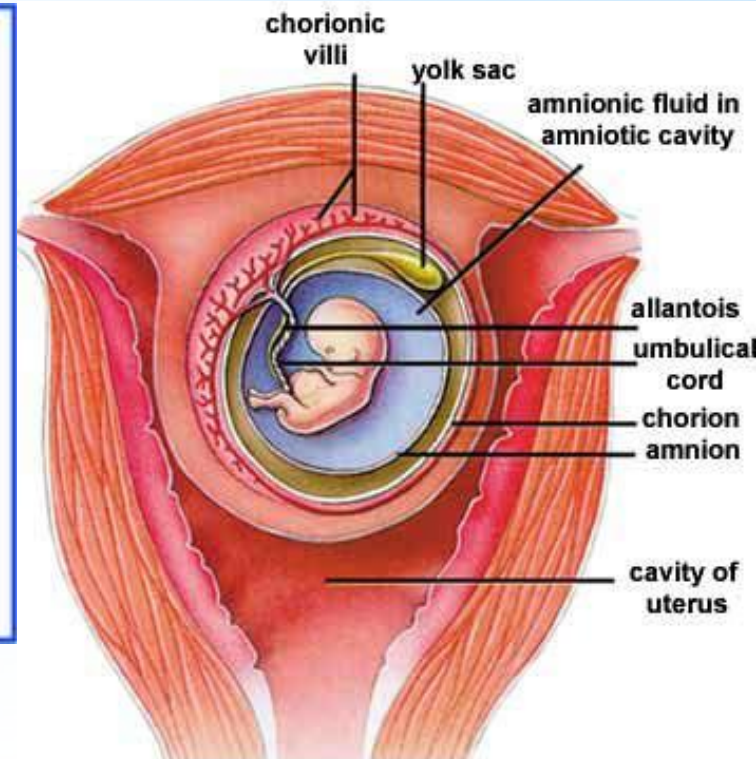
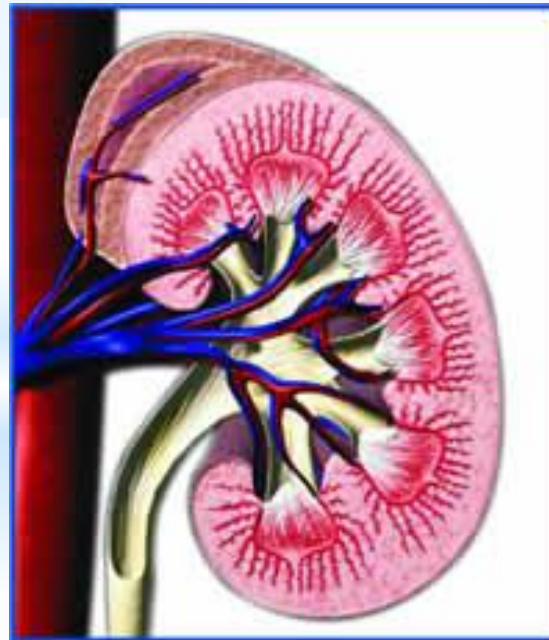
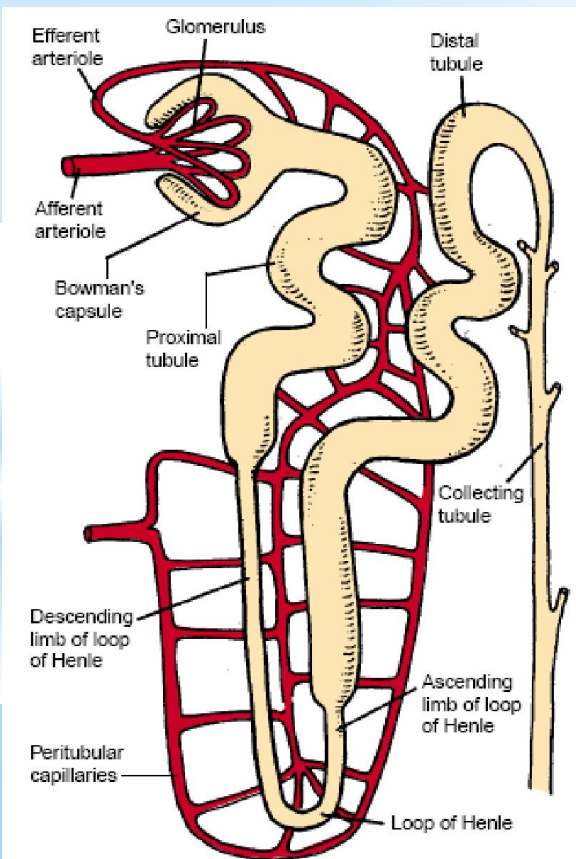


