ENZYMES

- **Functional plasma enzymes**: Present in plasma at a higher concentration than in tissues.

1- Mostly synthesized by the liver

2- Usually decreased in disease conditions (E. g. Clotting enzymes)

- **Non-functional plasma enzymes:**
  1-Present in plasma at a lower concentration than tissues
  2-Do does not have any function in the plasma
  3-Mostly synthesized by the liver, skeletal muscle, heart, brain

Usually increased in disease conditions (E. g. Creatine kinase, Alanine transaminase)

- **Assessment of Cell Damage and Proliferation**

Plasma enzyme activities can be used in the diagnosis of disease and the prognosis of treatment. Plasma enzyme levels depend on the balance between the rate of influx of active enzyme into the circulation and its eventual clearance from the blood.

- **Estimation of more than one enzyme**

Many enzymes are widely distributed, but their relative concentrations may vary in different tissues. For Ex., Alanine and aspartate transaminases (GOT&GPT) are abundant in the liver, and the concentration of aspartate transaminase (GOT) is much greater than that of alanine transaminase (GPT) in heart muscle

- **Isoenzyme's determination**

Some enzymes exist in more than one form: these isoenzymes may be separated by their different physical or chemical properties.

a-Amylase: Marked increase (five to 10 times the upper reference limit): Acute pancreatitis, Severe glomerular impairment

Moderate increase (up to five times the upper reference limit): Perforated peptic ulcer, Acute cholecystitis, Intestinal obstruction, Salivary gland disorders like mumps, salivary calculi

Lipase

Plasma lipase levels are elevated in acute pancreatitis and carcinoma of the pancreas. Clinical Significance

Serum **amylase** is increased in mumps, pancreatic disease, or due to some other cause, whereas **lipase** is increased only in pancreatitis. Therefore, the determination of both amylase and lipase together helps in the diagnosis of acute pancreatitis

Trypsin

• Trypsin: (TRY): is a serine proteinase that hydrolyzes the peptide bonds formed by the carboxyl groups of lysine arginine with other amino acids. Increased in pancreatic disease.

- **Liver enzymes:**

  There are three types of enzymes:

  1. Enzymes that are normally present inside the hepatocytes are released into the blood when there is hepatocellular damage = markers of hepatocellular damage.

  2. Enzymes that are primary membrane-bound (plasma membrane or side of hepatocytes) = markers of cholestasis

  3. Enzymes that are synthesized in the hepatocyte = indicate disturbances in the hepatocellular synthesis

Markers of hepatocellular damage:

1. Aminotransferases/Transaminases (GPT): Elevated plasma GPT is considered to be relatively specific for liver disease

• GOT may be elevated in other forms of tissue damage, such as myocardial infarction, muscle necrosis, and renal disorders.

Markers of cholestasis:

1. Alkaline phosphatase (ALP). Half-life= 10 days.

2. Gamma-glutamyl-transferase (glutamyl transferase; GGT): catalyzes the transfer of the–glutamyl group from peptides, GGT occurs mainly in the cells of the liver

Isoenzymes of creatine kinase

• CK consists of two protein subunits, M (for muscle) and B (for the brain), which combine to form three isoenzymes. BB (CK-1), MB (CK-2) and MM (CK-3).

• **CK-MM** is the predominant iso-enzyme in skeletal and cardiac muscle and is detectable in the plasma of normal subjects.

• **CK-MB** accounts for about 35 percent of the total CK activity in cardiac muscle and less than five percent in skeletal muscle

• **CK-BB** is present in high concentrations in the brain and in the smooth muscle of the gastrointestinal and genital tracts.

Lactate Dehydrogenase

• Lactate Dehydrogenase catalysis the reversible inter-conversion of lactate and pyruvate. The enzyme has high concentrations in cells of cardiac and skeletal muscle, liver, kidney, brain, and erythrocytes.

TUMOR MARKERS

These are biochemical indicators of the presence of a tumor. In clinical practice, it refers to a molecule that can be detected in plasma and body fluids.

Tumor markers are measurable biochemicals that are associated with malignancy. These markers are either produced by tumor cells (tumor-derived) or by the body in response to tumor cells (tumor-associated). They are typically substances that are released into the circulation and thus measured in the blood. Tumor markers are not the primary modalities for cancer diagnosis rather they can be used as a laboratory test to support the diagnosis.

