Kidney

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SHARE YOUR FEEDBACK

- Share Your Feedback

Rapid Review

Anatomy

1. The twin bean-shaped kidneys reside in the retroperitoneal space between the levels of T12 and L3.

2. We can divide the kidney into two parts:

   - Renal cortex – includes the glomerulus, Bowman's capsule, proximal tubules, and distal tubules
   - Renal medulla – includes the loops of Henle and collecting ducts

3. The nephron is the functional unit of the kidney.

Want to learn on a deeper level? IN-DEPTH REVIEW

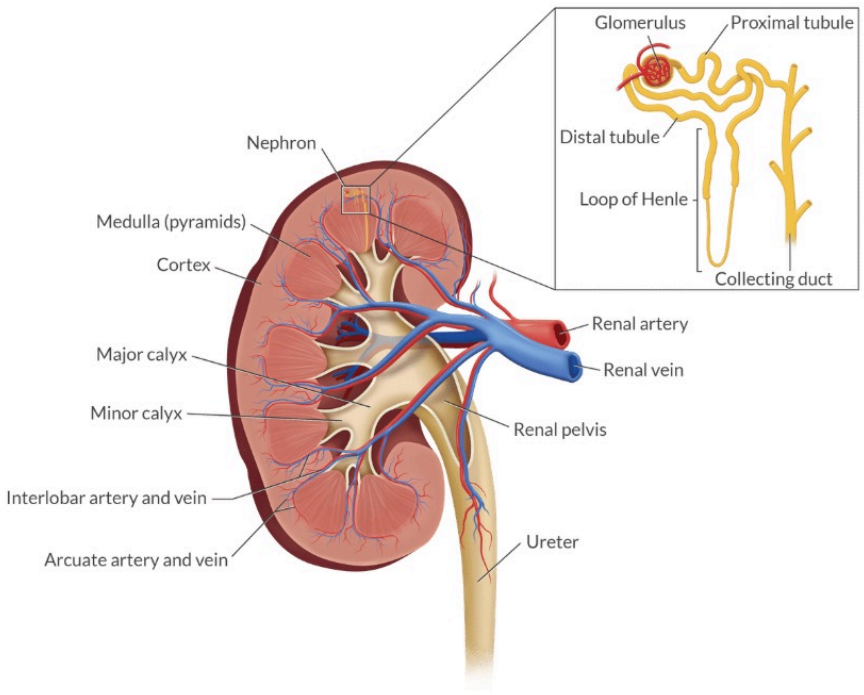
Ready to go to the next lesson? NEXT LESSON

In-Depth Review

Anatomy

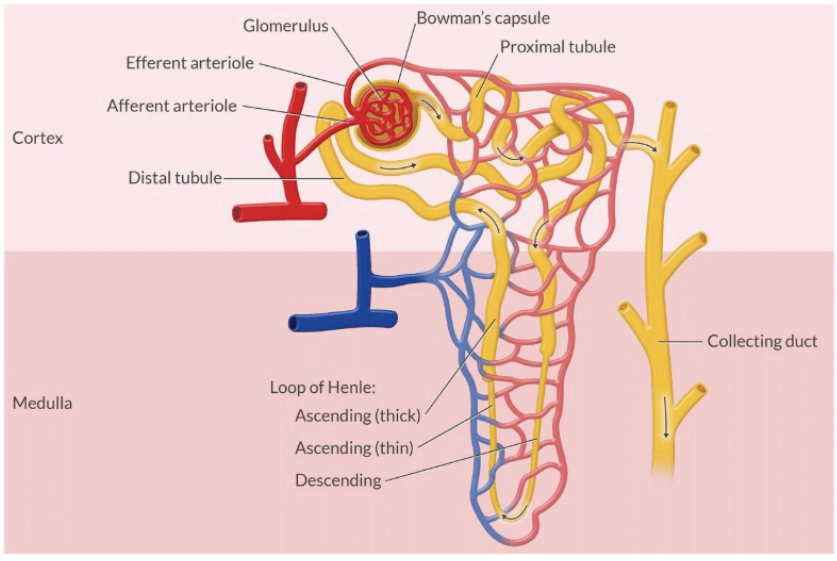
Gross Anatomy

The twin bean-shaped kidneys reside in the retroperitoneal space between the levels of T12 and L3. The right kidney is slightly more caudal to accommodate the liver. The hilum is an indentation that provides the point of entry and exit for the renal artery, renal vein, nerves, lymphatics, and ureters.



Anatomy of the Nephron

The nephron is the functional unit of the kidney. We'll learn more about it as you progress through this tutorial, but for now, you should learn the anatomy.



RENAL CORTEX | RENAL MEDULLA

- It is the outer section of the kidney (to help you remember, think about the location of the cerebral cortex).
- It houses the glomerulus, Bowman's capsule, proximal tubules, and distal tubules.

References +

Old References +

Want to practice what you learned in this lesson? LET ME PRACTICE

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Anatomy

Gross Anatomy

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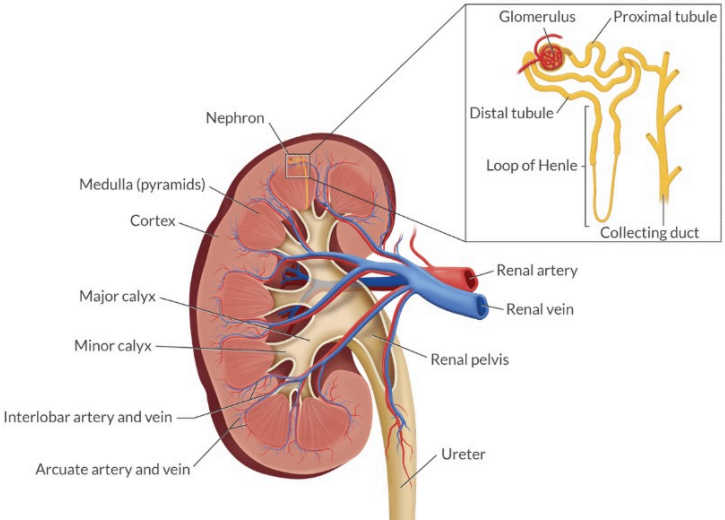

Pre-Lesson Question

The kidney produces: **(Select 3.)**

- [x] calcitriol.
- [x] antidiuretic hormone.
- [x] aldosterone.
- [x] renin.
- [x] erythropoietin.
- [x] angiotensinogen.

INCORRECT

Correct Answer:
Renin
Erythropoietin
Calcitriol

Explanation:
The kidney responds to, as well as produces, a wide variety of hormones and enzymes. In this question, we asked about the compounds that are produced in the kidney.

- Renin is produced by the juxtaglomerular apparatus - specifically in the fenestrated epithelium in the afferent arteriole.
- Erythropoietin is synthesized in the kidney and is secreted in response to hypoxia.
- Under the control of parathyroid hormone, the kidneys convert inactive vitamin D_3 to active vitamin D_3 (1,25 $[OH]_2$ vitamin D_3, or 1, 25-dihydroxycholecalciferol).

Why are the other answers wrong?

- Angiotensinogen is manufactured in the liver.
- Aldosterone is synthesized in the adrenal cortex.
- Antidiuretic hormone is produced by the supraoptic nuclei and paraventricular nuclei in the hypothalamus. It's released into the circulation from the posterior pituitary gland.

TAKE AGAIN

Pressed for time? Here are the highlights. RAPID REVIEW

Learn everything you need to know about this topic. IN-DEPTH REVIEW

Unit 7: Neuro

Unit 8: Regional Anesthesia

Unit 9: Fluids & Blood

Unit 10: Kidney, Liver & Endocrine

Tutorials

- [x] Kidney
- [ ] Liver
- [x] Endocrine

Flashcards

- [x] Unit 10: Kidney, Liver & Endocrine

Promote active recall and reinforce your memory by creating your own flashcards.

Review Exams

- [ ] Kidney (RE)
- [x] Diuretics (RE)

Rapid Review

The Six Functions of the Kidney

1 The kidney has 6 major functions:

1. Maintenance of extracellular volume and composition
2. Blood pressure regulation (long- and intermediate-term)
3. Excretion of toxins and metabolites
4. Maintenance of acid-base balance
5. Hormone production (erythropoietin, calcitriol, prostaglandins)
6. Blood glucose homeostasis

2 The lungs and the kidneys are the primary regulators of acid-base balance, where the lungs excrete volatile acids (CO_2), and the kidneys excrete non-volatile acids.

3 Inadequate oxygen delivery to the kidney causes it to release erythropoietin. Clinical examples include anemia, reduced intravascular volume, and hypoxia (high altitude, cardiac and pulmonary failure).

Rapid Review

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3. Inadequate oxygen delivery to the kidney causes it to release erythropoietin. Clinical examples include anemia, reduced intravascular volume, and hypoxia (high altitude, cardiac and pulmonary failure).

4. Severe kidney disease reduces EPO production and leads to chronic anemia.

5. A low blood calcium level increases parathyroid hormone release, which increases the serum calcitriol (active vit. D) level. As serum Ca^{+2} rises, it feeds back to reduce the serum level of PTH, which reduces the serum level of calcitriol (negative feedback).

Want to learn on a deeper level? IN-DEPTH REVIEW

Ready to go to the next lesson? NEXT LESSON

Rapid Review

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In-Depth Review

The Six Functions of the Kidney

Before we dig into the finer points of renal physiology, we're going to give you a bird's eye view of renal function. We certainly understand this is a perplexing topic, and it's easy to become distracted by the near-endless amount of minutiae in the textbooks. Our job is to condense this information into a smaller volume while ensuring you have everything you need for your exam. If you thirst for additional detail in this area, Guyton & Hall is a great place to start.

1. Maintenance of Extracellular Volume and Composition

- Aldosterone controls extracellular fluid volume (Na^+ and water are reabsorbed together).
- Antidiuretic hormone (vasopressin) controls plasma osmolarity (water is reabsorbed, but Na^+ is not).
- The kidneys also regulate potassium, chloride, phosphate, magnesium, hydrogen, bicarbonate, glucose, and urea.

2. Blood Pressure Regulation: Long- and Intermediate-Term

- Long-term control of BP is carried out by the thirst mechanism (intake) and sodium and water excretion (output).
- Intermediate-term control of BP is carried out by the renin-angiotensin-aldosterone system. Renin is produced by the juxtaglomerular cells, and aldosterone is synthesized in the adrenal cortex.
- Short-term control of BP is carried out by the baroreceptor reflex.

3. Excretion of Toxins and Metabolites

- Glomerular filtration and tubular secretion clear the blood of metabolic byproducts, toxins, and drugs.
- Like the liver, the kidney is capable of phase 1 and 2 biotransformations.

4. Maintenance of Acid-Base Balance

- The body's pH must be kept in a narrow range to ensure proper enzymatic and cellular function.
- The lungs and the kidneys are the primary regulators of acid-base balance.
- The lungs excrete volatile acids (CO_2), and the kidneys excrete non-volatile acids.
- The kidneys maintain acid-base balance by titrating hydrogen in the tubular fluid, which creates acidic or basic urine.

5. Hormone Production

Erythropoietin

- Inadequate oxygen delivery to the kidney causes it to release erythropoietin. Clinical examples include anemia, reduced intravascular volume, and hypoxia (high altitude, cardiac and pulmonary failure).
- EPO stimulates stem cells in the bone marrow to produce erythrocytes.
- Severe kidney disease reduces EPO production and leads to chronic anemia.

Prostaglandins

- PGE2 and PGI2 vasodilate the renal arteries.
- Thromboxane A2 constricts the renal arteries.

Calcitriol (Active Vitamin D3)

- In the skin, calciferol (vitamin D3 - inactive) is synthesized during exposure to ultraviolet light. We also absorb vitamin D compounds (also inactive) from food.
- In the liver, calciferol is converted to 25-hydroxycholecalciferol.
- In the kidney, 25-hydroxycholecalciferol is converted to 1,25-dihydroxycholecalciferol (calcitriol - active vitamin D3). Parathyroid hormone (PTH) regulates this process. An increased serum PTH level increases the serum calcitriol level.
- Calcitriol affects the serum Ca^{+2} level in three ways:
  - It stimulates the intestine to absorb Ca^{+2} from food (this raises the serum Ca^{+2} concentration).
  - It instructs the kidney to reduce Ca^{+2} and phosphate excretion (this raises the serum Ca^{+2} concentration).
  - It increases the deposition of Ca^{+2} into the bone. This may seem counterintuitive since calcitriol tends to increase the serum Ca^{+2} concentration. The other part of the story is that calcitriol causes resorption of "old" bone, which increases the serum Ca^{+2} concentration. This helps bone turnover over time.
- As serum Ca^{+2} rises, it feeds back to reduce the serum level of PTH. This reduces the serum level of calcitriol (negative feedback).

6. Blood Glucose Homeostasis

- The kidneys (like the liver) can synthesize glucose from amino acids, thereby preventing hypoglycemia during fasting.
- The kidneys rival the liver's ability to perform gluconeogenesis.

References +

Old References +

Want to practice what you learned in this lesson? LET ME PRACTICE

Ready to go to the next lesson? NEXT LESSON

Rapid Review

Renal Blood Flow

1. The kidneys receive 20 - 25% of the cardiac output (1,000~1,250 mL/min).
2. Of the blood delivered to the kidney, only 20% is filtered at the glomerulus. After filtration, ~ 99% of the ultrafiltrate is reabsorbed into the peritubular capillaries. The 1% of the ultrafiltrate that is not reabsorbed is excreted as urine (1 – 1.5 L/day).
3. Renal blood flow is directly proportional to the difference between MAP and renal venous pressure, and it's inversely proportional to renal vascular resistance.
4. Autoregulation maintains renal blood flow within a wide range of systemic blood pressures (MAP 50 – 180 mmHg). Understand that this range is highly patient-specific.
5. Key contributors of renal autoregulation include the myogenic mechanism, tubuloglomerular feedback, RAAS, atrial natriuretic peptide, prostaglandins, and autonomic tone.
6. The surgical stress response induces a transient state of vasoconstriction and sodium retention. This persists for several days, resulting in oliguria and edema. Vasoconstriction of the renal vasculature during this time predisposes the kidneys to ischemic injury and the effects of nephrotoxic drugs.

