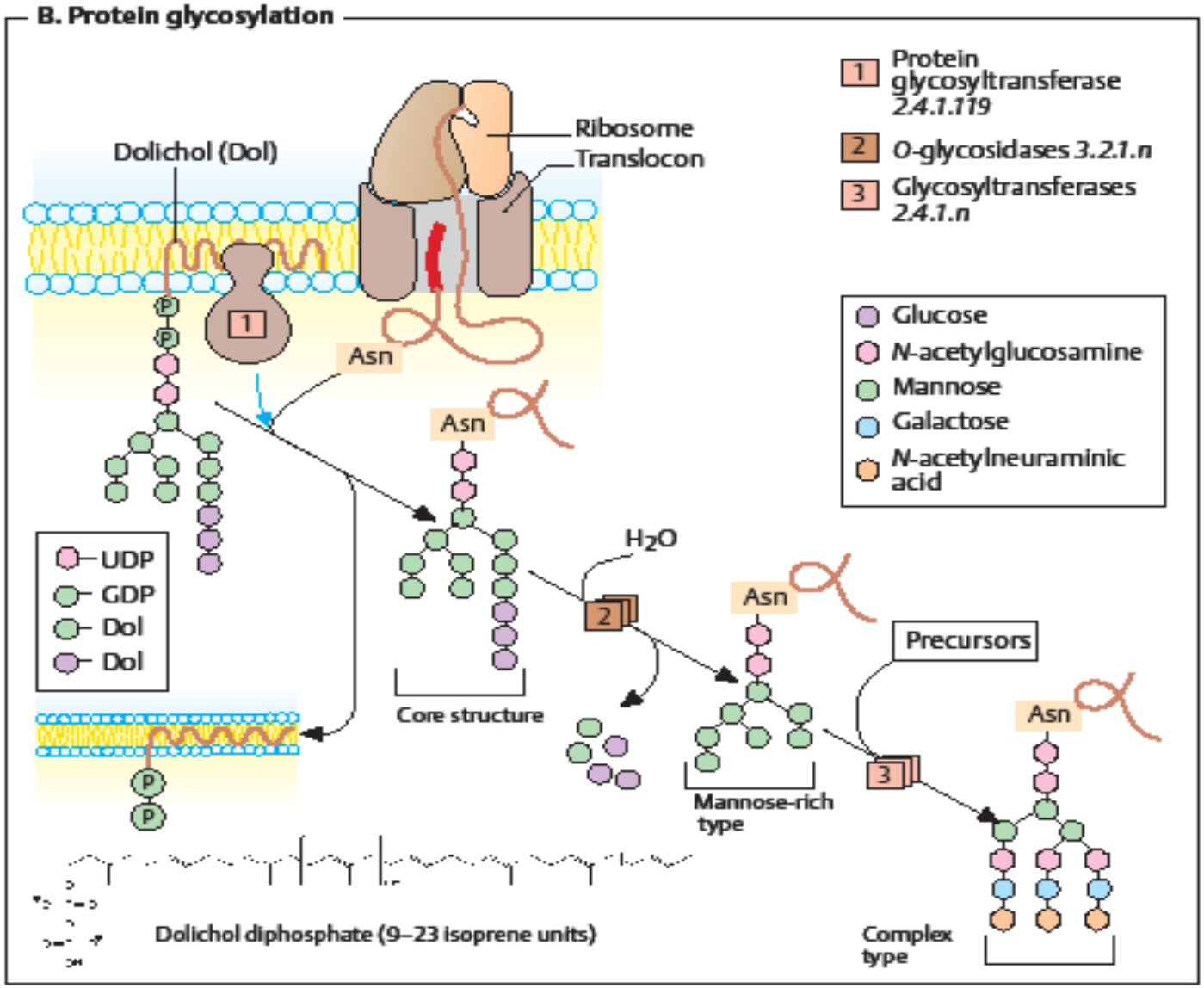
Translocation signal



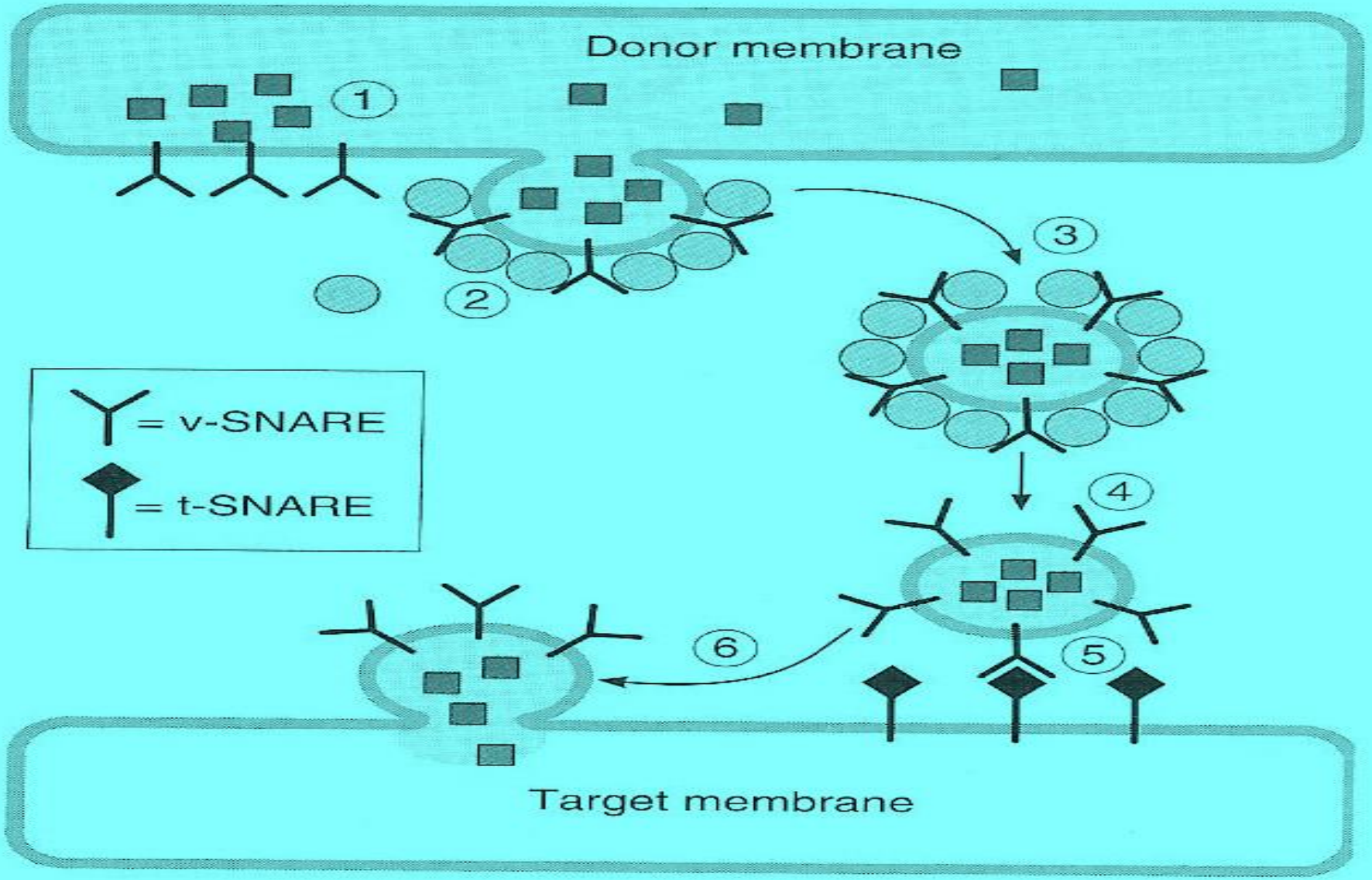
Protein synthesis in RER



Protein glycosylation



Intracellular Vesicular Traffic



Vesicle Sorting

- **Regulated secretory pathway:** specific stimulation, SNARE.
- **Constitutive secretory pathway:** No stimulation.
- **Content Segregation**
- **Lysosomal sorting:** GlcNAc, signal patch.
- **Endocytosis and Recycling:** coated pits, dynamin

Neurotransmitters and Thyroid Hormones

- ***Secretion of Catecholamines***
  - **Regulated Secretory Pathway:** Ca^{++}, vesicles
  - **Vesicles loaded with neurotransmitters and transports**
- ***Secretion of Thyroid Hormones***
  - **Vesicular and Nonvesicular trafficking**

    Thyroglobulin

    Colloid

    Transcytosis

Nonvesicular Hormone Transport

- ***Steroid Hormones***

  Synthesis

  Adrenal – gonads – placenta - nervous system.

  Cholesterol (de novo, acetate, stored, LDL).

  LDL (Receptor–mediated endocytosis).