Q/ Why use tumor markers?

Screening and Early Detection of Cancer. Screening refers to looking for cancer in people who have no symptoms of the disease. Some newer tumor markers help to assess how aggressive a cancer is likely to be or even how well it might respond to certain drugs. Cancer Markers are also used to detect cancers that recur after initial treatment. Some tumor markers can be useful once treatment has been completed and with no evidence of residual cancer left.

- **Determining direction**

  Tumor markers can be measured qualitatively or quantitatively by:

  1. Chemical methods.
  2. Immunological methods.
  3. Molecular biological methods to determine the presence of cancer.

Characteristics of Ideal Tumor Markers

1. Specificity for cancer: the substance should be produced only by the tumor.
2. Sensitivity for cancer: a very small tumor growth will produce measurable amounts of the marker.
3. The amount of marker produced: will correlate well with the tumor load.
4. The assay for the marker: must be inexpensive, easy to perform, and sensitive.
5. The half-life of the marker: must be short enough, so
6. That when production drops, the level falls off rapidly.

- **Classification of Tumor Markers**

  1. Enzymes and isoenzymes.
  2. Hormones, neurotransmitters, and their metabolites.
  3. Receptors (estrogen, progesterone, androgen, and corticosteroid).
  4. Serum proteins examples of (immunoglobulins, glycoproteins, carcinoembryonic proteins, or oncofetal antigens).

HORMONE

➢ Concept of hormones:

Hormones are chemicals that are responsible for controlling and regulating the activities of certain cells and organs. These hormones are secreted by ductless glands known as endocrine glands.

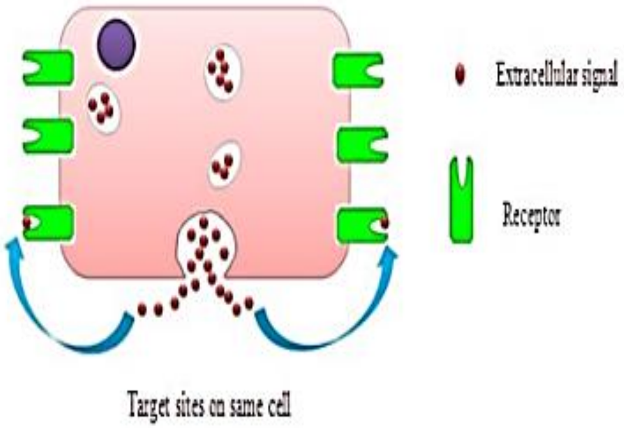
The nervous system and endocrine system are the major control mechanisms that integrate the functions of the tissues in the body. The nervous system transmits electrochemical signals between the brain and peripheral tissues for coordinating diverse body functions.

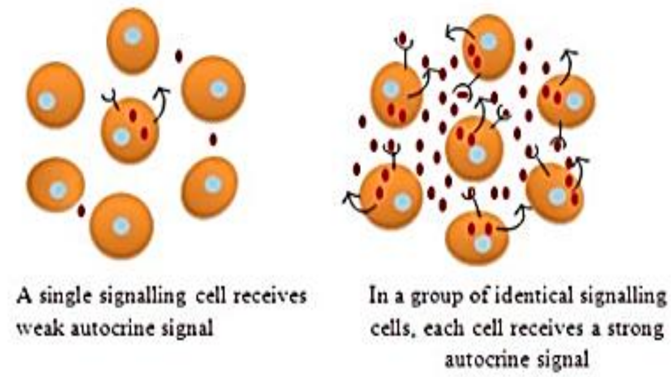
The endocrine system releases chemical mediators or hormones into circulation. However, both these systems converge, so that neural regulation of endocrine glands is affected.

