Urinary system

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Physiology
Mt SAC
Location of Kidney
Functions

• Primary: regulate ECF through urine formation

• Kidneys:
  - regulate volume of blood plasma
  - regulate concentration of waste products
  - regulate concentration of electrolytes
  - regulate acid-base balance
  - produce and secrete hormones
Structure of the kidney

- gross structure
  - capsule
  - cortex
  - medulla
  - renal pyramids
  - renal columns
  - calyces
Micturition reflex

• Internal urethral sphincter
• External urethral sphincter
• Pathway
  - Stretch receptors in bladder wall stimulated
  - Pelvic splanchnic nerves from sacral region of spinal cord respond by stimulating reflex contractions in bladder
  - Internal urethral sphincter relaxes as contractions increase
  - Urge to urinate
  - External sphincter under voluntary control
    • Delay ends contractions temporarily until additional urine accumulates
    • Stimulus resumes
Renal blood vessels
Nephrons
Renal tubules

- Nephrons
  - Cortical
  - Juxtamedullary
- Renal corpuscle
  - Bowmans capsule
  - glomerulus
Formation of Urine: Overview

KEY:

- **Filtration:** Water and solutes smaller than proteins are forced through the capillary walls and pores of the glomerular capsule into the renal tubule.

- **Reabsorption:** Water, glucose, amino acids, and needed ions are transported out of the filtrate into the tubule cells and then enter the capillary blood.

- **Secretion:** $H^+$, $K^+$, creatinine, and drugs are removed from the peritubular blood and secreted by the tubule cells into the filtrate.
Glomerular filtration

- Filtrate: protein-free, acellular
- restriction based on size and electrical charge
- size
  - podocytes
  - <18Å
  - 18-36Å
  - >36Å
- electrical charge
  - negatively charged surface = prevents movement of proteins
Ultrafiltrate

- Starling forces
  - hydrostatic pressure vs. osmotic pressure
- net filtration pressure: 10mmHg
- large surface area
- GFR = volume of filtrate produced by both kidneys/min
  - 115 ml/min in women
  - 125 ml/min in men
Regulation of GFR: Extrinsic

- Sympathetic effects = extrinsic
  - constriction of afferent arterioles in fight or flight
  - results: preservation of blood volume & diversion of blood
Regulation of GFR: intrinsic

• Renal autoregulation = intrinsic
  - ability to maintain relatively constant GFR with changing blood pressure
    • systemic arterial pressure <70mm Hg = dilation of afferent arteriole
    • systemic arterial pressure >70mm Hg = constriction of afferent arteriole

• Tubuloglomerular feedback
  - constriction of afferent arteriole due to increase in filtrate flow detected by macula densa cells
Reabsorption of water and salt

- 180 L of filtrate produced each day
- 99% reabsorbed
- Obligatory water loss = .444L
Reabsorption in the PCT

• filtrate osmolarity = plasma osmolarity
• epithelial cells
  - lower [Na+] than in filtrate
  - Na+/K+ ATPase pumps
  - osmotic gradient
    • Na+
  - electrical gradient
    • Cl-
  - RESULT: incr osmolarity in ECF
    • H₂O follows NaCl
Significance

- 65% H$_2$O + NaCl reabsorbed in PCT
- osmolarity remains unchanged due to equal transport of both substances
Countercurrent multiplier system

• Definition:
  - countercurrent: flow in opposite directions
  - multiplier = positive feedback

• Ascending limb
  - active transport of NaCl
  - impermeable to water

• Descending limb
  - no NaCl transport
  - permeable to water
Additional factors

• Vasa recta
  - around loops of Henle
  - juxtamedullary nephrons
  - countercurrent exchange

• Effects of urea
  - contributes to hypertonicity of tissues
Changes in filtrate osmolarity
Collecting duct: ADH

- Permeable to water, mostly impermeable to NaCl
- ADH increases number of water channels
- small change in % absorption = large changes in the amount of urine produced
Renal Plasma Clearance

• Inulin = measures GFR
  - freely filtered by glomerulus
  - not reabsorbed or secreted
  - not metabolized or produced by kidney
  - does not alter GFR

• para-aminohippuric acid (PAH) = measures renal blood flow
Renal clearance of inulin

- Polymer of fructose not produced, secreted or metabolized in the body
- Filtered without any reabsorption
- Renal plasma clearance = \( V \times \frac{U}{P} \)
  - \( v \) = urine volume per minute
  - \( u \) = [substance] in urine
  - \( p \) = [substance] in plasma
Clearance of PAH

- Not produced in body
- Secreted by PCT
- Cleared from blood in one pass
- total renal blood flow = PAH clearance/volume of plasma
  - On average = 1.1L/min
Renal plasma threshold for glucose

- How much glucose can you have in the blood (plasma) before you see it in the urine?
- Why is there a plasma threshold for glucose in the kidneys?
- Is there a threshold for glucose in the digestive tract?
\[ C_G = \frac{(U_G \times V)}{P_G} \]

- RPF = renal plasma flow = 700 ml/min
- GFR = glomerular filtration rate = 100 ml/min
- \( P_G \) = plasma glucose concentration
- \( U_G \) = concentration of glucose in urine
- \( C_G \) = glucose clearance
- Transporter maximum\( = Tm = 375 \text{ mg/min} \)
A: \( P_G = 1 \text{mg/ml} \)

Reabosorption: 100 mg/min

\( U_G \times \dot{V} = 0 \text{mg/min} \)

