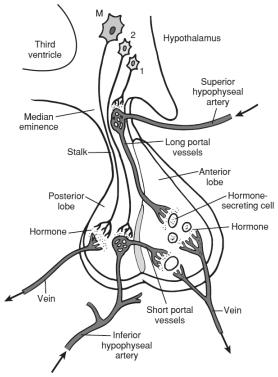
ENDOCRINE PHYSIOLOGY

POSTERIOR PITUITARY GLAND



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OBJECTIVES

At the end of this lecture you should be able to:

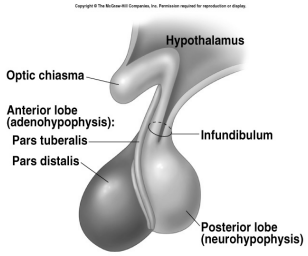
1. **List posterior pituitary hormones.**
2. **Identify and describe the function of ADH.**
3. **Identify and describe the regulatory mechanism, influencing factors and control of secretion of ADH.**
4. **Vasoconstrictor and Pressor Effects of ADH**
5. **Identify and describe the chemical nature, target effects and functions of oxytocin.**
6. **Describe Milk Let Down Reflex**
7. **Explain how Oxytocin Causes Contraction of the Pregnant Uterus.**

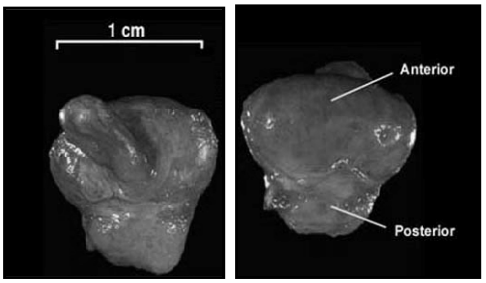
Pituitary Gland

- Pituitary gland is located in the diencephalon.
- Structurally and functionally divided into:

–Anterior lobe.

–Posterior lobe.



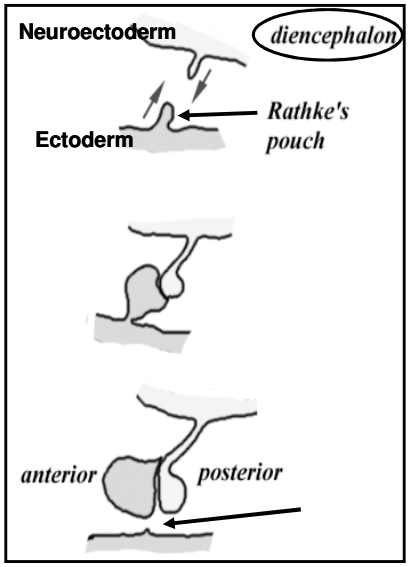


Sup view Inferior view

Pituitary Gland (continued)

- Anterior pituitary:
  - Master gland (adenohypophysis).
  - Derived from a pouch of epithelial tissue that migrates upward from the mouth.
    - Consists of 2 parts:
      - Pars distalis: anterior pituitary.
      - Pars tuberalis: thin extension in contact with the infundibulum.
- Posterior pituitary(neurohypophysis):
  - Formed by downgrowth of the brain during fetal development.
  - Is in contact with the infundibulum.
    - Nerve fibers extend through the infundibulum.

THE POSTERIOR PITUITARY
– Embryology -



The pituitary gland is derived from two sources.

The anterior lobe is an up growth of ectoderm called Rathke's pouch from the roof of the stomodeum, which will become the mouth.

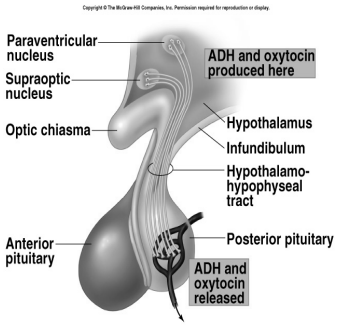
The posterior lobe is a down growth of neurectoderm from the diencephalon.

By the sixth week the connection between Rathke's pouch and the oral cavity degenerates.

THE POSTERIOR PITUITARY
– Relationship to the Hypothalamus -

Thus, the hormones secreted by the posterior lobe
Antidiuretic hormone (ADH) & oxytocin
are actually neuropeptides.

i.e. they are peptides released from neurons.



The connections between the hypothalamus & the posterior lobe of the pituitary are neural.

In fact, the posterior pituitary is a collection of nerve axons whose cell bodies are located in the hypothalamus.

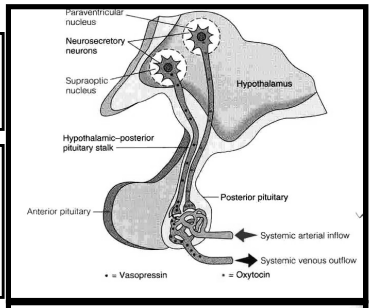
POSTERIOR PITUITARY & HYPOTHALAMUS

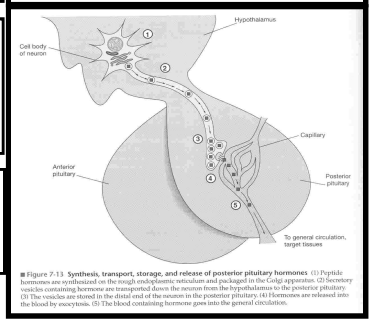
The posterior pituitary does not produce any hormones, it simply stores & secretes hormones produced by the hypothalamus

Once synthesized in the cell bodies, the hormones (neuropeptides) are transported down the axons in neurosecretory vesicles and stored in bulbous nerve terminals in the posterior pituitary.