Signal molecules are of different types and the process of transferring the signal into the cell is called signal transduction. There are two types of cells in signal transduction the sender cell where the signal originates and the target cell that receives the signal. The signal alters or modulates the activity/function of the cell. The types of these signals are:

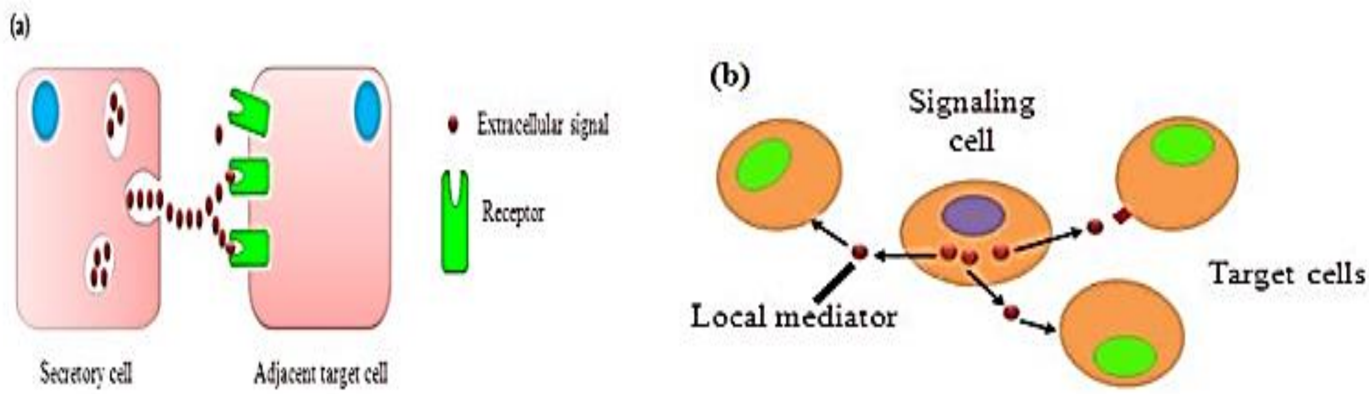
1- Autocrine signaling occurs when the same cell acts as sender and recipient,

e.g., growth.



