Step 1 Renal Physiology Review
Glomerular Filtration: barrier to filtration of protein
PHYSICAL BARRIER TO FILTRATION OF PROTEIN
ELECTRICAL BARRIER TO FILTRATION

[Graph showing relative filterability vs. effective molecular radius for different types of dextrans: polycationic dextran, neutral dextran, and polyanionic dextran. A star (*) indicates albumin.]
ELECTRICAL BARRIER TO FILTRATION OF PROTEIN

heparin sulfate
This patient’s proteinuria is likely caused by:

A. Reduced hepatic production of albumin.
B. Reduced negative charges on glomerular capillary endothelial cells.
C. Increased glomerular filtration rate.
D. Reduced distal tubular reabsorption of filtered protein.
E. Reduced proximal tubular reabsorption of protein.
Glomerular Filtration: determinants of GFR, renal plasma flow and filtration fraction.
\[ \text{GFR} = K_f (\text{Net Filtration Pressure}) \]

\[ \text{GFR} = K_f (P_{GC} - P_{BS} - \pi_{GC}) \]

Filtration Fraction = \frac{\text{GFR}}{\text{RPF}}
Intraglomerular mesangial cells

DCT
Which of the following will tend to increase the GFR?

A. Decreased Net Filtration Pressure.
B. Consumption of a large bowl of salty chicken broth and water, which decreases plasma oncotic pressure.
C. Afferent arteriolar constriction.
D. Ureteral constriction, which increases the hydrostatic pressure in Bowman’s Capsule.
E. Glomerular disease, which destroys glomerular capillaries.
F. Efferent arteriolar dilation.
G. Decreased glomerular capillary hydrostatic pressure.
H. Mesangial cell contraction, which decreases Kf.
A 68-year old woman with a history of diabetes and hypertension, who is recovering from a total hip replacement, is given ketorolac, a nonsteroidal anti-inflammatory drug, for the management of pain. Twenty-four hours later, her urine production decreases, and her serum blood urea nitrogen and creatinine levels rise to 44 mg/dL and 3.1 mg/dL, respectively. What is the effect of this medication on glomerular filtration rate, renal plasma flow, and filtration fraction?

A. Decreased renal plasma flow, decreased glomerular filtration rate and no change in filtration fraction.
B. Decreased renal plasma flow, increased glomerular filtration rate and increased filtration fraction.
C. Increased renal plasma flow, decreased glomerular filtration rate and increased filtration fraction.
D. No change in renal plasma flow, decreased glomerular filtration rate and decreased filtration fraction.
E. No change in renal plasma flow, increased glomerular filtration rate and increased filtration fraction.
Renal clearance.

\[ C_X = \frac{U_X \cdot V}{P_X} \]

\( C_{\text{inulin}} = \text{GFR} \)

\( C_{\text{creatinine}} \) slightly overestimates GFR

\( C_{\text{PAH}} \) estimates RPF
A previously well 12-year old boy is brought in to the Emergency Department with vomiting and severe abdominal cramps after a prolonged period of exercise. Elevated levels of serum creatinine and blood urea nitrogen suggest acute renal failure. Following treatment and recovery, his serum uric acid concentration (0.6 mg/dL) remains consistently below normal. To determine if his low serum uric acid level is related to renal dysfunction, uric acid clearance studies are conducted and the following data are obtained:

Urine flow: 1 mL/min
Urinary uric acid = 36 mg/dL

Which of the following is the patient’s uric acid clearance?

A. 6 mL/min
B. 12 mL/min
C. 24 mL/min
D. 48 mL/min
E. 60 mL/min
An 83-year-old woman with a history of hypertension presents to her family physician's office with oliguria. Serum creatinine and BUN are elevated and a CT reveals that the patient's left kidney is hypoplastic. Renal function studies are performed to assess the renal handling of various substances. Substance X is injected into an arterial line. All of substance X appears in the urine and none is detected in the renal vein. What do these findings indicate about the renal handling of substance X?

A. It must be filtered by the kidney.
B. It must be reabsorbed by the kidney.
C. Its clearance is equal to the glomerular filtration rate.
D. Its clearance is equal to the renal plasma flow.
E. Its urinary concentration must be higher than its plasma concentration.
Renal filtration, reabsorption, secretion, and excretion.