When the cell body is stimulated, the neurosecretory vesicles are released from the nerve terminals by exocytosis, and the secreted hormone enters the nearby capillaries.

Venous blood from the posterior pituitary enters the systemic circulation, which delivers the hormones to their target tissues.

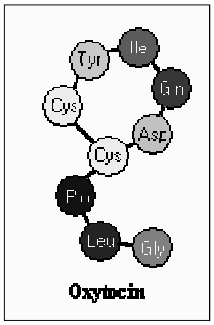




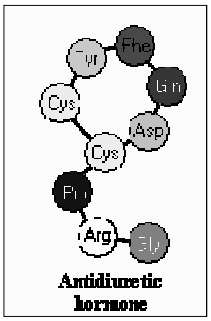
■ Figure 7-13 **Synthesis, transport, storage, and release of posterior pituitary hormones** (1) Peptide hormones are synthesized on the rough endoplasmic reticulum and packaged in the Golgi apparatus. (2) Secretory vesicles containing hormone are transported down the neuron from the hypothalamus to the posterior pituitary. (3) The vesicles are stored in the distal end of the neuron in the posterior pituitary. (4) Hormones are released into the blood by exocytosis. (5) The blood containing hormone goes into the general circulation.

THE POSTERIOR LOBE

Oxytocin

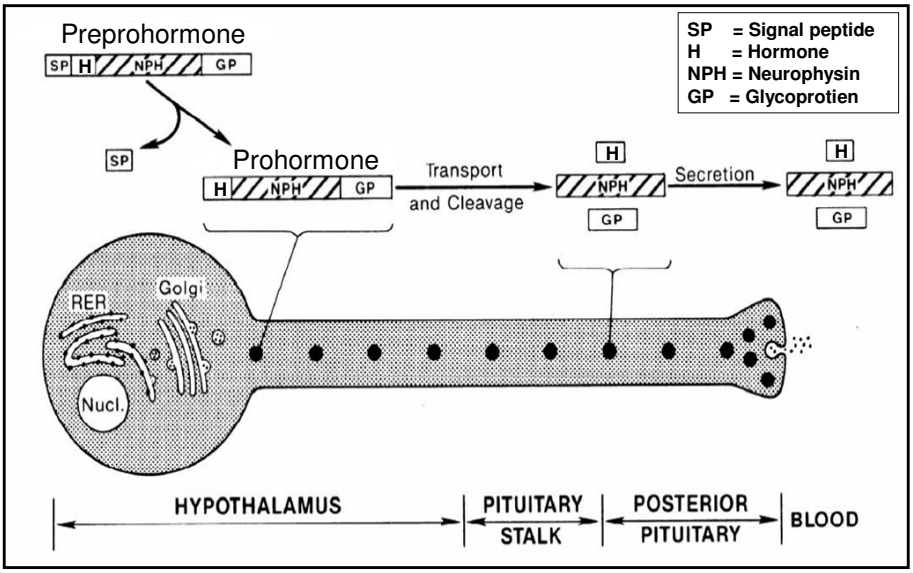


Antidiuretic Hormone



- **Vasopressin: Cys-Tyr-Phe-Gln-Asn-Cys-Pro-Arg-GlyNH2**
- **Oxytocin: Cys-Tyr-Ile-Gln-Asn-Cys-Pro-Leu-GlyNH2**

Synthesis and Secretion of Post. Pit. Hormones

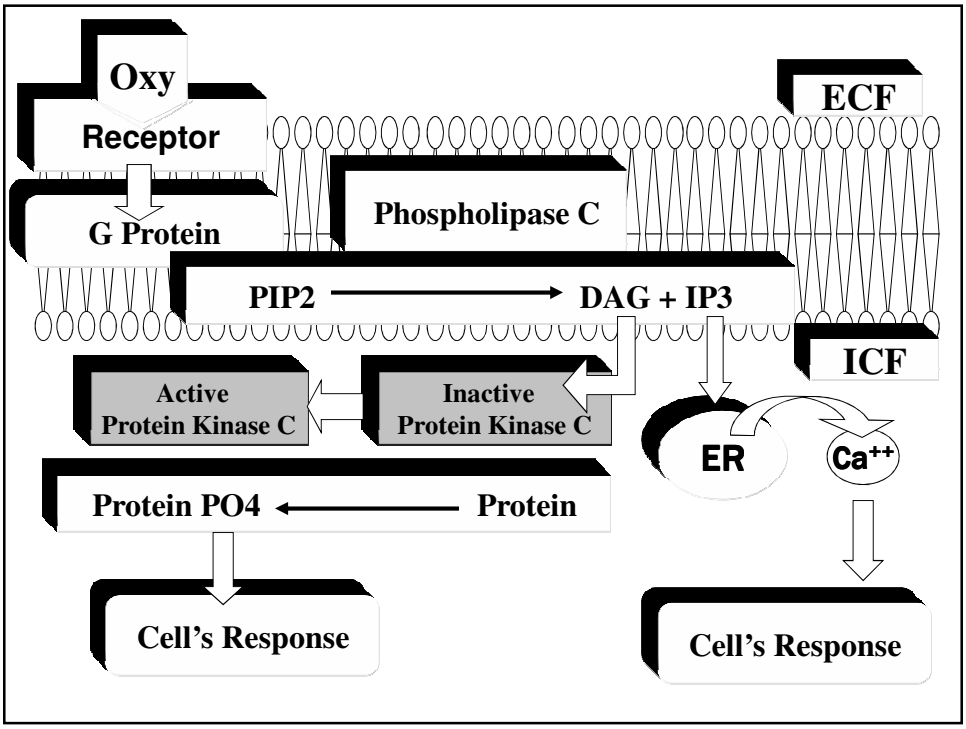


OXYTOCIN

- **Source Hypothalamus (Primarily Paraventricular Nucleus)**
- **Released from Posterior Pituitary (Gonads, Adrenal Cortex, Thymus)**
- **Chemistry Peptide 9 aa**
- **Half Life 6-20 min**
- **Daily Output**
- **Basal Levels 1-10 pg/ml**
- **Transport Neurophysins**
- **Pattern of Secretion Synchronous high frequency discharge**

