

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ



# VASOPRESSIN AXIS IN SHOCK STATES

*By*

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# Mansoura University Hospitals ICU, S

2 PICU (Pediatric H)

3 MICU (SMH)

14 ICU's !

120 ICU beds!

4 ICU (MUH)

SICU (MUNC)

1 MICU (MOC)

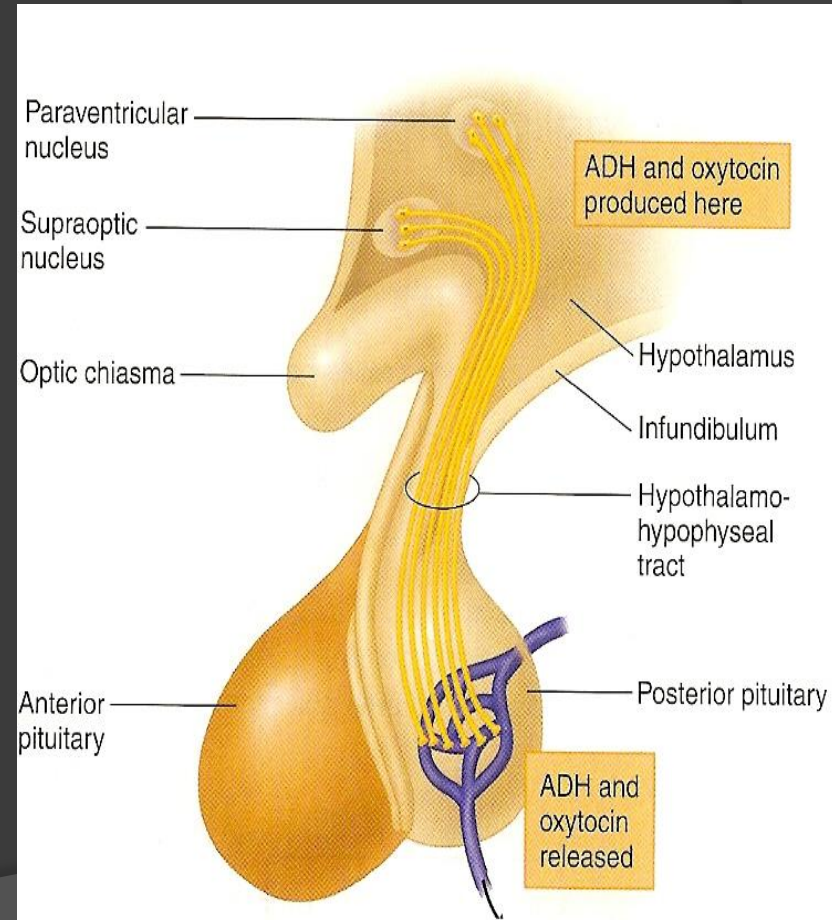
SICU (MGC)

2 MICU, 1 SICU  
(MEH)

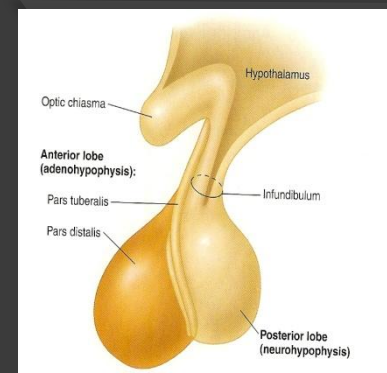


# The posterior pituitary gland

- Composed mainly of cells called 'Pituicytes', which act as packing & supporting cells.
- Stores & releases hormones into the close capillaries.
- These hormones are produced in hypothalamus.

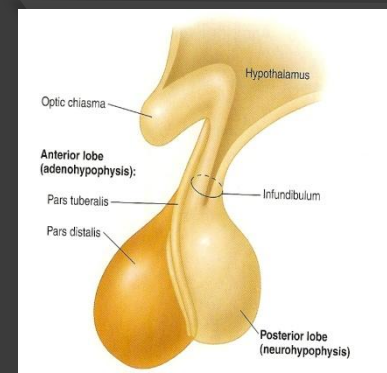


## The posterior pituitary gland hormones



- **Posterior pituitary gland releases 2 hormones:**
  1. Antidiuretic hormone (ADH), or arginine vasopressin (AVP).
  2. Oxytocin
- Both hormones are produced in hypothalamic nuclei:
  - Supraoptic nucleus → (ADH + 1/6 oxytocin)
  - Paraventricular nucleus → (Oxytocin + 1/6 ADH)