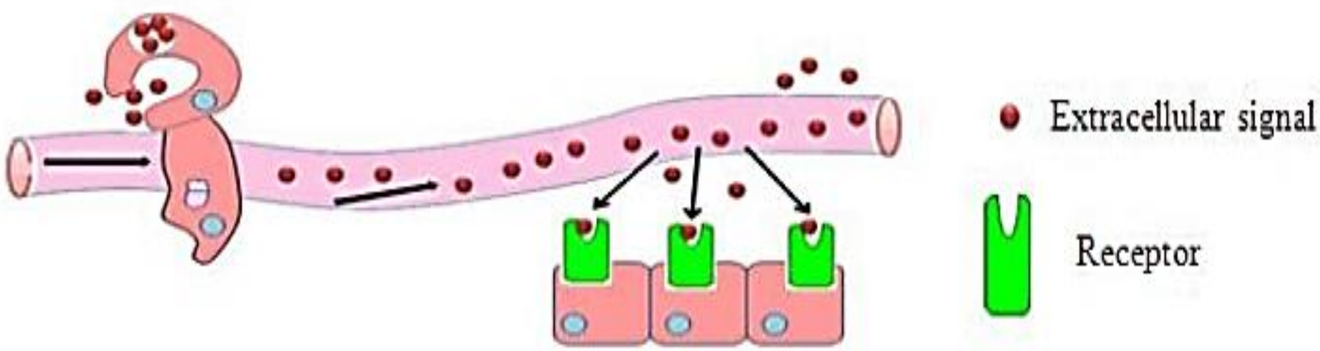


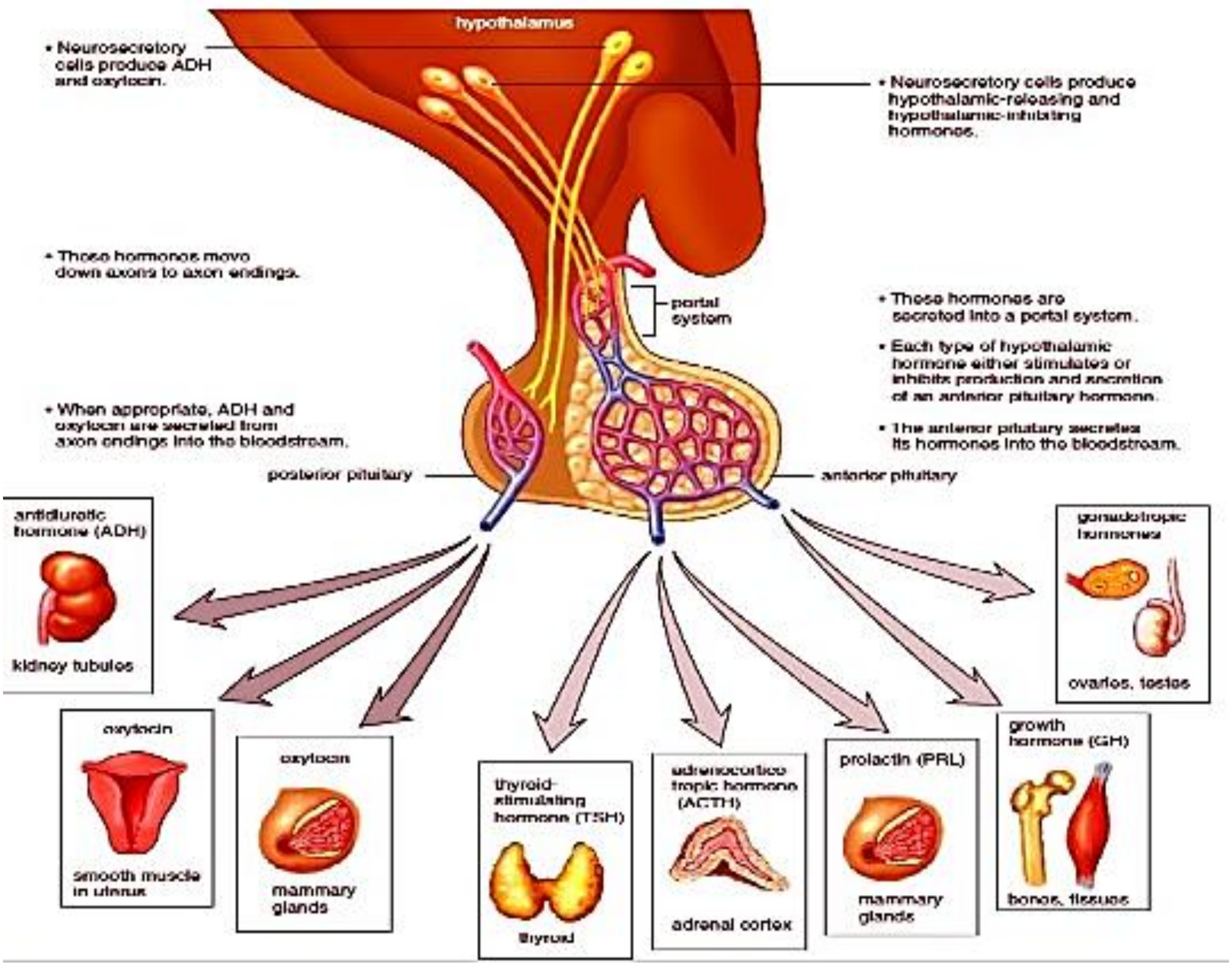
2- Paracrine signaling is affected by local mediators which have their effect near the site of secretion without entering the circulation.



3- Juxtracrine signaling occurs when the two types of cells are adjacent to each other.

4- Endocrine signaling is between cells that are located at a distance from each other and the signal may be hormones or chemical messengers secreted into circulation. Once they reach the target cell, they bind to specific target cell receptors with high affinity.


Extracellular signal
Receptor


hypothalamus
• Neurosecretory cells produce ADH and oxytocin.
• Neurosecretory cells produce hypothalamic-releasing and hypothalamic-inhibiting hormones.
• These hormones move down axons to axon endings.
portal system
• These hormones are secreted into a portal system.
• Each type of hypothalamic hormone either stimulates or inhibits production and secretion of an anterior pituitary hormone.
• When appropriate, ADH and oxytocin are secreted from axon endings into the bloodstream.
• The anterior pituitary secretes its hormones into the bloodstream.
posterior pituitary
anterior pituitary
antidiuretic hormone (ADH)
kidney tubules
gonadotropic hormones
ovaries, testes
oxytocin
smooth muscle in uterus
oxytocin
mammary glands
thyroid-stimulating hormone (TSH)
thyroid
adrenocorticotropic hormone (ACTH)
adrenal cortex
prolactin (PRL)
mammary glands
growth hormone (GH)
bones, tissues

The hypothalamus produces two types of endocrine factors;

a- Hypothalamic neuropeptides. These neurohormones are antidiuretic hormone (ADH) and oxytocin.

b- Hypothalamic releasing: The releasing factors are neurosecretions synthesized in the hypothalamus and released through the hypothalamic-pituitary portal circulation. They have an effect on the secretion of pituitary tropic hormones.

