Doctor 022

Physiology

Modified no.

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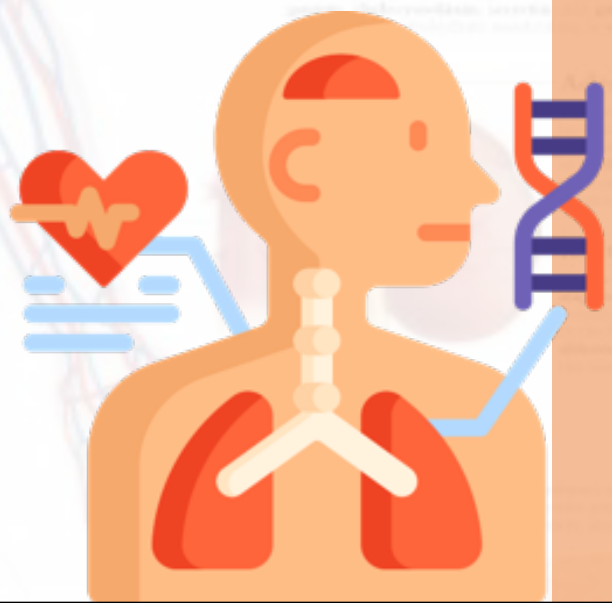

Signal Transduction

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Introduction to Physiology

2023

Chemical classes of hormones

- Lipid-soluble hormones- use transport proteins in the **plasma**
  - Steroid: Lipids derived from cholesterol.
    - Are lipophilic hormones.
      - Testosterone.
      - Estradiol.
      - Cortisol.
      - Progesterone.
  - Thyroid (amine but lipid soluble)
  - Nitric oxide (NO)

Chemical classes of hormones

- Water-soluble – circulate in "free" form in the plasma
  - Amines:
    - Hormones derived from tyrosine and tryptophan.
  - Polypeptides and proteins:
    - Polypeptides:
      - Chains of < 100 amino acids in length.
        - ADH.
    - Protein hormones:
      - Polypeptide chains with > 100 amino acids.
      - Growth hormone.
  - Eicosanoid (prostaglandins) derived from arachidonic acid (20 carbon 4 double bonds)

peptide hormones are synthesized by transcription and translation

Chemical Classification of Hormones

- Glycoproteins:
  - Long polypeptides (>100) bound to 1 or more carbohydrate (CHO) groups.
    - FSH and LH, TSH and hCG (human chorionic gonadotropin)

      They have α and β subunits (α is common and β is specific)
- Hormones can also be divided into:
  - Polar:
    - H_20 soluble.
  - Nonpolar (lipophilic):
    - H_20 insoluble.
      - Can gain entry into target cells.
      - Steroid hormones and T_4 (thyrxine –tetraiodothyronine))

* hormones sometimes are not synthesized in their final form

Prohormones and Prehormones

- Prohormone:
  - Precursor is a longer chained polypeptide that is cut and spliced together to make the hormone.
    - Proinsulin – gives insulin
- Preprohormone: The earlier step
  - Prohormone derived from larger precursor molecule.
    - Preproinsulin.
- Prehormone:
  - Molecules secreted by endocrine glands that are inactive until changed into hormones by target cells.
    - T_4 converted to T_3 (tri-iodothyronin)

T4 is inactive and it is activated when it change to T3 (by remove iodine group)

So preproinsulin cut and spliced to make proinsulin which is spliced to form insulin

