

ANSWER KEY WITH EXPLANATIONS FOR CHAPTER 14

Skill Drill Answers

SD 14.1: Diuretic Site of Action Matching

1. **B** — Loop diuretics act on thick ascending limb
2. **C** — Thiazides act on distal convoluted tubule
3. **A** — CA inhibitors act on proximal tubule
4. **D** — Aldosterone antagonists act on collecting duct
5. **D** — ENaC blockers act on collecting duct
6. **A-D** — Mannitol acts throughout the nephron (osmotic)

SD 14.2: True/False with Correction

1. **T** — Loop diuretics are the most potent.
2. **F** — Thiazides **DECREASE** calcium excretion; **LOOP** diuretics increase it.
3. **F** — Spironolactone is **NON-SELECTIVE**; **EPLERENONE** is selective.
4. **T** — All potassium-sparing diuretics can cause hyperkalemia.
5. **F** — Acetazolamide is a **WEAK** diuretic; **LOOP** diuretics are most potent.
6. **F** — Furosemide oral bioavailability is **VARIABLE** (10-100%).

SD 14.3: Fill in the Blank

1. **Na⁺/K⁺/2Cl⁻ (NKCC2)**
2. **Na⁺/Cl⁻ (NCC)**
3. **spironolactone (or eplerenone)**

4. **bicarbonate**
 5. **intracranial**
 6. **chlorthalidone**
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SD 14.4: Transporter Matching

1. **A** — Furosemide inhibits NKCC2
 2. **B** — HCTZ inhibits NCC
 3. **E** — Spironolactone blocks mineralocorticoid receptor
 4. **C** — Amiloride blocks ENaC
 5. **D** — Acetazolamide inhibits carbonic anhydrase
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SD 14.5: Electrolyte Effect Prediction

1. **hypo** — Loop diuretics cause hypokalemia
 2. **hypo** — Thiazides cause hypokalemia
 3. **hyper** — Aldosterone antagonists cause hyperkalemia
 4. **hyper** — ENaC blockers cause hyperkalemia
 5. **hypo** — CA inhibitors cause hypokalemia
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SD 14.6: Rapid Recall

1. **Loop diuretics**
 2. **Thiazides**
 3. **Gynecomastia**
 4. **Hypokalemia**
 5. **Mannitol**
 6. **Torsemide**
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SD 14.7: Complete the Sentence

1. **increase**

2. **decrease**
 3. **days**
 4. **immediate**
 5. **longer**
 6. **variable**
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SD 14.8: Diuretic Potency Ranking

Loop diuretics: **1** (most potent)

Thiazide diuretics: **2**

Carbonic anhydrase inhibitors: **3**

Potassium-sparing diuretics: **4** (least potent)

SD 14.9: Clinical Indication Matching

1. **A** — Furosemide for acute pulmonary edema
 2. **B** — Chlorthalidone for hypertension
 3. **C** — Spironolactone for HFrEF mortality benefit
 4. **D** — Acetazolamide for altitude sickness
 5. **E** — Mannitol for cerebral edema
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SD 14.10: Adverse Effect Identification

1. **A** — Loop diuretics cause ototoxicity
 2. **C** — Spironolactone causes gynecomastia
 3. **B** — Thiazides cause severe hyponatremia in elderly
 4. **D** — Acetazolamide causes metabolic acidosis
 5. **A** — Loop diuretics cause hypocalcemia
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SD 14.11: Combination Therapy Rationale

1. **T** — Metolazone + furosemide blocks sequential segments

2. **F** — Combination requires MORE monitoring
 3. **T** — Sequential blockade overcomes resistance
 4. **T** — K⁺-sparing diuretics prevent hypokalemia
 5. **T** — Fixed-dose combinations exist (e.g., HCTZ + triamterene)
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SD 14.12: Clinical Scenario Drug Selection

1. **B** — IV furosemide for acute pulmonary edema
2. **B** — Chlorthalidone (thiazide) reduces calcium excretion, preventing stones
3. **B** — Spironolactone has mortality benefit in HFrEF

Case Study Answers

Case 14.1: Diuretic Resistance in Heart Failure

Question 1. Multiple mechanisms: (1) Reduced absorption—intestinal edema decreases oral furosemide bioavailability; (2) Reduced secretion—worsening renal function decreases tubular secretion; (3) Distal nephron hypertrophy—chronic loop diuretic use causes compensatory increased reabsorption in DCT/CD; (4) Braking phenomenon—sodium retention between doses.

Question 2. Strategies include: IV administration (bypasses absorption), higher doses (steep dose-response curve), more frequent dosing (overcomes braking), continuous infusion, adding a thiazide-type diuretic (sequential nephron blockade), switching to torsemide (better absorption), and sodium restriction.

Question 3. Metolazone (thiazide-like) blocks the NCC in the distal tubule, preventing compensatory sodium reabsorption that occurs downstream from loop diuretic action. It also retains efficacy in renal impairment unlike traditional thiazides. The combination produces synergistic diuresis.

Question 4. Essential monitoring includes: potassium (severe hypokalemia risk), sodium (hyponatremia), magnesium (often depleted with loops), creatinine (prerenal AKI from overdiuresis), daily weights (response assessment), and volume status. Electrolytes may need checking daily during aggressive therapy.