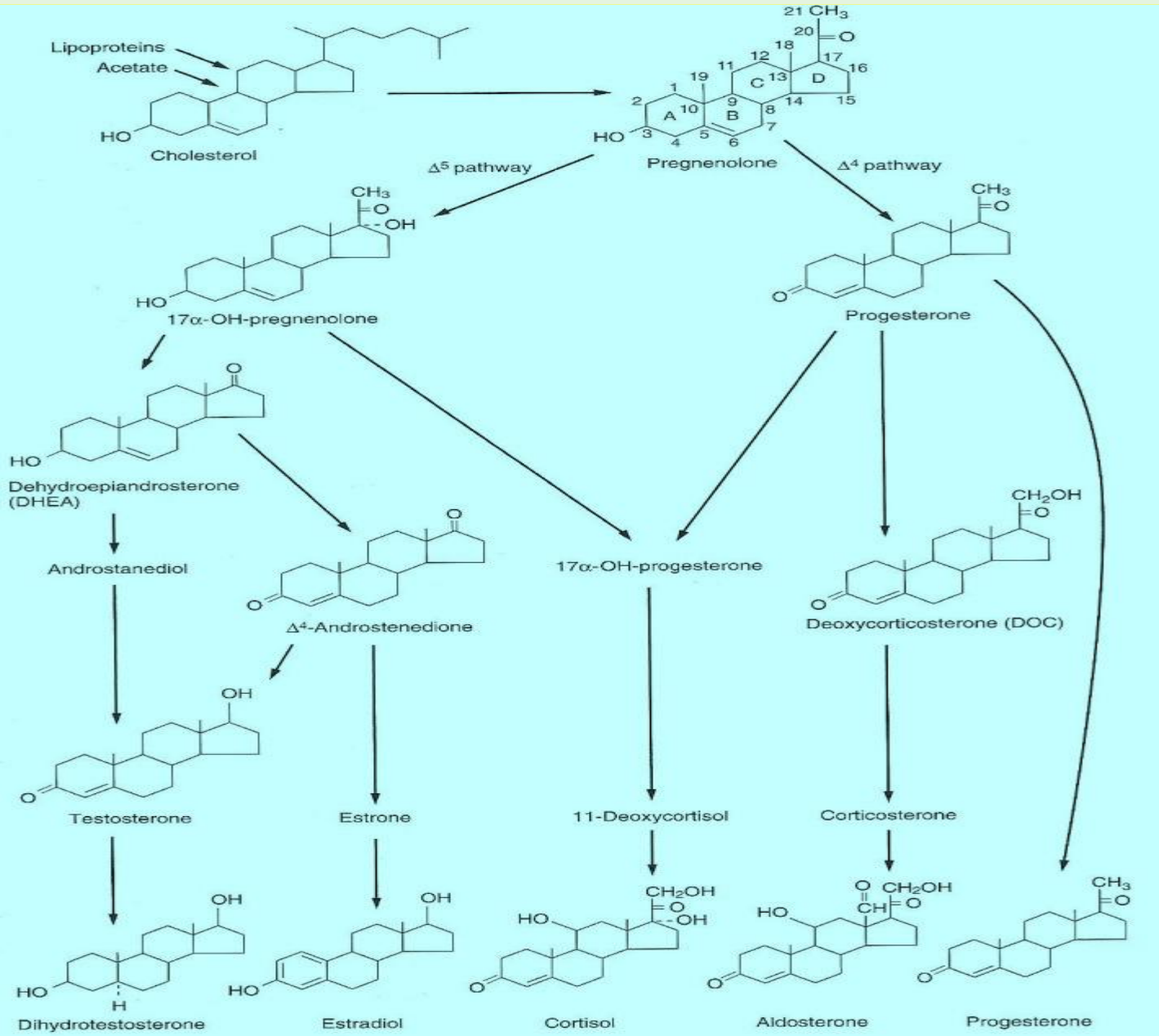
  P_{450}

- ***Vitamin D***

  Transportations

  Vitamin D transport protein, α–globulin

Nonvesicular Hormone Transport: Steroids



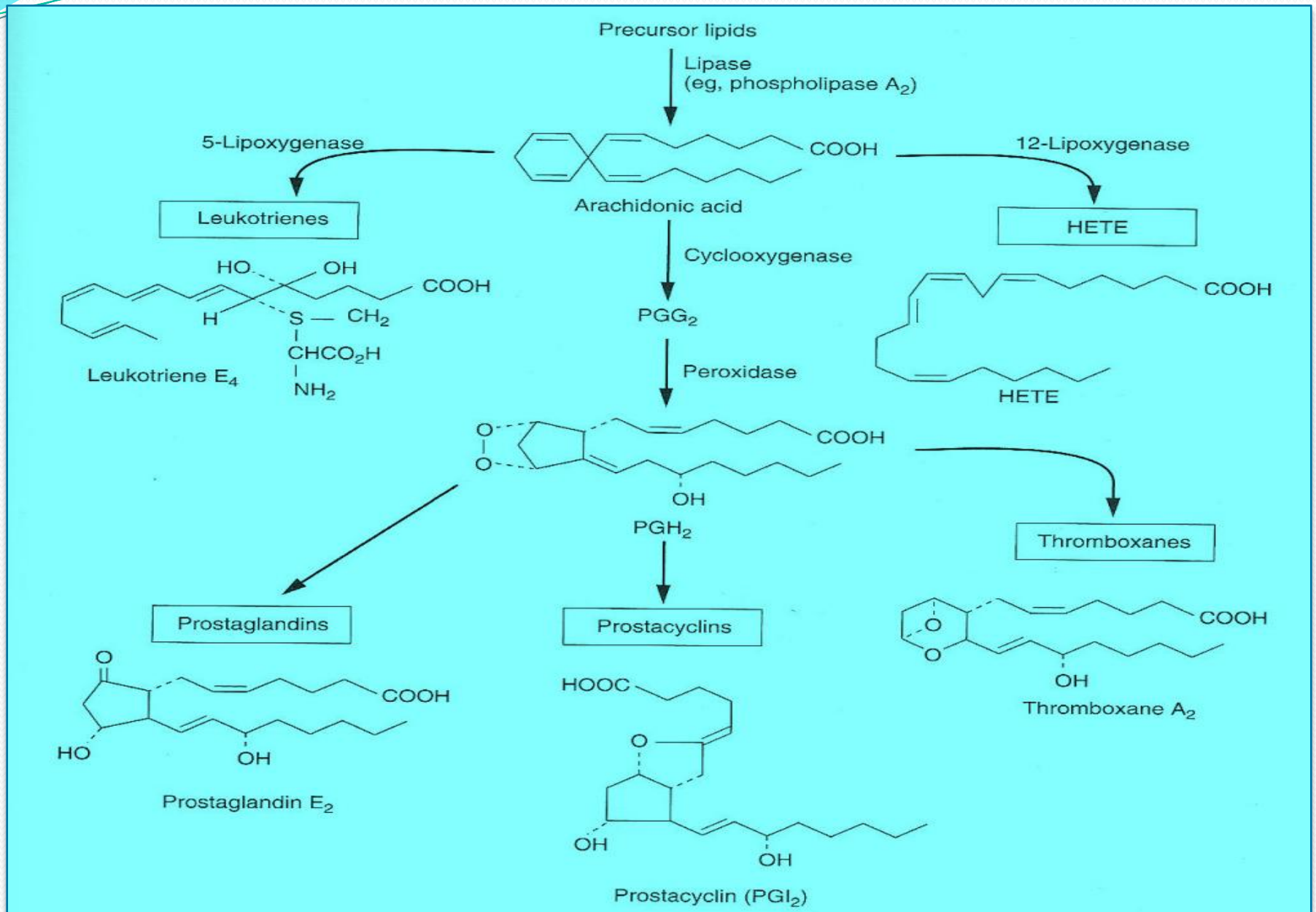
Nonvesicular Hormone Transport

- ***Eicosanoids***

  Synthesis

  Arachidonic acid → PGs, prostacyclins, thromboxanes, HETE.

