

ANSWER KEY WITH EXPLANATIONS FOR CHAPTER 24

Skill Drill Answers

SD 24.1: Insulin Preparation Matching

1. **A** — Lispro is rapid-acting
 2. **C** — NPH is intermediate-acting
 3. **D** — Glargine is long-acting
 4. **B** — Regular insulin is short-acting
 5. **A** — Aspart is rapid-acting
 6. **D** — Degludec is long-acting (ultra-long)
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SD 24.2: True/False with Correction

1. **F** — Metformin does NOT cause hypoglycemia when used alone; it is a euglycemic agent.
 2. **T** — Sulfonylureas bind to and close K-ATP channels, causing depolarization and insulin release.
 3. **F** — SGLT2 inhibitors work by BLOCKING glucose reabsorption in the kidney, not by stimulating insulin.
 4. **F** — Bisphosphonates must be taken on an EMPTY stomach with water only.
 5. **T** — GLP-1 agonists cause significant weight loss (5-15% with semaglutide).
 6. **F** — Teriparatide is an ANABOLIC agent (stimulates bone formation), not antiresorptive.
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SD 24.3: Fill in the Blank

1. **gluconeogenesis**
2. **urine (kidney)**
3. **15**

4. **osteoclast**
 5. **kidney**
 6. **RANK ligand**
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SD 24.4: Drug Mechanism Matching

1. **B** — Metformin reduces hepatic gluconeogenesis
 2. **A** — Glipizide (sulfonylurea) closes K-ATP channels
 3. **C** — Semaglutide activates GLP-1 receptors
 4. **D** — Empagliflozin blocks renal glucose reabsorption
 5. **E** — Sitagliptin inhibits DPP-4
 6. **F** — Alendronate inhibits osteoclast function
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SD 24.5: Cardiovascular/Renal Benefit Identification

1. **YES** — GLP-1 agonists reduce MACE in CV outcome trials
 2. **YES** — SGLT2 inhibitors reduce CV death and HF hospitalization
 3. **YES** — SGLT2 inhibitors slow CKD progression (DAPA-CKD, EMPA-KIDNEY)
 4. **NO** — Sulfonylureas have no proven CV benefit
 5. **NO** — DPP-4 inhibitors are CV neutral (no benefit or harm proven)
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SD 24.6: Rapid Recall

1. **Metformin**
 2. **Regular insulin**
 3. **Glucagon**
 4. **Bisphosphonates**
 5. **25-hydroxyvitamin D**
 6. **Genital mycotic infections**
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SD 24.7: Complete the Sentence

1. **medullary**
 2. **empty**
 3. **normal**
 4. **antiresorptive**
 5. **independent of**
 6. **reversible**
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SD 24.8: Hypoglycemia Risk Assessment

1. **A** — Insulin has high hypoglycemia risk
 2. **A** — Sulfonylureas have high hypoglycemia risk
 3. **C** — Metformin has minimal hypoglycemia risk
 4. **C** — SGLT2 inhibitors have minimal hypoglycemia risk
 5. **C** — GLP-1 agonists have minimal hypoglycemia risk (glucose-dependent)
 6. **C** — DPP-4 inhibitors have minimal hypoglycemia risk (glucose-dependent)
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SD 24.9: Osteoporosis Drug Classification

1. **A** — Alendronate is antiresorptive
 2. **N** — Teriparatide is anabolic
 3. **A** — Denosumab is antiresorptive
 4. **N** — Abaloparatide is anabolic
 5. **A** — Zoledronic acid is antiresorptive
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SD 24.10: Adverse Effect Matching

1. **C** — SGLT2 inhibitors cause genital mycotic infections
2. **A** — Metformin causes GI upset and B12 deficiency
3. **D** — GLP-1 agonists cause nausea and weight loss
4. **B** — Sulfonylureas cause hypoglycemia and weight gain
5. **E** — Bisphosphonates cause ONJ (with long-term use)

SD 24.11: Clinical Indication Identification

1. **T** — SGLT2 inhibitors reduce HF hospitalizations (major trial finding)
 2. **F** — Teriparatide is LIMITED to 2 years (theoretical osteosarcoma risk)
 3. **F** — GLP-1 agonists cause weight LOSS, not gain
 4. **T** — Zoledronic acid is given as once-yearly IV infusion
 5. **T** — Metformin should be held before contrast in renal impairment
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SD 24.12: Clinical Scenario Drug Selection

1. **B** — SGLT2 inhibitors have proven benefits for HF and CKD
2. **B** — Switch to anabolic agent (teriparatide) after bisphosphonate failure
3. **C** — GLP-1 agonists cause significant weight loss

Case Study Answers

Case 24.1: Type 2 Diabetes Medication Selection

Question 1. SGLT2 inhibitors are particularly appropriate because this patient has multiple compelling indications: ASCVD (prior MI), heart failure with reduced ejection fraction, and CKD (eGFR 55). Clinical trials have demonstrated that SGLT2 inhibitors reduce cardiovascular death, heart failure hospitalizations, and CKD progression in these populations. Guidelines now recommend SGLT2 inhibitors (or GLP-1 agonists) as preferred second-line agents after metformin in patients with these comorbidities.