ZSMU Pharmacology Department  
Lecture № 3

# DRUGS AFFECTING THE KIDNEY AND UTERUS FUNCTION

Lecturer - Associate Professor Irina Borisovna Samura



# DIURETICS

I. **Saluretics** - have the Sulfonamide Group -  $\text{SO}_2\text{NH}_2$

1. **Carbonic Anhydrase Inhibitors: Diacarbe** (*Acetazolamide*) – Tab. 0.25 g

2. **Loop Diuretics:**

**Furosemide** (*Lasix*)- Tab. 40 mg, Amp 1%-2 ml

**Ethacrynic acid** – Tab. and amp 50 mg

**Bumetanide** (*Burinex*) – Tab. 1 mg, amp 0.025% - 2 ml

3. **Benzothiadiazines** (acting on initial part of the distal tubule):

• **Thiazide Diuretics:**

**Hydrochlorothiazide** ( tab. 25 and 100 mg)

**Cyclomethiazide** (tab. 0.5 mg)

• **Thiazide-like Diuretics:**

**Clopamide** (*Brinaldix* – tab. 0.02 g)

**Oxodoline** (tab. 25; 50; 100 mg)

**Indapamide** (tab. 2.5 mg)

## II. K<sup>+</sup>- sparing Diuretics:

Amiloride – *Tab. 2.5 and 5 mg*

Triamteren – *Caps 50 mg*

Spiroinolactone – *Tab. 25 mg*



## III. Osmotic Diuretics:

Mannitol – *15% - 200, 400 ml*

Urea – *Vial 30, 45, 60 and 90 g*

## IV. Other diuretics:

Xanthine derivatives:

*Euphylline (Aminophylline)*



Accordingt to the ability to enhance  $\text{Na}^+$  excretion:

## 1. STRONG DIURETICS:

LOOP DIURETICS - Furosemide, Ethacrynic acid      OSMOTIC  
DIURETICS - Mannitol, Urea -

- inhibit  $\text{Na}^+$  reabsorption by up to 10-25%

## 2. AVERAGE STRENGTH:

THIAZIDES - Hydrochlorothiazide, Oxodoline -

- inhibit  $\text{Na}^+$  reabsorption by up to 5-10%

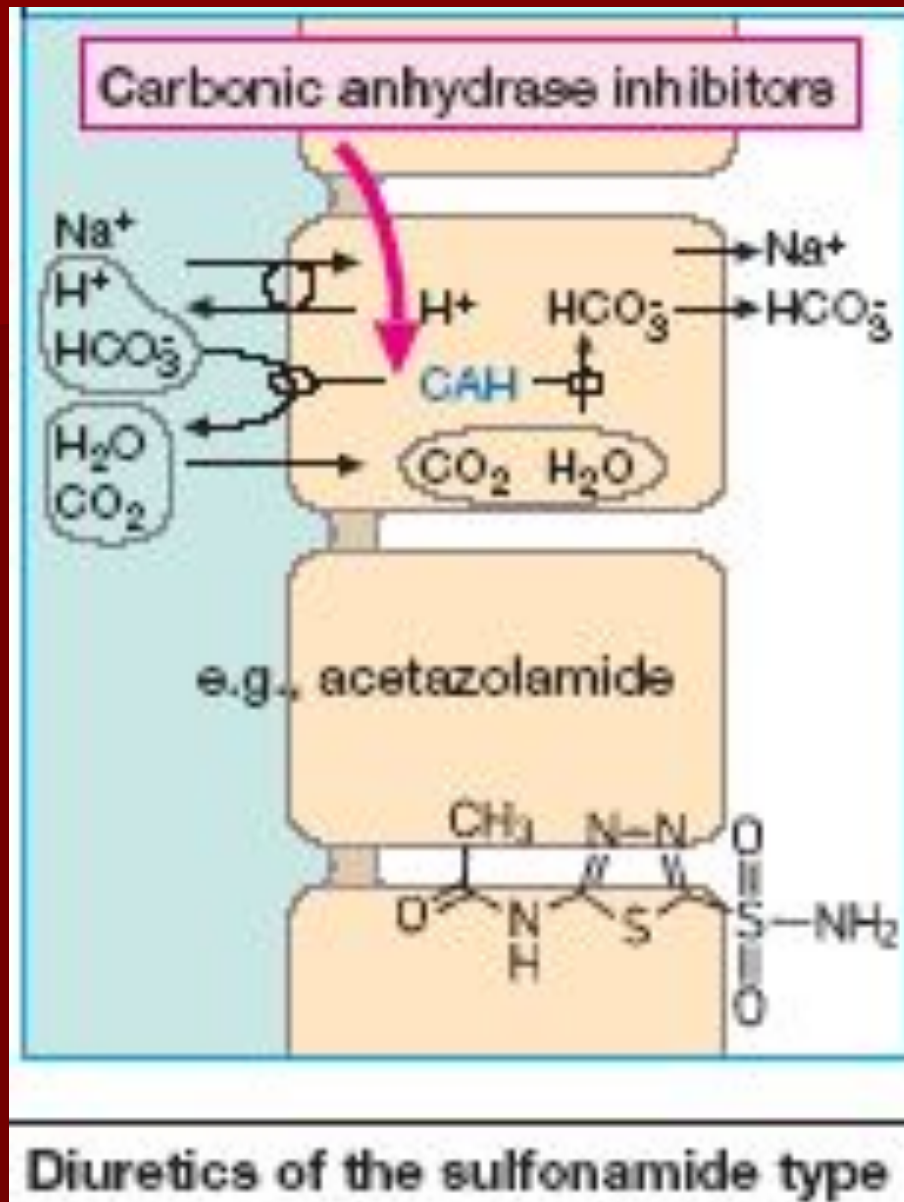
## 3. WEAK DIURETICS:

$\text{K}^+$ -SPARING - Spironolactone, Amiloride

Carbonic Anhydrase Inhibitor - Diamoxide -

- inhibit  $\text{Na}^+$  reabsorption by up to < 3%.





# **CLINICAL USES OF DIACARB:**



- **GLAUCOMA - at Open-Angle Glaucoma**
- **EPILEPSY - both Generalized and Partial -**
  - **the Severity and Magnitude of seizures**
  - **ACUTE MOUNTAIN SICKNESS**
  - **PULMONARY-CARDIAC FAILURE**

## 2. LOOP DIURETICS

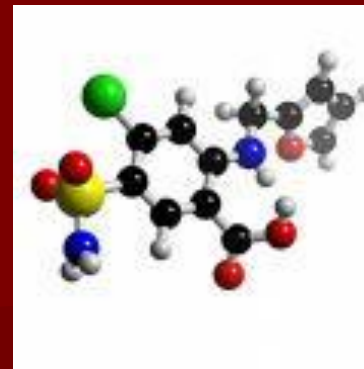
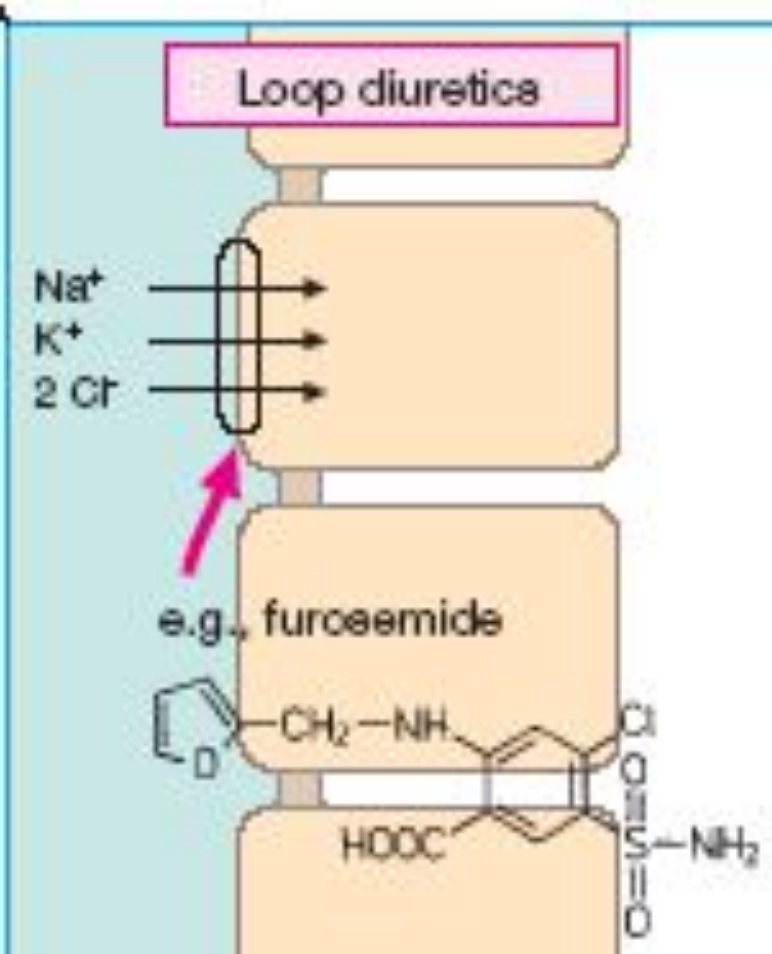


