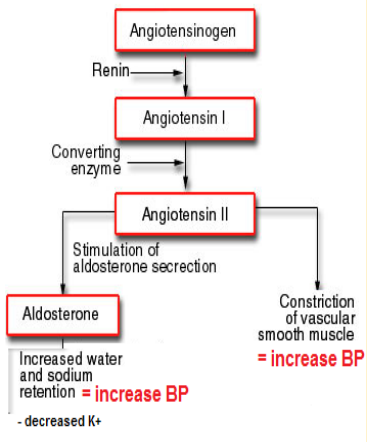
FUNCTIONS OF THE KIDNEY:

- Foreign & metabolic waste excretion
- Gluconeogenesis
- Regulation of:
  - Water & electrolyte balance
  - Extracellular fluid volume
  - Plasma osmolality
  - Red blood cell production
  - Vascular resistance
  - Acid-base balance
  - Vitamin D production

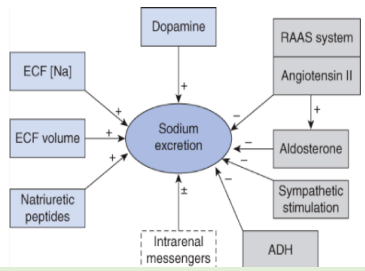
WATER AND ELECTROLYTE BALANCE:

- Nephron reabsorbs most (65%) Na, Cl, bicarbonate
  - > Extent of reabsorption depends on hydration status
- ADH secreted by pituitary gland
  - > Low volume = MORE ADH
  - > High osmotic pressure = LESS ADH
- ADH works at distal nephron (collecting duct) to increase reabsorption of water (↓diuresis)
- Alcohol inhibits release of ADH

RENIN ANGIOTENSIN ALDOSTERONE SYSTEM (RAAS)



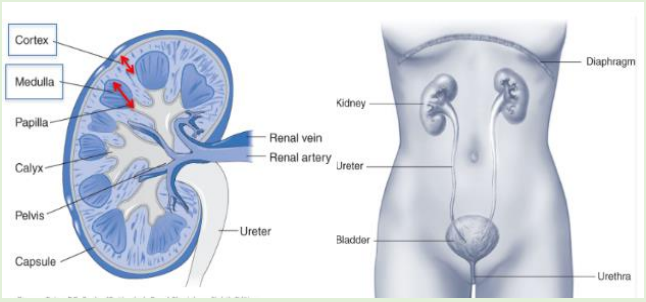
CONTROLLERS OF SODIUM EXCRETION:



HF – Na & H_2O EXCRETION OFF-TRACK:

1. Weakened cardiac muscle (chronic HT, MI, alcohol, infxn, AFIB, valvular disease, etc)
2. Pump volume & efficiency drops off
3. Body compensates: MORE renin, AT2, ADH → MORE sodium/water excretion → MORE BP
4. Stimulates heart
5. Excess fluid volume = edema in lungs/periphery
6. Solves problem temporarily but over time worsens structural changes in heart → further decreasing fxn

ANATOMY OF THE KIDNEY:



- **Afferent arteriole**: feeds blood TO glomerulus
- **Efferent arteriole**: drains blood OUT of glomerulus
- **Bowman's capsule**: hollow sphere of epithelial cells, receives filtrate
- **Glomerulus**: where filtration occurs
  - Fenestrated capillaries
  - Podocyte cell bodies
- **Juxtaglomeruluar apparatus**
  1. Detects flow rate
  2. Detects filtrate composition
  3. Produces renin (hormone that controls renal fxn via modifiying bp)
     - → STIMULATED BY:
       a. LOW renal perfusion pressure
       b. Activation of B1 receptors (epinephrine)

  * ALL will directly/indirectly affect GFR*

EXCRETION:

1. Glomerular Filtration
   - Fluid from glomerular capillaries into Bowman's capsule
   - Large plasma proteins (**albumin**) = 99.98% RETAINED in circulation
   - Protein-bound substances (Ca^{2+}) = RETAINED
   - Electrolytes (Na, K, Cl, bicarb), glucose, urea, amino acids, insulin, ADH = FREELY FILTERED
2. Tubular secretion (LITTLE)
   - K+ (in exchange with Na+)
   - H+ (in exchange with K+)
3. Tubular reabsorption (LOTS)
   - **Urea** (50% reabsorbed)
   - H_2O, electrolytes (99%)
   - **Glucose** (100%)

FILTRATION BARRIER: lined with "fixed polyanions" (-ve charge) = repels -ve macromolecules (plasma proteins) [but not minerals like Cl^- or bicarb)

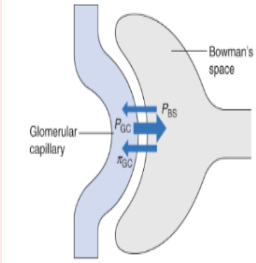
GLOMERULAR FILTRATION RATE:

- GFR = volume of filtrate formed per unit time (mL/min)
- GFR reference values
  1. Normal: ≥ 90 mL/min
  2. Mildly decreased: 60 – 89 mL/min
  3. Moderately decreased: 30-59 mL/min
  4. Severely decreased: 15-29 mL/min
  5. Kidney failure: < 15 mL/min

CONSIDER:

- Healthy young adult male GFR = 125 mL/min (= 180 L/day)
- Average total volume of plasma = 3L = kidney filters through body's plasma 60x per day
- As we age, GFR decreases as the number of functional nephrons diminishes

GFR IS SENSITIVE TO PRESSURES:



Forces

Favoring filtration:

Glomerular capillary blood pressure (P_{GC})

Opposing filtration:

Fluid pressure in Bowman's space (P_{BS})

Osmotic force due to protein in plasma (π_{GC})

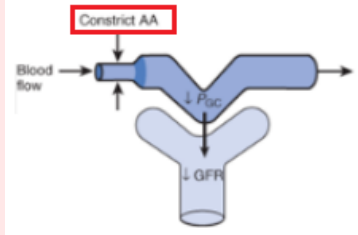
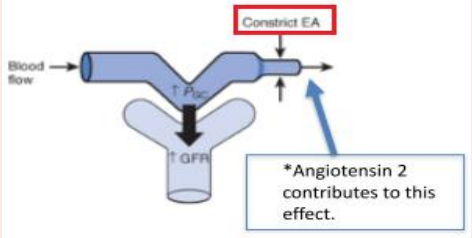
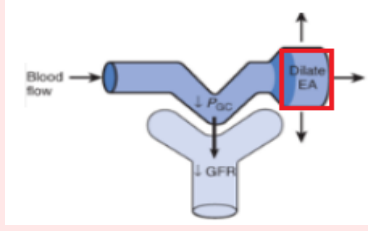
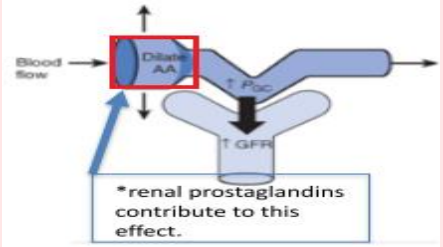
Net glomerular filtration pressure = $P_{GC} - P_{BS} - \pi_{GC}$

OBSTRUCTION:

↑ opposing forces (fluid pressure) because filtrate can't move through

↓ causes net decrease in filtration pressure = decreases GFR

GLOMERULAR CAPILLARY HYDROSTATIC PRESSURE:

	DECREASED GFR	INCREASED GFR
CONSTRICTION		
DILATION		

HEMATOPOIESIS:

- Production of erythrocytes, platelets, and leukocytes from undifferentiated stem cells
- Average person produces > 200 billion new blood cells per day
- Requires 3 essential nutrients **PLUS hematopoietic growth factor:**
  1. IRON: forms iron-porphyrin heme ring and binds oxygen
  2. VITAMIN B12 ([cyano]cobalamin): required for conversion of folate to its cofactors, reducing ability to synthesize DNA for rapidly dividing cells
  3. FOLIC ACID: essential for DNA synthesis
  4. **ERYTHROPOETIN (EPO):** hematopoietic growth factor produced by kidneys; stimulates production & release of reticulocytes when oxygen levels in blood are low (as a result of blood loss, pathological destruction, normal cell death…)

BONE-MINERAL METABOLISM **most dependent upon…**

Calcium	• 99% in bone as hydroxyapatite (complex of calcium & phosphate)
	• Of remaining 1% …
	  ○ Half is free ionized form
	  ○ Half is protein-bound (to albumin)
	• Critical to cell membrane depolarization and neurotransmission
	• Absorbed via GIT

Phosphate	• 85% in bone as hydroxyapatite; 14% intracellular; 1% ECF • Plentiful in our diet, absorbed from the GIT

Vitamin D (calcitriol)	• Binds and stimulates absorption of calcium from GIT
	• Inactive forms → hydroxylation at 25th position (hepatic) and at 1st position (**renal)** → calcitriol (active form)
	  ○ Vit D2 (ergocaliferol) – inactive form ingested in food
	  ○ Vit D3 (cholecalciferol) – inactive form synthesized in skin

PTH (parathyroid hormone)	• 4 glands embedded in thyroid gland in neck
	• Provides hormonal control of calcium and phosphate balance:
	  ○ Keeps plasma level of Ca at a range that doesn't require excitability of cell function
	  ○ Maintains bone integrity

Calcitonin	• Releasesd by thyroid gland • Inhibits action of osteoCLASTS (which inhibits calcium breakdown from bone) • Decreased plasma calcium levels
Fibroblast Growth Factor 23 (FGF 23)	