Question 2. SGLT2 inhibitors have demonstrated reduced cardiovascular death (empagliflozin in EMPA-REG OUTCOME), reduced heart failure hospitalizations across all trials, and slowed progression of CKD with reduced risk of dialysis, transplant, or renal death (dapagliflozin in DAPA-CKD, empagliflozin in EMPA-KIDNEY). These benefits appear to be independent of glucose-lowering effect, occurring even in patients without diabetes and those with reduced GFR.

Question 3. Counseling should include: (1) genital mycotic infections (yeast infections)—maintain good hygiene and report symptoms; (2) increased urination and thirst initially; (3) risk of volume depletion, especially if on diuretics—maintain hydration; (4) rare euglycemic DKA—report nausea, vomiting, or abdominal pain, especially during illness; (5) hold before surgery to reduce DKA risk; (6) possible UTI risk (though evidence is mixed).

Question 4. With a BMI of 34 kg/m², a GLP-1 agonist would provide significant weight loss (5-15% body weight with semaglutide), in addition to glucose lowering and cardiovascular benefit. This dual effect on glucose control and obesity is particularly valuable in overweight/obese patients with type 2 diabetes. Some patients may benefit from combination SGLT2 inhibitor + GLP-1 agonist for maximal cardiometabolic benefit.

Case 24.2: Osteoporosis Management

Question 1. Bisphosphonates reduce fracture risk by inhibiting osteoclast-mediated bone resorption. They bind to bone mineral and are internalized by osteoclasts during resorption, where they inhibit farnesyl pyrophosphate synthase in the mevalonate pathway. This disrupts osteoclast function and induces apoptosis. With reduced resorption, bone formation can proceed relatively unopposed, leading to increased bone density and reduced fracture risk at the spine, hip, and other sites.

Question 2. Critical administration instructions: (1) Take on an empty stomach first thing in the morning; (2) Swallow with a full glass of plain water only—not juice, coffee, or other beverages; (3) Remain upright (sitting or standing) for at least 30 minutes; (4) Do not eat, drink anything else, or take other medications for at least 30 minutes. These instructions prevent esophageal irritation (taking upright with water) and optimize absorption (empty stomach, no binding to food or minerals).

Question 3. Rare but serious adverse effects with long-term bisphosphonate use include: (1) Osteonecrosis of the jaw (ONJ)—jaw pain, exposed bone, especially after dental procedures; patients should have dental work completed before starting and avoid invasive dental procedures during treatment; (2) Atypical femoral fractures—stress fractures in the subtrochanteric region with prodromal thigh pain; risk increases with duration >5 years, prompting consideration of a "drug holiday" in patients at moderate fracture risk.

Question 4. Fracture despite 5 years of bisphosphonate therapy suggests she may benefit from anabolic therapy. Teriparatide (or abaloparatide) would be appropriate—these PTH analogues stimulate new bone formation rather than just preventing resorption. After completing 2 years of anabolic therapy, she should receive antiresorptive therapy (bisphosphonate or denosumab) to maintain the bone gains achieved.

Diagram/Table Exercise Answers

DT 24.1: Insulin Secretion and Drug Targets

1. Sulfonylureas close **K-ATP (ATP-sensitive potassium)** channels to stimulate insulin release.
 2. GLP-1 and GIP (incretins) enhance glucose-dependent **insulin** secretion.
 3. Metformin acts on the liver to reduce **gluconeogenesis (glucose production)**.
 4. SGLT2 inhibitors act on the **kidney (proximal tubule)** to block glucose reabsorption.
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DT 24.2: Bone Remodeling and Drug Targets

1. Bisphosphonates inhibit **osteoclast** function and induce their apoptosis.
2. Denosumab blocks **RANK ligand**, preventing osteoclast development.
3. Teriparatide stimulates **osteoblast** activity, increasing bone formation.
4. After stopping denosumab, patients experience rapid bone loss because its effects are **reversible**.