Want to learn on a deeper level? IN-DEPTH REVIEW

Ready to go to the next lesson? NEXT LESSON

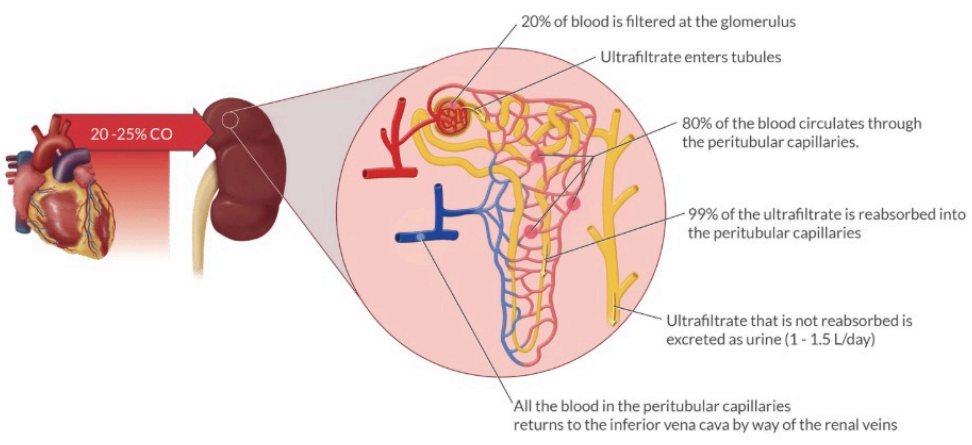
In-Depth Review

Renal Blood Flow

Overview

The kidneys receive 20 – 25% of the cardiac output (1,000 – 1,250 mL/min).

At any given time, there are two types of fluid moving through the kidney: blood + tubular fluid. You must understand what's happening with both as they flow through the nephron.



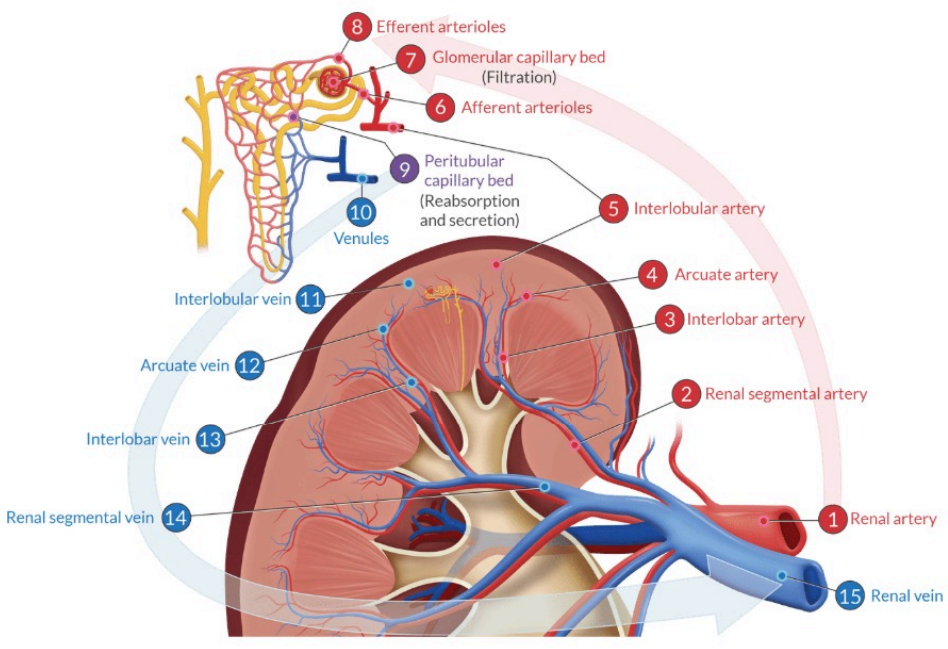
Distribution of Renal Blood Flow

Renal Blood Flow = (MAP - Renal Venous Pressure) / Renal Vascular Resistance

- The renal cortex receives 90% of the renal blood flow. The PO_2 in this region is 50 mmHg.
- The renal medulla and its juxtamedullary nephrons receive 10% of the renal blood flow. The PO_2 in this region is 10 mmHg.
- A lower PO_2 in the renal medulla explains why this region is more sensitive to ischemia.
- Renal blood flow decreases 10% per decade of life after age 50.
- In the neonate, RBF doubles in the first two weeks of life and achieves an adult level by two years of age.

Pathway of Blood Through the Kidney

You should understand how blood flows through the kidney.



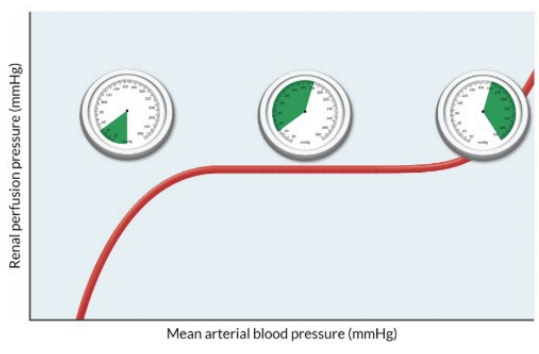
Control of Renal Blood Flow: Autoregulation

The purpose of autoregulation is to ensure a constant amount of blood flow is delivered to the kidneys over a wide range of arterial blood pressures. Glomerular filtration becomes pressure-dependent when MAP is outside the range of autoregulation.

- When renal perfusion is too low, autoregulation increases renal blood flow by reducing renal vascular resistance.
- When renal perfusion is too high, autoregulation decreases renal blood flow by increasing renal vascular resistance.

There's little agreement about the limits of RBF autoregulation, although we like 50 – 180 mmHg. We must stress, however, that autoregulation in any organ system is highly patient-specific.

- 70 –75 to 160 – 180 mmHg (Hall)
- 60 – 160 mmHg (Stoelting)
- 50 –150 mmHg (Hemmings)
- 50 – 180 mmHg (Nagelhout)
- 70 – 130 mmHg (Gropper)



*Urine output is NOT autoregulated. It's linearly related to MAP above 50 mmHg.

Renal autoregulation is carried out by several processes:

- Myogenic mechanism
- Juxtaglomerular apparatus and tubuloglomerular feedback
- Renin-angiotensin-aldosterone system
- Prostaglandins
- Atrial natriuretic peptide
- Sympathetic nervous system

Of these, the myogenic mechanism and tubuloglomerular feedback are the most important.

Myogenic Mechanism

- If the renal artery pressure is elevated, the myogenic mechanism constricts the afferent arteriole to protect the glomerulus from excessive pressure.
- When the renal artery pressure is too low, the myogenic mechanism dilates the afferent arteriole to increase blood flow going to the nephron.

Tubuloglomerular Feedback

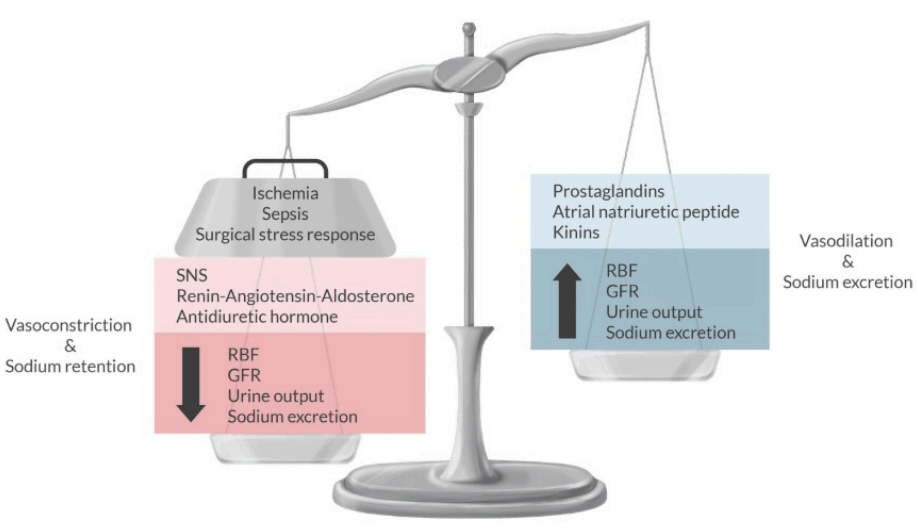
- The juxtaglomerular apparatus is located in the distal tubule, specifically the region that passes between the afferent and efferent arterioles.
- Tubuloglomerular feedback about the sodium and chloride composition in the distal tubule affects arteriolar tone. In turn, this creates a negative feedback loop to maintain renal blood flow. We've covered this in greater detail in the next lesson.

Renal Blood Flow During the Perioperative Period

The kidneys receive sympathetic innervation from T8-L1.

The SNS innervates the afferent and efferent arterioles. Under normal conditions, the internal autoregulatory mechanisms override the external effects of the SNS. In times of stress or when exogenous catecholamines are administered, the SNS can reduce renal blood flow. The PNS is not well represented in the kidney.

The surgical stress response induces a transient state of vasoconstriction and sodium retention (this outweighs the factors on the other side of the scale). This altered physiology persists for several days, leading to oliguria and edema. Vasoconstriction of the renal vasculature during this time predisposes the kidneys to ischemic injury and the effects of nephrotoxic drugs.



References +

Old References +

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Ready to go to the next lesson? NEXT LESSON

Rapid Review

Renin-Angiotensin-Aldosterone System

1. The juxtaglomerular apparatus, located in the distal tubule, monitors renal perfusion, and solute concentration. It maintains GFR by modulating renal vascular resistance and renin release.

2. The RAAS plays an integral role in regulating systemic vascular resistance and the composition of the extracellular volume. Conditions that increase renin release include:

   - Decreased renal perfusion pressure
   - SNS activation
   - Tubuloglomerular feedback

3. Aldosterone is a steroid hormone that's produced by the zona glomerulosa of the adrenal gland. It facilitates Na^+ and water reabsorption as well as K^+ and H^+ excretion. It doesn't meaningfully affect serum osmolarity.

4. Antidiuretic hormone controls serum osmolarity because it increases reabsorption of water but not sodium.

Want to learn on a deeper level? IN-DEPTH REVIEW

Ready to go to the next lesson? NEXT LESSON

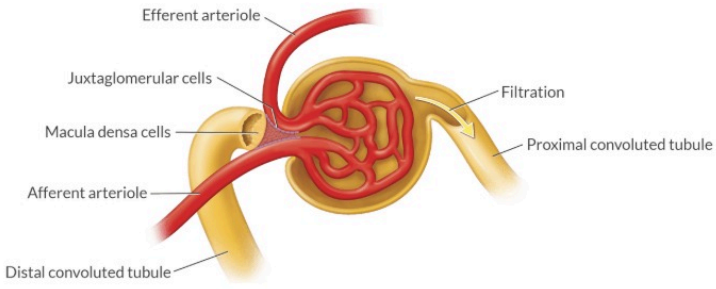
In-Depth Review

Renin-Angiotensin-Aldosterone System

Juxtaglomerular Apparatus

As a monitor of renal perfusion and ultrafiltrate solute concentration (Na^+ and Cl^-), the juxtaglomerular apparatus plays a vital role in regulating renal blood flow and GFR.

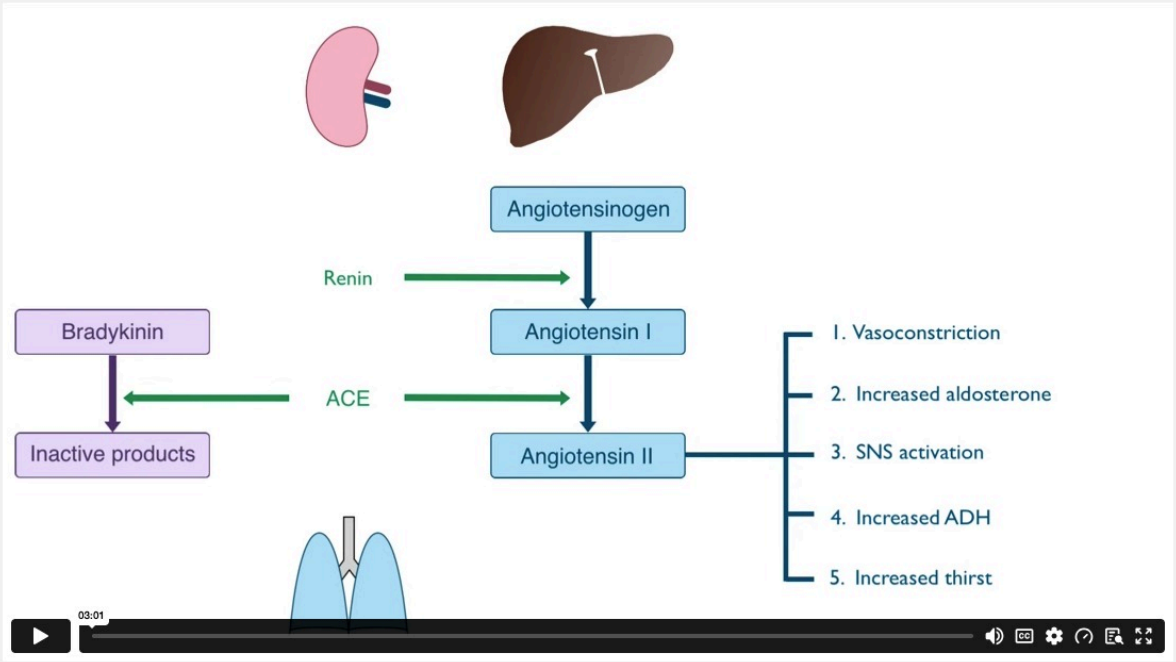
The juxtaglomerular apparatus is located in the distal tubule, specifically the region that passes between the afferent and efferent arterioles.