Synthesis of Eicosanoids



Membrane Traffic and Disease

- ***Cystic Fibrosis***

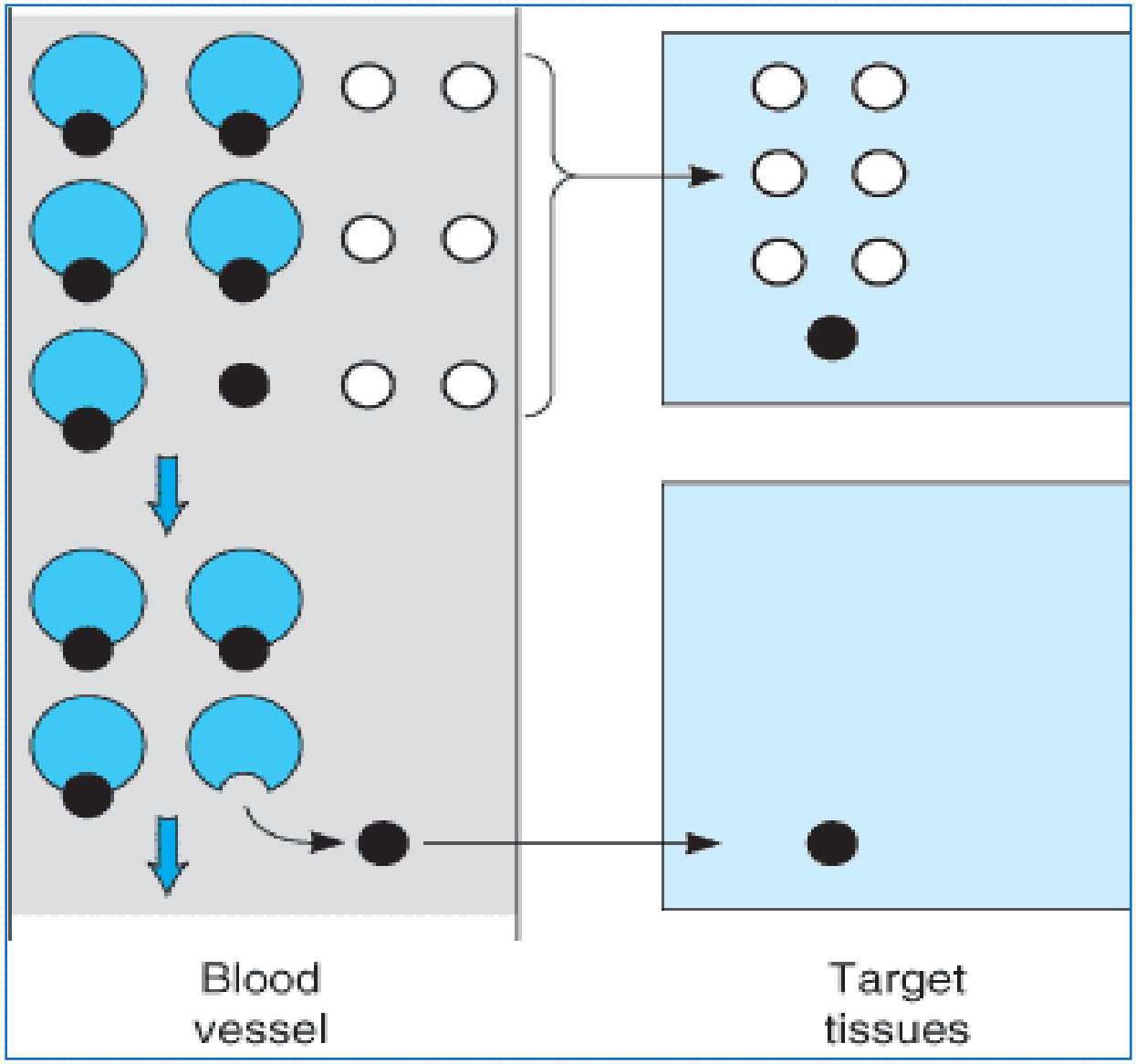