Name	*Chemical nature*	*Biological actions*
TRH; thyrotropin releasing hormone	Tripeptide; (pyro-Glu-His-Pro-NH_2)	Induces secretion of TSH and PRL; neuromodulator
GnRH; gonadotropin releasing hormone	Biologically active portion is a decapeptide	Releases LH and FSH; induces spermatogenesis, ovulation and testosterone
GHRH; growth hormone releasing hormone	37–44 amino acid; amino terminal end is tyrosine	Stimulates growth hormone secretion
CRF; corticotropin releasing factor	Amidated peptide with 41 amino acids	Release of ACTH. Inhibited by cortisol
Somatostatin; growth hormone inhibitory factor	Cyclic peptide with 14 amino acids	Inhibits secretion of GH and TSH. Inhibits gut hormones, pancreatic and gastric secretion
PIF; prolactin inhibitory factor	Dopamine	Inhibits PRL release

Direct connection between hypothalamus & adrenal medulla: it controls epinephrine & norepinephrine secretion.

The pituitary gland is the master gland: The pituitary is a small, pea-sized gland situated at the base of the brain, ant. The pituitary controls 3 endocrine glands: the thyroid, adrenal glands, and gonads. 3 endocrine glands not controlled by the pituitary; parathyroid, adrenal medulla, and pancreas

Acronym	*Full name*	*Chemical nature*	*Mol.wt. in kD*	*Amino acids*
GH	Growth hormone	Polypeptide	22	191
ACTH	Adrenocortico-tropic hormone	Polypeptide	4.5	39
LH	Luteinizing hormone	Glycoprotein; α,β chains	29	α = 89 β = 115
FSH	Follicle stimulating	Glycoprotein; α,β chains hormone	29	α = 89 β = 115
TSH	Thyroid stimulating hormone	Glycoprotein; α,β chains	28	α = 96 β = 115
MSH	Melanocyte stimulating hormone	Polypeptide	13	α = 13 β = 18 γ = 12
PRL	Prolactin b Endorphins	Polypeptide Polypeptides	22 4	198 31
LPH	Lipotropic hormone	Polypeptide	11	β = 91 γ = 60

Several other glandular tissues are considered to secrete hormones:

Heart: atrial natriuretic peptide (ANP).

kidney: produce the hormone erythropoietin, renin &1,25(OH)2cholecalciferol.

Thymus: This produces a hormone that circulates from this organ to stem cells in the lymphoid organ inducing them to become immunologically competent lymphocytes. **GI tract**: are called GI Hormones.

- **Biochemical structure & synthesis hormones: they are classified as:**

1. Steroid hormones: such as adrenocorticosteroid hormones, and progesterone.
2. Amino acid derivatives: such as epinephrine, norepinephrine and thyroid hormones.
3. Peptide/Protein hormones: such as Insulin, glucagon, parathormone, calcitonin, pituitary hormones,

Chemical structure & synthesis of hormones		
	Water soluble	Lipid soluble
Chemical nature	Protein & polypeptide (most hormones)	Steroid (sex hormones)
Gland	Pituitary, pancreas & parathyroid	Gonads & adrenal cortex
Action	Activation of enzymes	Synthesis of enzymes
Onset	Rapid action (minutes)	Slow action (hours or days)
Site of formation	In rER	In SER from cholesterol
Storge	more	Little
Release	By exocytosis	Carried plasma proteins

The Plasma carrier proteins exist for all classes of endocrine hormones. Carrier proteins for peptide hormones prevent hormone destruction by plasma proteases. Carriers for steroid and thyroid hormones allow these hydrophobic hormones to be present in the plasma. Carriers for small, hydrophilic amino acid-derived hormones prevent their filtration through the renal glomerulus, greatly prolonging their circulating half-life.

➢ The Character Of Endocrine Hormone:

1- They are secreted directly in blood in small amounts (very active).

2- Some hormones have generalizer action e.g., growth hormone & thyroxine. Others affect specific target organs e.g., sex hormones & ACTH.

3- Hormones are removed either by target cell uptake, metabolism inactivation by the liver, or excretion by the kidney.

4- Hormones play a key role in the regulation of almost all body functions including metabolism, growth, development, H2O and electrolyte balance, reproduction, and behavior.