ADH

- Nonapeptide-neurohormone, synthesized in the hypothalamus, stored & secreted in post. Pituitary
- Different names: Vasopressin, arginine vasopressin, argipressin.
- Has oxytocin-like activity which causes side effects with ADH drugs in ♀.

- Pharmacological & Physiological Actions:

Action	Receptor		
	V_1		V_2
	Neurotransmitter in V_1 R's, CNS		• ↑ H_2O reabsorption from collecting ducts (antidiuresis) • ↑ synthesis of certain clotting factors, e.g., VIII & Von Willebrand
	V_{1a}	V_{1b}	
	• Vasoconstriction • ↑ platelet aggregation	• ↑ ACTH release	

- Factors affecting ADH:

Factors	↑ ADH	↓ ADH
Physiologic	• **hypo**volemia, **hyper**osmolarity, pain, stress, nausea, fever, hypoxia • Ang II & prostaglandins	• **hyper**volemia, **hypo**osmolarity • ANP, GABA, Cortisol
Drugs	• Nicotine, **cholinergic agonists**, **β-adrenergics**, tricyclic antidepressants, insulin, morphine, vincristine (cancer drug)	• Alcohol, Phenytoin, **Anticholinergics**, **α-adrenergics**

- **Disorders affecting ADH release:**

Disorder	**Excess** ADH • **inappropriate ADH secretion (SIADH)** → consequence: dilutional hyponatremia	**Deficiency** of ADH • **Diabetes Insipidus (DI)** → consequence: polyuria
Cause	Head trauma, encephalitis, meningitis, oat cell carcinoma	• idiopathic, congenital, familial, gestational DI • hypothalamic surgery, head trauma,malignancies • overproduction Or ↓ clearance of vasopressinase
R_x	• water restriction (Rx of choice) • hypertonic saline solution • Fludrocortisone → ↑ Na^+ blood level • Loop diuretics (Furosemide) • ADH **antagonist**: - **Conivaptan** → V1 & V2 antagonist, IV administration - **Tolvaptan** → V2 antagonist (selective), P.O. E.g., Lixivaptan, Satavaptan *also used in fluid accumulation conditions like CHF & Liver Cirrhosis	• ADH **preparations**: (HRT) 1.**Pitressin** (Natural human ADH) short ½ life 15 mins, IM, SC 2. **Lypressin** (synthetic, porcine source) Short DOA (4hrs), intranasal, IM, IV 3. **Desmopressin** (synthetic ADH analogue) Most widely used, long DOA (12hrs), oral, intranasal, SC, IM 4. **Felypressin** (synthetic ADH analogue) Strong vasoconstrictor, used in dentistry **Clinical uses** of ADH drugs: DI, Nocturnal enuresis, Hemophilia, bleeding esophageal varices

Side effects of ADH drugs:
- Allergy, pallor
- headache, nausea, abdominal pain (♀)
- Anginal Pain (coronary artery vasospasm)
- H_2O intoxication in massive doses
- Gangrene → Desmopressin, V_2 Affinity

ADH Antagonists & Preparations

1) The antidiuretic action of Desmopressin is due to activation of which receptor?

a) V1a receptor
b) V2 receptor
c) V1b receptor
d) V1 and V2 receptor

2) All of the followings are non-renal actions of anti-diuretic hormone except

a) neurotransmitter in the central nervous system
b) promotes hemostasis
c) is a potent vasoconstrictor
d) increases the permeability of the membrane to water

3) Based on the V2 receptor, followings are the therapeutic uses of vasopressin, except:

a) Diabetes insipidus
b) Bedwetting in children
c) Bleeding esophageal varices
d) All of the above

4) What is the primary function of ADH drugs (preparations)?

a) Decrease blood pressure
b) Increase urine output
c) Promote water reabsorption
d) Inhibit sodium reabsorption

5) Which of the following conditions is commonly treated with ADH drugs?

a) Diabetes insipidus
b) Hypertension
c) Hyperthyroidism
d) Asthma

6) Which of the following ADH drugs is commonly used in the treatment of central diabetes insipidus?

a) Desmopressin
b) Furosemide
c) Spironolactone
d) Hydrochlorothiazide

7) ADH drugs are contraindicated in patients with:

a) Hypothyroidism
b) Hypertension
c) Hypernatremia
d) Diabetes mellitus

8) Which of the following ADH drugs is available in intranasal formulation?