1. Glomerular Filtration
2. Tubular Secretion
3. Tubular Reabsorption

Glucose filtered = GFR x $P_{glucose}$
Excreted = filtered - reabsorbed
Excreted = filtered + secreted
A 65-year-old man with uncontrolled type 2 diabetes and sustained hyperglycemia (serum glucose = 550 mg/dL) and polyuria (5 L/d) is evaluated in the hospital's clinical laboratory because his urine glucose concentration (<100 mM) was much lower than expected. The graph below illustrates the relationship between plasma glucose concentration and glucose excretion for this patient. The glomerular filtration rate (GFR) is 100 mL/min. Which of the following is the $T_{\text{max}}$ for glucose?

A. 100 mg/min  
B. 200 mg/min  
C. 300 mg/min  
D. 400 mg/min  
E. 500 mg/min
A patient with type 2 diabetes mellitus begins taking Canagliflozin, a SGLT2 inhibitor. As a result of the blockade of renal glucose transport, glucose clearance will:

A. Decrease and approach the clearance of PAH.
B. Decrease and approach the clearance of inulin.
C. Increase and approach the clearance of PAH.
D. Increase and approach the clearance of inulin.
E. Increase and approach the clearance of sodium.
Renal tubular physiology
Proximal tubular cell

filtrate

glutamine

Distal Convoluted Tubule

Principal Cell

α-Intercalated Cell

β-Intercalated Cell

Thick Ascending Limb Cell
Proximal tubular cell

fritrate →

HCO₃⁻

Na⁺ | H⁺ | glutamine

K⁺ | NH₄⁺

macula densa (in contact w/ afferent art)

Distal Convoluted Tubule

H⁺ | Na⁺ | Cl⁻ | Ca⁺⁺

Na⁺ | K⁺ | 2Cl⁻

Mg⁺⁺ | Ca⁺⁺

Thick Ascending Limb Cell

Na⁺ | K⁺ | 2Cl⁻

K⁺ |

PCT: Large brush border. Leaky epithelia. Reabsorbs all of the glucose and amino acids and most of the bicarbonate, salt and water. Secretes ammonium.
A patient with congestive heart failure is given the loop diuretic, furosemide, along with the potassium sparing diuretic, spironolactone. How does the distal nephron differ functionally from the proximal tubule?

A. The distal nephron is more permeable to hydrogen ion than the proximal tubule.
B. The distal nephron is less responsive to aldosterone than the proximal tubule.
C. The distal nephron has a more negative intraluminal potential than the proximal tubule.
D. The distal nephron secretes less potassium than the proximal tubule does.
E. The distal nephron secretes more hydrogen ion than the proximal tubule does.
The graph illustrates the relationship between tubular fluid concentration (TF/P) and plasma concentration (P) across different percentages of the proximal tubule length. The y-axis represents TF/P values ranging from 0.2 to 5, while the x-axis shows the percentage of proximal tubule length from 25% to 100%. The graph includes lines for various substances:

- PAH
- Inulin
- Chloride
- Sodium
- Osm
- HCO₃⁻
- Glucose

The formula for TF/P is given as:

\[
TF/P = \frac{\text{Tubular Fluid Concentration}}{\text{Plasma Concentration}}
\]
A 23-year-old woman presents with burning epigastric pain. A careful history reveals that the burning is exacerbated by fasting and improved with meals. The woman is prescribed the H$_2$ receptor antagonist, cimetidine, for suspected peptic ulcer disease (PUD). Cimetidine may also have an adverse effect on proximal tubular function. Which of the following substances will be more concentrated at the end of the proximal tubule than at the beginning of the proximal tubule?

A. Bicarbonate.
B. Creatinine.
C. Glucose.
D. Phosphate.
E. Sodium.
Angiotensin II
Sympathetic nerve activation

Principal Cell

Distal Convoluted Tubule

Proximal tubular cell

HCO₃⁻

glutamine

filtrate

Na⁺

H⁺

NH₄⁺

macula densa (in contact w/afferent art)

Na⁺

K⁺

2Cl⁻

K⁺

Thick Ascending Limb Cell

Aldosterone

(-)

Na⁺⁺

K⁺⁺

Principal Cell

a-Intercalated Cell

H⁺

+ NH₃

NH₄⁺

ANP
Control of renin secretion:

1. Renal baroreceptor

↑BP ➔ renin
Control of renin secretion:

1. Renal baroreceptor
2. Sympathetic nerves

↑ SYM ➔ ↑ renin
Control of renin secretion:

1. Renal baroreceptor

2. Sympathetic nerves

3. Macula densa

\[ \text{MD NaCl} \rightarrow \text{renin} \]
A 69-year-old man with chronic hypertension presents to his physician's office. His blood pressure is 165/105 mm Hg despite treatment with a diuretic, β-blocker, and an angiotensin receptor antagonist. It is decided that a fourth drug is needed for the patient's resistant hypertension, and he is prescribed the vasodilator diltiazem, a calcium channel antagonist. The effect of decreasing the resistance of the afferent arteriole in the glomerulus of the kidney is to decrease which of the following aspects of renal function?

A. Filtration fraction.
B. Glomerular filtration rate.
C. Oncotic pressure of the peritubular capillary blood.
D. Renal plasma flow.
E. Renin release from juxtaglomerular cells.
A 70-year-old man visits his primary care physician after going to a health fair and discovering that his blood pressure is 170/100 mm Hg. The previous year, his blood pressure was 135/85 mm Hg. The man also has a history of hypercholesterolemia. At the physician's office, his blood pressure is 150/100 mm Hg and heart rate is 80/min. An abdominal bruit is detected in the epigastric region to the right of midline. Laboratory findings are significant for a serum sodium level of 147 mEq/L and a serum potassium level of 3.3 mEq/L.

Decreased perfusion of which of the following structures results in renin release that is responsible for this patient’s condition?

A. Adrenal medulla.
B. Afferent arteriole.
C. Distal convoluted tubule.
D. Loop of Henle.
E. Zona glomerulosa.
Control of sodium balance in response to:

Increased salt intake
iv isotonic saline infusion
Exercise/sweating
Decreased salt intake
Diarrhea
Congestive Heart Failure
Hemorrhage
A 40-year-old woman with severe manic-depressive episodes is given lithium to control her symptoms. Unfortunately, this results in the onset of nephrogenic diabetes insipidus which was most evident from her constant thirst and drinking. If she is prevented from drinking, which of the following changes from normal would reflect this condition?

<table>
<thead>
<tr>
<th></th>
<th>Hematocrit</th>
<th>Extracellular Fluid Osmolality</th>
<th>Intracellular Fluid Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>decreased</td>
<td>increased</td>
<td>decreased</td>
</tr>
<tr>
<td>B</td>
<td>decreased</td>
<td>increased</td>
<td>increased</td>
</tr>
<tr>
<td>C</td>
<td>increased</td>
<td>decreased</td>
<td>increased</td>
</tr>
<tr>
<td>D</td>
<td>increased</td>
<td>increased</td>
<td>decreased</td>
</tr>
<tr>
<td>E</td>
<td>increased</td>
<td>increased</td>
<td>increased</td>
</tr>
</tbody>
</table>
A 58-year old patient is hospitalized following an acute myocardial infarction. Several days later, the patient’s 24-hour urine output is lower than normal. An increase in which of the following contributes to a reduced urine flow in a patient with heart failure and reduced effective circulating volume?

A. Atrial natriuretic peptide.
B. Renal perfusion pressure.
C. Renal sympathetic nerve activity.
D. Sodium delivery to the macula densa.
E. Angiotensinogen.
Diuretics

Proximal tubular cell

filtrate

HCO_3^- 

Na^+ 

H^+

NH_4^+

glutamine

macula densa (in contact w/ afferent art)

Thiazide diuretics

Amiloride Triamterene

Loop diuretics

Carbonic anhydrase inhibitors

Principal Cell

Distal Convolved Tubule

Na^+ 

Cl^- 

Ca^{++}

H^+

NH_4^+

HCO_3^- 

NH_3 

H_2O

Thick Ascending Limb Cell

Vasopressin Antagonists

Diuretics

Amiloride

Triamterene

Vasopressin Antagonists

Thiazide diuretics

Carbonic anhydrase inhibitors
Control of water excretion.

Water deprived: High vasopressin

Low urine flow

V2
Control of water excretion.

Water excess: Low vasopressin

High urine flow
A 57-year-old woman with chronic cardiac failure presented at the University Medical Center to participate in a clinical research study on the genetics of heart failure. Genetic analysis showed an increase in vasopressin gene expression and associated hypothalamic biosynthesis of the hormone, in addition to increased release of the hormone from the posterior pituitary. In the presence of antidiuretic hormone (ADH), the filtrate will be isotonic to plasma in which of the following parts of the kidney?