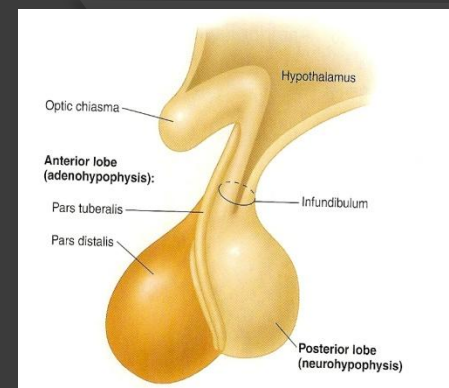
## The posterior pituitary gland hormones ... cont.



- Both hormones are polypeptides, each contains 9 amino acids.
- Both are transported slowly along the ‘hypothalamo-hypophyseal tract’ in combination with carrier protein called ‘neurophysin’, to the nerve endings in the posterior pituitary gland where they are stored.

## The posterior pituitary hormones –

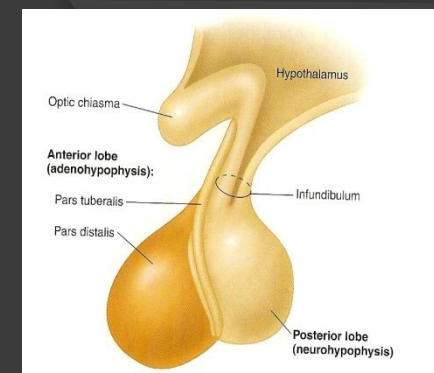
### 1. ADH (vasopressin):



- Antidiuretic hormone (ADH), or arginine vasopressin (AVP), is produced mainly in **SON** of hypothalamus.
- ADH activates (2) second messenger systems:
  1. cAMP
  2.  $IP_3/Ca^{2+}$



# Action of ADH



- **ADH has 2 main effects:**

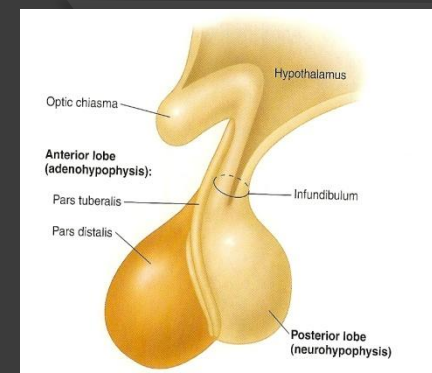
1. ↑ water re-absorption (retention) by distal tubules & collecting ducts of the kidneys → decrease osmotic pressure of the blood.

- \* This effect is regulated by  $V_2$  receptors, through the action of cAMP.