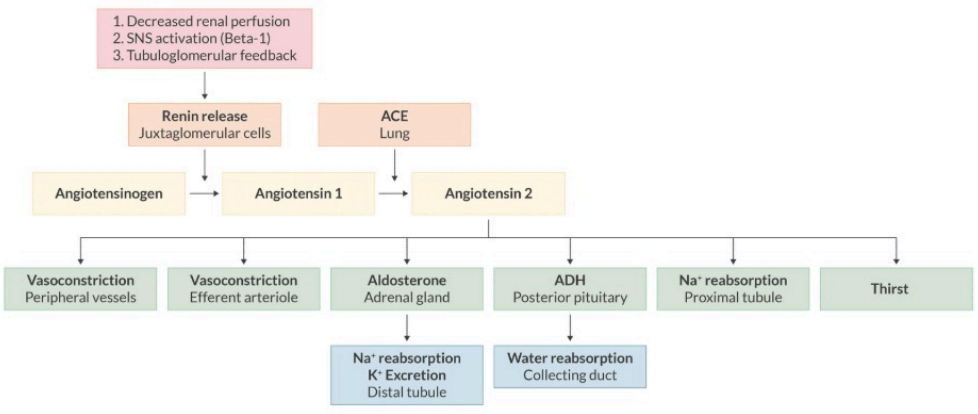
When renal blood flow decreases, GFR also declines which reduces Na^+ and Cl^- delivery to the juxtaglomerular apparatus (sensed by the macula densa). This leads to the dilation of the afferent arterioles, which restores GFR. Additionally, a lower Cl^- concentration in the ultrafiltrate triggers renin release from the juxtaglomerular cells, which activates the renin-angiotensin-aldosterone system. Angiotensin 2 causes constriction of the efferent arteriole, which also increases GFR.

Unlike renal blood flow, urine output is not auto-regulated. Instead, there's a linear relationship between urine output and MAP. Urine output typically comes to a halt when MAP is less than 50 mmHg.

Renin-Angiotensin-Aldosterone System



The RAAS plays an integral role in regulating systemic vascular resistance and the composition of the extracellular volume. By extension, the RAAS greatly influences cardiac output and arterial blood pressure.



Conditions That Increase Renin Release	Causes
1. Decreased Renal Perfusion Pressure	Hemorrhage PEEP CHF Liver failure with ascites Sepsis Diuresis
2. SNS Activation (Beta-1)	Circulating catecholamines Exogenous catecholamines
3. Tubuloglomerular Feedback	Decreased sodium & chloride in distal tubule

Aldosterone

Aldosterone is a steroid hormone that is produced in the zona glomerulosa of the adrenal gland.

By stimulating the Na/K-ATPase in the principal cells of the distal tubules and collecting ducts, aldosterone facilitates Na^+ and water reabsorption and K^+ and H^+ excretion.

Aldosterone does not meaningfully change serum osmolarity. This is because the water follows sodium in direct proportion when it's reabsorbed into the peritubular capillaries. Antidiuretic hormone controls serum osmolarity, because it increases reabsorption of water but not sodium.

In addition to RAAS stimulation, aldosterone release is increased by:

- Hyperkalemia
- Hyponatremia

While the sodium retaining effect of angiotensin 2 is almost immediate, there is a 1 - 2 hour delay between aldosterone release and its physiologic effects.

Disorders of Aldosterone Release

Conn's disease occurs with excess aldosterone production. It causes sodium retention and potassium loss.

Inadequate aldosterone production in isolation is uncommon. Addison's disease is usually the result of adrenocortical insufficiency (destruction of all of the cortical zones).

References +

Old References +

Want to practice what you learned in this lesson? LET ME PRACTICE

Ready to go to the next lesson? NEXT LESSON

Rapid Review

Osmolality & Antidiuretic Hormone

1. Sodium concentration is the principal determinant of osmolarity. Glucose and BUN also play a role.

2. Normal serum osmolarity = 280 – 290 mOsm/L

3. Antidiuretic hormone is released into the systemic circulation from the posterior pituitary gland when:

   - Osmolarity of the ECF is increased
   - Blood volume is decreased

4. ADH restores blood pressure in two ways:

   1. V_1 receptor stimulation causes vasoconstriction in the vasculature (increased SVR).
   2. V_2 receptor stimulation in the collecting ducts causes water retention.

5. Perioperative factors that increase ADH release (and renal water retention) include PEEP, positive pressure ventilation, hypotension, and hemorrhage.

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In-Depth Review

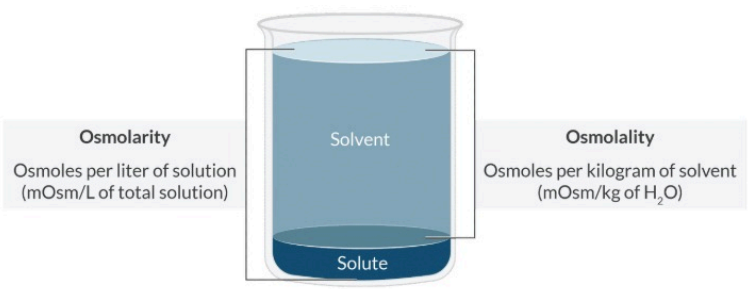
Osmolality & Antidiuretic Hormone

Definitions

Osmolarity and osmolality are measures of concentration. Learn these terms:

- Concentration is an amount per volume.
- Osmolality measures the number of osmoles per kilogram of solvent.
- Osmolarity measures the number of osmoles per liter of solvent.
- Osmoreceptors are monitors of sodium concentration in the extracellular fluid.

For our purposes, the difference between osmolarity and osmolality is so minuscule that we're going to pretend they're the same thing. As such, we'll use these terms interchangeably.



Sodium concentration is the principal determinant of osmolarity. For completeness, you should understand that it's also affected by glucose and blood urea nitrogen.

$$\text{Normal Osmolarity} = 280 - 290 \text{ mOsm/L}$$

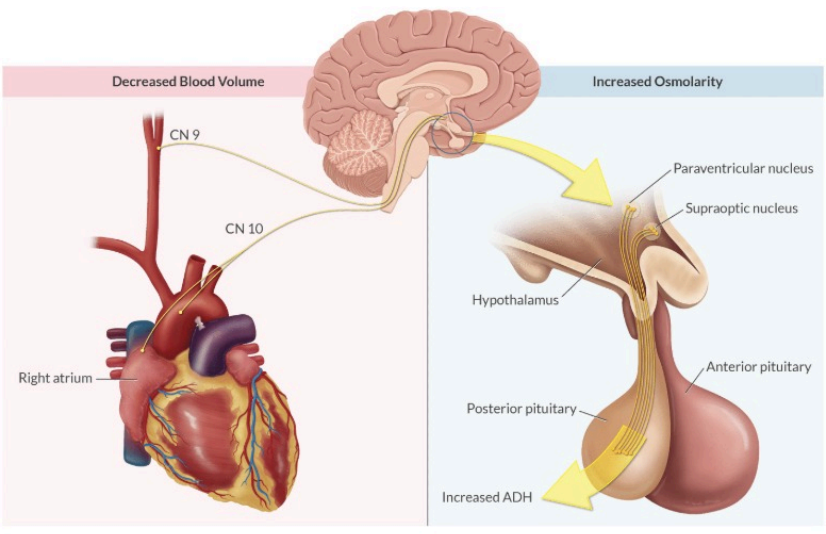
$$\text{Plasma osmolarity} = 2[Na^+] + \frac{\text{Glucose}}{18} + \frac{\text{BUN}}{2.8}$$

Antidiuretic Hormone (Vasopressin)

ADH is produced in the supraoptic and paraventricular nuclei of the hypothalamus. It's released from the posterior pituitary gland. Remember, vasopressin, arginine vasopressin (AVP), and antidiuretic hormone (ADH) are the same thing.

There are two mechanisms that control ADH release:

1. Increased Osmolarity of the ECF:
    a. An increased ECF sodium concentration shrinks the osmoreceptors in the hypothalamus. This initiates the process of transporting ADH from the hypothalamus to the posterior pituitary gland. After this, ADH is released into the systemic circulation.
    b. The thirst reflex is activated, and antidiuresis prevents additional water loss. As the kidneys conserve water, the urine becomes more concentrated (osmolarity increases).
2. Decreased Blood Volume:
    a. When blood volume declines, unloading of the baroreceptors in the carotid sinuses, transverse aortic arch, great veins, and right atrium stimulate ADH release.



How ADH Restores Blood Pressure

1. ADH stimulates the V1 receptor and causes vasoconstriction in the peripheral vasculature (↑IP_3, DAG, Ca^{+2}).
    a. The net result is an increased SVR.
    b. The half-life of ADH is 5 – 15 min.
    c. While anesthetic agents do not directly affect ADH homeostasis, they do impact arterial blood pressure and venous blood volume. In turn, these changes increase ADH release. Examples include PEEP, positive-pressure ventilation, hypotension, hemorrhage.
2. ADH stimulates the V2 receptor in the collecting ducts (↑ cAMP).
    a. Under the direction of ADH, aquaporin-2 channels (water channels) are inserted into the walls of the collecting ducts.
    b. This facilitates water reabsorption, reduces plasma osmolarity, and increases urine osmolarity.
    c. The net result is an expansion of the plasma volume.

References +

Old References +

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Ready to go to the next lesson? NEXT LESSON

Rapid Review

Mechanisms of Renal Vasodilation

1. Three pathways promote renal vasodilation:

   - Vasodilating prostaglandins—antagonize the effects of RAAS
   - Natriuretic peptides—inhibit RAAS and stimulates sodium and water excretion
   - Dopamine receptors:
     - DA_1 → Vasodilation, increased renal blood flow, increased GFR, diuresis, Na+ excretion
     - DA_2 → Decreased NE release from the presynaptic SNS nerve terminal

2. While dopamine increases urine output, there's no solid evidence to support the age-old notion that renal-dose dopamine either prevents or treats AKI.

Want to learn on a deeper level? IN-DEPTH REVIEW

Ready to go to the next lesson? NEXT LESSON

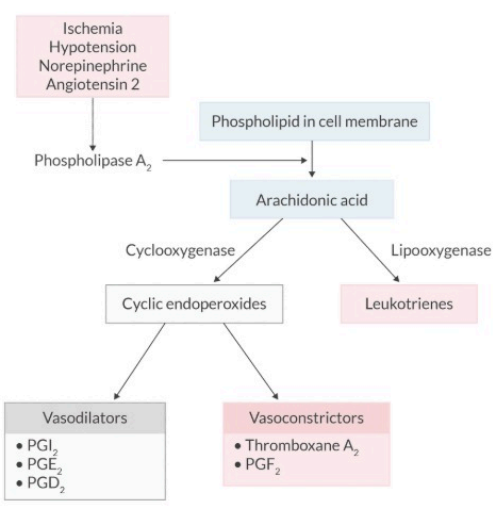
In-Depth Review

Mechanisms of Renal Vasodilation

Three pathways promote renal vasodilation:

1. Prostaglandins
2. Natriuretic peptide
3. Dopamine receptors

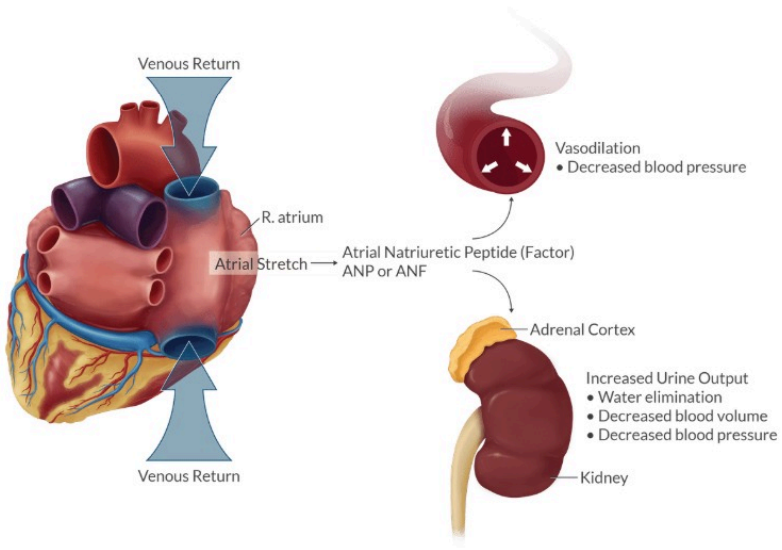
1. Prostaglandins



- Prostaglandins (produced in the afferent arteriole) play an important role in renal protection by promoting renal blood flow.
- Arachidonic acid is liberated from the cell membrane in response to ischemia, hypotension, norepinephrine, and angiotensin 2. In effect, the factors that initiate the stress response also activate a process designed to preserve renal blood flow.
- NSAIDs inhibit cyclooxygenase. These drugs can reduce renal blood flow by inhibiting the production of vasodilating prostaglandins.
- Under hypoxic conditions, the cyclic endoperoxide pathway favors the production of renal vasoconstrictors (thromboxane A2 and PGF2). These substances also reduce GFR.
- Endotoxin increases leukotriene production, which leads to renal vasoconstriction.

2. Natriuretic Peptide

- In response to atrial distension, the myocardium produces atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP).
- Natriuretic peptides:
  - Inhibit renin release (negative feedback on RAAS → vasodilation and decreased BP).
  - Promote sodium and water excretion into the collecting ducts.
- We can use BNP as a biomarker to assess disease severity in heart failure patients.



3. Dopamine Receptors

- There are two types of dopamine receptors: DA1 and DA2
  - DA1 receptors are present in the kidney and the splanchnic circulation.
  - DA2 receptors are present on the presynaptic adrenergic nerve terminal.

	DA1 Receptor	DA2 Receptor
Location	Renal vasculature Tubules	Presynaptic SNS nerve terminal
2nd Messenger	Increased cAMP	Decreased cAMP
Function	Vasodilation Increased renal blood flow Increased GFR Diuresis Sodium excretion	Decreased norepinephrine release

Does Dopamine Improve Outcome in Acute Kidney Injury?

No. While dopamine increases urine output, there's no solid evidence to support the age-old notion that renal-dose dopamine either prevents or treats AKI.

What About Fenoldopam?

Fenoldopam is a selective DA1 receptor agonist that increases renal blood flow. Low-dose fenoldopam (0.1 - 0.2 mcg/kg/min) is a renal vasodilator and increases RBF, GFR, and facilitates Na^+ excretion without affecting arterial blood pressure.

It may offer renal protection during aortic surgery and during cardiopulmonary bypass.

Fenoldopam reduces the requirement for dialysis and in-hospital mortality in cardiac surgery patients.

References +

Old References +

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Ready to go to the next lesson? NEXT LESSON

Rapid Review

Nephron Function: Part 1

1. The normal glomerular filtration rate is 125 mL/min. Water, electrolytes, and glucose are freely filtered, but plasma proteins (e.g., albumin) are not filtered.
2. The most important determinant of GFR is glomerular hydrostatic pressure, which is determined by arterial blood pressure, afferent arteriole resistance, and efferent arteriole resistance.
3. Reabsorption is the process where a substance is transferred from the tubule to the peritubular capillaries. For some substances, there's a maximum amount that can be reabsorbed into the peritubular blood. After the maximum value is achieved, the excess substance will be excreted in the urine (think of the diabetic who spills sugar in his urine).
4. Secretion is the process where a substance is transferred from the peritubular capillaries to the tubule.
5. Excretion is the process where a substance is removed from the body in the urine.
6. Kidney disease destroys the basement membrane, which allows the filtration of proteins into the tubules. For instance, patients with interstitial nephritis lose protein in the urine (proteinuria), which explains why they may experience hypoalbuminemia.

