Renal Physiology
Part II

Bio 219
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Fluid and Electrolyte balance

• As we know from our previous studies:
  • Water and ions need to be balanced in order to maintain proper homeostatic ranges in the body in order to preserve proper functionality
  • Can regulate concentration of specific substances (osmolarity) and/ or total fluid volume
Regulation of ECF osmolarity

- ECF osmolarity affects movement of H₂O in/out of cells
- Normal ECF = 290 mOsm
  - ↑ ECF osmolarity → ↓ ICF volume
  - ↓ ECF osmolarity → ↑ ICF volume
Figure 5.16

Cells placed in distilled water
Cells swell and burst

H₂O

Cells placed in concentrated salt solution
Cells shrink and shrivel

H₂O
Hypothalamus

• Osmoreceptors respond to changes in plasma osmolarity
  • Neurosecretory cells produce ADH (vasopressin), secreted by posterior pituitary
• high ADH levels:                      low ADH levels:
  • ↑ permeability of CD to H2O         • ↓ permeability of CD to H2O
  • ↑ H2O reabsorbed from CD           • ↓ H2O reabsorbed from CD
  • concentrated urine, less H2O lost  • dilute urine, more H2O lost
    (e.g. diabetes insipidus)
ADH Regulation

1. High blood osmotic pressure stimulates hypothalamic osmoreceptors.
2. Osmoreceptors activate the neurosecretory cells that synthesize and release ADH.
3. Nerve impulses liberate ADH from axon terminals in the posterior pituitary into the bloodstream.
4. Kidneys retain more water, which decreases urine output.
5. Low blood osmotic pressure inhibits hypothalamic osmoreceptors.
6. Inhibition of osmoreceptors reduces or stops ADH secretion.

Target tissues:
- Arterioles constrict, which increases blood pressure.
- Sudoriferous (sweat) glands decrease water loss by perspiration from the skin.
Regulation of ECF Volume

- ECF volume affects blood pressure
- Kidneys help control ECF volume via:
  1. Regulation of H2O reabsorption/excretion - controlled by ADH
  2. Regulation of solute reabsorption/excretion
- Na+ and Cl- are the most abundant ECF solutes
- Total amount of Na+ in the ECF affects ECF volume
  - ↑ Na+ in ECF → ↑ ECF osmolarity → ↑ ADH → ↑ H2O reabsorption → ↑ ECF volume
Fluid Imbalances:

• Fluid imbalances may involve change in osmolarity, volume, or both.
  • e.g., hypertonic dehydration: ↑ ECF osmolarity and ↓ ECF volume
  • isotonic dehydration: ↓ ECF volume with normal ECF osmolarity
Electrolyte Balance: Na\(^+\) and K\(^+\) regulation

- most Na\(^+\) and K\(^+\) filtered into nephrons is reabsorbed in the PCT
  - regulated reabsorption and secretion of Na\(^+\) and K\(^+\) in the DCT and upper CD

- **aldosterone** - secreted by the adrenal cortex
  - stimulates Na\(^+\) reabsorption and K\(^+\) secretion in principle (P) cells of DCT and CD
  - activates apical Na\(^+\) and K\(^+\) channels and basolateral Na\(^+\)-K\(^+\) pumps
Aldosterone

• Stimulated by:
  • 1. high plasma [K+]
  • 2. renin-angiotensin-aldosterone system: responds to low BP and low [Na+]
    • juxtaglomerular apparatus
    • granular (juxtaglomerular) cells - sense BP in afferent arteriole
    • macula densa - senses [Na+] in tubular fluid

• renin - enzyme secreted into blood by granular cells
  • in blood, renin converts angiotensinogen to angiotensin I
  • in capillaries, angiotensin converting enzyme (ACE) converts ANG I to ANG II
Renin-Angiotensin-Aldosterone

• Juxtaglomerular Apparatus – area where the distal tubule comes between the afferent and efferent arteriole
  • Consists of the extraglomerular matrix cells, macula densa cells and granular cells
  • Macula densa cells sense [NaCl]. A decrease in [NaCl] will cause the release of a chemical signal to the granular cells to release renin
  • Granular cells produce, store and regulate the release of renin (protease)
• Angiotensin II promotes the release of **Aldosterone** from the adrenal gland
  • Aldosterone is a mineralcortacoid hormone
  • Aldosterone will act on the cells of the distal tubule and collecting ducts to **increase** sodium reabsorption (and therefore also water reabsorption) and decrease potassium reabsorption
Angiotensin II

- angiotensin II effects:
  - 1. vasoconstriction $\rightarrow$ ↑ peripheral resistance $\rightarrow$ ↑ BP
  - 2. stimulates aldosterone secretion $\rightarrow$ ↑ Na+ reabsorption $\rightarrow$ ↑ plasma volume $\rightarrow$ ↑ BP
Atrial Natriuretic Peptide (ANP)

• Synthesized and secreted by cells in the cardiac atria
• Released when pressure (or stretch) in the atrium gets too high, i.e. high BP.
• Causes relaxation of afferent arteriole into the renal corpuscle
• Inhibits release of renin
  – Which will cause an increase or decrease in Na+ reabsorption? Water reabsorption?
ANP and BNP promote local anti-hypertrophic actions

↓ Sympathetic Tone
↓ Salt/water Appetite

Vasodilation
Endothelial Permeability

Aldosterone Inhibition
Natriuresis, Diuresis, Renin Inhibition
Renal Acid-Base Regulation

• Kidneys control excretion of metabolic (non-CO2) acids and bases
• - normally secrete $H^+$ and reabsorb $HCO_3^-$
• - rates of $H^+$ secretion and $HCO_3^-$ reabsorption are adjusted to respond to alterations in pH and $[HCO_3^-]$ of the plasma
• - net result is regulation of plasma $[HCO_3^-]$ and pH
Acid-Base Balance

• Body naturally produces acid from metabolism, respiration and food

• Acid-base balance is maintained by the reabsorption of virtually all filtered HCO$_3^-$ and the secretion of H$^+$

• Most of the bicarbonate is reabsorbed in the proximal tubule (80%) and loop of henle (10-20%) and the rest is absorbed in the distal tubules and collecting ducts

• Acid (H$^+$) is secreted using buffers:
  • HPO$_4^{2-}$ + H$^+$ --> H$_2$PO$_4^-$
  • Kidney hydrolyzes glutamine to produce NH$_3$ and HCO$_3^-$
  • The HCO$_3^-$ is reabsorbed and the NH$_3$/NH$_4^+$ buffers the H$^+$ in the lumen
Renal-Acid Base Regulation

• Negative feedback control

• normal pH = 7.4 and [HCO3-] = 24 mM

• ↓ [HCO3-] and/or ↓ pH → ↑ H+ secretion and ↑ HCO3-reabsorption → ↑ [HCO3-], ↑ pH

• ↑ [HCO3-] and/or ↑ pH → ↓ H+ secretion and ↓ HCO3-reabsorption → ↓ [HCO3-], ↓ pH
Mechanisms of Bicarbonate Reabsorption

• 1. HCO3- in tubular fluid (PCT and DCT) combines with H+ to form CO2 + H2O
  • (catalyzed by carbonic anhydrase in the tubule)
• 2. CO2 diffuses into the tubule epithelial cells
• 3. CO2 is converted to H+ + HCO3- (via carbonic anhydrase inside the cell)
• 4. HCO3- is transported to ECF,
  H+ is pumped back out to the tubule lumen