Lec 7

notes

- ↑ in hydrostatic or ↓ in oncotic pressure of peritubular capillaries leads to ↓ net reabsorption so fluid accumulates in interstitial space & leaks through tight junctions of tubule cells

now lets discuss hormones that affect Reabsorption

Aldosterone

- stimulated by angiotensin II due to hypovolemia from renal cortex & acts on late distal, cortical, & medullary collecting tubules

effects principal cells by:

- ↑ Na^+ reabsorption by ↑ activity of Na^+/K^+ ATPase
- ↑ K^+ secretion by ↑ activity of Na^+/K^+ channels

effects intercalated cells by:

- ↑ H^+ secretion

Excess Aldosterone (Conn's Syndrome/Primary aldosteronism)

- A condition that results in: ↑ Na^+ retention & hypokalemia
  - water retention → hypertension
- ↑ H^+ secretion → leading to Alkalosis

Aldosterone deficiency (Addisons Disease)

- Adrenal glands dont secrete aldosterone
- Na^+ wasting (more Na^+ in urine), hyperkalemia
  - hypotention due to water loss

- Acidosis from ↓ H^+ Secretion

Control of Aldosterone Secretion

- Mainly activated due to released Angiotensin II
  - ↳ released by Renin
- ↑ plasma K^+ levels stimulate Aldosterone release
- ACTH also plays a role in Aldosterone release
- Atrial Natriuretic factor (ANF/ANP) & ↑ plasma Na^+ inhibit Aldosterone release

Angiotensin II (ATII)

- Affects Reabsorption, especially Na^+ by:

Stimulating Aldosterone Secretion

Directly ↑ Na^+ Reabsorption

- directly on proximal, loop, distal, & collecting tubules transporters by ↑ activity of Na^+/K^+ ATPase, Na/HCO_3 Cotransport, & Na^+/K^+ exchanger

Constricting efferent arterioles

- will ↓ peritubular capillary hydrostatic pressure to ↑ reabsorption
- ↓ Renal plasma flow will ↑ FF → ↑ peritubular oncotic pressure → ↑ reabsorption

Blocking effect of AT II on Reabsorption by:

- ACE inhibitors (captopril, benazepril, Ramipril)
- AT II antagonist (losartan, candesartan, irbesartan)
- Renin inhibitor (aliskirin)

- they work by ↓ ATII & aldosterone secretion → inhibit Na^+ reabsorption in all sections of nephron → ↓ efferent arteriolar resistance → ↑ peritubular hydrostatic pressure → ↓ net reabsorption = natriuresis, diuresis, ↓ BP

Antidiuretic Hormone (Vasopressin)

- secreted by posterior pituitary to ↑ H_2O reabsorption in distal & collecting tubules = ↓ in urine volume, & ↑ urine concentration

* important controller in extracellular fluid osmolarity

MOA

Vasopressin binds V_2 receptor (g-protein coupled) → activates CAMP → activates PKA → phosphorilates aquaporins (AQP-2) → water reabsorption via osmosis

This mechanism depends on negative feedback

- when extracellular osmolarity ↑, osmoreceptors in hypothalamus stimulate ADH secretion from pituitary to ↓ H_2O excretion

ADH Abnormalities

- Inappropriate ADH Syndrome (Excess ADH)
  - ↓ plasma osmolarity due to ↑ H_2O reabsorption & hyponatremia
- Central Diabetes insipidus (insufficient ADH)
  - ↑ plasma osmolarity, hypernatremia, excessive thirst

Atrial Natiuretic Peptide (ANP)

- Diuretic hormone secreted by Atria in response to stretch from ↑ BP
- Inhibits Na^+ reabsorption
- Inhibits Renin & ADH release
- Vasodialator on efferent arterial → ↑ GFR & FF → ↓ reabsorption & ↑ excretion
- minimizes blood volume & ↓ BP

Parathyroid Hormone (PTH)

- released from parathyroid in response to ↓ extracellular Ca^{++}
- ↑ Ca^{++} reabsorption in Kidney's & gut
- ↓ phosphate reabsorption by kidney

* releases Ca^{++} from bones; activates vitamin D3 to ↑ intestinal reabsorption of Ca^{++}

Sympathetic Nervous System

- Catecholamines (epi & norepi) stimulate Na^+ reabsorption by ↑ activity of transporters, & stimulates Renin release

* under high sympathetic stimulation, GFR & RBF ↓

Effects of Renal Arterial Pressure on Urinary Na^+ Excretion

- normal mean arterial pressure = 100 mm hg
- if Na^+ intake ↑ beyond normal, MAP will ↑
- this results in ↑ urinary Na^+ output called pressure natiuresis
- Pressure natiuresis causes ↓ Na^+ reabsorption, inhibition

of renin angiotensin system & aldosterone; ↑ release of intrarenal natiuretic factors (postaglandins, EDRF) to ↑ GFR & ↓ Na^+ reabsorption

- chronic changes in MAP leads to faster pressure natiuresis response, so Na^+ output ↑ sharply at a much higher rate than acute MAP changes

Osmotic effect on Reabsorption

- H_2O is reabsorbed by osmosis paracellularly or through aquaporins
- increasing amount of unreabsorbed solutes in the tubules will ↑ osmotic pressure & less H_2O will be reabsorbed

Diabetes mellitus

- glucose secreted into tubule → ↑ osmotic pressure → diuresis & water loss

Osmotic diuretics (mannitol)

- ↑ mannitol conc. in tubules → ↑ osmotic pressure → diuresis

Ways to Assess Kidney Function

- plasma conc. of waste products
- urine specific gravity & concentrating ability
- urinalysis test (glucose, proteins)
- Biopsy
- Albumin excretion
- isotope renal scans
- imaging

- creatine clearance method

- **Clearance** → the rate that substances are removed from plasma

$$Cs \times Ps = Us \times V$$

$$Cs = \frac{Us \times V}{Ps} = \text{urine excretion rate} \;/\; \text{Plasma conc. s}$$

Where: Cs = clearance of substance S
Ps = plasma conc. of substance S
Us = urine conc. of substance S
V = urine flow rate

- **Renal clearance** of substance is the volume of plasma completely cleared of a substance / min by kidneys

* different substances = different clearance

- **glucose & albumen** → **zero clearance** b/c zero excretion

- **filtered substance** that <u>arnt reabsorbed or secreted</u> (inulin, creatine, iothalmate) → their **clearance = GFR**

$$GFR \times Pin = Uin \times V$$

$$GFR = \frac{Uin \times V}{Pin}$$

P_{in} → Plasma concentration of inulin

U_{in} → Urine concentration of inulin

* so we can find GFR

* Substance **completely cleared** should tell us RPF

↓ Cx = renal plasma flow

- **PAH** is filtered, secreted, & almost completely cleared (90% cleared) ... so we use it to estimate plasma flow

$$ERPF = \frac{U_{PAH} \times V}{P_{PAH}}$$

ERPF = Clearance PAH

* b/c 10% is not cleared, **PAH must be corrected** to get RPF ... but calculation is not needed from us