Want to learn on a deeper level? IN-DEPTH REVIEW

Ready to go to the next lesson? NEXT LESSON

In-Depth Review

Nephron Function: Part 1

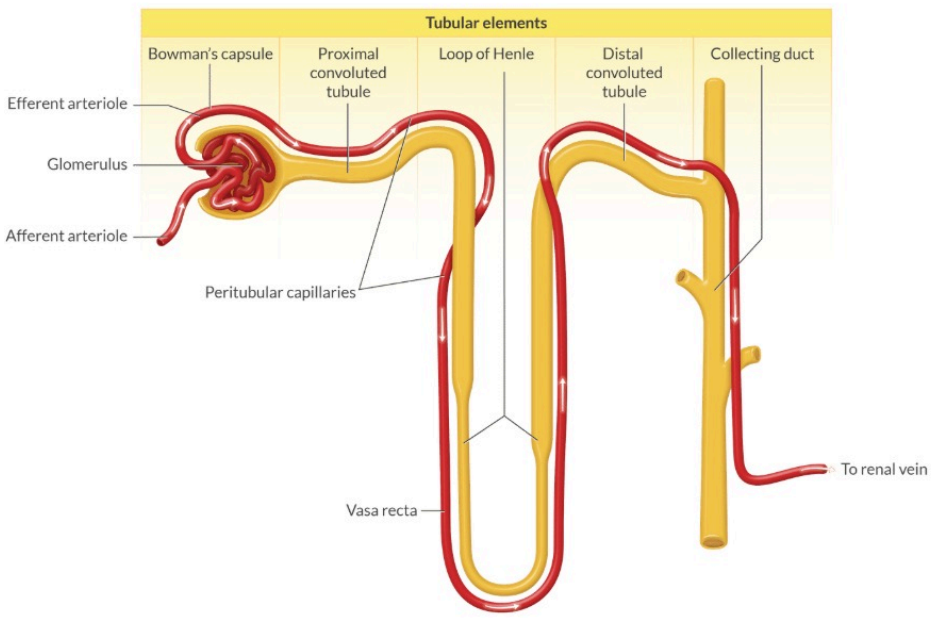
Overview

Each nephron contains two main components:

1. The glomerulus, which is a tuft of glomerular capillaries.
2. The renal tubule, where filtered fluid becomes urine.

Bowman's capsule is a thin membranous structure at the beginning of the renal tubule. It surrounds the glomerulus.

Together the glomerulus and Bowman's capsule form a united structure called the renal corpuscle. This is where the initial process of glomerular filtration begins.



Glomerular Filtration

- The normal glomerular filtration rate is 125 mL/min.
- The filtration fraction is ~ 20%. This means that ~ 20% of the renal blood flow is filtered by the glomerulus, and ~ 80% is delivered to the peritubular capillaries.
- Water, electrolytes, and glucose are freely filtered.
- Plasma proteins (e.g., albumin) are not filtered.
- The glomerular filtrate is identical to plasma except that it doesn't contain plasma proteins, erythrocytes, or white blood cells.
- Kidney disease destroys the basement membrane, which allows proteins to enter the tubules. For instance, patients with nephrotic syndrome or interstitial nephritis lose protein in the urine (proteinuria), which explains why they experience hypoalbuminemia.

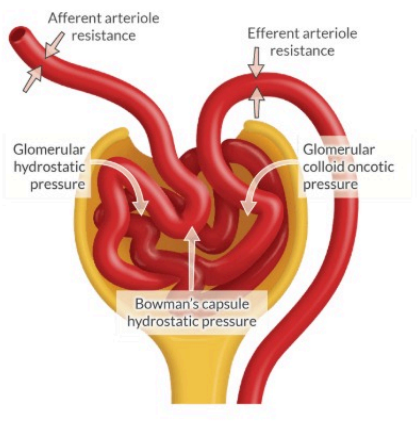
Glomerular Hydrostatic Pressure

The net filtration pressure (NFP) is the driving force that pushes fluid from the blood (glomerulus) into Bowman's capsule.

NFP = Glomerular Hydrostatic P − Bowman's Capsule Hydrostatic P − Glomerular Oncotic P

Glomerular hydrostatic pressure is the most important determinant of GFR. There are three determinants of glomerular hydrostatic pressure:

1. Arterial blood pressure
2. Afferent arteriole resistance
3. Efferent arteriole resistance



Effect	RBF	GFR	Filtration Fraction
Constriction of afferent arteriole	▼	▼	No Δ
Constriction of efferent arteriole	▼	▲	▲
Increased plasma protein	No Δ	▼	▼
Decreased plasma protein	No Δ	▲	▲

1. Arterial Blood Pressure

- Increased MAP increases GFR, and decreased MAP decreases GFR.
- Autoregulation safeguards against hypo- and hypertension (so long as the driving pressure is within the upper and lower limits of autoregulation).

2. Afferent Arteriole Resistance

- Constriction of the afferent arteriole reduces GFR.
- Dilation of the afferent arteriole increases GFR.

3. Efferent Arteriole Resistance

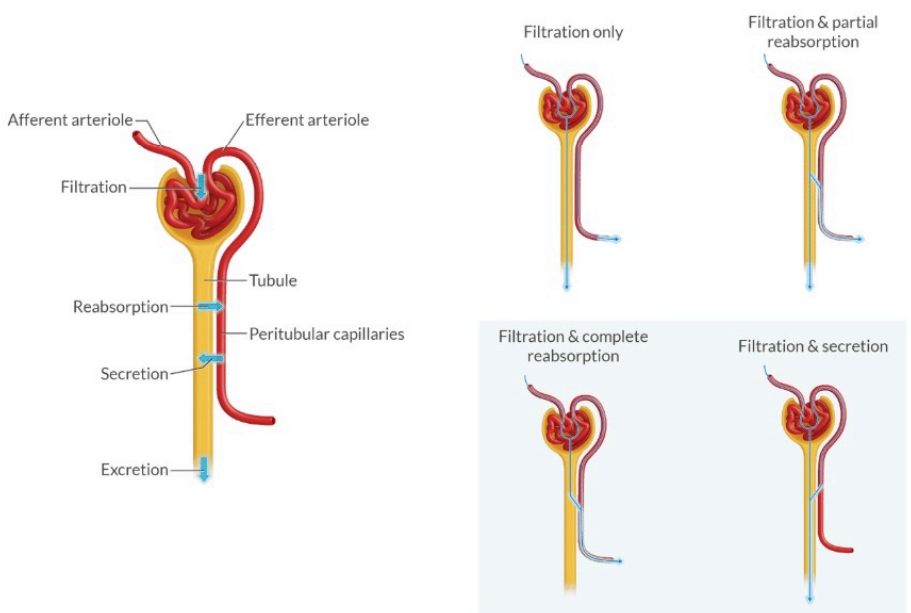
- Constriction of the efferent arteriole follows a biphasic pattern.
- Mild constriction reduces flow towards the peritubular capillaries and increases GFR.
- Excessive constriction reduces renal blood flow as well as GFR.
- Dilation of the efferent arteriole increases flow towards the peritubular capillaries and reduces GFR.

Reabsorption, Secretion, and Excretion

Since water, electrolytes, and glucose are freely filtered by the glomerulus, the body requires a mechanism to return these substances to the systemic circulation. Indeed, 99% of all that is filtered is reabsorbed as the glomerular filtrate makes its way through the nephron.

We know the concept of secretion and reabsorption can be confusing. If you think of these actions as originating from the efferent arteriole (not the tubule), everything will make more sense.

- Reabsorption — substance is transferred from the tubule to the peritubular capillaries
- Secretion — substance is transferred from the peritubular capillaries to the tubule
- Excretion — substance is removed from the body in the urine



Maximum Transport

For some substances, there's a maximum amount that can be reabsorbed into the peritubular blood. After the maximum value is achieved, the excess substance will be excreted in the urine. This occurs regardless of the plasma concentration of that substance.

A clinical example is a patient with hyperglycemia. Once the glucose concentration in the ultrafiltrate exceeds the maximum transport for glucose, the excess glucose is eliminated in the urine.

Urine Production

Urine formation is the sum of glomerular filtration, tubular reabsorption, and tubular secretion.

Urinary Excretion Rate = Filtration − Reabsorption + Secretion

References +

Old References +

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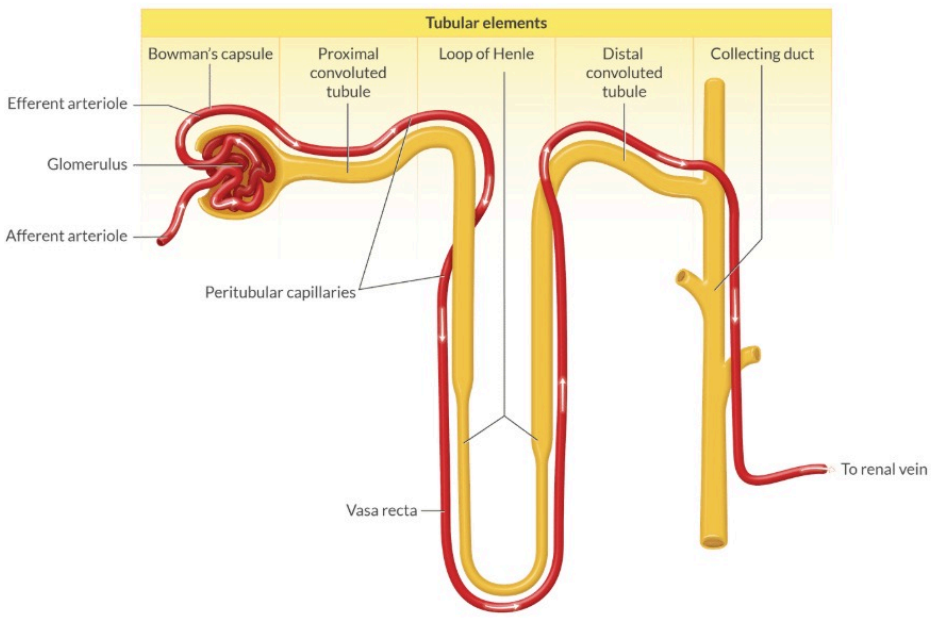

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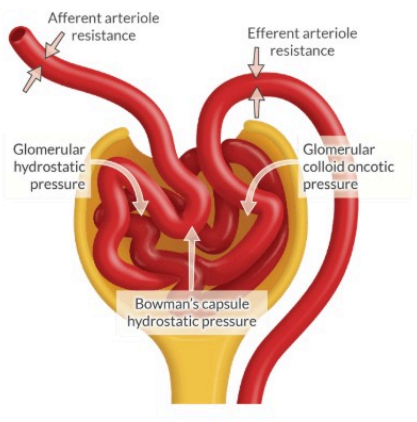

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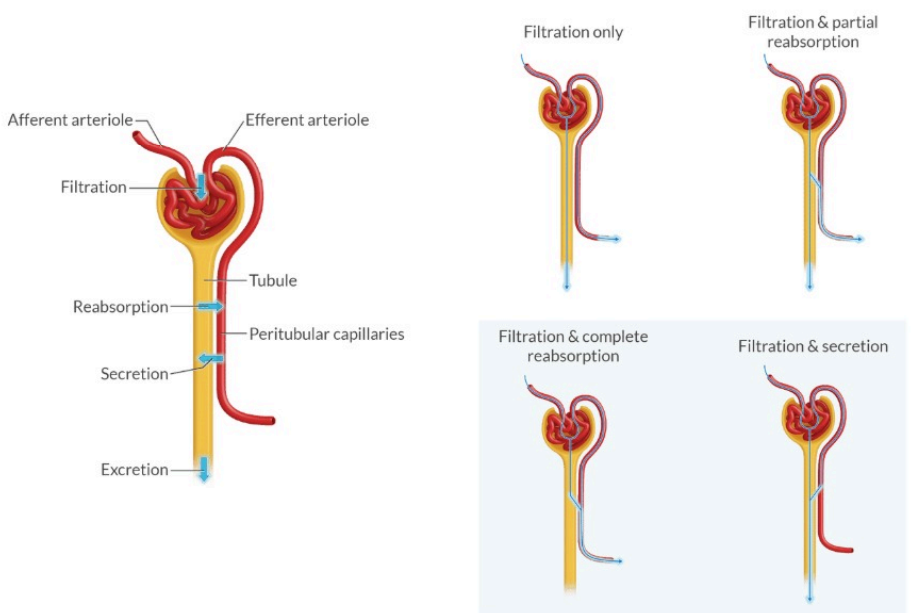

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Ready to go to the next lesson? NEXT LESSON

Rapid Review

Nephron Function: Part 2

1. Proximal tubule:
   - 65% of the filtered sodium load is actively transported out of the proximal tubule, 65% of filtered water follows.
   - Potassium, chloride, and bicarbonate follow suit in direct proportion.
   - Organic bases, acids, and hydrogen ions are secreted into the proximal tubule.
2. Descending loop of Henle:
   - The descending limb of the loop of Henle is highly permeable to water (20% of water is absorbed here) and modestly permeable to ions.
   - The descending limb participates in the countercurrent system, where the primary objective is to concentrate the urine by transferring water from the tubular fluid, to the peritubular interstitium, and ultimately returning it to the blood.
3. Ascending loop of Henle:
   - Unlike the descending limb, the ascending limb is impermeable to water.
   - 20% of the filtered sodium load is actively pumped from the tubular fluid to the peritubular interstitium. This process also contributes to the countercurrent mechanism.
   - Since water cannot follow sodium into peritubular interstitium, the ultrafiltrate becomes more dilute, and the peritubular interstitium becomes concentrated.
4. Distal tubule:
   - 5% of filtered sodium load is reabsorbed.
   - The late distal tubule is impermeable to water except in the presence of aldosterone or antidiuretic hormone.
5. Collecting duct:
   - 5% of the filtered sodium load is reabsorbed.
   - ADH and aldosterone also work in the collecting duct.
   - Atrial natriuretic peptides work here, too.

