MULTIFACETED ROLE OF VASOPRESSIN & OXYTOCIN

The **posterior pituitary gland**, also called the **neurohypophysis**, is composed mainly of glial-like cells called **pituicytes**. The pituicytes do not secrete hormones; they act simply as a supporting structure for large numbers of **terminal nerve fibers** and **terminal nerve endings** from nerve tracts that originate in the **supraoptic** and **paraventricular nuclei** of the hypothalamus. These tracts pass to the neurohypophysis through the **pituitary stalk** (hypophysial stalk).The nerve endings are bulbous knobs that contain many secretory granules. These endings lie on the surfaces of capillaries, where they secrete two posterior pituitary hormones: (1) **antidiuretic hormone** (ADH), also called vasopressin, and (2) **oxytocin**.

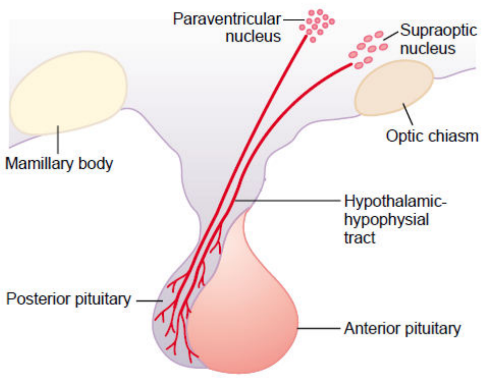

Fig : Hypothalamic control of the posterior pituitary

ADH is initially synthesized in the cell bodies of the supraoptic nuclei (SON) whereas oxytocin is synthesized primarily in the paraventricular nuclei (PVN). These hormones are then transported in combination with "carrier" proteins called **neurophysins** down to the nerve endings in the posterior pituitary gland. When nerve impulses are transmitted downward along the fibers from the supraoptic or paraventricular nuclei, the hormone is immediately released from the secretory granules in the nerve endings by the usual secretory mechanism of ***exocytosis*** and is absorbed into adjacent capillaries. Both the neurophysin and the hormone are secreted together, but because they are only loosely bound to each other, the hormone separates almost immediately.

Chemical Structures of ADH and Oxytocin :

Both oxytocin and ADH (vasopressin) are polypeptides, each containing nine amino acids. Their amino acid sequences are the following:

Vasopressin: Cys-Tyr-Phe-Gln-Asn-Cys-Pro-Arg-GlyNH2

Oxytocin: Cys-Tyr-Ile-Gln-Asn-Cys-Pro-Leu-GlyNH2

Note that these two hormones are almost identical except that in vasopressin, phenylalanine and arginine replace isoleucine and leucine of the oxytocin molecule. The similarity of the molecules explains their partial functional similarities.

Physiological Functions of ADH :

Minute concentrations of ADH cause increased water conservation by the kidneys; higher concentrations of ADH have a potent effect of constricting the arterioles throughout the body and therefore increasing the arterial pressure. For this reason, **ADH** has another name, **vasopressin**.

ADH is the main hormone involved in regulation of **water homeostasis** and osmolarity of body fluids. Plasma **osmolality** and **blood volume** are monitored by specialized receptors of the cardiovascular system (e.g., carotid bodies and juxtaglomerular apparatus). An increase in osmolality or a decrease in blood volume stimulates ADH release. Additionally, the cell bodies of the hypothalamic secretory neurons may also serve as osmoreceptors, initiating ADH release. Pain, trauma, emotional stress, and drugs such as nicotine also stimulate release of ADH.

When osmolarity of the body fluids increased above normal (that is, the solutes in the body fluids become too concentrated), the posterior pituitary gland secretes more ADH, which increases the permeability of the distal tubules and collecting ducts to water. This allows large amounts of water to be reabsorbed and decreases urine volume but does not markedly alter the rate of renal excretion of the solutes.

When there is excess water in the body and extracellular fluid osmolarity is reduced, the secretion of ADH by the posterior pituitary decreases, thereby reducing the permeability of the distal tubule and collecting ducts to water, which causes large amounts of dilute urine to be excreted. Thus, the rate of ADH secretion determines, to a large extent, whether the kidney excretes dilute or concentrated urine.

1. **Antidiuresis :** (ADH facilitates resorption of water from the distal tubules and collecting ducts of the kidney by altering the permeability of the cells to water)

In the absence of ADH, the collecting tubules and ducts become almost impermeable to water, which prevents significant reabsorption of water and therefore allows extreme loss of water into the urine, also causing extreme dilution of the urine. Conversely, in the presence of ADH, the permeability of the collecting ducts and tubules to water increases greatly and allows most of the water to be reabsorbed as the tubular fluid passes through these ducts, thereby conserving water in the body and producing very concentrated urine.