a) Desmopressin
b) Vasopressin
c) Conivaptan
d) Tolvaptan

9) Which of the following is an example of a synthetic ADH analog?

a) Vasopressin
b) Desmopressin
c) Conivaptan
d) Tolvaptan

10) A 63-year-oldwoman with euvolemic hyponatremia due to heart failure was started on a medication to help with the excretion of free water with minimal electrolyte loss. The to the concern for osmotic demyelination. What medication was most likely prescribed?

a) Bumetanide
b) Desmopressin
c) Eplerenone
d) Mannitol
e) Tolvaptan

11) Nephrogenic diabetes insipidus (NDI) is a condition in which the kidneys are unable to respond to antidiuretic hormone (ADH), also known as vasopressin. This leads to an inability to concentrate urine and excessive urination, which can cause dehydration, electrolyte imbalances, and other complications.
Drug of choice for nephrogenic diabetes insipidus is:

a) Lypressin
b) Hydrochlorothiazide
c) Terlipressin
d) Vasopressin

Extra

12) Which statement about antidiuretic hormone (ADH) is true?

A) It is synthesized in the posterior pituitary gland
B) It increases salt and water reabsorption in the collecting tubules and ducts
C) It stimulates thirst
D) It has opposite effects on urine and plasma osmolality

13) A patient has nephrogenic diabetes insipidus. Of the following options, which outcome would be expected or which intervention would be suggested?

A) Expected outcome: decreased plasma sodium con- centration
B) Expected outcome: increased secretion of ADH from the supraoptic and paraventricular nuclei
C) Expected outcome: high urine osmolality
D) Suggested intervention: water restriction
E) Suggested intervention: ADH antagonists (vaptans)

Answers:

1) B	**2) D**	**3) D**
4) C	**5) A**	**6) A**
7) C	**8) A**	**9) B**
10) E	**11) B**	**12) D**
13)B		

NOTES:

Q2 Explanation: ADH has several non-renal actions. it acts as a neurotransmitter in the central nervous system, where it plays a role in social behavior, memory, and learning. It also promotes hemostasis by causing vasoconstriction and increasing platelet aggregation, which can help to prevent bleeding. In addition, ADH is a potent vasoconstrictor, which can increase blood pressure by constricting blood vessels. This effect is mediated by a specific type of receptor called V1 receptors.

Q3: Nocturnal enuresis → bedwetting in children

Q11 Explanation: Two types of diabetes insipidus: either **(Central DI)** due to insufficient secretion of ADH from pituitary also known as ADH deficiency, drugs of choice are ADH drugs (preparations) **OR** **(Nephrogenic DI)** failure of the kidneys to respond to ADH where thiazides are used for Tx.

Uterine Stimulants

Oxytocin

- MOA: ↑ intracellular Ca^{+2} → depolarization → contraction of uterine muscle
  ↑ Prostaglandin release

∴ Clinical **uses**: **labor induction** (*Drug of choice* I.V) & **abortifacient** (I.V, ≥ 20 WG)

∴ most serious side effect is **rupture of uterus**

- ineffective in early pregnancy **X** due to ↓ uterus sensitivity
- Ejects milk by contracting myoepithelial cells of the breast.

∴ Clinical **use**: **breast engorgement** (intranasal)

- ADH-like activity → side effect: water intoxication & hypertension
- Antagonist: tocolytics e.g., Atosiban

Prostaglandins

Drug	**Dinoprostone**	**Dinoprost**	**Carboprost**	**Gemeprost**
PG	PGE_2	PGF_α	$PGF_{2\alpha}$	PGE_1
Use	• Abortifacient • labor induction		• Abortifacient • Postpartum hemorrhage	Prime the cervix & uterine contraction induction
Administration	Pessaries, inserts, gel, tab	IV & Intraamniotic	IM & Intraamniotic	Pessaries

Ergot alkaloids

- ***Drugs of choice for postpartum hemorrhage***
  → potency > oxytocin; produces prolonged, sustained contractions + less toxic
- Examples: Ergonovine, (Methyl)ergonovine
- Administration: IM, Oral
- **Contraindicated** as delivery inducers (↑ fetal distress & mortality)

Uterine Relaxants

- Also known as Tocolytics
- Clinical Use: premature delivery (weeks 20-30) to improve the survival of the newborn
- **Contraindicated** in fetal distress.