Synthesis and secretion of peptide hormones

Transcription

↓

translation

↓

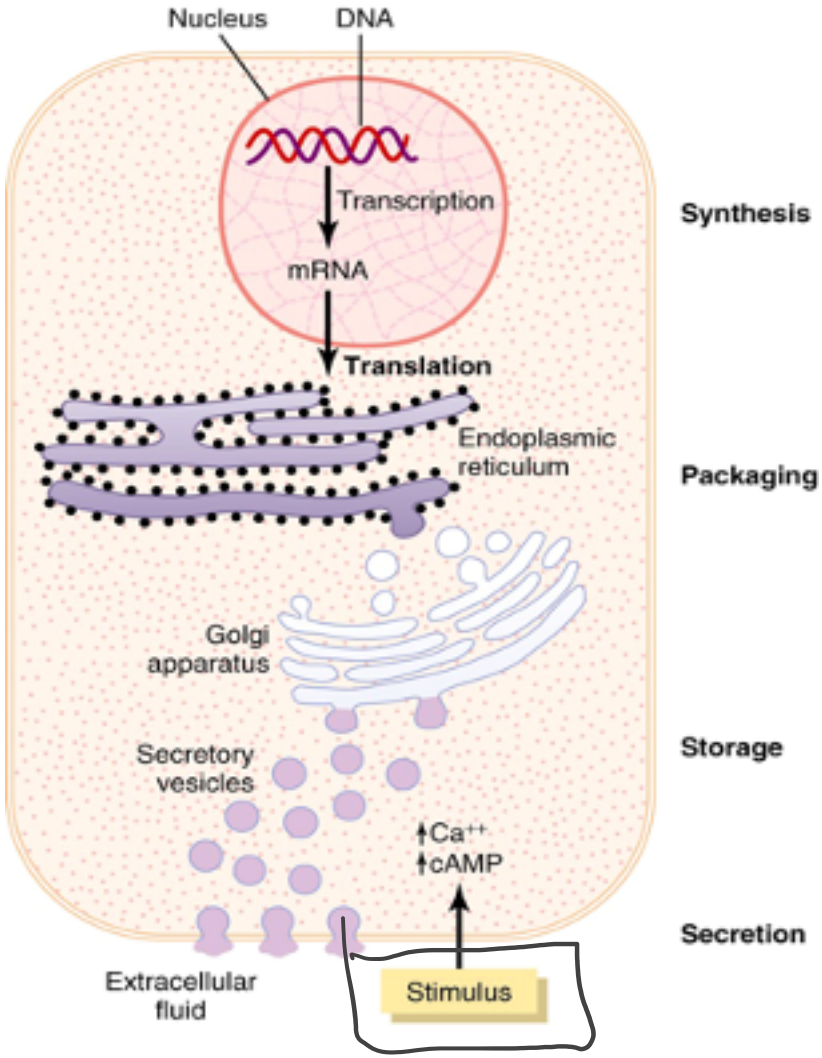
Synthesize polypeptide

↓

Golgi for modification

↓

Store in vesicles



To stimulate the secretion of hormones from its vesicles ,there must be a signal

Chemical classification of hormones

Table 10-4 Chemical Classification and Function of Hormones

Chemical Classification	Examples	Regulated Function
Endocrine Hormones		
Amino acid derivatives	Epinephrine (adrenaline) and norepinephrine (both derived from tyrosine)	Stress responses: regulation of heart rate and blood pressure; release of glucose and fatty acids from storage sites
They are amino acids with modifications Ex: carboxylation ,decarboxylation …etc		
They are not peptides BUT derived from amino acid	Thyroxine (derived from tyrosine)	Regulation of metabolic rate
Peptides	Antidiuretic hormone (vasopressin)	Regulation of body water and blood pressure
	Hypothalamic hormones (releasing factors)	Regulation of tropic hormone release from pituitary gland
	↳ These factors stimulate other hormones from other glands	
Proteins	Anterior pituitary hormones	Regulation of other endocrine systems
Steroids	Sex hormones (androgens and estrogens)	Development and control of reproductive capacity
	Corticosteroids	Stress responses; control of blood electrolytes
Paracrine Hormones		
Amino acid derivative	Histamine	Local responses to stress and injury
Arachidonic acid derivatives	Prostaglandins	Local responses to stress and injury

The doctor did not say anything about functions

Lipid BUT soluble in water BECAUSE it is negatively charged

Peptide & Protein Hormones

These hormones can not enter the cell so receptors are required on cell surface

Gland/Tissue	Hormones
Hypothalamus	▪ TRH, GnRH, CRH GHRH, Somatostatin,
Anterior pituitary	▪ ACTH, TSH, FSH, LH, PRL, GH
Posterior pituitary	▪ Oxytocin, ADH
Thyroid	▪ Calcitonin
Pancreas	▪ Insulin,Glucagon, Somatostatin
Liver	▪ Somatomedin C (IGF-1)
Parathyroid	▪ PTH