Want to learn on a deeper level? IN-DEPTH REVIEW

Ready to go to the next lesson? NEXT LESSON

In-Depth Review

Nephron Function: Part 2

You must understand the physiology of the nephron. Common test questions include anatomy, handling of electrolytes or glucose, and the site of action for diuretics. These are terrific hotspot questions. Completing the mind map in the workbook will help you tremendously.

- Because it helps you understand diuretic therapy, you must know sodium's fate at each point in the nephron.
- Reabsorption of electrolytes requires energy in the form of ATP, while reabsorption of water occurs by osmosis (no energy required).

Key Functions of Each Part of the Nephron

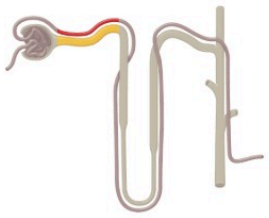
Under normal circumstances, excretion of water is regulated separately from excretion of solutes. For this to occur, the kidneys must be able to excrete urine that is either hypoosmotic or hyperosmotic with respect to body fluids. This ability to excrete urine of varying osmolality, in turn, requires that solute be separated from water at some point along the nephron.

Said another way, in order to produce dilute or concentrated urine, certain segments of the nephron tubules must separate the handling of water from sodium. The rule, "where sodium goes, water follows", is often broken in the nephron!

In the next section, we'll review the nephron tubules segment-by-segment. Pay special attention to the handling of water and solutes in each segment.

1

Proximal Convoluted Tubule



Bulk Reabsorption of Solutes and Water

- Sodium (65%) is actively transported from the proximal tubule and into the peritubular interstitium. This consumes a large quantity of oxygen.
- Water (65%) follows sodium by osmosis. ("Where sodium goes, water follows" holds true here.)
- Potassium, chloride, and bicarbonate follow sodium in direct proportion by the sodium co-transport mechanism. That means that 65% of these ions are also absorbed in the proximal tubule.
- Said another way, reabsorption of solutes and water is proportional in the PCT.
- Organic bases, acids, and hydrogen ions are secreted into the proximal tubule by the sodium counter-transport mechanism.
- Examples of organic acids and bases include bile salts, uric acid, catecholamines, toxins, and certain drugs.

References +

Old References +

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In-Depth Review

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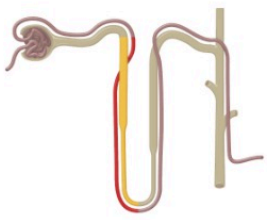
2

Descending Loop of Henle



Countercurrent Mechanisms + High Permeability to H_2O

- The primary function of the loop of Henle is to participate in forming concentrated or dilute urine. To accomplish this goal, **the loop of Henle separates the handling of sodium and water**.
- The ability of the kidneys to produce concentrated or dilute urine depends on the presence of a graduated hyperosmotic peritubular interstitium.
    - Said another way, there must be an osmotic gradient across the renal medulla, from the cortex to the papilla, to produce variable urine concentration
- Two countercurrent systems are needed to create and maintain the graduated hyperosmotic peritubular interstitium:
    - Loop of Henle = Countercurrent **multiplier** system that **creates** the osmotic gradient.
    - Vasa recta = Countercurrent **exchanger** system that **maintains** the medullary osmotic gradient.
- The descending limb of the loop of Henle is highly permeable to water (20% of water is reabsorbed here) and modestly permeable to ions. Therefore, the descending limb concentrates NaCl in the tubular fluid, which is delivered to the thick ascending limb.
- The osmolarity of the peritubular interstitium progressively increases (there is a gradient) as the descending limb travels from the cortex towards the medulla (osmolarity starts at 300 mOsm/L and increases to 1,500 mOsm/L in the renal pelvis). The increasing osmolarity provides the energy for passively reabsorbing water (osmosis).
- The vasa recta are peritubular capillaries that run parallel to the loop of Henle. This vascular network is essential because it returns the reabsorbed water to the blood, allowing the osmolarity in the peritubular interstitium to remain high.

References +

Old References +

Want to practice what you learned in this lesson? LET ME PRACTICE

Ready to go to the next lesson? NEXT LESSON

In-Depth Review

Nephron Function: Part 2

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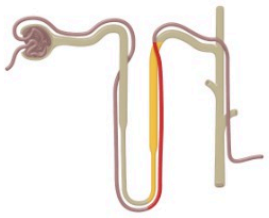
Ascending Loop of Henle



Countercurrent Mechanisms + No Permeability to H_2O

- In contrast to the descending limb of the loop of Henle, the thin and thick segments of the ascending limb are not permeable to water.
- Ions are pumped from the tubular fluid into the peritubular interstitium. The most important pump is the sodium-potassium-(2) chloride co-transporter (the target of loop diuretics). This system removes (reabsorbs) about 20% of the tubular sodium.
- Since water cannot follow sodium into the peritubular interstitium, the tubular fluid becomes more dilute, and the peritubular interstitium becomes concentrated. This is a key process of the countercurrent multiplier system function of the loop of Henle.
- Recall that the kidney contains two types of nephrons, superficial cortical nephrons and juxtamedullary nephrons. The juxtamedullary nephrons play a more significant role in the countercurrent multiplier.
- The two countercurrent systems work together to transfer water from the tubular fluid to the peritubular interstitium, and then return the water to the blood. Without this system, we would produce a ton of dilute urine, leading to dehydration.
- Hydrogen is excreted via the sodium-hydrogen exchange mechanism.

References +

Old References +

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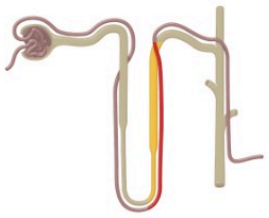

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- Recall that the kidney contains two types of nephrons, superficial cortical nephrons and juxtamedullary nephrons. The juxtamedullary nephrons play a more significant role in the countercurrent multiplier.
- The two countercurrent systems work together to transfer water from the tubular fluid to the peritubular interstitium, and then return the water to the blood. Without this system, we would produce a ton of dilute urine, leading to dehydration.
- Hydrogen is excreted via the sodium-hydrogen exchange mechanism.

References +

Old References +

Want to practice what you learned in this lesson? LET ME PRACTICE

Ready to go to the next lesson? NEXT LESSON

In-Depth Review

Nephron Function: Part 2

You must understand the physiology of the nephron. Common test questions include anatomy, handling of electrolytes or glucose, and the site of action for diuretics. These are terrific hotspot questions. Completing the mind map in the workbook will help you tremendously.

- Because it helps you understand diuretic therapy, you must know sodium's fate at each point in the nephron.
- Reabsorption of electrolytes requires energy in the form of ATP, while reabsorption of water occurs by osmosis (no energy required).

Key Functions of Each Part of the Nephron

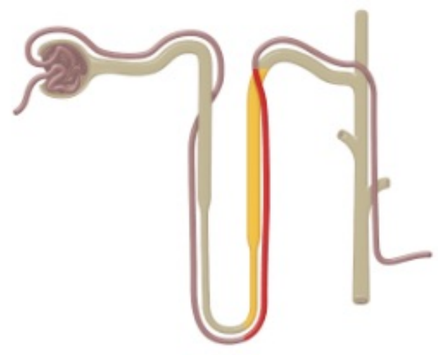
Under normal circumstances, excretion of water is regulated separately from excretion of solutes. For this to occur, the kidneys must be able to excrete urine that is either hypoosmotic or hyperosmotic with respect to body fluids. This ability to excrete urine of varying osmolality, in turn, requires that solute be separated from water at some point along the nephron.

Said another way, in order to produce dilute or concentrated urine, certain segments of the nephron tubules must separate the handling of water from sodium. The rule, "where sodium goes, water follows", is often broken in the nephron!

In the next section, we'll review the nephron tubules segment-by-segment. Pay special attention to the handling of water and solutes in each segment.

3

Ascending Loop of Henle



Countercurrent Mechanisms + No Permeability to H_2O

- In contrast to the descending limb of the loop of Henle, the thin and thick segments of the ascending limb are not permeable to water.
- Ions are pumped from the tubular fluid into the peritubular interstitium. The most important pump is the sodium-potassium-(2) chloride co-transporter (the target of loop diuretics). This system removes (reabsorbs) about 20% of the tubular sodium.
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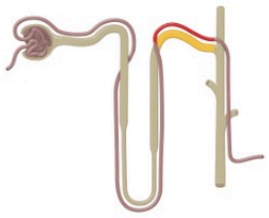
Distal Convoluted Tubule



Fine Tunes Solute Concentration

- Sodium (5%) is reabsorbed, and potassium, chloride, and bicarbonate follow via the sodium co-transport mechanism.
- The late distal tubule is impermeable to water except in the presence of aldosterone or antidiuretic hormone. These hormones can fine-tune the final urine concentration.
- Aldosterone increases Na^+ and water reabsorption and increases K^+ and H^+ secretion.
- ADH (vasopressin) increases water reabsorption only (no solutes).
- Parathyroid hormone increases calcium reabsorption.
- Is home to the juxtaglomerular apparatus (JGA). The JGA lies at the junction of the thick ascending limb and the distal tubule.
- Adjusts urea concentration.

References +

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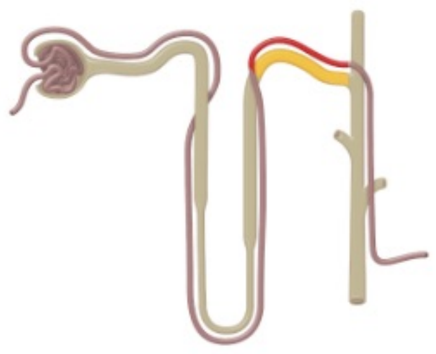

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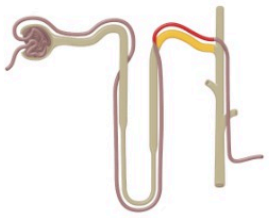

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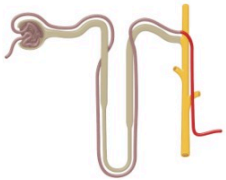
5

Collecting Duct



Regulates Final Concentration of Urine

- Reabsorbs sodium (5%).
- ADH (vasopressin) and aldosterone also work in the collecting duct.
- Atrial natriuretic peptide inhibits water and sodium reabsorption.
- Adjusts hydrogen concentration.

References +

Rapid Review

Diuretics

1. Carbonic anhydrase inhibitors noncompetitively inhibit carbonic anhydrase in the cells that make up the proximal tubule. This reduces the reabsorption of HCO_3^-, Na^+, and water.

2. Because carbonic anhydrase inhibitors produce a mild hyperchloremic metabolic acidosis, they're used to treat high altitude sickness and central sleep apnea. They're also useful for open-angle glaucoma.

3. Osmotic diuretics are sugars that undergo filtration but not reabsorption. They inhibit water reabsorption in the proximal tubule (primary site) as well as the loop of Henle. Water is excreted in excess of electrolytes.

4. Osmotic diuretics transiently increase intravascular volume. This can lead to pulmonary edema in the patient with congestive heart failure.

5. Loop diuretics disrupt the Na-K-2Cl transporter in the medullary region of the thick portion of the ascending loop of Henle (primary site). The amount of sodium that remains in the tubule overwhelms the distal tubule's reabsorption capability, so the patient eliminates a large volume of dilute urine.

6. Key complications of loop diuretics include hypokalemia, hypocalcemia, metabolic alkalosis, and ototoxicity.

7. Thiazides inhibit the Na-Cl co-transporter in the distal tubule.

8. Unique side effects of thiazide diuretics include hypercalcemia, hyperuricemia, and hyperglycemia.

9. Potassium-sparing diuretics are designed to prevent hypokalemia—a common side effect of other diuretics. This benefit can be problematic because it leads to hyperkalemia, a problem for patients who take NSAIDs, beta-blockers, or ACE inhibitors.

Want to learn on a deeper level? IN-DEPTH REVIEW

Ready to go to the next lesson? NEXT LESSON

In-Depth Review

Diuretics

Basis of Action

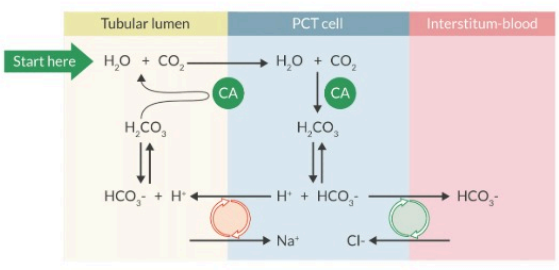
The kidney expends most of its oxygen on the Na/K-ATPase in the basolateral membrane of the tubular cells (the side that faces the peritubular capillaries). This pump maintains the concentration gradient for sodium so that sodium moves from the tubule to the peritubular capillaries. This system also powers a variety of other pumps that drive reabsorption of the rest of the electrolytes. These pumps are often the target of diuretic therapy.

By inhibiting sodium reabsorption, we're inhibiting water reabsorption as well. Remember that water follows sodium by osmosis. Also, by inhibiting sodium reabsorption, we're disrupting the other systems that drive reabsorption of chloride, calcium, magnesium, and bicarbonate. There are a few exceptions to this, which we've pointed out below.

Carbonic Anhydrase Inhibitors: Acetazolamide, Dorzolamide

Here's the big picture:

1. CO_2 and water diffuse into the proximal convoluted tubule cells.
2. Carbonic anhydrase facilitates the production of H_2CO_3.
3. H_2CO_3 dissociates into H^+ and HCO_3^-.
4. HCO_3^- diffuses into the interstitium then the blood.
5. H^+ is returned to the tubular lumen.



Mechanism of Action

Carbonic anhydrase inhibitors noncompetitively inhibit carbonic anhydrase in the cells that make up the proximal tubule.

- Inhibition of carbonic anhydrase reduces the reabsorption of HCO_3^-, Na^+, and water.
- Loss of HCO_3^- to the urine produces alkaline urine and mild hyperchloremic metabolic acidosis.

DOSE	CLINICAL USE	COMPLICATIONS
• Acetazolamide 250 – 500 mg		

Osmotic Diuretics: Mannitol, Glycerin, Isosorbide

Mechanism of Action

Osmotic diuretics are sugars that undergo filtration but not reabsorption. They inhibit water reabsorption in the proximal tubule (primary site) and the loop of Henle. Water is excreted in excess of electrolytes.