Mechanism: The primary physiologic effect of ADH on the kidney is the insertion of water channels (aquaporins) into cells of the distal convoluted tubules and collecting ducts, which increases the permeability for water. Immediately inside the cell membrane are a large number of special vesicles that have highly water permeable pores called *aquaporins.* ADH acts through its specific V2 receptor on the basolateral domain of cells lining the distal convoluted tubules and collecting ducts (mutation of this receptor is responsible for nephrogenic diabetes insipidus). Binding of ADH with its membrane receptors activate adenylyl cyclase and cause the formation of cAMP inside the tubular cell cytoplasm. This causes phosphorylation of elements in the special vesicles, which then causes the vesicles to insert into the apical cell membranes (Insertion of aquaporin-2 (AQP-2) into the apical domain and aquaporin-3 (AQP-3) into the basolateral domain of these cells is responsible for rapid resorption of water across the tubule epithelium), thus providing many areas of high water permeability. All this occurs within 5 to 10 minutes. Then, in the absence of ADH, the entire process reverses in another 5 to 10 minutes. Thus, this process temporarily provides many new pores that allow free diffusion of water from the tubular fluid through the tubular epithelial cells and into the renal interstitial fluid.

2. **Chloride resorption**: ADH enhances excretion of chloride by decreasing chloride resorption.

3. **Effects on cardiovascular system**: Vasopressin increases blood pressure. Simultaneously heart rate decreases.

4. **Respiration :** Change in blood pressure stimulate the respiratory centre, which increases rate of respiration.

5. **Metabolic changes**: Liver Glycogenolysis increases, causing rise in blood glucose level, glucose excretion increases in urine, BMR decreases.

6. **Peristalsis**: Vasopressin increases peristalsis of stomach & intestine.

7. **Non voluntary muscles contraction:** It stimulates the contraction of non voluntary muscles of small intestine, gall bladder, ureter, urethra.

Physiological Functions of Oxytocin Hormone :

1. **Contraction of the Pregnant Uterus:** It generally promotes contraction of uterine smooth muscle during orgasm, menstruation, and parturition. It powerfully stimulates contraction of the pregnant uterus,

especially toward the end of gestation, helping in the expulsion of child through the vaginal opening.also it helps in the expulsion of p;acenta after parturition.

2. **Aids in Milk Ejection by the Breasts :** In lactation, oxytocin causes milk to be expressed from the alveoli into the ducts of the breast so that the baby can obtain it by suckling.

Milk is secreted continuously into the alveoli of the breasts, but milk does not flow easily from the alveoli into the ductal system and therefore, does not continually leak from the breast nipples. Instead, the milk must be *ejected* from the alveoli into the ducts before the baby can obtain it. This is caused by a combined neurogenic and hormonal reflex that involves the posterior pituitary hormone *oxytocin.*

Milk letdown mechanism: When the baby suckles, it receives virtually no milk for the first half minute or so. The suckling stimulus on the nipple of the breast for the first time causes signals (sensory impulses) to be transmitted through somatic sensory nerves from the nipples to the mother's spinal cord and then to her Hypothalamus, where they cause nerve signals that promote *oxytocin* secretion at the same time that they cause prolactin secretion. The oxytocin is then carried by the blood to the breasts, where it causes contraction of ***myoepithelial cells*** (smooth muscles which surround the outer walls of the alveoli of the mammary glands), thereby expressing the milk from the alveoli into the ducts at a pressure of +10 to 20 mm Hg. Then the baby's suckling becomes effective in removing the milk. Thus, within 30 seconds to 1 minute after a baby begins to suckle, milk begins to flow.This mechanism is called ***milk letdown*** or ***milk ejection***.

3. **Semen transport:** During sexual intercourse oxytocin assists transportation of ejaculated semen within vagina.
4. **Metabolic change:** High concentration of oxytocin increases blood glucose level, especially in dog.

TABLE 21.4 Hormones of the Posterior Lobe of the Pituitary Gland

Hormone	Composition	Source	Major Functions
Oxytocin	Polypeptide containing 9 amino acids	Cell bodies of neurons located in the supraoptic and paraventricular nuclei of the hypothalamus[a]	Stimulates activity of the contractile cells around the ducts of the mammary glands to eject milk from the glands; stimulates contraction of smooth muscle cells in the pregnant uterus
Antidiuretic hormone (ADH; vasopressin)	Polypeptide containing 9 amino acids; two forms: arginine-ADH (most common in humans) and lysine-ADH	Cell bodies of neurons located in the supraoptic and paraventricular nuclei of the hypothalamus[a]	Decreases urine volume by increasing reabsorption of water by collecting ducts of the kidney; decreases the rate of perspiration in response to dehydration; increases blood pressure by stimulating contractions of smooth muscle cells in the wall of arterioles

[a] Immunocytochemical studies indicate that oxytocin and ADH are produced by separate sets of neurons within the supraoptic and paraventricular nuclei of the hypothalamus. Biochemical studies have demonstrated that the supraoptic nucleus contains equal amounts of both hormones, whereas the paraventricular nucleus contains more oxytocin than ADH, but less than the amount found in the supraoptic nucleus.