Facts

- **(1) In a hypophysectomized animal, the duration of labor is prolonged indicating a possible effect of oxytocin during delivery.**
- **(2) The amount of oxytocin in the plasma increases during labor, especially during the last stage.**
- **(3) Stimulation of the cervix in a pregnant animal elicits nervous signals that pass to the hypothalamus and cause increased secretion of oxytocin.**



Oxytocin
– Regulation of Secretion –

Factors that

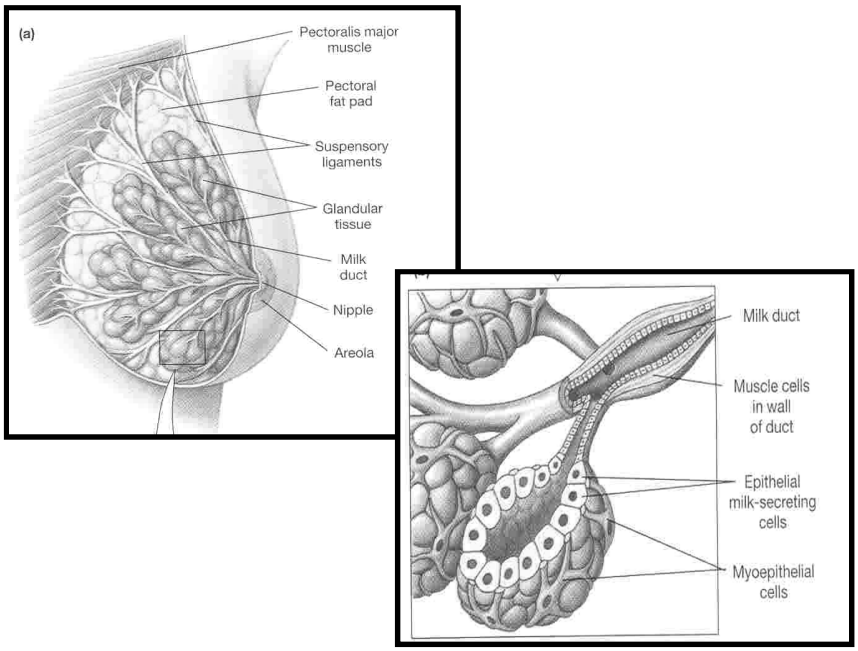
Stimulate secretion
1- Suckling
2- Sight, sound, or smell of the infant
3- Dilation of the cervix.
4- Orgasm

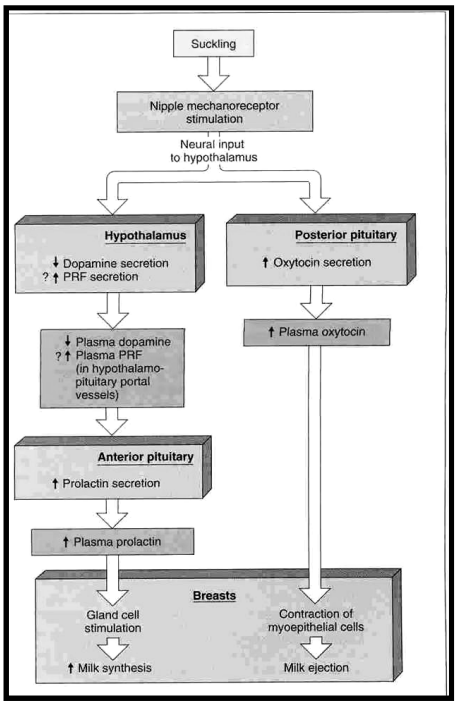
Inhibit secretion
1- Opioids (endorphins)

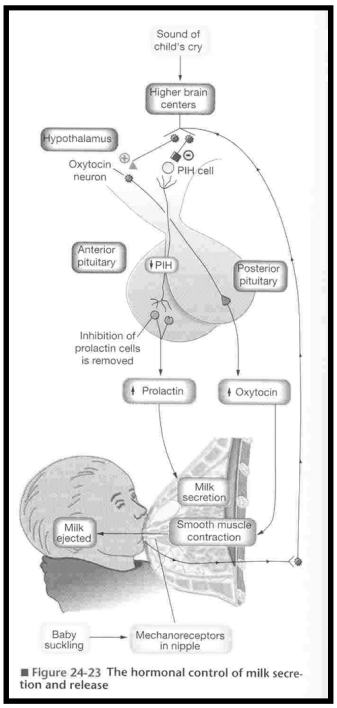
Physiologic Effects

- **Stimulation of milk ejection (milk letdown)**
- **Stimulation of uterine smooth muscle contraction at birth**
- **Establishment of maternal behavior**
- **Facilitate Sperm transport in Female Genital Tract**
- **Increased Contraction of Vas Deferens (Ejaculation)**
- **Curb salt appetite**

Physicians and veterinarians sometimes administer oxytocin ("pitocin") to further stimulate uterine contractions





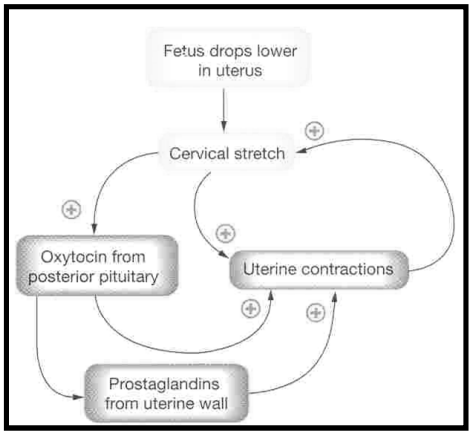


■ Figure 24-23 The hormonal control of milk secretion and release

(2) Uterine contraction

At a very low concentration, oxytocin causes powerful rhythmic contractions of uterine smooth muscle.