A. Ascending limb of the Loop of Henle.
B. Descending limb of the Loop of Henle.
C. Cortical Collecting duct.
D. Medullary collecting duct.
E. Renal pelvis.
A patient who is dehydrated because of severe sweating and inadequate water intake would be expected to exhibit which one of the following?

A. Decreased plasma vasopressin.
B. Decreased plasma albumin concentration.
C. Hyperosmotic urine.
D. Low plasma sodium concentration.
E. Increased urine flow.
CASE 20

A 60-year-old man with a 30-year smoking history presents to his physician with complaints of cough, fatigue, and a recent 9.1-kg (20-lb) weight loss. X-ray of the chest reveals a 2-cm hilar mass that is identified on biopsy as small cell lung cancer. On physical examination, the patient has some cachexia but normal skin turgor, no edema or jugular venous distention, and no orthostatic hypotension. Relevant laboratory findings are as follows:

<table>
<thead>
<tr>
<th>Serum:</th>
<th>Urine:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium: 128 mEq/L</td>
<td>Sodium: Normal</td>
</tr>
<tr>
<td>Potassium: 4 mEq/L</td>
<td>Osmolality: 610 mOsm/kg H₂O</td>
</tr>
<tr>
<td>Blood urea nitrogen (BUN):</td>
<td></td>
</tr>
<tr>
<td>8 mg/dL</td>
<td></td>
</tr>
<tr>
<td>Glucose: 90 mg/dL</td>
<td></td>
</tr>
</tbody>
</table>

In this patient, which of the following will be decreased:

A. Urinary flow rate.
B. Intracellular volume.
C. Extracellular volume.
D. Principal cell cAMP levels.
E. Principal cell apical membrane aquaporin levels.
### Acid-base pathophysiology

<table>
<thead>
<tr>
<th>Acid-base physiology</th>
<th>pH</th>
<th>PCO₂</th>
<th>[HCO₃⁻]</th>
<th>Compensatory response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic acidosis</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>Hyperventilation (immediate)</td>
</tr>
<tr>
<td>Metabolic alkalosis</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>Hypoventilation (immediate)</td>
</tr>
<tr>
<td>Respiratory acidosis</td>
<td>↓</td>
<td>↑</td>
<td>↑</td>
<td>↑ renal [HCO₃⁻] reabsorption (delayed)</td>
</tr>
<tr>
<td>Respiratory alkalosis</td>
<td>↑</td>
<td>↓</td>
<td>↓</td>
<td>↓ renal [HCO₃⁻] reabsorption (delayed)</td>
</tr>
</tbody>
</table>

Key: ↑ ↓ = 1° disturbance; ↓ ↑ = compensatory response.
Acid-base pathophysiology

Acidosis/alkalosis

Check arterial pH

- pH < 7.4
  - Acidemia
    - $\text{PCO}_2 > 40 \text{ mmHg}$
      - Respiratory acidosis
        - Hypoventilation
          - Airway obstruction
          - Acute lung disease
          - Chronic lung disease
          - Opioids, sedatives
          - Weakening of respiratory muscles
        - Hypoventilation
          - Anion gap
            - $\text{Na}^+ - (\text{Cl}^- + \text{HCO}_3^-)$
          - Anion gap
            - MUDPILES:
              - Methanol (formic acid)
              - Uremia
              - Diabetic ketoacidosis
              - Propylene glycol
              - Iron tablets or INH
              - Lactic acidosis
              - Ethylene glycol (oxalic acid)
              - Salicylates (late)

- pH > 7.4
  - Alkalemia
    - $\text{PCO}_2 < 40 \text{ mmHg}$
      - Respiratory alkalosis
        - Hyperventilation
          - (e.g., early high-altitude exposure)
          - Salicylates (early)
        - Check anion gap
          - Normal anion gap (8–12 mEq/L)
          - HARD-ASS:
            - Hyperalimentation
            - Addison's disease
            - Renal tubular acidosis
            - Diarrhea
            - Acetazolamide
            - Spironolactone
            - Saline infusion
    - $\text{PCO}_2 > 40 \text{ mmHg}$
      - Metabolic alkalosis with compensation (hyperventilation)
        - Loop diuretics
        - Vomiting
        - Antacid use
        - Hyperaldosteronism