  Mutations in membrane transporter

  ER→ PM

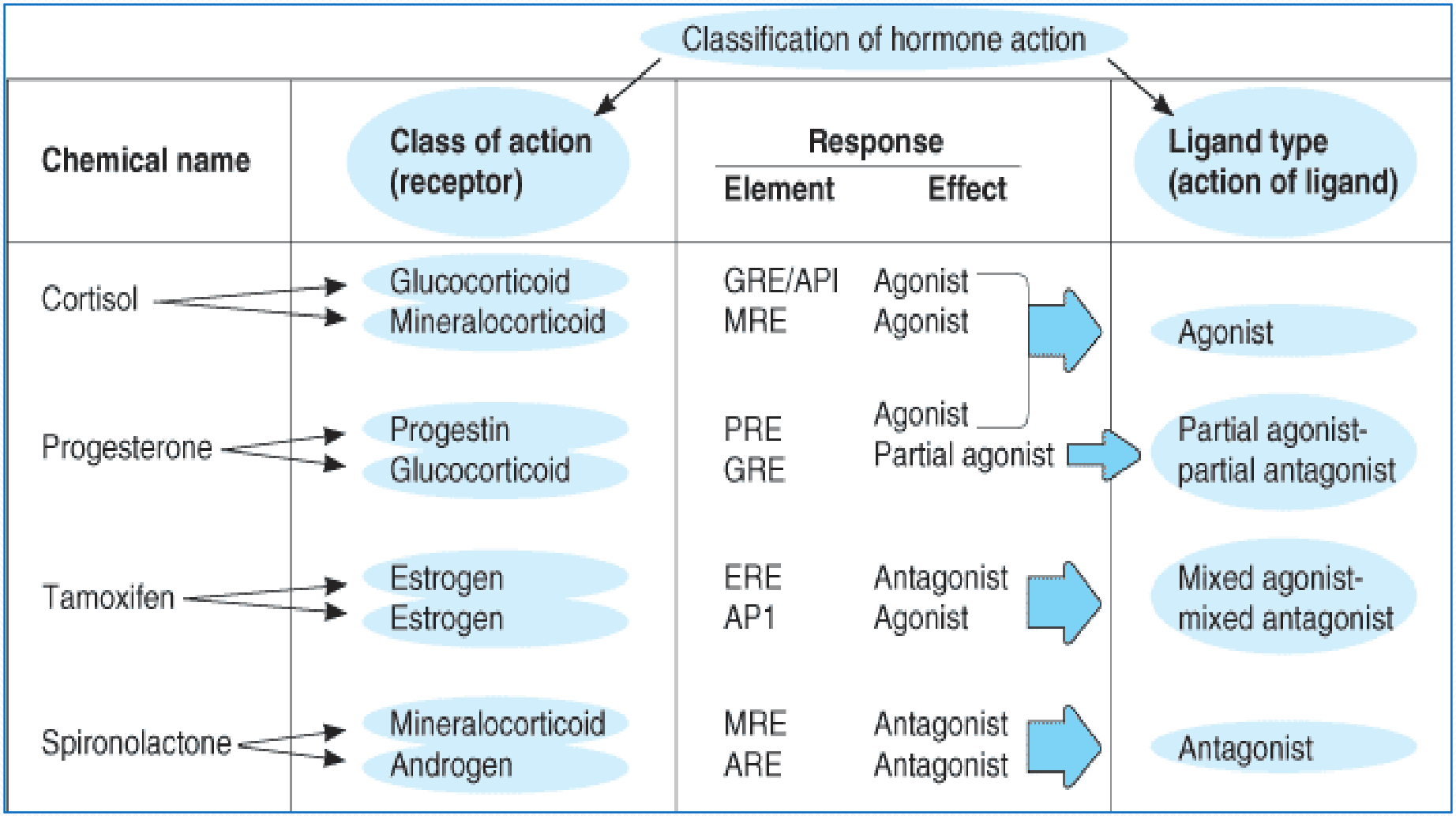
- ***Emphysema***

  α_1 – anti protease deficiency