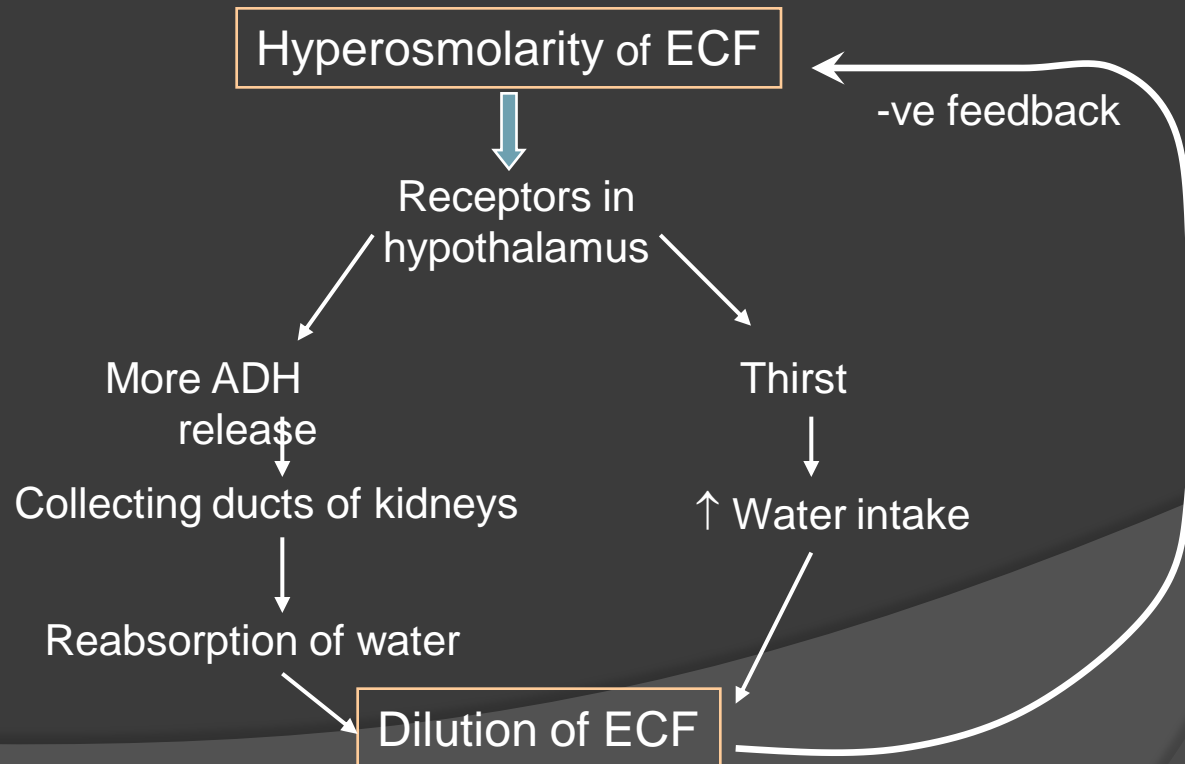
2. Contraction of vascular smooth muscles → generalized vasoconstriction.

- \* This effect is regulated by  $V_1$  receptors, through the action of  $IP_3/Ca^{2+}$ .

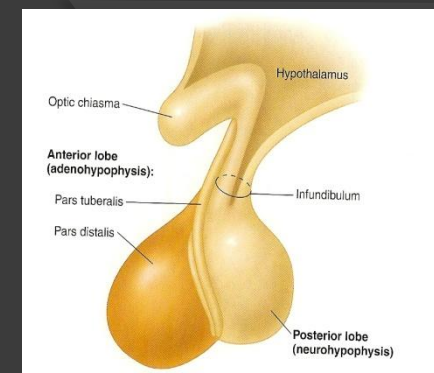
# Control of ADH release



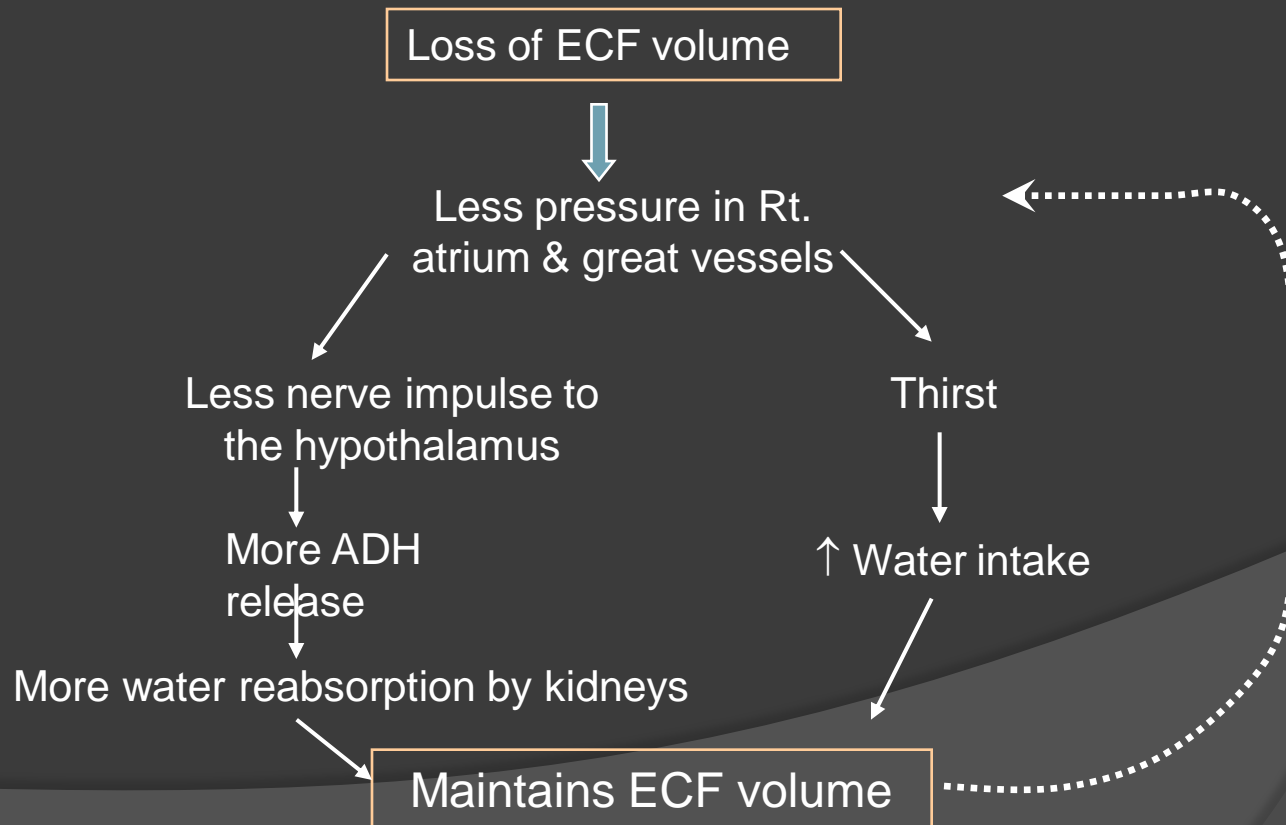
1.  $\uparrow$  in osmotic pressure of the ECF ( $\uparrow$  in plasma osmolality), as in dehydration which will stimulate osmoreceptors in the hypothalamus  $\rightarrow \uparrow$  ADH.