β-adrenergics	Magnesium Sulfate
• MOA: ↑cAMP → ↓ cytoplasmic Ca^{+2} • Examples: - Ritodrine: IV, **Highly effective** ∴ most widely used - Terbutaline: Oral, SC, IV • Side Effects: sweating, tachycardia, chest pain	• MOA: Activates Adenylate Cyclase & Stimulates Ca^{+2} dependent-ATPase • IV • Used in premature delivery & pre-eclampsia convulsions

Progesterone	Oxytocin competitive antagonist	PG synthesis inhibitors	Nifedipine
• Dydrogesterone • Oral, IM	Atosiban	• Indomethacin • Meloxicam	-

Drugs Acting on The Uterus

1. The drug used for cervical priming to facilitate labour is
(a) Oxytocin
(b) Stilboestrol
(c) Progesterone
(d) Prostaglanding E2

2. Following delivery of a healthy baby, a young woman begins to bleed extensively because her uterus has failed to contract. Which one of the following drugs should be administered to this woman?
(a) Desmopressin
(b) Octreotide
(c) Oxytocin
(d) Prolactin

3. A 29-year-old woman who was in her 41st week of gestation had been in labor for 12 hours. Although her uterine contractions had been strong and regular initially, they had diminished in force during the past hour. Which of the following drugs would be administered to facilitate this woman's labor and delivery?
(a) Dopamine
(b) Leuprolide
(c) Oxytocin
(d) Prolactin

4. which one of the following is the clinical use of ergot alkaloids?
a) Induction of birth
b) Postpartum bleeding
c) Both

5. The effect of oxytocin on the uterus is?
a) Increase ca influx
b) Increase k influx
c) Decrease ca influx

6. Which one of the following consider as a side effect of oxytocin?
a) Vaginal bleeding
b) Hypertension
c) gangrene

7. A 29-year-old pregnant lady came to the clinic complaining of ankle edema that she noticed 5 days ago. After taking the history she said that she is taking a drug for premature labor but she forgot the name of the drug. Which one of the following drugs she most likely uses?
a) Ergometrine
b) Misoprostol
c) Nifedipine
d) Ritodrine

8. A 16-year-old pregnant girl came to the ER with severe vaginal bleeding. After doing routine procedures it is learned that the baby is dead.
While taking the history the patient told the doctor that her friend gave her a suppository to induce abortion. Which one of the following drugs she most likely took?
a) Dinoprost
b) Dinoprostone
c) Carboprost
d) Oxytocin

9. The drug of choice for controlling postpartum Hemorrhage is:
a) Oxytocin
b) Methylergonovine
c) Dihydroergotamine
d) Prostaglandin E2

10. Select the drug that has been used to suppress Labor:
a) Atropine
b) Ritodrine
c) Prostaglandin E2
d) Progesterone

11. Use of ritodrine to arrest premature labor can cause the following complications except:

a) Tachycardia
b) Fall in blood pressure
c) Hypoglycaemia
d) Pulmonary edema

12. A 36-year-old multiparous pregnant lady (who had cesarean sections for all her previous pregnancies) is now 10 months pregnant, her obstetrician decides to induce labor so he gave her an intra-amniotic injection. After giving birth to a healthy baby the patient complained of abdominal pain and died of a hypovolemic shock a few hours later. Which one of the following drugs did the doctor give her?

a) Carboprost
b) Dinoprostone
c) Oxytocin
d) Ergometrine

13. Which pituitary hormone has a chemical structure most similar to that of ADH?

A) Oxytocin
B) ACTH
C) TSH
D) FSH
E) Prolactin

14. Release of which hormone is an example of neuroendocrine secretion?

A) GH
B) Cortisol
C) Oxytocin
D) Prolactin
E) ACTH

15. For milk to flow from the nipple of the mother into the mouth of the nursing infant, what must occur?

A) Myoepithelial cells must relax
B) Prolactin levels must fall
C) Oxytocin secretion from the posterior pituitary must take place
D) The baby's mouth must develop a strong negative pressure over the nipple
E) All the above

16. Which of the following could inhibit the initiation of labor?

A) Administration of an antagonist of the actions of progesterone
B) Administration of LH
C) Administration of an antagonist of PGE2 effects
D) Mechanically dilating and stimulating the cervix
E) Administration of oxytocin

Answers: 1-D 2-C 3-C 4-B 5-A 6-A 7-C 8-B 9-B 10-B 11-C 12-B 13-A 14-C 15-C 16-C