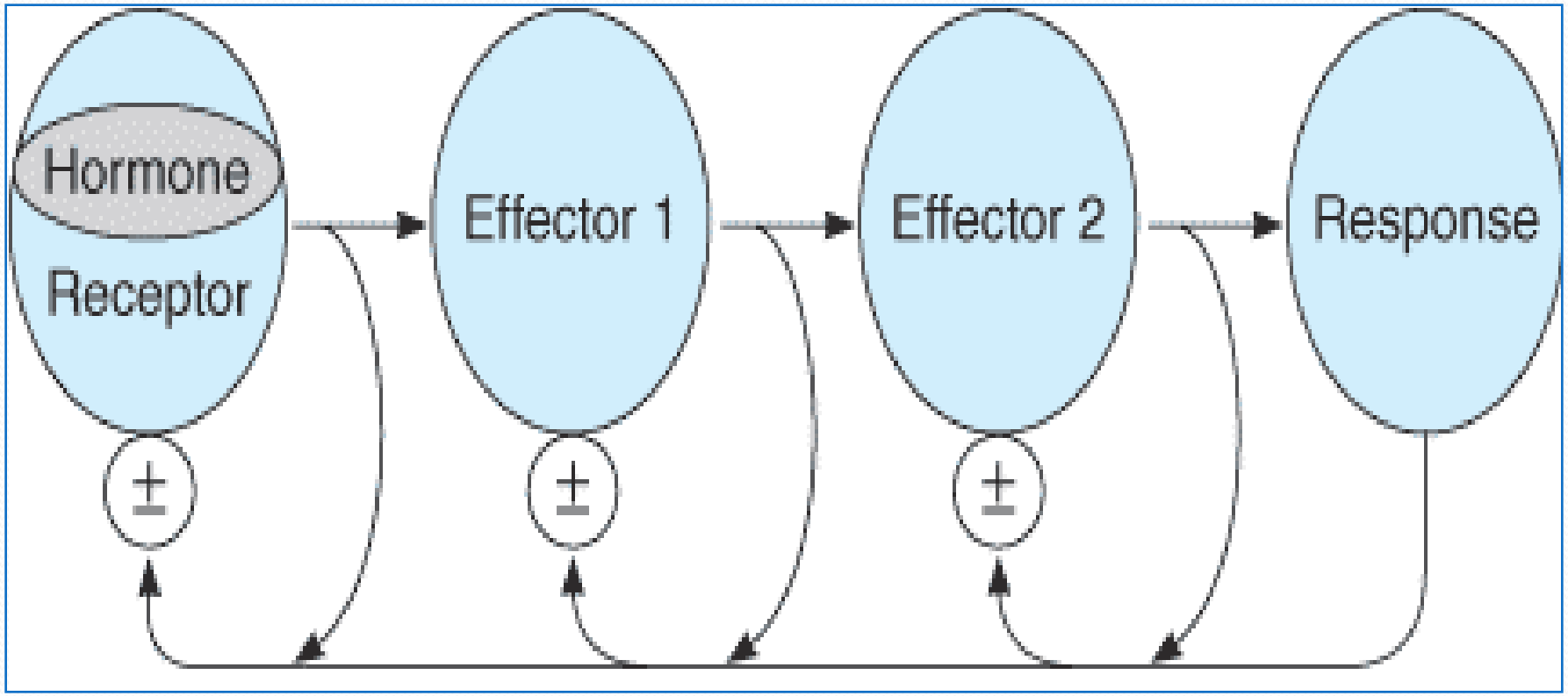
Role of Binding proteins



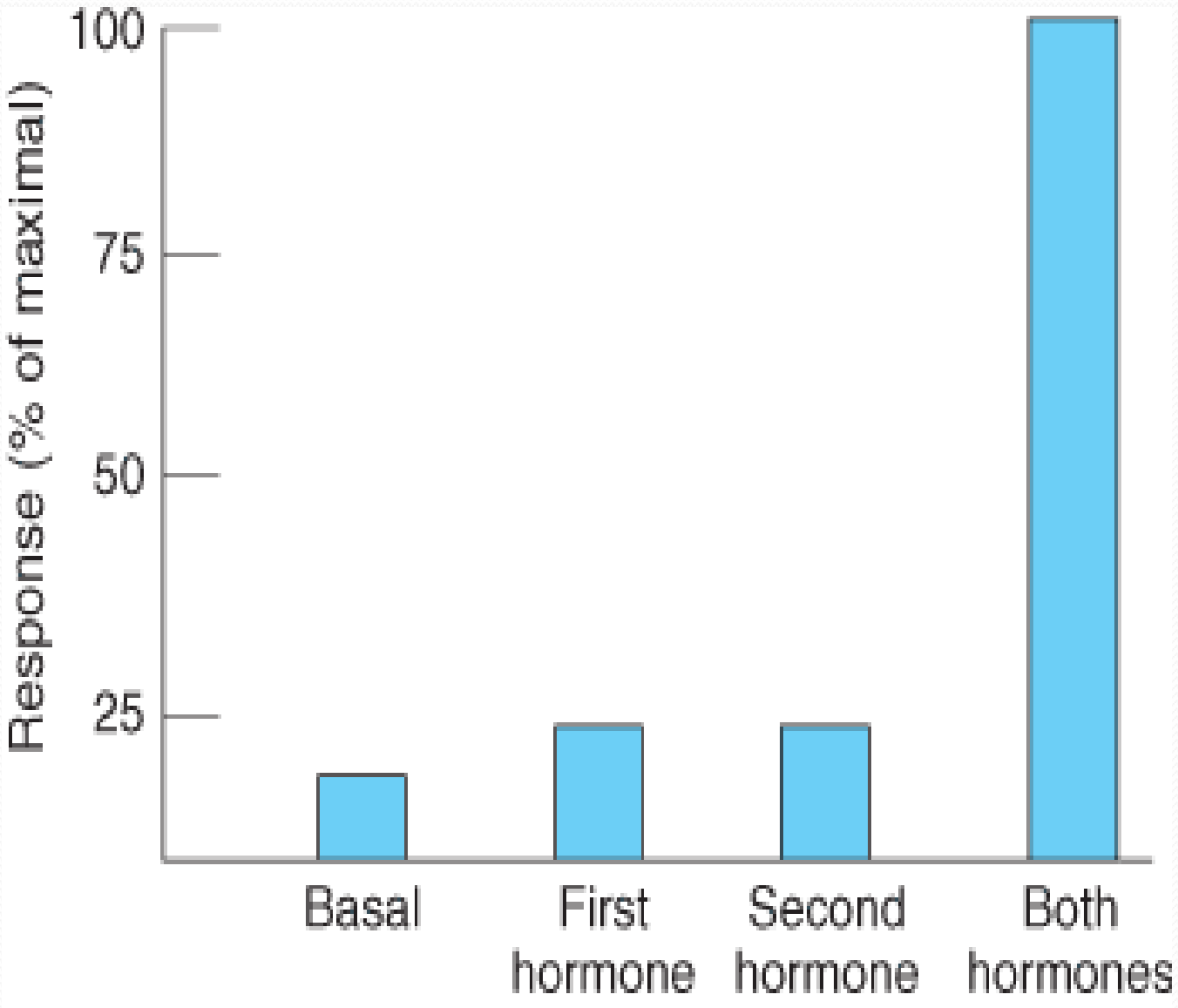