DT 24.3: Diabetes Medication Comparison Table

Drug Class	Mechanism	Hypoglycemia Risk	Weight Effect	CV/Renal Benefit
Metformin	Reduces hepatic gluconeogenesis	Low	Neutral/loss	Possible (not definitively proven)
Sulfonylureas	Closes K-ATP channels, stimulates insulin	High	Gain	None proven
GLP-1 agonists	GLP-1 receptor activation	Low	Loss	Yes (MACE reduction)
SGLT2 inhibitors	Blocks renal glucose reabsorption	Low	Loss	Yes (HF, CKD, CV death)
DPP-4 inhibitors	Inhibit incretin degradation	Low	Neutral	None proven

DT 24.4: Osteoporosis Medication Comparison Table

Drug	Mechanism	Administration	Key Consideration
Alendronate	Inhibits osteoclasts	Oral weekly	Strict administration requirements (empty stomach, upright)
Zoledronic acid	Inhibits osteoclasts	IV yearly	Flu-like symptoms first dose
Denosumab	Blocks RANK ligand	SC every 6 months	Rapid bone loss if stopped—must transition to another agent
Teriparatide	Stimulates osteoblasts (anabolic)	SC daily	Limited to 2 years

Multiple-Choice Question Answers

Question 1. Answer: B

Metformin primarily works by reducing hepatic gluconeogenesis via AMPK activation. It does not stimulate insulin secretion and does not cause hypoglycemia when used alone.

Question 2. Answer: C

Regular insulin is the only insulin preparation appropriate for IV administration. Other insulins (rapid-acting, NPH, long-acting) are formulated for subcutaneous use only.

Question 3. Answer: B

Bisphosphonates inhibit osteoclast-mediated bone resorption. They are internalized by osteoclasts and disrupt their function by inhibiting the mevalonate pathway.

Question 4. Answer: B

Hypoglycemia is the major adverse effect limiting tight glycemic control with insulin. It causes symptoms ranging from tremor and sweating to seizures and loss of consciousness.

Question 5. Answer: C

GLP-1 receptor agonists cause significant weight loss (5-15%) through delayed gastric emptying and central appetite suppression. Sulfonylureas and TZDs cause weight gain; DPP-4 inhibitors are weight-neutral.

Question 6. Answer: C

SGLT2 inhibitors have proven benefits for heart failure (reduced HF hospitalizations) and CKD (slowed progression). Sulfonylureas have no proven benefit; TZDs are contraindicated in heart failure.

Question 7. Answer: B

SGLT2 inhibitors cause genital mycotic infections (yeast infections) because glucosuria creates a favorable environment for candida growth. They have low hypoglycemia risk and do not cause lactic acidosis.

Question 8. Answer: B

Oral bisphosphonates must be taken on an empty stomach with a full glass of water, remaining upright for at least 30 minutes to prevent esophageal irritation and optimize absorption.

Question 9. Answer: B

GLP-1 agonists are contraindicated in patients with personal or family history of medullary thyroid carcinoma or MEN2 syndrome, based on thyroid C-cell tumor findings in rodent studies.

Question 10. Answer: B

The "Rule of 15" for hypoglycemia: give 15 grams of fast-acting carbohydrate, wait 15 minutes, recheck glucose, and repeat if still below 70 mg/dL.

Question 11. Answer: B

Teriparatide is an anabolic agent that stimulates bone formation (osteoblast activity). Bisphosphonates are antiresorptive (inhibit osteoclast activity). This is a fundamental difference in mechanism.

Question 12. Answer: B

Euglycemic DKA occurs with normal or near-normal glucose levels. SGLT2 inhibitors can cause this because they lower glucose through glucosuria while ketoacidosis develops from other metabolic shifts.

Question 13. Answer: B

Denosumab effects are fully reversible. Stopping it causes rapid bone loss and increased vertebral fracture risk within 6-12 months. Patients must transition to a bisphosphonate or other antiresorptive agent.

Question 14. Answer: B

SGLT2 inhibitors reduce heart failure hospitalizations—a consistent finding across multiple cardiovascular outcome trials (EMPA-REG, CANVAS, DECLARE, DAPA-HF).

Question 15. Answer: B

ONJ is most likely after dental extractions or invasive dental procedures. Patients should complete necessary dental work before starting bisphosphonates and avoid invasive procedures during treatment.

Question 16. Answer: C

Acarbose inhibits intestinal disaccharidases, preventing sucrose digestion. Patients on acarbose who develop hypoglycemia must use glucose (dextrose) tablets—not sucrose, juice, or complex carbohydrates.