Glucose clearance = 0 mL/min

B: \( P_G = 5 \text{mg/ml} \)

Reabsorption: 375 mg/min

\( U_G \times \dot{V} = 125 \text{mg/min} \)

Glucose clearance = 25 mL/min
Renal control of electrolyte and acid-base balance

• Role of aldosterone in Na+/K+ balance
  - sodium reabsorption
  - potassium reabsorption

  remember:
  - $\uparrow$aldosterone $= \uparrow$Na$^+$ reabsorbed $= \uparrow$H$_2$O
    $= \uparrow$blood pressure
  - When Na$^+$ is reabsorbed, K$^+$ is excreted!
Na⁺ reabsorption

• 90% reabsorbed before DCT
• without aldosterone
  - 8% reabsorbed
  - 2% filtered Na⁺ into urine
• with aldosterone
  - all Na⁺ reabsorbed
K⁺ reabsorption

- Normal ECF values range between 3.5-5.0 mmol/L
- 90% reabsorbed in PCT
- without aldosterone
  - all K⁺ reabsorbed in DCT
- with aldosterone
  - K⁺ secretion into DCT & CD
Control of aldosterone secretion

• Stimulus:
  - direct: increase in blood $K^+$
  - indirect: decrease in blood $Na^+$

• Juxtaglomerular apparatus
  - releases renin

• Regulation of renin secretion
  - decreased blood volume
  - sympathetic nervous activity

• Naturetic hormone
  - $Na^+$ and $H_2O$ secretion
Juxtaglomerular apparatus

- **Granular cells**
  - afferent arteriole
  - renin secretion

- **macula densa**
  - Ascending Limb of Loop of Henle
  - renin inhibition
Relationship between Na\(^+\), K\(^+\), & H\(^+\)

- Na\(^+\) reabsorption encourages K\(^+\) secretion = electrical gradient
- Increase extracellular H\(^+\)
  - H\(^+\) into cells
  - drives K\(^+\) into ECF
- DCT and CD
  - H\(^+\) & K\(^+\) secreted as Na\(^+\) reabsorbed
Metabolic Acidosis

Due to:

1. increased intake of acid
2. increased production of acid by metabolism
3. decreased acid excretion by the kidneys
4. increased loss of alkali

Causes

- Diabetic ketoacidosis
- Renal failure
- Diarrhea
- Starvation
- Hypoaldosteronism
Metabolic alkalosis

• **Due to:**
  - Excessive loss of H\(^+\) from body
  - Retaining too much HCO\(_3^-\)
  - Too much HCO\(_3^-\) production (rare)

• **Causes:**
  - Vomiting
  - Loop diuretics/thiazide diuretics
  - Adrenal steroids
Acid-Base Balance

• Adults produce about 100 mmol/day of $H^+$

• **Goal**: maintain relatively constant plasma pH in spite of daily variations in production of acids from metabolism and food intake

• Role of the kidney
  - Reabsorb all $HCO_3^-$ filtered and excreting $H^+$ into urine
    • 90-95% reabsorbed in PCT and DCT
    • Excreting 1-2L of unbuffered urine only eliminates 1mmol/day of $H^+$

  - Generate new $HCO_3^-$
    • Filterable phosphate is primary buffer anion in urine
    • Nitrogen is excreted as ammonium rather than urea, sparing bicarbonate
Reabsorption of HCO$_3^-$

- **Carbonic anhydrase**
  - apical membrane
  - cytoplasm
- **Acidic urine in filtrate**
- **Adjustments**
  - acidosis
    - H$^+$ into filtrate
    - reabsorb HCO$_3^-$
  - alkalosis
    - HCO$_3^-$ excreted
Urinary buffers spare $\text{HCO}_3^-$ for plasma

$\text{Glutamine} \rightarrow \text{ECF} \rightarrow \text{HCO}_3^- + \text{NH}_4^+ \rightarrow \text{ECF} \rightarrow \text{tubules}$

$\text{HPO}_4^{\text{=} \rightarrow \text{HCO}_3^- + \text{H}^+ \rightarrow \text{H}_2\text{CO}_3 \rightarrow \text{H}_2\text{O} + \text{CO}_2 \rightarrow \text{ECF}$

Normal urinary pH = 5 to 7
Clinical applications

• Diuretics
  - inhibit salt and water reabsorption

• Glomerulonephritis
  - autoimmune
  - results: decrease in bv and edema

• Renal insufficiency
  - destruction of nephrons, obstruction, damage
  - result: hypertension, uremia, acidosis

• Pyelonephritis
Glomerulonephritis

- Thickened capillary loops reflect the large number antibodies attaching to surface
- Triggers complement cascade
- Inflammation allows large molecules and blood cells to move out into the filtrate
Kidney disease: Treatment options

• Hemodialysis
  – Home hemodialysis
• Peritoneal dialysis
• Kidney transplant
Artificial Kidney: Hemodialysis
Dialysis Machine
Hemodialysis catheter
Loop configuration
Home hemodialysis
Kidney transplant
Kidney transplant: Harvesting donor organs

- Two punctures and 3-inch abdominal incision allow for laparoscopic harvest of kidney from living donor
Kidney transplant

- Patients own kidneys remain in place
- Transplanted kidney connected via transplanted ureter directly to bladder
- Blood supply to new kidney redirected from blood vessels supplying recipient’s leg
- Surgical procedure usually requires approx 3 hours