Classification of hormone action



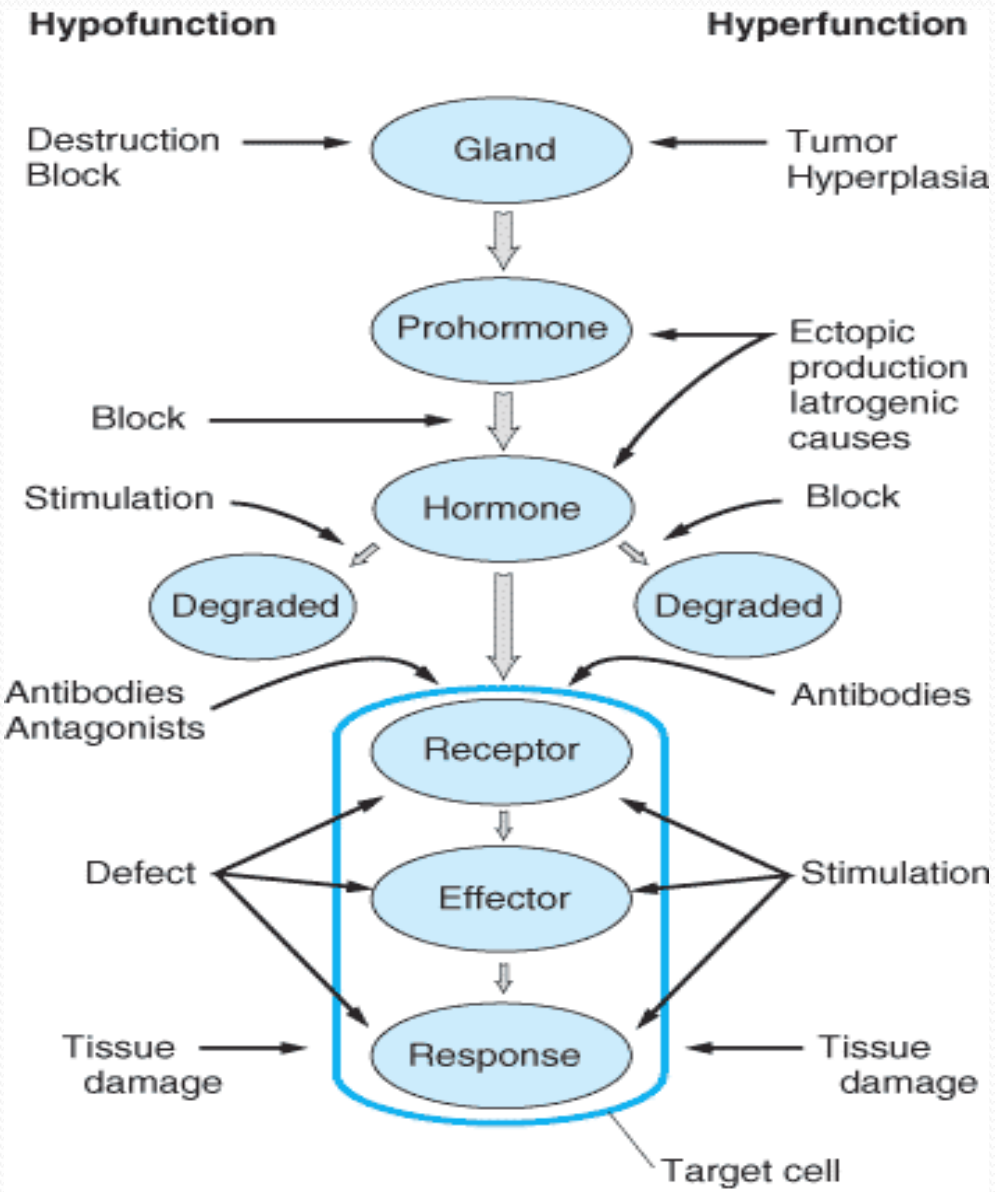
Regulation of hormone responsiveness: Feedback regulation



