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**Pharmacology**

**PHA304(endocrine and system pharmacology) ASSIGNMEN**

Hormones have a longer response time than nerve impulses, requiring from seconds to days, or longer, to cause a response that may last for weeks or months} The endocrine system releases hormones into the bloodstream, which carries these chemical messengers to target cells throughout the body }The neuroendocrine system, controlled by the pituitary and hypothalamus, coordinates body functions by transmitting messages between individual cells and tissues The release of hormones could be stimulated or inhibited by the nervous system, and some hormones can stimulate or inhibit nerve impulses} The nervous system and the endocrine system are closely interrelated }

The hormones of the anterior pituitary are regulated by neuropeptides that are called either “releasing” or “inhibiting” factors or hormones produced in the hypothalamus} The hormones secreted by the hypothalamus and the pituitary are all peptides or low-molecular- weight proteins that act by binding to specific receptor sites on their target tissues } The protein precursors then undergo post- translational modification to produce hormones released into the circulation} The interaction of the releasing hormones with their receptors results in the activation of genes that promote the synthesis of protein precursors }

The hypothalamus also synthesizes the precursor proteins of vasopressin and oxytocin, which are stored in the posterior pituitary} The hypothalamic-releasing hormones are primarily used for diagnostic purposes (to determine pituitary insufficiency) } Each hypothalamic regulatory hormone controls the release of a specific hormone from the anterior pituitary }

Hormones of the anterior and posterior pituitary are administered either IM, SC, or intranasally but not orally, because their peptidyl nature makes them susceptible to destruction by the proteolytic enzymes in GIT} Some pituitary hormone preparations are used therapeutically for specific hormonal deficiencies but most have limited therapeutic applications }Adrenocorticotropic hormone (ACTH), or corticotropin is a product of the posttranslational processing of this precursor polypeptide} Corticotropin-releasing hormone (CRH) is responsible for the synthesis and release of the peptide pro- opiomelanocortin by the pituitary } Stress stimulates ACTH secretion, whereas cortisol acting via negative feedback suppresses its release} ACTH is released from the pituitary in pulses with an overriding diurnal rhythm, with the highest concentration occurring at approximately 6 AM and the lowest in the late evening } CRH is used diagnostically to differentiate between Cushing syndrome and ectopic ACTH-producing This pathway ends with the synthesis and release of the adrenocorticosteroids and the adrenal androgens} The occupied receptors activate G protein-coupled processes to increase cAMP, which in turn stimulates the rate-limiting step in the adrenocorticosteroid synthetic pathway (cholesterol to pregnenolone) } The target organ of ACTH is the adrenal cortex, where it binds to specific receptors on the cell surfaces }Mechanism of action.ACTH is used in the treatment of multiple sclerosis and infantile spasm (West syndrome)} Diagnostic use for differentiating between primary adrenal insufficiency (Addison disease, associated with adrenal atrophy) and secondary adrenal insufficiency (caused by the inadequate secretion of ACTH by the pituitary) }Therapeutic uses: Similar to those of glucocorticoids ◦ Osteoporosis ◦ Hypertension ◦ Peripheral edema ◦ Hypokalemia ◦ Emotional disturbances ◦ Increased risk of infection}Adverse effects:

* + Growth hormone (GHRH)-- anterior pituitary synthesis
    - Growth regulation
    - Intermediary metabolism effects
  + Prolactin (PRL)-- anterior pituitary synthesis
    - Required for lactation
  + Luteinizing hormone (LH) and Follicle-stimulating hormone (FSH)--anterior pituitary synthesis
    - Male and female gonadal control
  + Thyroid-stimulating hormone (TSH, thyrotropin)--anterior pituitary synthesis
    - Thyroid function regulation
  + Adrenocorticotropin (ACTH)--anterior pituitary synthesis
    - Regulation: adrenocortical glucocorticoid functions
  + Vasopressin (AVP; antidiuretic hormone, ADH) --synthesis site: hypothalamic neurons; storage site: posterior pituitary.
    - AVP: regulation of renal water conservation
  + Oxytocin: --synthesis site: hypothalamic neurons; storage site: posterior pituitary.
    - Oxytocin: required for milk let-down; may assist in parturition
* Feedback Relationships:
  + Feedback between anterior pituitary and its three target glands:
    - gonads
      * if gonads fail or removed then LH and FSH increased ­ (primary hypogonadism)
    - adrenal cortex
      * with adrenal cortex destruction/removal, primary adrenal-insufficiency occurs (Addison's disease) with increased­ serum ACTH concentration
    - thyroid
      * thyroid failure  leads to  primary hypothyroidism resulting in increased ­ TSH
  + With removal/destruction of the pituitary gland, trophic hormone is lost:
    - Secondary hypogonadism
    - Adrenal-insufficiency
    - Hypothyroidism
  + With removal/destruction of the pituitary gland: no effect on vasopressin (AVP) and oxytocin provided intact hypothalamus