Gland/Tissue	Hormones
Placenta	▪ HCG, HCS or HPL
Kidney	▪ Renin
Heart	▪ ANP
G.I. tract	▪ Gastrin, CCK, Secretin, GIP, Somatostatin
Adipocyte	▪ Leptin

You do not have to distinguish between protein and peptide hormones

Amine Hormones

Gland/Tissue	Hormones
Hypothalamus	▪ Dopamine water soluble
Thyroid	▪ T_3, T_4 Lipid soluble
Adrenal medulla	▪ Epinephrine and Norepinephrine (NE, EPI) water soluble

Synthesis of Amine Hormones

Enzymes are not important to memorize

Tyrosine

tyrosine hydroxylase

L-Dopa

dopa decarboxylase

Dopaminergic Neurons

Dopamine

dopamine β-hydroxylase

Adrenergic Neurons

Norepinephrine

phenylethanolamine-N-methyltransferase

Epinephrine

Adrenal Glands

Thyroid Hormones

Thyroid Gland

The main point to remember that depending on the enzymes that found in a specific cell , the hormone synthesized

So for example because of enzymes that present in adrenal glands , Tyrosine is converted to Epinephrine not dopamine ☺

Steroid Hormones

Gland/Tissue	Hormones
Adrenal Cortex	■ Cortisol, Aldosterone, Androgens
Testes	■ Testosterone
Ovaries	■ Estrogens, Progesterone
Corpus Luteum	■ Estrogens, Progesterone
Placenta	■ Estrogens, Progesterone
Kidney	■ 1,25-Dihydroxycholecalciferol (calcitriol)

Hormone Activity

- Hormones affect only specific target tissues with specific receptors
- Receptors are dynamic and constantly synthesized and broken down
  - Down-regulation- decrease in receptor number or esponse
  - Up-regulation- increase in receptor number or activity

To get a response :

1-The concentration of hormone must be suitable
2-Have a receptor on target cell

without receptors there will be no response even if the concentration of hormone is high

There is no constant number of receptors on the cells , the receptors are dynamic and the same cell may have different densities of receptors depending on the condition of the cell

Effects of [Hormone] on Tissue Response

- Priming effect (upregulation):
  - Increase number of receptors formed on target cells in response to particular hormone.
  - Greater response by the target cell.
- Desensitization (downregulation):
  - Prolonged exposure to high [polypeptide hormone].
    - Subsequent exposure to the same [hormone] produces less response.
      - Decrease in number of receptors on target cells.
        - Insulin in adipose cells.
  - Pulsatile secretion may prevent downregulation.

Glands secrete hormones as pulses so it is not continuous secretion of hormone all the time and this prevent downregulation

Diabetes type II is an example of Desensitization
Insulin is stimulated for along time , this makes insulin receptors less sensitive to insulin and thus the response will be decreased

Effects of hormone concentration on Tissue Response

Hormone concentration in the blood depends on:
1-the rate of secretion of the gland.
2-half-life

- [Hormone] in blood reflects the rate of secretion.
- Half-life:
  - Time required for the blood [hormone] to be reduced to ½ reference level.
    - Minutes to days.
- Affinity of receptors to ligands, Kd