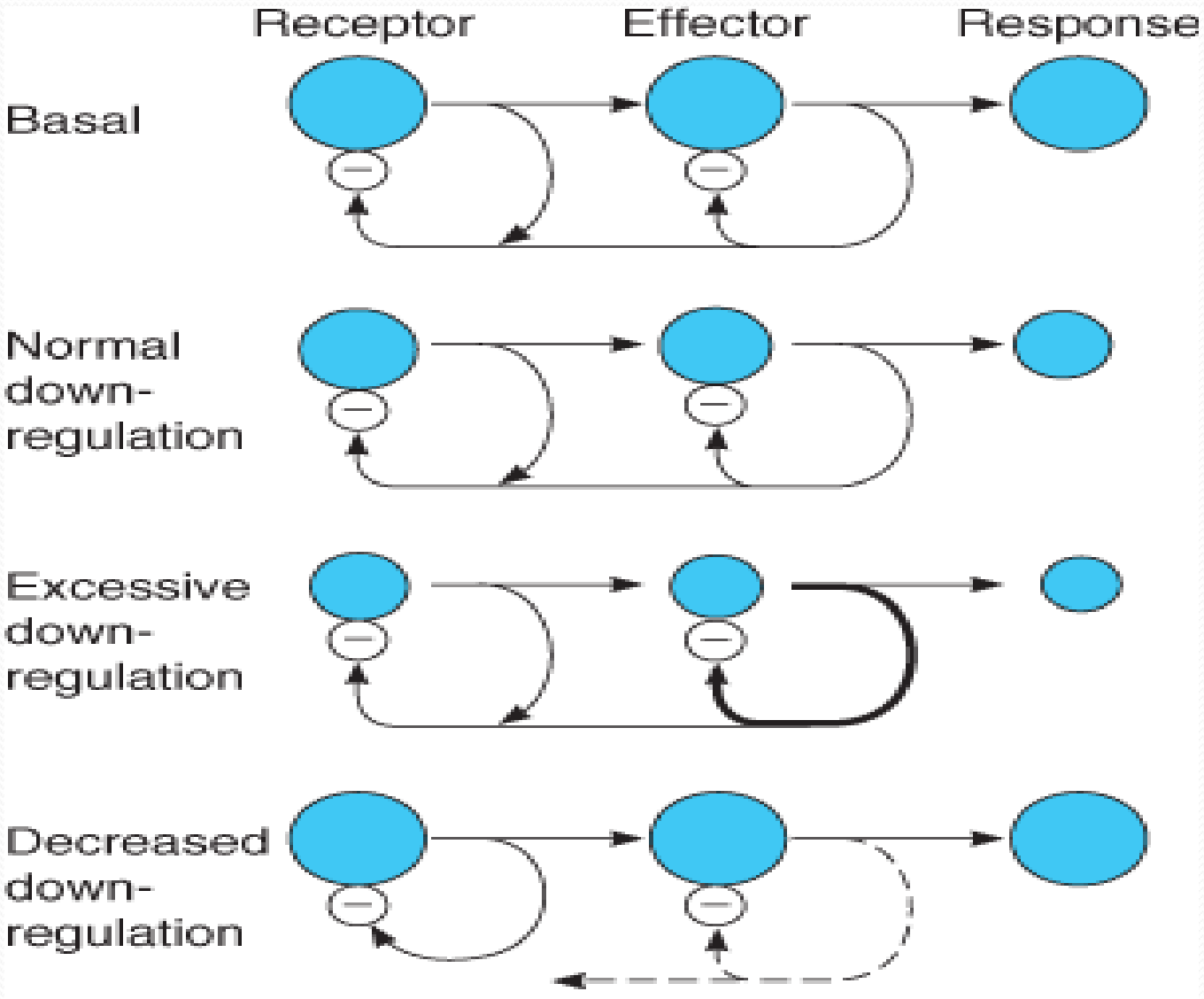
Synergistic Hormone Response



Hypofunction and hyperfunction



Hypo- and hyperesponsiveness



Actions of Hormones

- Hormone Release
- Fetal Development
- Cell Growth and Cancer
- Intermediary Metabolism
- Mineral and water Metabolism
- Cardiovascular and Renal Function:
- Skeletal Function
- Reproductive Function
- Immune System
- Central Nervous System

Disorders of the Endocrine System (1)

Hypofunction:

- **Destruction of the Gland:**
  - Autoimmune disease
- **Extraglandular Disorders:**
  - Renal disease:
- **Defect in Hormone Biosynthesis:**
  - Defects in genes
  - Dietary iodine deficiency

Disorders of the Endocrine System (2)

Hyperfunction

- **Tumors**
- **Ectopic tumors**
- **Hyperplasia**
- **Autoimmune Stimulation**
- **Hormone administration**

Sensitivity

- **Genetic defects**
- **Acquired Defects**

Approaches to Endocrine Patients (1)

Evidence-Based endocrinology

History and Physical Examination

Laboratory Studies

- **Measurement of Hormone Levels:** basal levels, precursor, metabolites.
- **Plasma and Urine Assays:** Urine assays for steroids and catecholamine.
- **Free Hormone Levels:** equilibrium dialysis, ultrafiltration, competitive binding.
- **Immunoassays:** RIA, ELISA, Sandwich technique.
- **Nonimmunologic Assays:** chemical, bioassays, receptor-binding.
- **Diagnosis of genetic Diseases:** DNA sequence (PCR), RFLP.

Approaches to Endocrine Patients (2)

Laboratory Studies

- **Indirect Measurements:** hormone effects (glucose, Ca^{++}, …)
- **Provocative Test:** adrenal insufficiency, glucocorticoid excess.
- **Imaging Studies: MRI, CT for endocrine tumors.**
- **Biopsy procedures:** thyroid gland.

Screening of Endocrine Diseases

- Hypertension, diabetes.

Interpretation of Lab. Tests

Treatment of Endocrine Diseases

- Hormone replacement, blockers, surgery.

Metabolism, Transport and Elimination of Hormones (1)

Polypeptide Hormones

- **Metabolism**
  Degradation, lysosomes
- **Transport**
  Free IGF-1 binding proteins, neurophysins, GH.
  Glycosylation.

Metabolism, Transport and Elimination of Hormones (2)

Steroid Hormones & Vitamin D

- **Transport**

  CBG (transcortin), SHBG, vit. D binding protein.

- **Metabolism**

  Inactivation (water-soluble forms)

  Activation: T, vit. D

  Aldosterone

Metabolism, Transport and Elimination of Hormones (3)

Thyroid Hormone

- **Transport**
  Free Bound: (TBG), TBPA, Albumin.
- **Metabolism**
  Degradation (deiodinases: type I, type II)

Catecholamines

- **Metabolism**
  COMT, MAO → VMA