Furosemide (*Lasix*) – Tab. 40 mg

Amp. 1%-2 ml

Ethacrinic acid – Tab. and Amp. 50 mg

Bumetanide (*Burinexe*) – Tab. 1 mg



## Mechanism of action of Loop Diuretics:

They produce  **$\text{Na}^+ / \text{K}^+ / 2\text{Cl}^-$  cotransport inhibition** of the Luminal Membrane in the Proximal Part of the Ascending Loop of Henle =>

=> increase the excretion  **$\text{Na}^+$ , Water,  $\text{Cl}^-$ , and  $\text{K}^+$**





# CLINICAL USES of LOOP DIURETICS

1. Pulmonary Edema
2. Refractoriness to Thiazides
3. Prophylaxis of Acute Renal Hypovolemic Failure
4. Hypercalcemia



# Adverse Effects of Loop Diuretics:

1. Ototoxicity
2. Hyperurecemia
3. Acute Hypovolemia: with the possibility of Hypotension, Shock, and Cardiac Arrhythmias
4.  $K^+$  depletion: the loss of  $K^+$  from cells in exchange for  $H^+$  => **Hypokalemic Alkalosis**



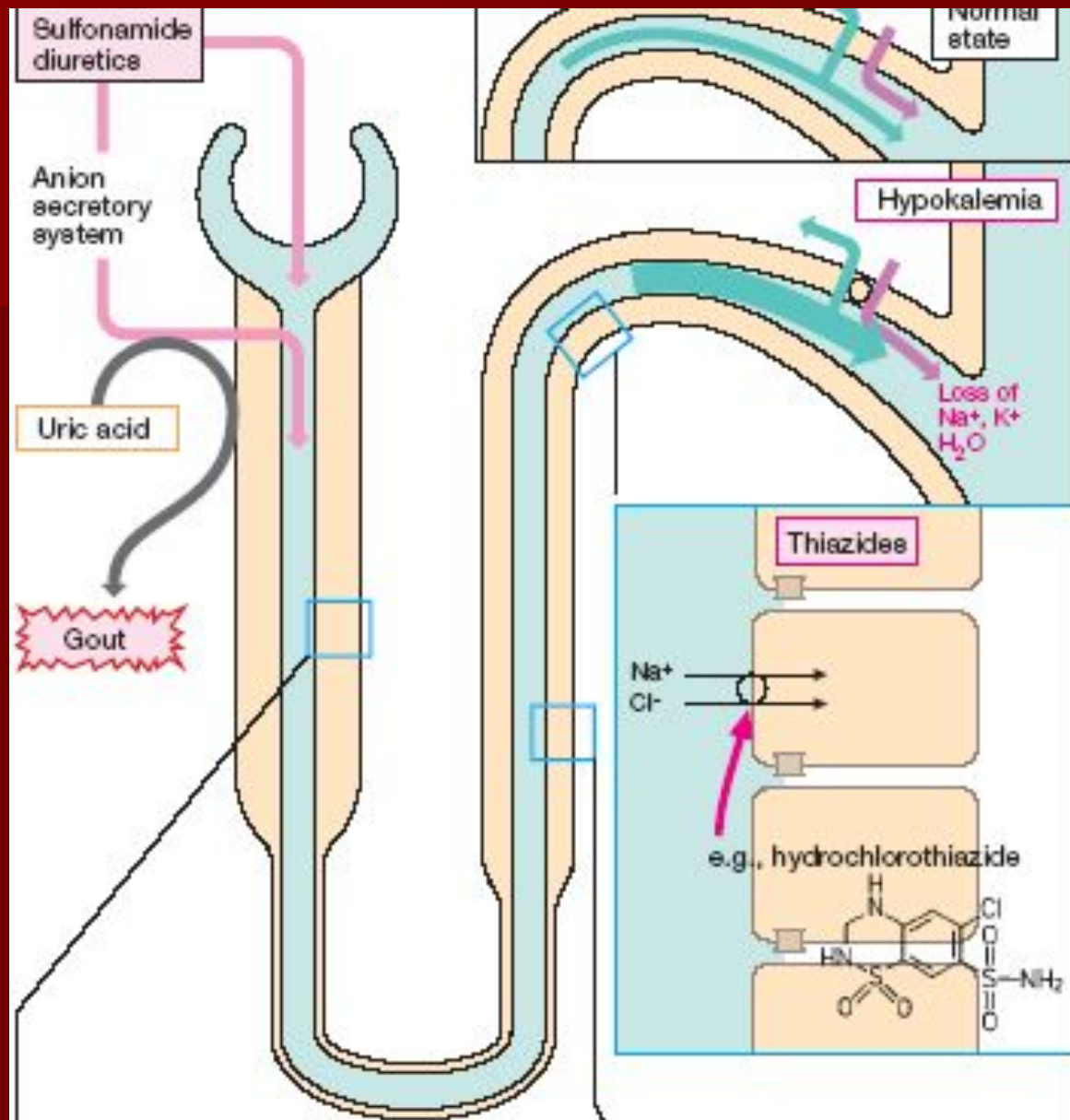
## THIAZIDE DIURETICS:

Hydrochlorothiazide – tab. 25 and 100 mg

Cyclomethiazide – tab. 0.5 g

Oxodoline – tab. 25; 50; 100 mg





**THIAZIDES:** Inhibition a Na<sup>+</sup>/Cl<sup>-</sup> cotransport

# CLINICAL USES OF THIAZIDES:

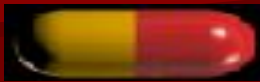
1. Hypertension
2. CHF. Thiazides can be the diuretic of choice  
in ↓ *Extracellular Volume*  
If the *thiazide* fails - *Loop diuretic*
3. Hypercalciuria:  
**Thiazides** inhibit urinary  $\text{Ca}^{2+}$  excretion
4. Diabetes Insipidus.





## ADVERSE EFFECTS of THIAZIDES :

1. Hypokalemia
2. Hyperglycemia and Glycosuria.
3. Hyperuricemia - □ Plasma Urate Levels => **Gout**
4. Hyperlipidemia





ALDOSTERONE promotes the reabsorption of Na+

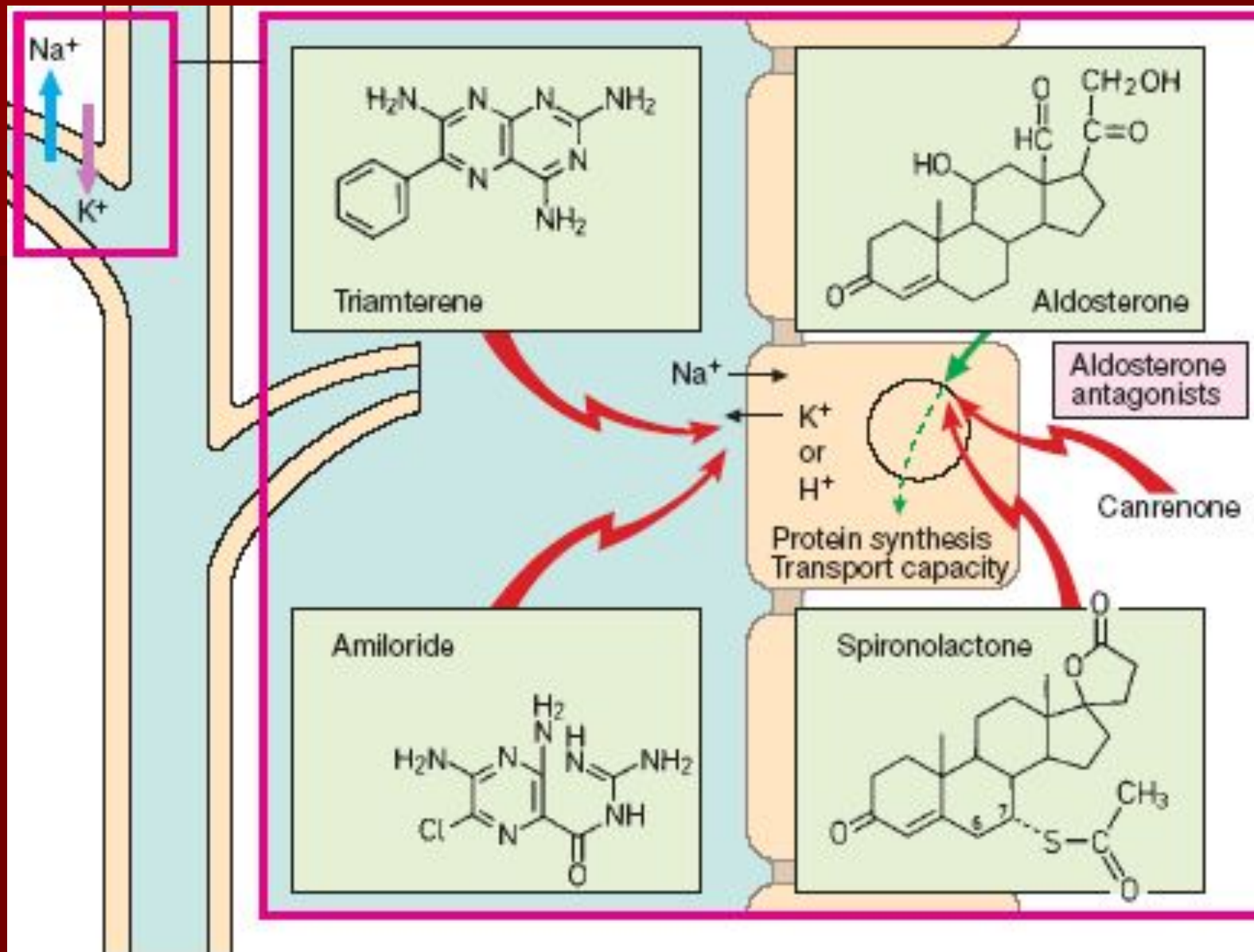
(Cl<sup>-</sup> and H<sub>2</sub>O follow) in exchange for K+.