Osmotic diuretics increase plasma osmolarity, which reduces brain water (decreases ICP). The increased plasma volume augments RBF. In patients with poor myocardial function, expansion of the intravascular volume can precipitate heart failure and pulmonary edema.

Mannitol is also a free radical scavenger. This effect may limit cellular edema and decrease obstruction of the renal tubules.

DOSE	CLINICAL USE	COMPLICATIONS
• Mannitol 0.25 – 1 g/kg		

Loop Diuretics: Furosemide, Bumetanide, Ethacrynic Acid

Mechanism of Action

The ascending limb of the loop of Henle is impermeable to water. As the ultrafiltrate flows upward, the Na-K-2Cl transporter removes these ions from the ultrafiltrate and dilutes the urine. This region is responsible for 25% of the sodium reabsorption in the nephron.

Loop diuretics disrupt the Na-K-2Cl transporter in the medullary region of the thick portion of the ascending loop of Henle (primary site). The amount of sodium that remains in the tubule overwhelms the distal tubule's reabsorption capability. Thus, a large volume of dilute urine is excreted. Potassium, calcium, magnesium, and chloride are lost to the urine as well.

DOSE	CLINICAL USE	COMPLICATIONS
• Furosemide 20 – 200 mg • Bumetanide 0.5 – 2 mg • Ethacrynic acid 25 – 100 mg		

Thiazide Diuretics: Hydrochlorothiazide, Chlorthalidone, Metolazone, Indapamide

Mechanism of Action

Thiazides inhibit the Na-Cl co-transporter in the distal tubule. Stoelting says their primary site of action is the cortical region of the thick ascending loop of Henle, but this book seems to be an outlier.

Inhibition of the Na-Cl co-transporter in the distal tubule activates the Na-Ca antiporter. This increases Ca^{+2} reabsorption, ultimately increasing serum calcium.

A unique feature of thiazide diuretics is that they cause hyperglycemia. Possible mechanisms for this include reduced insulin release from the pancreas or impaired cellular glucose utilization in the body.

DOSE	CLINICAL USE	COMPLICATIONS
• Hydrochlorothiazide 12.5 – 50 mg • Chlorthalidone 12. 5 – 50 mg • Metolazone 1.25 – 5 mg • Indapamide 1.25 – 5 mg		

Potassium-Sparing Diuretics: Spironolactone, Amiloride, Triamterene

Mechanism of Action

- Amiloride and triamterene inhibit potassium secretion and sodium reabsorption in the collecting ducts. Their function is independent of aldosterone.
- Spironolactone exists in a subclass of potassium-sparing diuretics called aldosterone antagonists. By blocking aldosterone at mineralocorticoid receptors, spironolactone inhibits potassium secretion and sodium reabsorption in the collecting ducts.

DOSE	CLINICAL USE	COMPLICATIONS
• Spironolactone 12.5 – 100 mg • Amiloride 5 –10 mg • Triamterene 50 – 150 mg		

References +

Old References +

Rapid Review

Renal Function Tests

1. Renal function tests provide an assessment of either glomerular function or tubular function (concentrating ability).

2. Tests of glomerular function include:

   - Blood urea nitrogen (10 – 20 mg/dL)
   - Serum creatinine (0.7 – 1.5 mg/dL)
   - Creatinine clearance (110 – 150 mL/min)

3. Tests of tubular function (concentrating ability) include:

   - Fractional excretion of sodium (1 – 3%)
   - Urine osmolality (65 – 1,400 mOsm/L)
   - Urine sodium concentration (130 – 260 mEq/day)
   - Urine specific gravity (1.003 – 1.030)

4. Creatinine is a metabolic byproduct of creatine breakdown. It undergoes renal filtration but not reabsorption. Creatinine clearance is the best indicator of GFR.

5. You should be able to evaluate renal function tests to determine the cause of renal dysfunction.

Want to learn on a deeper level? IN-DEPTH REVIEW

Ready to go to the next lesson? NEXT LESSON

In-Depth Review

Renal Function Tests

Renal function tests provide an assessment of either glomerular function or tubular function.

Tests of Glomerular Function		Tests of Tubular Function (Concentrating Ability)	
Blood urea nitrogen	10 – 20 mg/dL	Fractional excretion of Na^+	1 – 3%
Serum creatinine	0.7 –1.5 mg/dL	Urine osmolality	65 – 1,400 mOsm/kg
Creatinine clearance	110 – 150 mL/min	Urine sodium concentration	130 – 260 mEq/day
		Urine specific gravity	1.003 – 1.030

Blood Urea Nitrogen

Urea is the primary metabolite of protein metabolism in the liver (amino acids → ammonia → urea)

Because urea undergoes filtration AND reabsorption, It's a better indicator of uremic symptoms than as a measurement of GFR.

Blood Urea Nitrogen	Etiology
< 8 mg/dL	Overhydration Decreased Urea Production • Malnutrition • Severe liver disease
20 – 40 mg/dL	Dehydration Increased Protein Input • High protein diet • GI bleed • Hematoma breakdown Catabolism • Trauma • Sepsis Decreased GFR
> 50 mg/dL	Decreased GFR

Serum Creatinine

- Creatine is produced by skeletal muscle, and creatinine is a metabolic byproduct of creatine breakdown.
- Creatinine production is constant and is directly proportional to muscle mass (It's lower in women and in the elderly)
- It undergoes renal filtration but not reabsorption. This makes it a useful indicator of GFR.
- A 100% increase in creatinine indicates a 50% reduction in GFR.

BUN: Creatinine Ratio

Since BUN undergoes filtration AND reabsorption, but creatinine undergoes filtration but NOT reabsorption, the ratio of these substances in the blood can help use evaluate the state of hydration.

- The normal BUN:Cr ratio is 10:1.
- A BUN:Cr ratio of > 20:1 suggests prerenal azotemia.
- The aforementioned non-renal causes of elevated BUN can also increase this ratio.

Creatinine Clearance

- Creatinine clearance is the most useful indicator of GFR.

$$GFR = \frac{[(140 - age) \bullet body\ weight\ (kg)]}{72 \bullet serum\ cr\ (mg/dL)}$$

*In women, this value should be multiplied by 0.85 to account for a smaller muscle mass

Fractional Excretion of Sodium

- $Fe(Na^+)$ relates sodium clearance to creatinine clearance.
- If $Fe(Na^+) < 1\%$, then more sodium is conserved relative to the amount of creatinine cleared. This suggests prerenal azotemia.
- If $Fe(Na^+) > 3\%$, then more sodium is excreted relative to the amount of creatinine cleared. This suggests impaired tubular function.

Urinary Sodium

- Working kidneys can conserve sodium, while failing kidneys waste sodium.

Urinalysis

URINE PROTEIN | SPECIFIC GRAVITY | URINE OSMOLALITY

- A large amount of protein in the urine indicates glomerular injury (> 750 mg/day or > +3 by urinalysis).

Differential Diagnosis of Prerenal Oliguria vs. Acute Tubular Necrosis

Diagnostic Test	Prerenal Oliguria	Acute Tubular Necrosis
Fractional excretion of Na^+ (%)	< 1	> 3
Urinary Na^+ (mEq/L)	< 20	> 20
Urine osmolality (mOsm/kg)	> 500	< 400
BUN:Creatinine ratio	> 20:1	10 – 20:1
Sediment	Normal Possible hyaline casts	Tubular epithelial cells Granular casts

References +

Old References +

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Ready to go to the next lesson? NEXT LESSON

Rapid Review

Acute Kidney Injury

1. Acute kidney injury (AKI) is a significant source of perioperative morbidity and mortality. The most common cause of perioperative kidney injury is ischemia-reperfusion injury.

2. Patients at greatest risk include those who have pre-existing kidney disease, CHF, advanced age, and sepsis.

3. The problem with using urine output as a surrogate of renal perfusion is that oliguria is often the result of the physiologic response to perioperative stress (increased ADH release during surgery). It's not specific for renal injury or risk of injury.

4. We can classify AKI on the basis of prerenal, intrinsic, or post renal injury. Understand that the treatment is not the same for a given classification.

    - Prerenal injury—Hypoperfusion
        - There is inadequate perfusion of the kidneys, but there is no intrinsic damage.
        - Restoration of renal blood flow with IVF, hemodynamic support, and PRBCs can halt the progression to ATN.
    - Intrinsic injury—Parenchymal
        - Intrinsic injury can be caused by injury of the tubules, glomerulus, or the interstitial space.
        - Causes of acute tubular necrosis include ischemia and nephrotoxic drugs.
        - Treatment is supportive.
    - Postrenal injury—Obstruction
        - The source of the obstruction can arise anywhere between the collecting system and the urethra.
        - Treatment is to remove the obstruction.

5. Attempting to convert oliguric to nonoliguric AKI with diuretics increases the risk of additional renal injury as well as mortality.

6. Renal dose dopamine does not prevent or treat AKI.

7. The KDIGO guidelines include a bundle designed to reduce the risk of AKI in high-risk patients, and several investigations have demonstrated a significant risk reduction.

Want to learn on a deeper level? IN-DEPTH REVIEW

Ready to go to the next lesson? NEXT LESSON

In-Depth Review

Acute Kidney Injury

Acute kidney injury (AKI) is a significant source of perioperative morbidity and mortality. The nephron (particularly the proximal tubule and thick ascending limb of the loop of Henle) has a high ATP consumption, and research reveals that impaired energetics is the fundamental basis of AKI. The underlying problems that give rise to AKI include renal hypoxia, exposure to nephrotoxic substances, and inflammation. The most common cause of perioperative kidney injury is ischemia-reperfusion injury.

The following patients are at risk for acute kidney injury during the perioperative period:

- Pre-existing kidney disease
- Prolonged renal hypoperfusion
- Congestive heart failure
- Advanced age
- Sepsis
- Jaundice
- High-risk surgery (Use of aortic cross-clamp and liver transplant)

Classification of Kidney Injury

Oliguria is common during the perioperative period and is usually prerenal in origin. The problem with using urine output as a surrogate of renal perfusion is that oliguria is often the result of the physiologic response to perioperative stress (increased ADH release during surgery). It's not specific for renal injury or risk of injury. Even so, a Foley catheter is the standard monitor of urine production. Finally, a weight-based urine output requirement doesn't take obesity into account.

There are three methods used to classify the severity of renal injury. All of them use the same urine output criteria, but there are minor differences in the creatinine values used to define AKI.

RIFLE | AKIN | KDIGO

RIFLE Criteria: Risk, Injury, Failure, Loss, End-Stage Kidney Disease

Class	SCr	Urine Output
Risk	Increase in SCr to > 1.5x baseline	UOP < 0.5 mL/kg/hr for > 6 hrs
Injury	Increase in SCr to > 2x baseline	UOP < 0.5 mL/kg/hr for > 12 hrs
Failure	Increase in SCr to > 3x baseline or... Increase ≥ 0.5 mg/dL to absolute value of ≥ 4 mg/dL	UOP < 0.3 mL/kg/hr > 12 hr or... Anuria for > 12 hr
Loss	Need for renal replacement therapy > 4 weeks	
End-Stage	Need for renal replacement therapy > 3 months	

Another problem with these approaches is that they tell you that renal injury has already occurred. There's currently a quest to discover renal biomarkers that warn of impending injury (so that it can be treated before it occurs). Examples include NGAL, cystatin C, and TIMP-2. More research is needed to determine how to best use these in the prevention of AKI.

Pseudo-Anatomic Classification of AKI

We can classify AKI on the basis of prerenal, intrinsic, or post renal injury. Understand that the treatment is not the same for a given classification. For instance, let's consider two very different patients, both with prerenal injury:

1. An oliguric patient with heart failure who requires a diuretic
2. A hypovolemic patient needs hydration (the opposite treatment).

The key takeaway is that not all oliguria is treated the same!

PRERENAL INJURY | INTRINSIC | POSTRENAL INJURY

Cause = Hypoperfusion

- There is inadequate perfusion of the kidneys, but there is no intrinsic damage.
- Perfusion is impaired as a result of hypovolemia, decreased cardiac output, systemic vasodilation, renal vasoconstriction, or increased intra-abdominal pressure.

Treatment

- Restoration of renal blood flow with IVF, hemodynamic support, and PRBCs (if insufficient DO_2) can halt the progression to ATN.
- Renal prostaglandins mediate vasodilation in the kidney. NSAIDs reduce prostaglandin synthesis, thereby causing constriction of the renal vasculature. Avoid NSAIDs in patients at risk for kidney injury.
- An improvement in UOP following an intravenous fluid bolus confirms the diagnosis of prerenal azotemia.

Etiologies of Acute Kidney Injury

This is a really intimidating list! We don't recommend that you memorize the whole thing. We've grouped each pathology under a general concept. Learn the concepts, and you'll be in great shape.

Prerenal Injury	Intrinsic Injury	Postrenal Injury
Intravascular Volume Depletion • Hemorrhage • Dehydration • GI losses (diarrhea, NGT, vomiting) • Cirrhosis • Nephrotic syndrome **Decreased Cardiac Output** • CHF • Sepsis • Cardiogenic shock **Systemic Vasodilation** • Sepsis • Anaphylaxis • Cirrhosis **Renal Vasoconstriction** • Early sepsis • Hepatorenal syndrome • Hypercalcemia • NSAIDs • Iodine containing IV contrast dye **Increased Abdominal Pressure** • Abdominal compartment syndrome	**Tubular Injury** • Ischemia from hypoperfusion • Myoglobin • Free hemoglobin (transfusion rxn) • Antibiotics • Contrast agents • Chemotherapeutics **Tubulointerstitial Injury** • Acute allergic interstitial nephritis • Infection • Infiltration **Glomerular Injury** • Inflammatory disease • Hemolytic uremic syndrome • Thrombotic thrombocytopenic purpura **Renal Vasculature** • Toxemia of pregnancy • Hypercalcemia • Contrast agents • Malignant hypertension • Scleroderma **Large Vessels** • Thrombosis • Vasculitis • Dissection • Trauma	**Urinary Tract Obstruction** • Retroperitoneal tumor/lymph nodes • Hematoma • Fibrosis • Surgical trauma to ureter • Nephrolithiasis • Blood clots/debris • Tumor • Stricture • Infection • Enlarged prostate • Bladder obstruction • Stones • Neurogenic bladder

Fluid Management

- The risk of prerenal azotemia is reduced by maintaining MAP > 65 mmHg and providing appropriate hydration.
- While there is no clear benefit between crystalloids and colloids, the use of hydroxyethyl starches is associated with an increased risk of renal morbidity.
- Excessive use of 0.9% NaCl can cause hyperchloremic metabolic acidosis.
- Attempting to convert oliguric to nonoliguric AKI with diuretics increases the risk of additional renal injury as well as mortality.