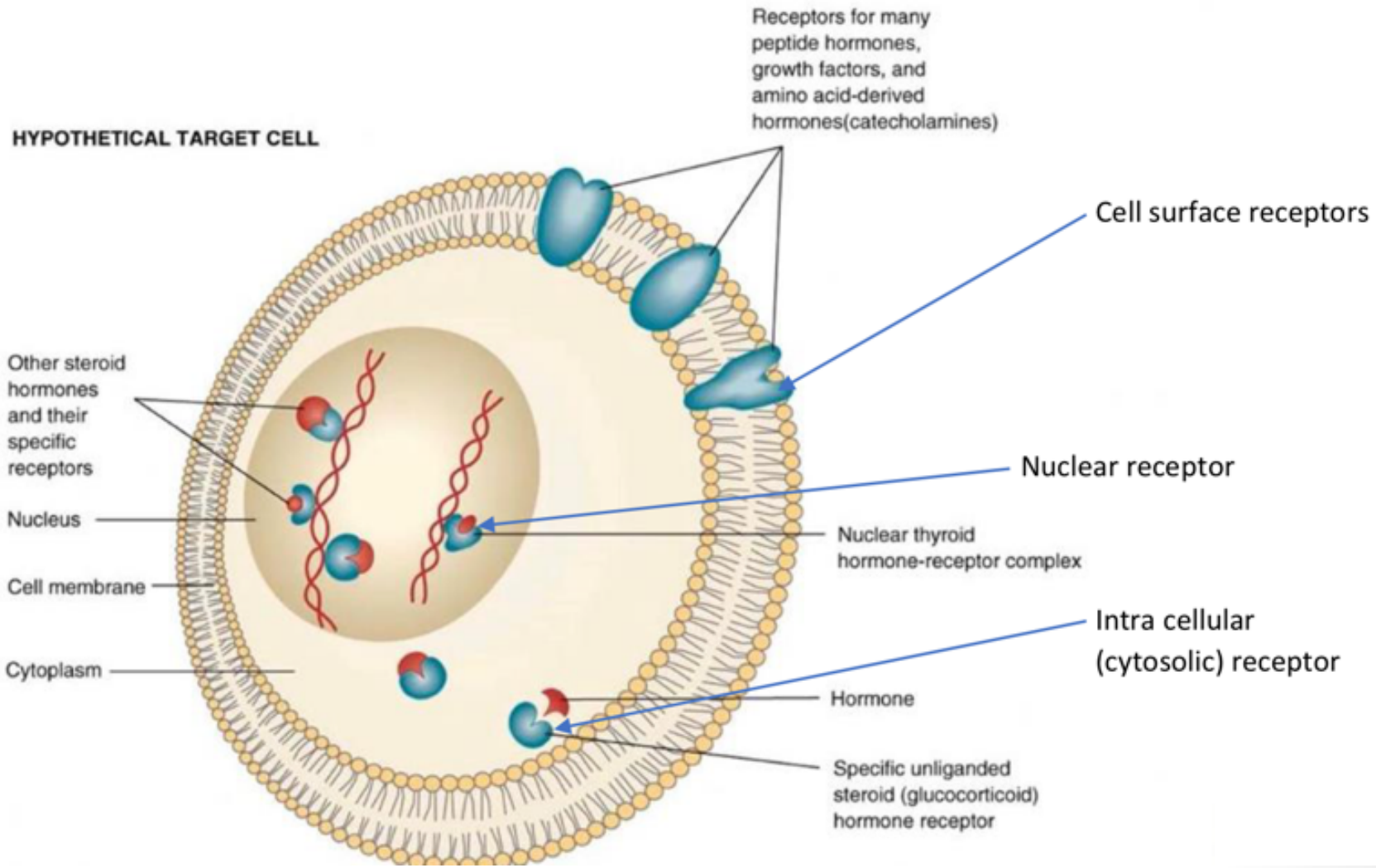
Dissociation constant

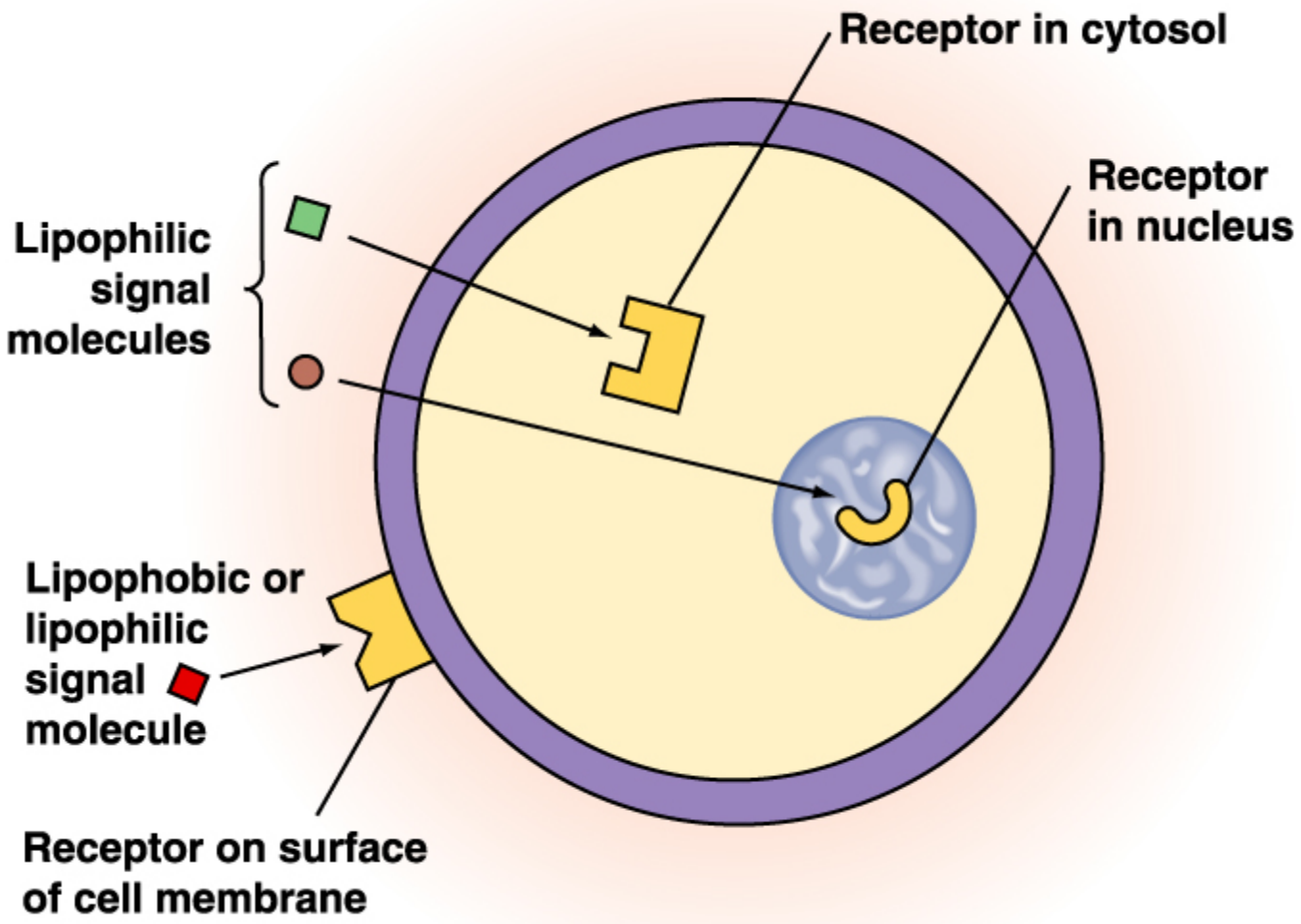
When hormone is favorable binding to its receptors . This means that we need lower concentrations to cause the response

As Kd increase , this means less affinity of hormone toward the receptor . So we need a higher concentration of hormone to cause response.

As Kd decrease , this means higher affinity of hormone toward receptor .So we need a lower concentration of hormone to cause response.

- Normal tissue responses are produced only when [hormone] are present within physiological range.
- Varying [hormone] within normal, physiological range can affect the responsiveness of target cells. The response may differ if concentration is more or less than physiological response


HYPOTHETICAL TARGET CELL
Receptors for many peptide hormones, growth factors, and amino acid-derived hormones(catecholamines)
Cell surface receptors
Other steroid hormones and their specific receptors
Nucleus
Nuclear receptor
Nuclear thyroid hormone-receptor complex
Cell membrane
Intra cellular (cytosolic) receptor
Cytoplasm
Hormone
Specific unliganded steroid (glucocorticoid) hormone receptor


Receptor in cytosol
Receptor in nucleus
Lipophilic signal molecules
Lipophobic or lipophilic signal molecule
Receptor on surface of cell membrane