Hormonal effect on protein synthesis => augmentation of the reabsorptive capacity of tubule cells.

*SPIRONOLACTONE* - a synthetic *aldosterone antagonist* that competes with **aldosterone** for intracellular cytoplasmic receptor sites =>

Retention of K<sup>+</sup> and Excretion of Na<sup>+</sup>.





Potassium-sparing diuretics

# Clinical uses of Spironolactone:

- Edemas
- Secondary Hyperaldosteronism –  
Liver Cirrhosis with Ascites

# Adverse effects of Spironolactone:

- Gynecomastia
- Hyperkalemia
- Lethargy
- Mental Confusion



## Triamterene and Amiloride:

- Block  $\text{Na}^{\pm}$  transport channels =>  
=>  $\square \text{Na}^+ - \text{K}^+$  exchange
- Have  $\text{K}^+$ -sparing diuretic actions
- the ability to block  $\text{Na}^+ - \text{K}^+$  exchange **does not depend on the presence of aldosterone**
- Have diuretic activity even in individuals with Addison's disease.
- are frequently used in combination with other diuretics for their  $\text{K}^+$ -sparing properties:  
they prevent  $\text{K}^+$  loss that occurs with **thiazides** and *Furosemide*.

### III. OSMOTIC DIURETICS:

**Mannitol** Vial 15% - 200, 400 ml

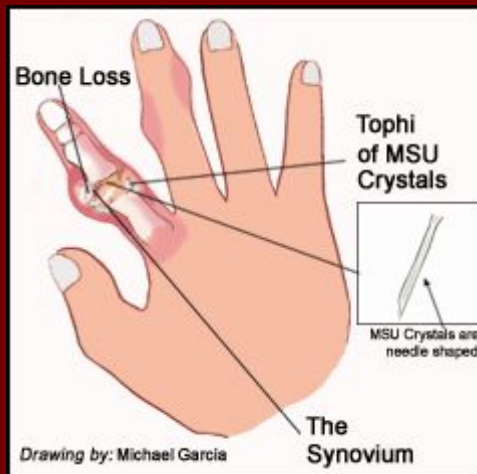
**Urea** – Vial 30, 45, 60 and 90 g

- are filtered through the glomerulus
- carry water with them into the tubular fluid
- are used to produce increased water excretion rather than  $\text{Na}^+$  excretion
- a mainstay of treatment for patient with:
  - Increased Intracranial Pressure
  - BRAIN EDEMA
  - Acute Renal Failure due to shock, drug toxicities and trauma.

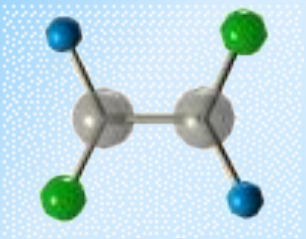


**GOUT** - a metabolic disease in which plasma **URATE** concentration is raised because of overproduction or impaired secretion of **PURINES**

- Intermittent attacks of Acute Arthritis produced by **Urate Crystals Deposition**







## ANTIGOUTY AGENTS

### 1. Inhibitors of Uric Acid synthesis:

**Allopurinol** - *Tab. 0.1 g*

### 2. Inducers of Uric Acid excretion -

#### **Uricosuric Agents:**

**Anturan** (*Sulfinpyrazone*) - *Tab 0.1 g*

**Probenecid** - *Tab. 0.5 g*

**Ethamid** - *Tab . 0.35 g*

**Urodan** - granules 100 g

**Urolesan** - vial 15 ml

### 3. Inhibiting leukocyte migration into the joint:

**Colchicine:** *Tab. 2 mg, 0.5% Ointment*

a *Colchicum autumnale* -

Meadow Saffron alkaloid



### 4. Anti-inflammatory and analgesic drugs: **NSAIDs:**

**Indomethacin, Aspirin, Diclofenac-sodium**





**URODAN**— granules 100.0 g -

1 teasp. in  $\frac{1}{2}$  glass of water 3-4 times a day  
before meals

Contains:

*Piperazine phosphate*

*Hexamethylenetetramine*

*Na<sup>+</sup> and Li<sup>+</sup> benzoates*

*Na<sup>+</sup> phosphate*

*Na<sup>+</sup> hydrocarbonate*

*Tartaric acid, sugar*



■ **UROLESAN** - vial 15 ml: 8-10 drops on a bit of sugar

Contains:

Fir Oil

Peppermint Oil

Castor Oil

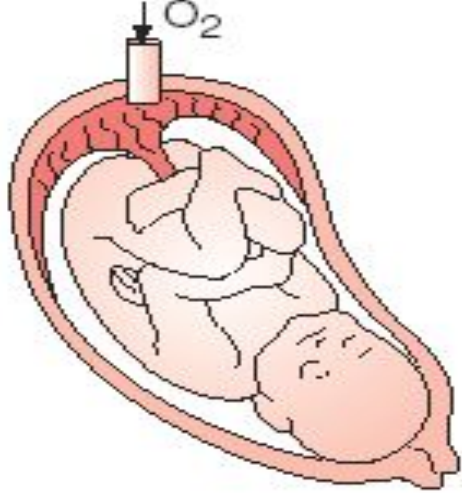
Hop Cones

Extract from Carrot Seeds

Extract from Origanum Grass







# Agents Affecting the Uterus Function

Inhibition of labor

$\beta_2$ -  
Sympathomimetics

Induction of labor

Oxytocin

Prostaglandins  
 $F_{2\alpha}$ ,  $E_2$



# AGENTS AFFECTING MAINLY THE UTERUS CONTRACTILITY

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## 1. Enhancing mainly the Contractive Activity:

Oxytocin - amp. 5 units/mL

Pituitrin -amp. 5 units/mL

Dinoprost (PG F<sub>2α</sub>) – amp. 0.1%-1 ml

Dinoprostone (PG E<sub>2</sub>)-amp. 0.1%-0.75 ml

Tab. 0.5 mg, Vaginal gel 1 mg

Misoprostole (PG E<sub>1</sub>)

Ru-486 (Anti Progestin)



**OXITOCINE** (amp. 5 units/ml) -

□ **Na<sup>+</sup> permeability** of *uterine myofibrils*,  
indirectly Stimulating the Contraction of  
Uterine Smooth Muscle.

The threshold for response **is lowered**  
in the presence of □ **ESTROGEN**





## Clinical uses of OXITOCINE:

- to induce or augment Labour when the Uterine muscle is not functioning adequately
- to treat Postpartum Haemorrhage
- to induce "*Milk let-down*"



# DINORPOSTONE (PG E<sub>2</sub>)

amp. 0.1%-1 ml,  
vaginal supp. 20 mg

- Stimulates myometrial contractions in the gravid uterus similar to the contractions of term labor.
- Softens the cervix by  $\square$ proteoglycan content and changing the biophysical properties of collagen



## CLINICAL USES:

Induction

Induction / augmentation of labour

Cervical priming

Postpartum hemorrhage

**RU-486** - is an antiprogestin (**Antigestagen**) –  
it has been combined with  
an oral oxytocic PG **MISOPROSTOL**  
to produce early abortion.



## 2. TOCOLYTICS



- $\beta_2$ -AMs: *Fenoterol, Terbutaline, Ritodrine*
- $\text{MgSO}_4$  and  $\text{Mg}^{2+}$  agents
- $\text{Ca}^{2+}$  Channels Blockers - *Nifedipine, Diltiazem*
- Blockers of PGs' synthesis - *Indomethacin*
- Phosphodiesterase Blockers - *Aminophylline*
- General Anesthetics: *Sodium oxybutirate*