This action of oxytocin is the basis for its use in:
- Inducing labor
- Reducing postpartum bleeding



The postive feedback loop of Parturition

Stops when the fetus is delivered

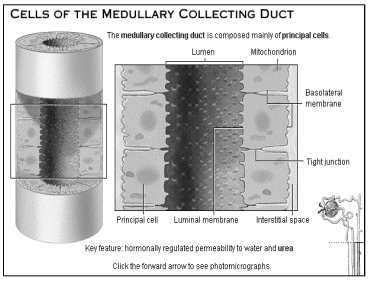
ANTIDIURETIC HORMONE

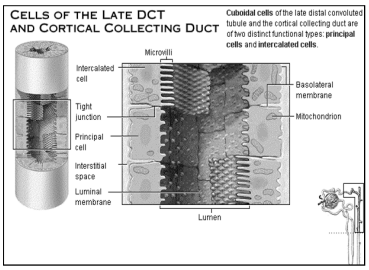
ADH (AVP)

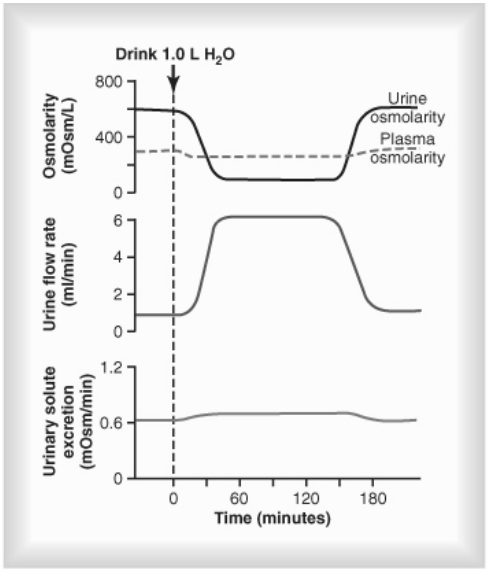
- **Source Hypothalamus Posterior Pituitary**
  (Primarily SupraOptic Nucleus)
  (Gonads, Adrenal Cortex)
- **Chemistry Peptide 9 aa**
- **Half Life 2-3 minutes**
- **Basal Levels 1pg/ml**
- **Transport Neurophysins**
- **Pattern of Secretion**
  - **Initial steady increase in discharge**
  - **Prolonged Phasic Bursting**

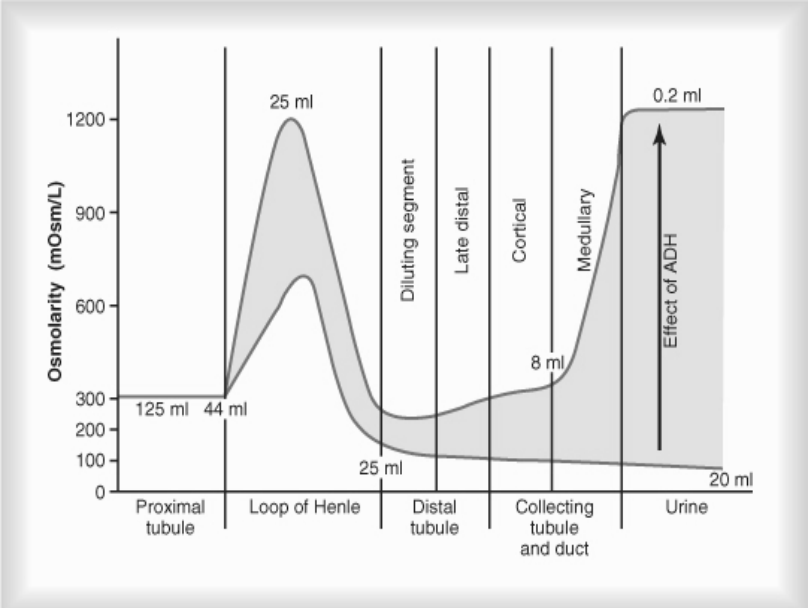
Physiologic Effects

- **Water retention in excess of solutes (V2 Receptors)**
- **Blood Pressure homeostasis (Vasoconstriction V1A receptor, vascular smooth muscle)**
- **Glycogenolysis in Liver (V1A)**
- **Neurotransmitter in brain & spinal cord**
  - **Lowers body temperature**
  - **Facilitate memory Consolidation & Retrieval**
- V1B receptors are unique to anterior pituitary and mediate increased ACTH secretion









Antidiuretic Hormone (ADH)
– Actions –

ADH (vasopressin) has two actions

1- kidney → for Water retention

2- vascular smooth muscle → for Vasoconstriction

These actions are mediated by
different receptors
different intracellular mechanisms
different second messengers

Antidiuretic Hormone (ADH)
– Water retention – Vasoconstrection –

- Site of Action:
- The principal cells of late distal tubule and collecting duct.