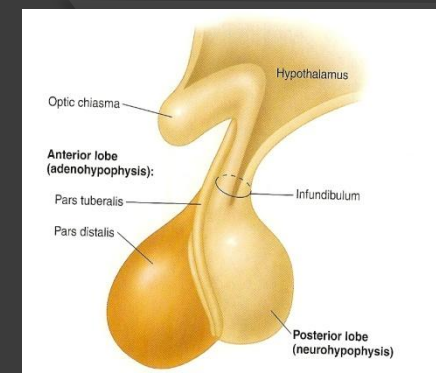
## Control of ADH release ... cont.



2. ↓ blood volume ( $\geq 10\%$ ) → stimulate mechanoreceptors in the great arteries (aorta & carotids) & right atrium → ↑ ADH.



## Control of ADH release ...cont.



3. ↓ arterial blood pressure, due to ↓ blood volume → ↑ ADH.
4. Age: → ↑ ADH secretion → water retention & hyponatremia.
5. Pain, emotional stress & physical trauma → ↑ ADH secretion.
6. Drugs, e.g. morphine, barbiturates, & nicotine → ↑ ADH secretion.
7. Alcohol → ↓ ADH secretion.

# Introduction:

- Arginine vasopressin is released from the posterior pituitary in response to increased serum osmolality or reduced plasma volume. Under normal conditions, the major physiological role of vasopressin is the regulation of water balance. It does not appear to play a major role in the vascular regulation of blood pressure and abnormally high endogenous vasopressin levels (syndrome of IADH secretion) do not produce hypertension.

- Vasopressin, also called antidiuretic hormone is a 9 amino acid peptide, synthesized from a precursor containing neurophysin II, by neurons from the supraoptic and periventricular nuclei and then stored in the posterior hypophysis.

- ⦿ Vasopressin regulates plasmatic osmolality and volaemia via V2 receptor at the level of the kidney and vascular smooth muscle tone via V1 arterial receptors.
- ⦿ In addition, vasopressin interacts with the main hormonal system involved in the response to stress, including hypothalamic pituitary adrenal axis, other anterior pituitary hormones mainly prolactin and growth hormone, RAAS and regulates insulin synthesis and glucose metabolism.

- ⦿ During critical illness, exogenous vasopressin administration showed little effect on the circulating levels of these various hormones except prolactin.



⦿ In shock states, endogenous vasopressin release has an important vasoconstrictor mechanism.