Vasopressors

- In healthy patients, alpha-1 agonists can reduce RBF.
- The septic patient will benefit from an alpha-1 agonist as long as it supports MAP. The benefits of increased renal perfusion outweigh the renal vasoconstrictive effects.
- Vasopressin preferentially constricts the efferent arteriole. It maintains GFR and UOP better than norepinephrine or phenylephrine.
- Renal dose dopamine does not prevent or treat AKI.

KDIGO Guidelines to Prevent AKI in High-Risk Patients

The KDIGO guidelines include a bundle designed to reduce the risk of AKI in high-risk patients, and several investigations have demonstrated a significant risk reduction. We'll highlight the components of this bundle that apply to the perioperative period.

- Use protocol-based management of hemodynamic and oxygenation parameters to prevent the development or worsening of AKI in high-risk patients.
- Do not use diuretics to prevent AKI.
- Do not use diuretics to treat AKI except in the setting of volume overload.
- Do not use the following to prevent or treat AKI: low-dose dopamine, fenoldopam, atrial natriuretic peptide, or recombinant human (rh)IGF-1.
- Avoid aminoglycoside antibiotics unless there is no suitable alternative available.
- Avoid IV amphotericin B when possible, but if not, then a lipid formulation is preferred over the conventional formulation.
- In critically ill patients, initiate insulin therapy to a target serum glucose of 110 – 149 mg/dL.
- Off-pump cardiopulmonary bypass should not be selected solely based on reducing the risk of AKI.

References +

Old References +

Want to practice what you learned in this lesson? LET ME PRACTICE

Ready to go to the next lesson? NEXT LESSON

Rapid Review

Chronic Kidney Disease

1. Chronic kidney disease is a progressive and irreversible disorder that reflects the ongoing inability of the kidneys to sustain their normal functions.

   - The most common cause of CKD is diabetes mellitus.
   - The second most common cause is hypertension.

2. Complications of chronic kidney disease include:

   - Uremic syndrome
   - Uremic bleeding
   - Anemia
   - HTN
   - Congestive heart failure
   - Coronary artery disease
   - Gap metabolic acidosis
   - Hyperkalemia
   - Osteodystrophy
   - Restrictive ventilatory defect
   - Peripheral neuropathy
   - Autonomic dysfunction
   - Infection

3. Dialysis is the cornerstone CKD treatment. Indications include:

   - Volume overload
   - Hyperkalemia
   - Severe metabolic acidosis
   - Symptomatic uremia
   - Overdose with a drug that is cleared by dialysis

4. Hypotension is the most common event during dialysis. This is due to intravascular volume depletion and osmotic shifts.

Want to learn on a deeper level? IN-DEPTH REVIEW

Ready to go to the next lesson? NEXT LESSON

In-Depth Review

Chronic Kidney Disease

Chronic kidney disease is a progressive and irreversible disorder that reflects the ongoing inability of the kidneys to sustain their normal functions.

The most common cause of CKD is diabetes mellitus. The second most common cause is hypertension.

Stages of Kidney Disease

Stage	Description	GFR mL/min
1	Normal	≥ 90
2	Mildly decreased	60 – 89
3	Moderately decreased	30 – 59
4	Severely decreased	15 – 29
5	Kidney failure *Requires dialysis	≤ 15

Uremic Syndrome

- S/Sx: include anemia, fatigue, N/V, anorexia, and coagulopathy.
- The blood urea nitrogen level parallels uremic symptoms and can be used to guide management.

Uremic Bleeding

- Uremic patients are at an increased risk of bleeding.
- Bleeding time is a measure of platelet function. It's elevated by uremia and is the most accurate predictor of bleeding risk.
- The PT, PTT, and platelet counts are normal.
- The first-line treatment is desmopressin (von Willebrand factor 8).
- Cryoprecipitate may be used to provide 8-vWF, however its use is associated with an increased risk of viral transmission.
- Dialysis improves bleeding time, so it should be performed within 24 hours of surgery.

Anemia

- Decreased production of erythropoietin leads to normochromic normocytic anemia.
- Excess parathyroid hormone also contributes to anemia by replacing bone marrow with fibrotic tissue.
- Treatment consists of exogenous EPO or darbepoetin + iron supplementation.
- EPO can cause hypertension.
- Blood transfusion is not a first-line treatment because it increases the risk of HLA sensitization and future rejection of a transplanted kidney.

Cardiovascular

- Hypertension is the result of RAAS activation leading to sodium retention and fluid overload.
- Salt and water retention contribute to congestive heart failure and pulmonary edema.
- Coronary artery disease is the most common cause of death. Assume all patients with chronic kidney disease have CAD.
- Pericarditis is common with uremia. There is a risk of pericardial effusion and cardiac tamponade.

Acid-Base Balance

- Decreased excretion of non-volatile acid contributes to a gap metabolic acidosis.
- Remember that a gap acidosis is the result of an accumulation of non-volatile acids, while a non-gap acidosis is the result of a loss of HCO_3^- ions.
- Acidosis shifts the oxyhemoglobin dissociation curve to the right. This partially compensates for anemia.

Potassium

- Hyperkalemia is the result of impaired potassium excretion.
- Dialysis is indicated when serum potassium exceeds 6 mEq/L.
- Other treatments that reduce serum potassium include:
  - Glucose (25 - 50g) + insulin (10 - 20 units).
  - Hyperventilation (for every 10 mmHg decrease in $PaCO_2$, the serum potassium level decreases by 0.5 mEq/L).
  - Sodium bicarbonate (50 - 100 mEq).
- Calcium chloride (1g) does not alter serum potassium concentration. Instead, it raises threshold potential in the myocardium and reduces the risk of lethal dysrhythmias.

Osteodystrophy

Renal osteodystrophy is caused by:

- Decreased vitamin D production
- Secondary hyperparathyroidism

Pathophysiology:

- An inadequate supply of vitamin D impairs calcium absorption in the GI tract.
- The body responds to hypocalcemia by increasing parathyroid hormone release. In this situation, PTH demineralizes bone to restore serum calcium concentration.
- Additionally, hyperphosphatemia contributes to low serum calcium. Phosphate clearance parallels GFR (low GFR → increased serum phosphate).
- The net result is a decreased bone density and increased risk of bone fractures.

Respiratory

- Increased intravascular volume and uremia create a restrictive ventilatory defect.
- Volume overload may lead to pulmonary edema.
- Metabolic acidosis is compensated by respiratory alkalosis (hyperventilation).

Neurologic

- Uremia impairs nerve conduction.
- Autonomic dysfunction contributes to reduced baroreceptor responsiveness (hemodynamic instability) as well as delayed gastric emptying.
- Peripheral neuropathies are both sensory and motor. They contribute to silent myocardial ischemia.
- Central symptoms may be mild (impaired abstract thinking, insomnia) and may progress to severe (seizures, encephalopathy, coma).

Infection

- Impaired white cell function and a low protein diet contribute to the high risk of infection.
- Frequent exposure to blood products increases the risk of viral transmission.

Dialysis

Dialysis is the cornerstone of treatment. There are five indications for its use:

- Volume overload
- Hyperkalemia
- Severe metabolic acidosis
- Symptomatic uremia
- Overdose with a drug that is cleared by dialysis

Considerations for the patient on dialysis:

- Hemodialysis is more efficient than peritoneal dialysis.
- Peritoneal dialysis is favored in patients who cannot tolerate fluid shifts associated with hemodialysis (CHF or unstable angina).
- Emergent dialysis is carried out by obtaining central access via the internal jugular or femoral vein.
- Hypotension is the most common event during dialysis. This is due to intravascular volume depletion and osmotic shifts.
- Anesthetic options for graft placement include brachial plexus blockade, local infiltration, or general anesthesia.
- Infection is a leading cause of death in dialysis patients. A strict aseptic technique is required.

References +

Old References +

Rapid Review

Anesthetic Drugs & Impaired Renal Function

1. The modern halogenated anesthetics (Des, Sevo, and Iso) do not directly cause kidney dysfunction.
2. Although there's no human data that links AKI and compound A, the FDA recommends that sevoflurane be administered at a rate of 1 L/min for no more than 2 MAC hours.
3. The rate of compound A production is increased by a low FGF, high sevo vol%, warm soda lime, and increased CO_2 production.
4. Succinylcholine can increase serum potassium by 0.5–1.0 mEq/L for up to 10 – 15 min. It's safe in patients with renal failure who have a normal potassium level.
5. Due to their organ-independent elimination, cisatracurium and atracurium are the best nondepolarizing NMBs for renal failure.
6. Both anticholinesterases and anticholinergics do not require dosage adjustments in patients with kidney disease.
7. Sugammadex is not recommended in patients with severe renal impairment.
8. Propofol may need an upward dosage adjustment due to a hyperdynamic circulation and disruption of the blood-brain barrier secondary to uremia.
9. Morphine is metabolized to morphine-6-glucuronide. This product is more potent than morphine, and it relies on renal excretion. Accumulation can contribute to respiratory depression.
10. Meperidine is metabolized to normeperidine. Accumulation of normeperidine can cause convulsions.

Want to learn on a deeper level? IN-DEPTH REVIEW

Ready to go to the next lesson? NEXT LESSON

In-Depth Review

Anesthetic Drugs & Impaired Renal Function

Instead of giving you a huge list of drugs that are acceptable in patients with impaired renal function, we're going to focus our discussion on the exceptions, controversies, and misconceptions.

Altered responses to anesthetic drugs are usually due to one or more of the following:

- Active metabolites
- Decreased protein binding increases the free fraction
- Impaired elimination of active metabolites
- Acidosis alters the proportion of ionized and nonionized drug
- Uremia-induced disruption in the blood-brain barrier

Patients may experience exaggerated hemodynamic effects due to:

- Antihypertensive medications, specifically ACE inhibitors and angiotensin receptor blockers
- Attenuation of SNS tone
- Positive pressure ventilation

Halogenated Anesthetics

Although their metabolism liberates free fluoride ions, the modern halogenated anesthetics (Des, Sevo, and Iso) do not directly cause kidney dysfunction. In the sense that they can induce hypotension and depress cardiac output, they can indirectly cause renal injury by reducing perfusion. Additionally, a reduction in renal perfusion coupled with renal vasoconstriction or nephrotoxic agents further increases the likelihood of acute kidney injury.

SEVOFLURANE | METHOXYFLURANE

Compound A is produced when sevoflurane is degraded by soda lime.

Although there is no human data that links AKI and compound A, the FDA recommends that sevoflurane be administered at a rate of 1 L/min for no more than 2 MAC hours. After 2 MAC hours have elapsed, the fresh gas flow should be increased to 2 L/min.

Factors associated with increased compound A production include:

- High concentrations over a long period of time
- Low fresh gas flow
- High temperature of CO_2 absorbent
- Increased CO_2 production

Muscle Relaxants

SUCCINYLCHOLINE | BENZYLISOQUINOLINES | AMINOSTEROIDS

- Opening of the nAChR at the neuromuscular junction can increase serum potassium by 0.5 – 1.0 mEq/L for up to 10 – 15 min. In patients with upregulation of extrajunctional receptors, the potassium concentration may rise even further.
- Renal failure does not cause upregulation of extrajunctional receptors, so succinylcholine is safe in patients with renal failure and a normal potassium level. In the patient with hyperkalemia (K^+ > 5.5 mEq/L), the normal response to succinylcholine may increase serum potassium to a dangerous level.
- In patients with renal disease, succinylcholine should not be administered as a continuous infusion, because its primary metabolite (succinylmonocholine) is excreted by the kidney. Succinylmonocholine is weakly pharmacologically active, however it may prolong the period of paralysis.

Reversal Agents

- Both anticholinesterases and anticholinergics used to reverse neuromuscular blockers undergo renal elimination, and thus share a similar increase in duration. They do not require dosage adjustments.
- Sugammadex is not recommended in patients with severe renal impairment.

Induction Agents

- Propofol may need an upward dosage adjustment due to a hyperdynamic circulation and disruption of the blood-brain barrier secondary to uremia.

Opioid Agonists

- Morphine is metabolized to morphine-6-glucuronide. This product is more potent than morphine, and it relies on renal excretion. Accumulation can contribute to respiratory depression.
- Meperidine is metabolized to normeperidine. Accumulation of normeperidine can cause convulsions.
- Hydromorphone is metabolized to an active metabolite, hydromorphone-3-glucuronide. This can cause prolonged respiratory depression and myoclonus. The books are inconsistent about this (some say there's no active metabolite), so if you are asked about renally excreted metabolites, then morphine or meperidine are the best answer choices. Whether or not hydromorphone produces an active metabolite, renal impairment does necessitate a dose reduction.
- Fentanyl, sufentanil, alfentanil, and remifentanil do not produce active metabolites and are better choices with renal failure.

Dexmedetomidine

- Dexmedetomidine is biotransformed by the liver and may be used safely in this population. Its duration may be prolonged.

References +

Old References +

Want to practice what you learned in this lesson? LET ME PRACTICE

Ready to go to the next lesson? NEXT LESSON

Rapid Review

Nephrotoxic Agents

1. The risk of AKI related to nephrotoxic agents is increased in patients with pre-existing kidney disease as well as those with other risk factors, including hypovolemia, sepsis, and congestive heart failure.

2. Prevention of contrast-induced nephropathy (CIN):

   - Use nonionic iso- or low-osmolar contrast instead of hyperosmolar contrast.
   - Use the lowest volume of contrast as the procedure will allow.
   - Withhold other drugs with known nephrotoxic effects.
   - Hydrate with intravenous 0.9% NaCl before administration of contrast dye.
   - Sodium bicarbonate injection or infusion.
   - *N*-acetylcysteine is a free radical scavenger. It has fallen out of favor for lack of efficacy.

3. Radiographic contrast media can also cause anaphylaxis.

4. Myoglobin is nephrotoxic and can lead to tubular obstruction and acute tubular necrosis. It's best treated with aggressive IV hydration and an agent to alkalize the urine (e.g., sodium bicarbonate or acetazolamide).

5. There are two ways that sevoflurane can theoretically impair renal function—compound A (produced in the breathing circuit) and production of free fluoride ions (produced by the liver).