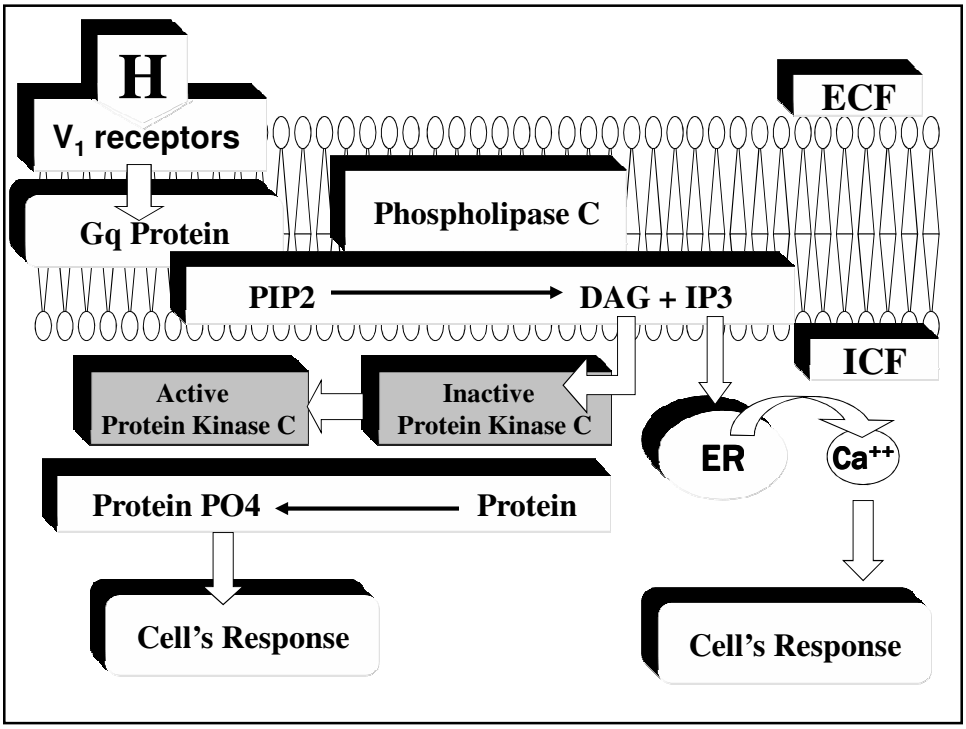
- The receptor for ADH:
- **V2 receptor,** which is coupled to adenyl cyclase via a Gs protein.

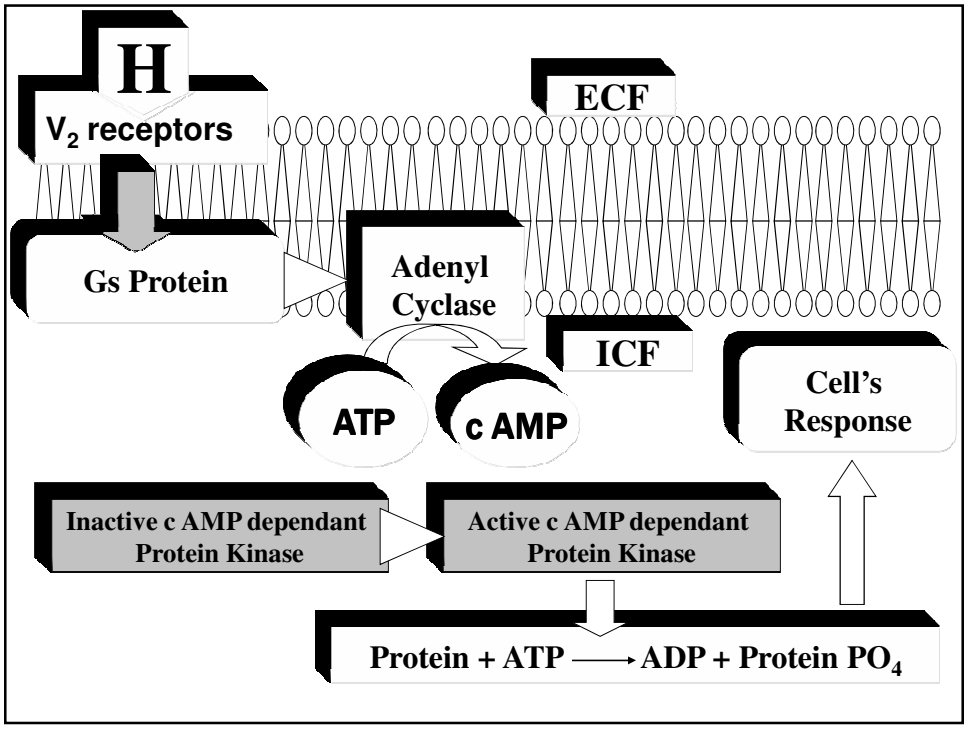
- The second messenger:
- **cAMP**, which, via phosphorylation steps, directs the insertion of water channels, **aquaporin 2 (AQP2)**, in the luminal membranes.

- Site of Action:
- vascular smooth muscle .

- The receptor for ADH:
- **V1 receptor,** which is coupled to phospholipase C via a Gq protein.