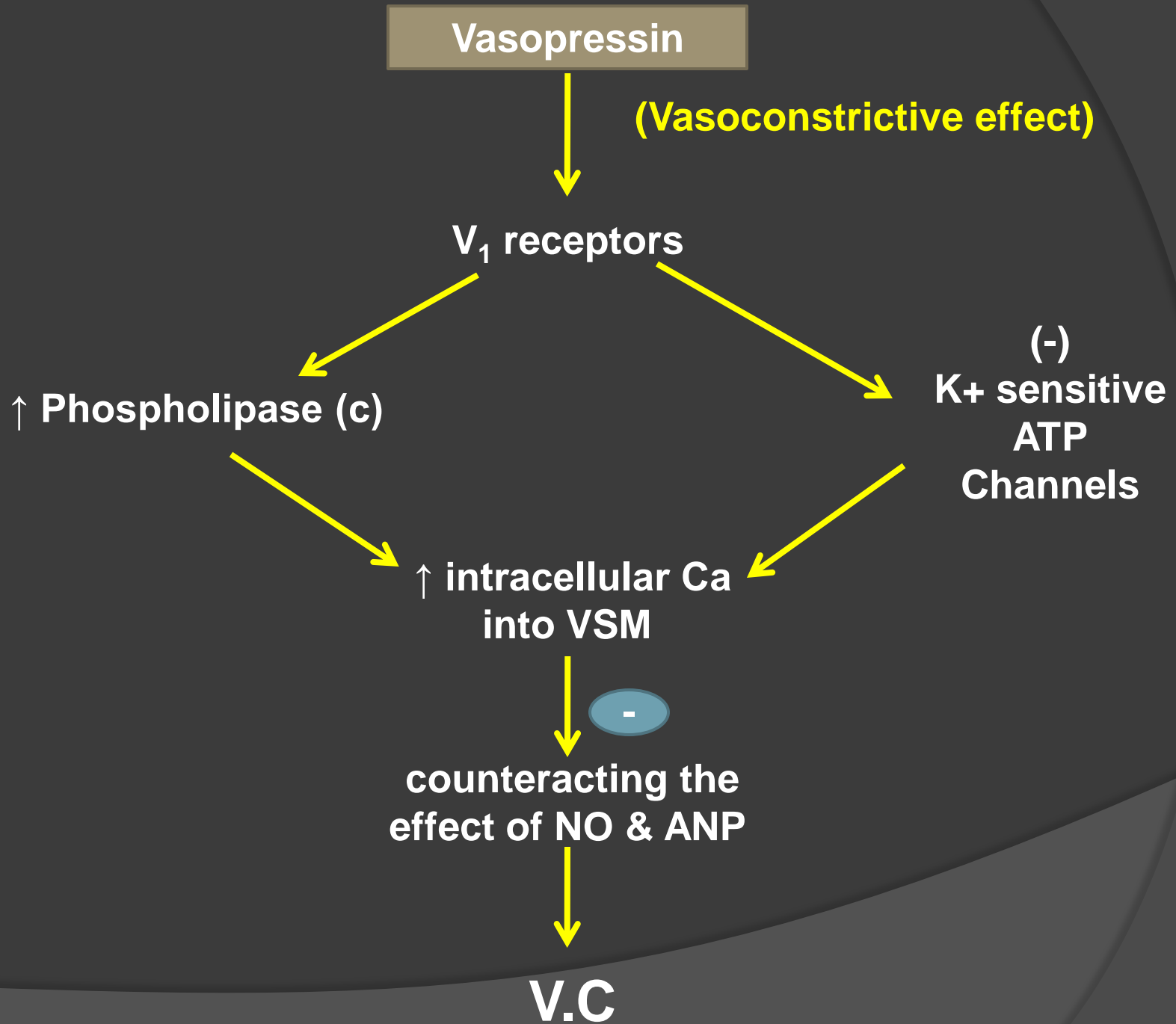
⦿ Plasma level of vasopressin increases within a few minutes of circulatory arrest and also rise in response to:

Hge, sepsis, MI, CPR, epidural and general anesthesia, surgery and exercise.

- ⦿ Prolonged hypovolaemia, sepsis, CPB may lead to vasopressin levels that are inappropriately low this may contribute to the development of pathologic vasodilatation that may occur during advanced shock

- ① The use of low dose vasopressin infusion has become an accepted alternative for the management of vasodilatory shock refractory to catecholamines.