Case 14.2: Thiazide Complications

Question 1. The patient demonstrates: (1) Severe hyponatremia (Na⁺ 118)—common in elderly on thiazides; (2) Hypokalemia (K⁺ 2.9); (3) Hyperglycemia (glucose 186, new)—thiazide-induced; (4)

Hyperuricemia (uric acid 9.2); (5) Hypercalcemia (Ca 11.2). This represents the classic "hyper-GLUC" plus hyponatremia/hypokalemia profile.

Question 2. Thiazide-induced hyponatremia results from: (1) Impaired diluting capacity—blocking NCC prevents sodium reabsorption in the "diluting segment"; (2) Continued ADH-driven water reabsorption in collecting duct; (3) Increased thirst; (4) Elderly patients are especially susceptible due to reduced free water excretion capacity and dietary factors.

Question 3. Thiazides impair insulin release through hypokalemia. Potassium is required for normal pancreatic beta-cell function—K⁺ depletion reduces insulin secretion in response to glucose, causing hyperglycemia. This is generally reversible with potassium replacement and thiazide discontinuation.

Question 4. Thiazides increase calcium reabsorption in the DCT. By blocking NCC, they hyperpolarize DCT cells, enhancing calcium entry through TRPV5 channels. Mild hypercalcemia is expected, but significant hypercalcemia (>11 mg/dL) may unmask underlying primary hyperparathyroidism. This patient needs PTH measurement.

Diagram/Table Exercise Answers

DT 14.1: Nephron Sites of Diuretic Action

1. Site 1 (PCT): **Carbonic anhydrase inhibitors**
2. Site 2 (TAL): **Loop diuretics**
3. Site 3 (DCT): **Thiazide diuretics**
4. Site 4 (CD): **Potassium-sparing diuretics (aldosterone antagonists, ENaC blockers)**

DT 14.2: Potassium Handling and Diuretics

1. Loop and thiazide diuretics cause hypokalemia by increasing **sodium delivery** to the collecting duct.
 2. Aldosterone antagonists cause hyperkalemia by blocking **mineralocorticoid** receptors.
 3. ENaC blockers cause hyperkalemia by directly blocking **epithelial sodium channels (ENaC)**.
 4. Example of aldosterone antagonist: **Spironolactone**; Example of ENaC blocker: **Amiloride**
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DT 14.3: Diuretic Comparison Table

Diuretic Class	Site of Action	Transporter/Target	Potency	K ⁺ Effect
Loop	Thick ascending limb	NKCC2	High	Hypokalemia
Thiazide	Distal convoluted tubule	NCC	Moderate	Hypokalemia
K⁺-sparing (aldo antagonist)	Collecting duct	Mineralocorticoid receptor	Weak	Hyperkalemia
K⁺-sparing (ENaC blocker)	Collecting duct	ENaC	Weak	Hyperkalemia
CA inhibitor	Proximal tubule	Carbonic anhydrase	Weak	Hypokalemia

DT 14.4: Diuretic Effects on Calcium

Property	Loop Diuretics	Thiazide Diuretics
Effect on calcium excretion	Increased	Decreased
Effect on serum calcium	May decrease	May increase
Use in hypercalcemia	Yes (with saline)	No
Use in osteoporosis/stones	No	Yes (beneficial)

Multiple-Choice Question Answers

Question 1. Answer: B

Loop diuretics inhibit the Na⁺/K⁺/2Cl⁻ cotransporter (NKCC2) in the thick ascending limb.

Question 2. Answer: B

Thiazide diuretics are first-line for hypertension due to efficacy, safety, and low cost.

Question 3. Answer: C

Spironolactone reduced mortality by 30% in the RALES trial for HFrEF.

Question 4. Answer: B

Loop diuretics increase calcium excretion, potentially causing hypocalcemia. Useful for treating hypercalcemia.

Question 5. Answer: B

Acetazolamide induces metabolic acidosis, which stimulates hyperventilation and accelerates altitude acclimatization.

Question 6. Answer: A

Thiazide-induced hyponatremia is common, especially in elderly women, and can be severe.

Question 7. Answer: B

Chlorthalidone has a longer half-life (40-60 hours) and better cardiovascular outcome data than HCTZ.

Question 8. Answer: B

Both spironolactone (K⁺-sparing) and lisinopril (ACE inhibitor) increase potassium—combination increases hyperkalemia risk.

Question 9. Answer: B

Metolazone retains efficacy in renal impairment, unlike other thiazides, making it useful for resistant edema.

Question 10. Answer: C

Rapid IV furosemide administration increases ototoxicity risk, especially with concurrent aminoglycosides.

Question 11. Answer: B

Thiazides decrease calcium excretion, reducing calcium concentration in urine and preventing stone formation.

Question 12. Answer: B

Metolazone blocks the DCT NCC, preventing compensatory distal sodium reabsorption that limits loop diuretic response.

Question 13. Answer: B

Spironolactone blocks mineralocorticoid receptors (nuclear receptors), affecting gene transcription—a genomic mechanism requiring days.

Question 14. Answer: B

Thiazide-induced hypokalemia impairs insulin secretion from pancreatic beta cells, causing hyperglycemia.

Question 15. Answer: B

Mannitol requires renal excretion. In anuria, it cannot be eliminated and will cause severe volume overload.

Question 16. Answer: B

Furosemide + metolazone (loop + thiazide) causes profound natriuresis with high risk of severe electrolyte disturbances.