- The second messenger:
- **IP3/Ca2+**, which produces contraction of vascular smooth muscle, constriction of arterioles, and increased total peripheral resistance




H
V2 receptors
ECF
Gs Protein
Adenyl Cyclase
ICF
ATP
c AMP
Cell's Response
Inactive c AMP dependant Protein Kinase
Active c AMP dependant Protein Kinase
Protein + ATP → ADP + Protein PO4

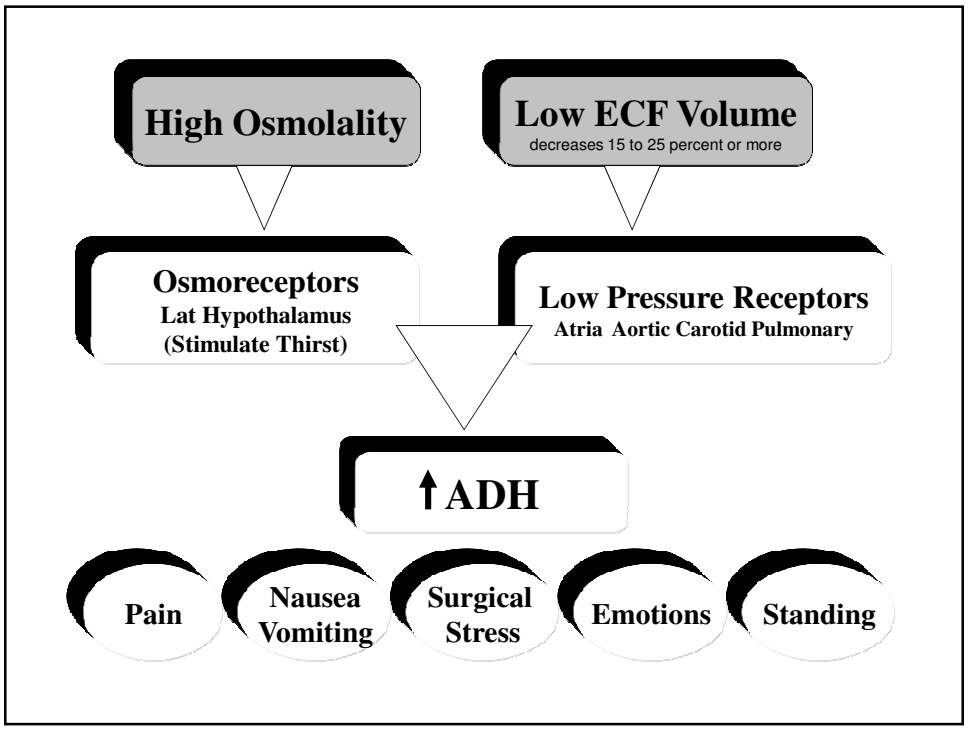
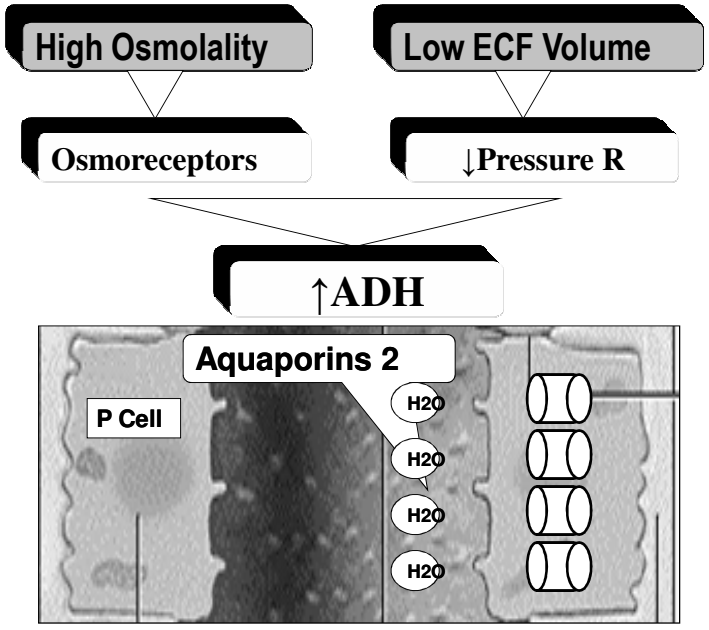

High Osmolality
Low ECF Volume
decreases 15 to 25 percent or more
Osmoreceptors
Lat Hypothalamus
(Stimulate Thirst)
Low Pressure Receptors
Atria Aortic Carotid Pulmonary
↑ADH
Pain
Nausea Vomiting
Surgical Stress
Emotions
Standing