# Mechanism of Action



- ◎ The resulting V.C occurs predominately in the small vessels of the skin, skeletal m, small intestine and fat

- ⦿ Blood flow within the coronaries as well as cerebral, pulmonary and renal vascular bed is preserved; promoting shunting to those areas.

# Vasodilator effect of vasopressin

interplay

$V_1$  Rs

Endothelial

Oxytocin Rs

$V_3$

↑ Nitric oxide  
NO



The antidiuretic effects of vasopressin are mediated through V2 receptors

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graph TD; A[The antidiuretic effects of vasopressin are mediated through V2 receptors] --> B[↑ cAMP in the distal tubules of the kidney]; B --> C[↑ Capillary permeability in the distal tubules and collecting ducts]; C --> D[↑ reabsorption of water]; D --> E[↑ systemic blood volume];
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↑ cAMP in the distal tubules of the kidney

↑ Capillary permeability in the distal tubules and collecting ducts

↑ reabsorption of water

↑ systemic blood volume

- ⦿ In addition to these direct effects vasopressin may also enhance or restore catecholamine sensitivity.
- ⦿ Synthetic vasopressin acts at the same receptor sites as endogenous vasopressin producing an identical response

- ⦿ During shock circulating vasopressin levels initially increase in an effort to maintain cardiovascular homeostasis, reaching values as high as 1,000 pg/ml, normal plasma vasopressin levels (<5pg). After this initial increase, however plasma vasopressin appear a rapidly decline despite continued stress.

◎ It has been speculated that this relative vasopressin deficiency during the later stages of shock may be due to:

1. Impairment in baroreceptor mediated hormone secretion
2. Stemming from depletion of pituitary vasopressin stores.

**Use in adults**

- In many studies 0.04 unit/min exogenous vasopressin → ↑syst. Blood Pressure from 92-146 mm/Hg within 15 minutes and ↑ in SVR (systemic vascular resistance)

- ⦿ Stopping the infusion → rapid fall in blood pr
- ⦿ Restarting 0.01 unit/min → ↑ syst BI,Pr from 83 to 115 mmHg.

- In 2002 Masetti and Colleagues → open label study of vasopressin in 16 adults with hypotension following cardio-pulmonary bypass. All had failed to respond to maximal nor-epinephrine doses  $> 30\text{mcg/kg/min}$ .





- ⊙ Vasopressin – 0.1 to 1 unit/min for average  $58.8 \pm 37.3$  hours.
- ⊙ Syst. BI pr  $\rightarrow$   $\uparrow$  from  $89.6 \pm 7$  to  $119 \pm 10.5$  mmHg and SVR  $\uparrow$  d

- Because vasopressin is destroyed by gastric trypsin. It must be administered parenterally. It is rapidly degraded by enzymes in the liver and kidney.
- Half life → 10 to 35 minutes.

# Drug interaction:

- V.C effect of vasopressin are counteracted by vasodilatory drugs such as nitroglycerine or nitroprusside.
- Antidiuretic effect ↑d by concomitant administration of carbamazepine, chlorpropamide, clofibrate, fludrocortisone, tricyclic anti-depressants.

# Adverse effects:

- ⦿ High dose vasopressin → HTN, bradycardia arrhythmias and MI.
- ⦿ Administration without fluid resuscitation → ischemia e.g G.I.T & kidney.
- ⦿ Ischemic skin & mm → 10 -30% → low dose.
- ⦿ Extravasations → intense local V.C → severe tissue necrosis & gangrene.
- ⦿ Venous thrombosis, tremor, vertigo, sweating, ↓Na, abdominal cramps.

- ⦿ Because of the ability of vasopressin to rapidly increase extracellular water content, it should be used with caution in patients with chronic nephritis, CHF, asthma, epilepsy migraine.

- ⦿ Randomized controlled trial of vasopressin and corticosteroid. Vasopressin in septic shock trial (VASST). The primary finding of this study is that low-dose vasopressin infusion plus corticosteroids was associated with lower 28 day mortality compared with nor-epinephrine plus corticosteroid.

- ◎ The combination of low dose vasopressin infusion plus corticosteroid, compared with nor-epinephrine plus corticosteroid was also associated with less organ dysfunction as shown by more days a live and free from shock, ventilation and renal failure.

**Thank  
You**