## B. Agents Enhancing mainly Tonus of Myometrium

### 1. Plant Origin - Alkaloids and Preparation of *Ergot*

Ergotamine maleate – *amp. 0.02%-1 ml*      Ergotal –  
*amp. 0.05%-1 ml*

Ergotamine hydrotartrate

### 2. Synthetic agents:

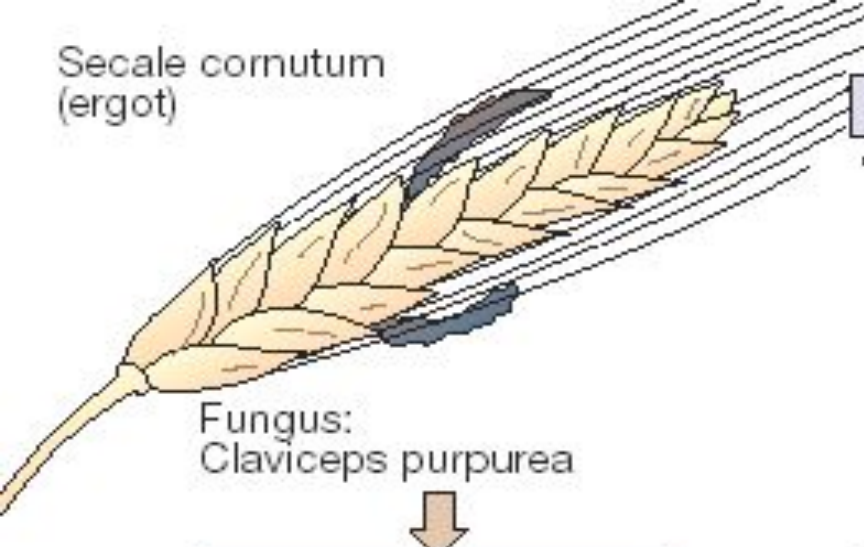
Cotarnine chloride

Anaprilin





Secale cornutum (ergot)



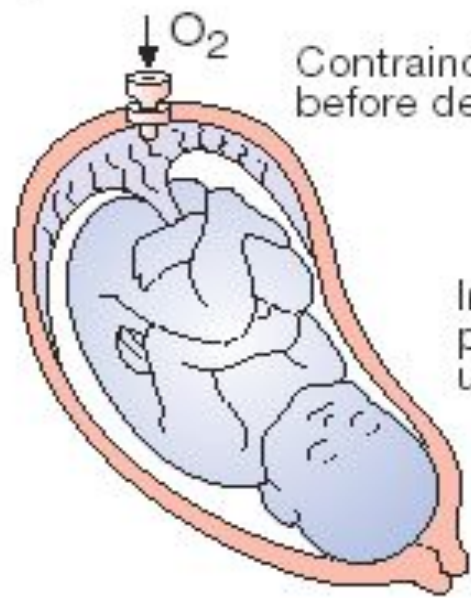
Fungus: Claviceps purpurea

Secale alkaloids

Effect on vasomotor tone

Tonic contraction of uterus

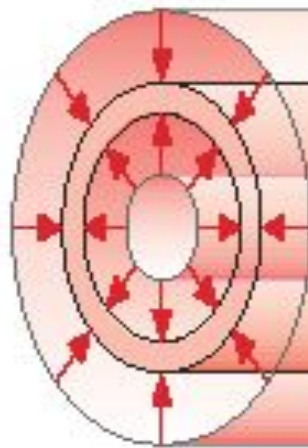
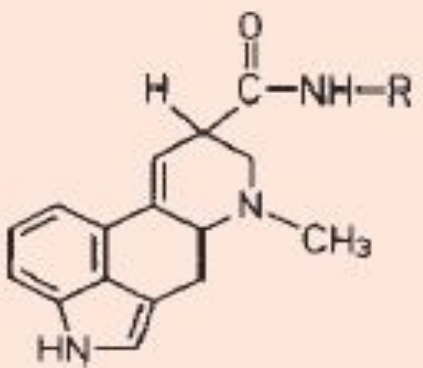
e.g., ergometrine



Contraindication: before delivery

Indication: postpartum uterine atonia

e.g., ergotamine



Fixation of lumen at intermediate caliber

# ERGOT ALKALOIDS

- *Ergotamine maleate*
- *Ergotamine hydrotartrate*
- *Ergotal*
  - act on several types of receptors.
- Effects include Agonist, Partial Agonist, and Antagonist actions at :
  - $\alpha$  - Adrenoreceptors
  - Serotonin Receptors
  - Agonist actions at CNS Dopamine Receptors.
- A Powerful Stimulant Effect on the Uterus appears to combine  $\alpha$ -Agonist, Serotonin and other effects.

## Adverse Effects of ERGOT ALKALOIDS:

- Nausea, vomiting, diarrhea
- Dementia with florid hallucinations
- Prolonged Vasospasm => Gangrene
- Stimulation of uterine smooth muscle, which in pregnancy may result in abortion.

### Creeping sickness - Ergotism -

ergot poisoning, producing either burning pains **and** eventually gangrene in the limbs **or** itching skin and convulsions

# C. Agents Reducing Tonus of the Uterine Neck

- M-cholinoblockers: *Atropine sulfate*
- Myotropic spasmolytics:  
*Papaverine hydrochloride*  
*No-spa*
- Prostaglandins:  
*Dinoprost*  
*Dinoprostone*





*Thank you for  
attention!*