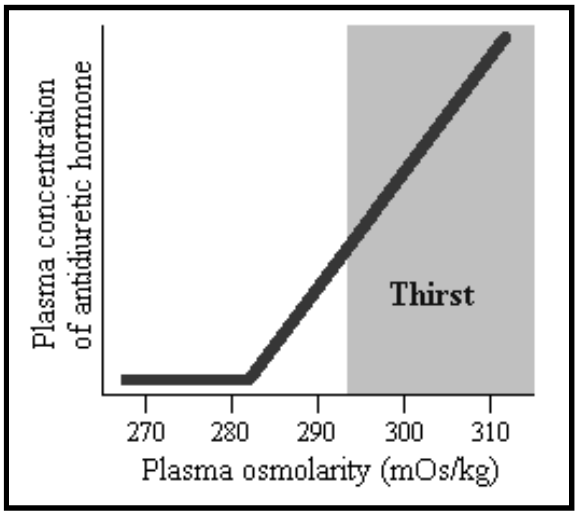
Table 28–2

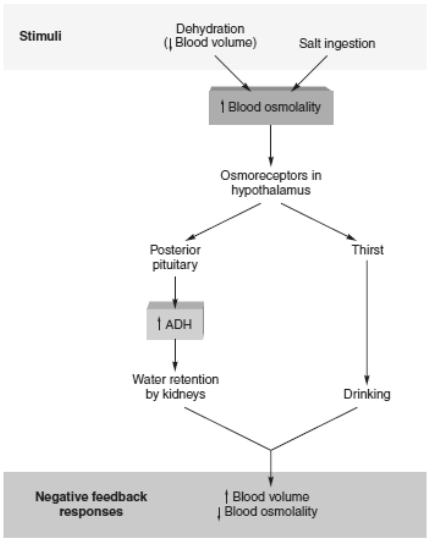
Regulation of ADH Secretion

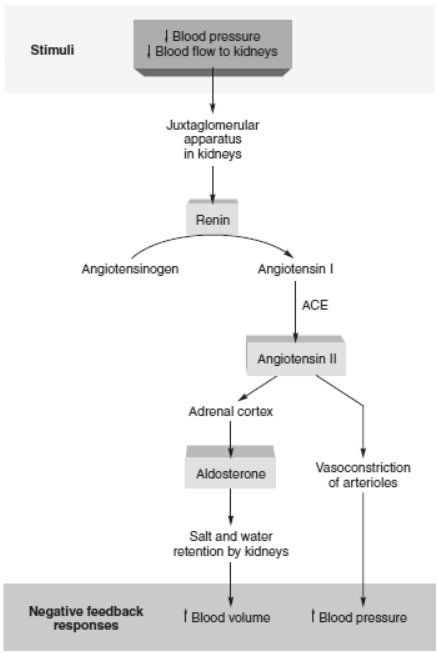
Increase ADH	Decrease ADH
↑ Plasma osmolarity	↓ Plasma osmolarity
↓ Blood volume	↑ Blood volume
↓ Blood pressure	↑ Blood pressure
Nausea	
Hypoxia	
Drugs:	Drugs:
Morphine	Alcohol
Nicotine	Clonidine (antihypertensive drug)
Cyclophosphamide	Haloperidol (dopamine blocker)



Plasma Osmolarity and ADH







DISORDERS OF URINARY CONCENTRATING ABILITY

- Types and causes of DI
  - Central
  - Nephrogenic DI
- Syndrome of inappropriate ADH secretion

It must be differentiated from other polyuric states such as primary polydipsia & osmotic duiresis.

DIABETES INSIPIDUS

- Failure to Produce ADH: **"Central"** Diabetes Insipidus.
  - Defect in hypothalamus, pituitary stalk or posterior pituitary
- Inability of the Kidneys to Respond to ADH: **"Nephrogenic"** Diabetes Insipidus.
  - In this condition, renal tubules are resistant to normal or high levels of plasma vasopressin Cause: abnormality in the vasopressin-2 receptor, or as an autosomal post-receptor defect in an ADH-sensitive water channel, aquaporin-2

CAUSES OF CENTRAL DI

- Brain tumors
  - Lung cancer, leukemia, lymphoma most common
- Head trauma
- Post-neurosurgery
- Idiopathic – 30-50%
  - Pituitary atrophy, possible autoimmune
- Congenital
  - Mutations of ADH gene, usually autosomal dominant
- Infiltrative diseases, such as Histiocytosis X or sarcoidosis

CAUSES OF NEPHROGENIC DI

- **Acquired**
  - **Drugs: lithium, amphotericin, gentamicin, loop diuretics**
  - **Electrolyte disorders: hypercalcemia, hypokalemia**
  - **Renal dz: obstructive uropathy, chronic renal failer , polysystic kidney, post-transplant, pyelonephritis**
  - **Systemic processes: sarcoid, amyloid, multiple myeloma, sickle cell disease, pregnancy**
- **Congenital – rare**
  - **Present in 1st week of life**
  - **V2 ADH receptor defect – X-linked recessive**
  - **AQP2 water channel defect – will respond to ADH**

Symptoms and signs of DI

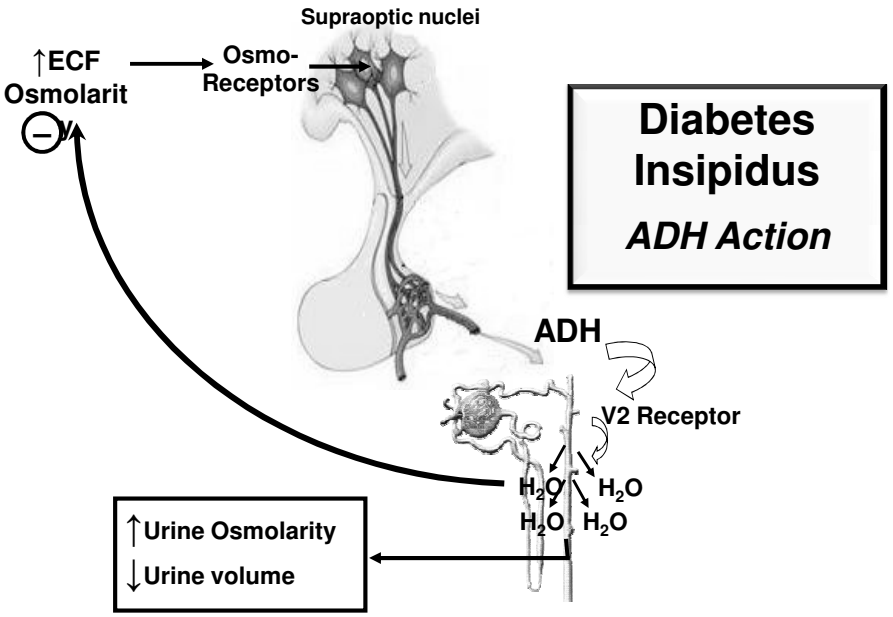
- **Dehydration which can cause:**
  - **Dry mouth**
  - **Muscle weakness**
  - **Hypotension (low blood pressure)**
  - **Sunken appearance of the eyes**
- **Rapid heart rate**
- **Weight loss**