6. Select nephrotoxic antibiotics include gentamycin, tobramycin, amikacin, vancomycin, and amphotericin B.

7. Calcineurin inhibitors (cyclosporine and tacrolimus) are immunosuppressant agents that prevent the rejection of transplanted organs. Sirolimus is a non-calcineurin inhibitor that carries a much lower risk of nephrotoxicity.

Want to learn on a deeper level? IN-DEPTH REVIEW

Ready to go to the next lesson? NEXT LESSON

In-Depth Review

Nephrotoxic Agents

Because a primary function of the kidney is to eliminate toxins from the body, it should be logical that the kidneys may succumb to the damaging effects of these compounds. By concentrating the toxins inside the tubules, this region is at particular risk. The concentration of the toxin, as well as the duration of exposure, determine the extent of its nephrotoxic effects.

The risk of AKI related to nephrotoxic agents is increased in patients with pre-existing kidney disease as well as those with other risk factors including hypovolemia, sepsis, and congestive heart failure.

Radiographic Contrast Media

There are two mechanisms by which radiographic contrast media causes nephrotoxicity:

- Ischemic injury due to vasoconstriction in the renal medulla
- Direct cytotoxic effects

Signs of AKI begin at 24 - 36 hours and peak between 3 - 5 days.

Prevention of contrast-induced nephropathy (CIN):

- Use nonionic iso- or low-osmolar contrast instead of hyperosmolar contrast.
- Use the lowest volume of contrast as the procedure will allow.
- Withhold other drugs with known nephrotoxic effects.
- Hydrate with intravenous 0.9% NaCl before administration of contrast dye.
- Sodium bicarbonate injection or infusion.
- N-acetylcysteine is a free radical scavenger. It has fallen out of favor for lack of efficacy.

Don't forget - radiographic contrast media can also cause anaphylaxis.

Myoglobin

Myoglobin is released into the circulation during a hemolytic reaction or rhabdomyolysis. Hemolytic reactions were covered in Blood 2: Transfusion, so we'll focus our discussion on rhabdomyolysis.

Rhabdomyolysis and myoglobinemia are sequelae of direct muscle trauma, muscle ischemia, or prolonged immobilization. Myoglobin binds oxygen inside of the myocyte. When it's released into the circulation, it's freely filtered at the glomerulus. In the presence of acidic urine (pH < 5.6), myoglobin precipitates in the proximal tubule. This causes tubular obstruction and acute tubular necrosis. In addition, myoglobin scavenges nitric oxide, leading to renal vasoconstriction and ischemia.

Creatine phosphokinase is also released during muscle injury. A level above 10,000 units/L is associated with an increased risk of kidney injury.

Preventative strategies include:

- Maintenance of renal blood flow and tubular flow with IV hydration
- Osmotic diuresis with mannitol
- Keep UOP > 100 - 150 mL/hr
- Administer sodium bicarbonate and/or acetazolamide to alkalize the urine

Hemolysis from a hemolytic reaction is treated in the same way.

Sevoflurane

There are two ways that sevoflurane can theoretically impair renal function. Before we go any further, however, we'd like to point out that there is no solid human data that support these concerns.

Compound A (Produced in the Breathing Circuit)

- Compound A is produced when sevoflurane is exposed to soda lime.
- The FDA says that a minimum FGF of 1 L/min is safe for up to 2 MAC hours.
- Example: 2% x 2 hours or 1% x 4 hours.
- After two MAC hours have elapsed, the minimum FGF is 2 L/min.
- The rate of compound A production is increased by a low FGF, high sevo vol%, warm soda lime, and increased CO_2 production.

Free Fluoride Ions (Produced in the Liver)

- ~5% of sevoflurane is metabolized by the liver.
- Hepatic metabolism liberates inorganic fluoride ions.
- Inorganic fluoride ions are nephrotoxic; they impair the concentrating mechanism in the renal tubules.
- Previous research with methoxyflurane concluded that the risk of nephrotoxicity was increased when [Fl-] exceeded 50 µM/L. This does not seem to be the case with sevoflurane.

Aminoglycosides (Gentamycin, Tobramycin, and Amikacin)

These drugs are polycationic compounds that bind to the anionic brush border in the proximal tubules. They are transported into the cytosol, where they induce free radical damage.

The risk of AKI is reduced with intravenous fluids, correction of correctable risk factors, and close monitoring of serum trough levels.

Other Antibiotics

- Amphotericin B
- Vancomycin
- Sulfonamide
- Tetracyclines
- Cephalosporins

NSAIDs

The nephrotoxic actions of NSAIDs have been addressed previously.

Calcineurin Inhibitors (Cyclosporine and Tacrolimus)

These are immunosuppressant agents that prevent the rejection of transplanted organs. Side effects include hypertension and renal vasoconstriction.

Sirolimus is a non-calcineurin inhibitor that carries a much lower risk of nephrotoxicity.

References +

Old References +

Want to practice what you learned in this lesson? LET ME PRACTICE

Ready to go to the next lesson? NEXT LESSON

Rapid Review

Transurethral Resection of the Prostate (TURP)

1. Neuraxial anesthesia (spinal is preferred) is the most common approach to TURP. A T10 level is required. This approach allows for earlier detection of complications because you can assess the patient's neurologic status throughout the surgical procedure.

2. TURP requires a continuous fluid source. Irrigation fluid is absorbed through the open venous sinuses of the prostate. This means there is a risk of circulatory overload and toxicity from irrigation solutes.

3. The absorbed volume can be estimated as 10 – 30 mL/min of resection time. Resection time should be limited to 1 hour.

4. Absorption of a large volume of hypo-osmolar irrigation solution can produce TURP syndrome. The classic triad includes hypertension, bradycardia, and a change in mental status.

5. You must be aware of the pros and cons of all the options for irrigation solutions. See the In-Depth review for details.

6. Glycine absorption can lead to transient blindness. No treatment is required.

7. Treatment for TURP syndrome includes providing cardiopulmonary support, correcting serum sodium levels, and administering midazolam for seizures.

8. Other complications of TURP include bladder perforation (abdominal and shoulder pain), bleeding, and hypothermia.

Want to learn on a deeper level? IN-DEPTH REVIEW

Ready to go to the next lesson? NEXT LESSON

In-Depth Review

Transurethral Resection of the Prostate (TURP)

TURP is indicated for prostate removal for benign prostatic hypertrophy.

- A resectoscope is inserted into the urethra to allow access to the prostate.
- Neuraxial anesthesia (spinal is preferred) is the most common approach to TURP. A T10 level is required.
- This approach allows for earlier detection of complications because you can assess the patient's neurologic status throughout the surgical procedure.
- General anesthesia is an acceptable alternative, however it removes the monitoring benefit of a conscious patient.

Irrigation Solutions

TURP requires a continuous fluid source to facilitate visualization and irrigation of the bladder and prostate.

- Irrigation fluid is absorbed through the open venous sinuses of the prostate. This means that a portion of the irrigation fluid will be absorbed into the patient's systemic circulation (risk of circulatory overload and toxicity from irrigation solutes).
- The absorbed volume can be estimated as 10 – 30 mL/min of resection time (the longer the resection time, the more fluid is absorbed, and the greater the likelihood of complications).
- The height of the solution should be kept no more than 60 cm above the OR table. Some texts say the height should be reduced towards the end of the case because more venous sinuses are open → increased intravascular absorption.
- Resection time should be limited to 1 hour.

Characteristics of Irrigation Solutions

- The ideal irrigation fluid provides good surgical visibility (it should be clear), is isotonic, and is absent of toxicity.
- 0.9% NaCl or LR would be great choices, however they're highly ionized, so they're good conductors of electricity. Therefore, these fluids are contraindicated when monopolar electrocautery is used, however the introduction of bipolar cautery in newer resectoscopes permits the use of ionic solutions.
- Water is absent of electrolytes, and free water absorption can decrease serum osmolality and cause dilutional hyponatremia and hemolysis.

Solution	Osmolality (mOsm/L)	Pros	Cons
Distilled Water	0	Good surgical visibility	Increased risk of TURP syndrome: • Hyponatremia • Hemolysis • Hemoglobinuria → renal failure
Glycine	200	Decreased risk of TURP syndrome	Increased ammonia → decreased LOC Transient postop visual syndrome • Blindness or blurry vision x 24 – 48 hrs • Glycine is an inhibitory neurotransmitter in the eye
Sorbitol 3.3%	165	Decreased risk of TURP syndrome	Hyperglycemia Osmotic diuresis Lactic acidosis (following massive absorption)
Mannitol 5%	275	Osmolarity similar to plasma Renal filtration and excretion (no metabolism)	Osmotic diuresis Transient plasma expansion (risk of LV failure)
NaCl 0.9%	308	Osmolarity just a bit higher than plasma Absent of many of side effects associated with other solutions	Can only be used with bipolar electrocautery Do NOT use with unipolar electrocautery • Can transmit electrical current to the patient!!!

TURP Syndrome

Absorption of a large volume of hypo-osmolar irrigation solution can produce TURP syndrome. The classic triad includes hypertension (with increased pulse pressure), bradycardia (reflex), and a change in mental status.

- Serum Na^+ < 120 mEq/L increases the risk of complications.
- Serum Na^+ < 110 mEq/L is associated with seizure, coma, and lethal ventricular dysrhythmias.

Cardiopulmonary	CNS	Metabolic	Misc.
Circulatory overload • Hypertension • Reflex bradycardia • CHF • Pulmonary edema • Dysrhythmias • Myocardial infarction	Restlessness Nausea and vomiting Cerebral edema Seizures Coma	Hyponatremia	Hemolysis Hypo-osmolality

Treatment

- Support oxygenation and cardiovascular support.
- Tell the surgeon to abort the procedure.
- Lab data includes electrolytes, hematocrit, creatinine, glucose, and 12-lead EKG.
- If Na^+ > 120 mEq/L, then restrict fluids and give + furosemide (loop diuretic).
- If Na^+ < 120 mEq/L, then give 3% NaCl at < 100 mL/hr (discontinue when Na^+ > 120 mEq/L).
- Correcting serum Na^+ too quickly increases the risk of central pontine myelinolysis.
- Midazolam may be used for seizures.
- Proceed with tracheal intubation and mechanical ventilation if the patient has difficulty with oxygenation and/or pulmonary edema (Chest auscultation and CXR will be helpful).

Other Complications

BLADDER PERFORATION | BLEEDING | HYPOTHERMIA

Bladder perforation can occur if the resectoscope punctures the bladder wall.

- Inadvertent stimulation of the obturator nerve through the bladder wall can cause lower extremity movement, which may cause the resectoscope to puncture the bladder wall.
- This complication is more easily recognized in a conscious patient, especially if sensory anesthesia does not extend much beyond T10.
- Presentation includes abdominal and shoulder pain.
- A reduction of irrigation fluid return is an early sign of bladder rupture.
- Treatment is supportive (IVF, vasopressors, etc.) with a serial assessment of H&H and transfusion as indicated.
- The patient will require emergent suprapubic cystostomy or possibly exploratory laparotomy.

References +

Old Reference +

Want to practice what you learned in this lesson? LET ME PRACTICE

Ready to go to the next lesson? NEXT LESSON

Rapid Review

Lithotripsy

1. Lithotripsy is a procedure that breaks up stones in the kidney, ureter, or bladder.
2. Extracorporeal shock wave lithotripsy (ESWL) delivers shock waves in rapid succession that are directed at the stone.
3. Absolute contraindications to ESWL include pregnancy and coagulopathy. The presence of a pacemaker is a relative contraindication.
4. The shock wave can produce dysrhythmias (probably due to mechanical influence), and the pulse wave is timed to the R wave on the EKG to minimize the risk of "R-on-T" phenomenon.
5. Percutaneous nephrolithotomy is often used when ESWL has been ineffective. Urethral stents are placed, and then the urologist places a nephrostomy tube to access the stone. The patient most commonly receives GETA and is placed in the prone position.
6. Laser lithotripsy uses a laser to break up the stone. Irrigation fluid is used, so the considerations listed in our TURP coverage apply here. Follow laser precautions.

Want to learn on a deeper level? IN-DEPTH REVIEW

Test your understanding of this tutorial with a quiz. QUIZ

Share your feedback to help us improve your experience. SHARE FEEDBACK

In-Depth Review

Lithotripsy

Lithotripsy is a procedure that breaks up stones in the kidney, ureter, or bladder.

- Nephrolithiasis = Kidney stone
- Ureterolithiasis = Ureter stone
- Cystolithiasis = Bladder stone

The presence of stones causes severe pain, but can also cause obstructive renal failure.

Extracorporeal Shock Wave Lithotripsy

ESWL delivers shock waves in rapid succession that are directed at the stone.

- Because the acoustic impedance of water and human tissue is roughly similar, the shock wave moves through the body until it reaches the body-stone interface.
- At this point, the energy is released, breaking up the stone, producing smaller stone fragments that are eliminated via the urine.
- It's important that there's nothing between the energy source and the stone.

Contraindications

For your exam, we think you'll need to be familiar with the contraindications to ESWL.

Absolute Contraindications	Relative Contraindications
Pregnancy Risk of bleeding (bleeding disorder or anticoagulation)	Pacemaker / ICD Calcified aneurysm of the aorta or renal artery (problem of density) UTI (untreated) Obstruction beyond the renal stone (can't eliminate fragments) Morbid obesity (further distance from energy source to stone)

Complications

- The shock wave can produce dysrhythmias (probably due to mechanical influence), and the pulse wave is timed to the R wave on the EKG to minimize the risk of "R-on-T" phenomenon.
- Any internal organ in the path of the shock wave is at risk for perforation.
- Skin bruising and petechiae may occur.
- Hematuria is a common side effect.

Percutaneous Nephrolithotripsy

- This approach is often used when ESWL has been ineffective.
- Urethral stents are placed, and then the urologist places a nephrostomy tube to access the stone.
- The patient most commonly receives GETA and is placed in the prone position.
- Irrigation fluid is used, so the considerations listed in our TURP coverage apply here.
- Pneumothorax is a possible complication.

Laser Lithotripsy

- Laser lithotripsy uses a laser to break up the stone.
- Follow laser precautions. These are covered in the Miscellaneous Topics tutorial in Unit 12.
- Irrigation fluid is used, so the considerations listed in our TURP coverage apply here.
- Patients are typically placed in the lithotomy position.

References +

Old References +