Symptoms and signs of DI

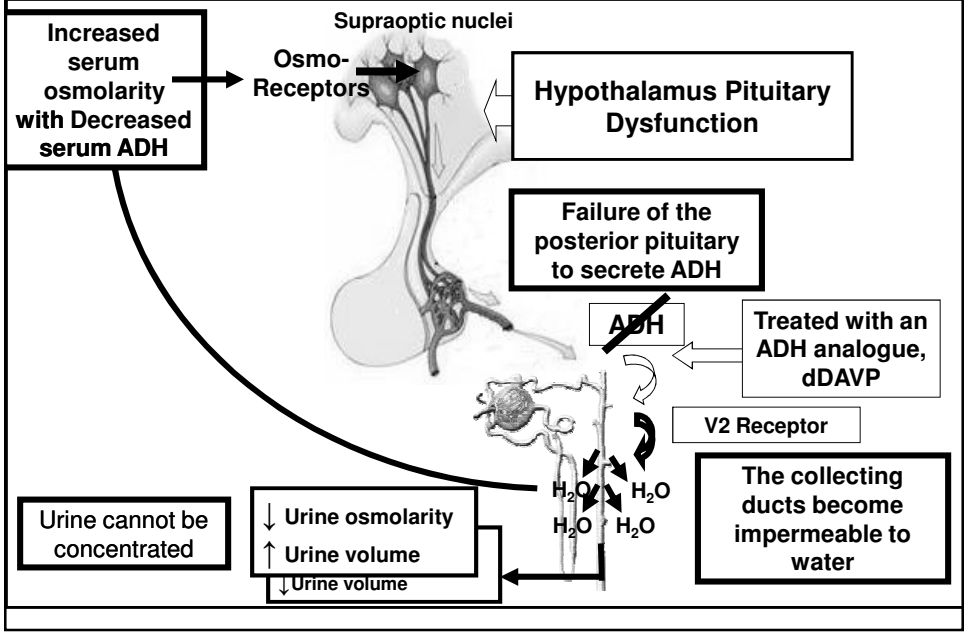
- **Electrolyte imbalance**
  - **Hypernatremia**
  - **Hyperchloremia**
- **Electrolyte imbalance can cause**
  - **Headache**
  - **Fatigue**
  - **Irritability and muscle pains**
- **Impaired consciousness**
- **Seizures secondary to Hypernatremia can happen**

TREATMENT

- Desmopressin
  - Desamino-desarginino-vasopressin(DDAVP)
  - V2-selective analogue
  - Little V1 (vasoconstrictor) activity
  - Drug of choice in Diabetes insipidus
- Thiazide Diuretics for Nephrogenic DI



– Central Diabetes Insipidus –



Diagnosis

- **High or high-normal plasma osmolality**
- **low urine osmolality < 200 mosm/L (in primary polydipsia plasma osmolality tends to be low).**
- **Resultant high or high-normal plasma sodium.**
- **High 24-h urine volumes (less than 2 L excludes the need for further investigation).**
- **Failure of urinary concentration with fluid deprivation.**
- **Restoration of urinary concentration with vasopressin or an analogue.**
- **Anorexia, constipation**

Water-deprivation test

Procedure

Fasting and no fluids from 0730 h. Monitor serum and urine osmolality, urine volume and weight hourly for up to 8 hours. Abandon fluid deprivation if weight loss > 3% occurs If serum osmolality > 300 mOsm/kg and/or urine osmolality < 600 mOsm/kg give desmopressin 2 µg i.m. at end of test. Allow free fluid but measure urine osmolality for 2–4 hours

Interpretation

Normal response. Serum osmolality remains within normal range (275–295 mOsm/kg). Urine osmolality rises to > 600 mOsm/kg.
Diabetes insipidus (DI). Serum osmolality rises above normal without adequate concentration of urine osmolality (i.e. serum osmolality > 300 mOsm/kg; urine osmolality< 600 mOsm/kg).
Nephrogenic DI – if DDAVP does not concentrate urine.
Cranial DI – if urine osmolality rises by > 50% after desmopressin.

DISORDERS OF URINARY CONCENTRATING ABILITY

Inappropriate secretion of ADH (SIADH) leads to retention of water and hyponatraemia.

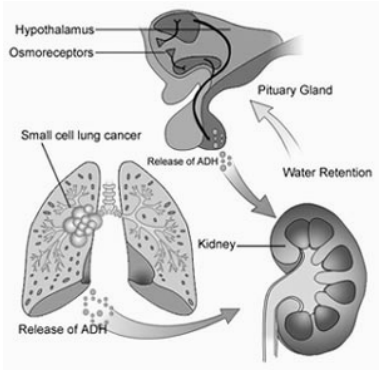
Syndrome of Inappropriate antidiuretic Hormone (SIADH)

- The syndrome of inappropriate secretion of ADH (SIADH) is characterized by
  - Non-physiologic release of ADH
  - Impaired water excretion with normal sodium excretion
- SIADH is associated with disease that affect osmoreceptor in the hypothalamus

Causes

–Cancer - small cell cancer of lung
–Brain –
- Meningitis
- Cerebral abscess
- Head injury
- Tumors

–Lungs(pneumonia,TB)
–Metabolic
–Drugs



Diagnosis

- Fluid retention
- Serum hypo-osmolarity
- Dilutional hyponatraemia
- Hypochloremia
- Concentrated urine in the presence of normal or increased intravascular volume
- Normal renal function

Hyponatraemia and hypo-osmolarity lead to acute edema of the brain cells (> 5-10% water in brain is incompatible with life)

Clinical Features

- Headache
- Nausea
- Vomiting
- Impaired consciousness
- Neurological signs (severe hyponatraemia)
  - Drowsiness
  - Disorientation
  - Delirium
  - Seizures
- Coma & death (severe cases)

THANKS