

ANSWER KEY WITH EXPLANATIONS FOR CHAPTER 18

Skill Drill Answers

SD 18.1: Anticoagulant Mechanism Matching

1. **C** — Warfarin blocks vitamin K-dependent factor synthesis
 2. **A** — UFH enhances antithrombin (inhibits IIa and Xa)
 3. **B** — LMWH enhances antithrombin (primarily Xa)
 4. **D** — Rivaroxaban directly inhibits Xa
 5. **E** — Dabigatran directly inhibits thrombin
 6. **B** — Fondaparinux enhances antithrombin (Xa only)
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SD 18.2: True/False with Correction

1. **F** — Warfarin has DELAYED effect (3-5 days to deplete existing factors).
 2. **F** — DOACs do NOT require routine monitoring.
 3. **T** — Aspirin irreversibly inhibits COX.
 4. **F** — HIT causes THROMBOSIS (paradoxically), not bleeding.
 5. **T** — Statins inhibit HMG-CoA reductase.
 6. **F** — Clopidogrel is a PRODRUG requiring CYP2C19 activation.
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SD 18.3: Fill in the Blank

1. **K**
2. **idarucizumab**
3. **thromboxane A2 (TXA2)**

4. **plasmin**
 5. **cholesterol**
 6. **clopidogrel**
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SD 18.4: Anticoagulant Monitoring Matching

1. **B** — Warfarin: PT/INR
 2. **A** — UFH: aPTT
 3. **C** — Enoxaparin: anti-Xa (if needed)
 4. **D** — Apixaban: no routine monitoring
 5. **D** — Dabigatran: no routine monitoring
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SD 18.5: Antiplatelet Agent Classification

1. **A** — Aspirin: COX inhibitor
 2. **B** — Clopidogrel: P2Y₁₂ inhibitor
 3. **B** — Ticagrelor: P2Y₁₂ inhibitor
 4. **C** — Abciximab: GP IIb/IIIa inhibitor
 5. **B** — Prasugrel: P2Y₁₂ inhibitor
 6. **C** — Eptifibatide: GP IIb/IIIa inhibitor
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SD 18.6: Rapid Recall

1. **II, VII, IX, X**
 2. **Protamine (sulfate)**
 3. **Myopathy (rhabdomyolysis)**
 4. **Heparin (UFH > LMWH)**
 5. **Fibrates**
 6. **Dabigatran**
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SD 18.7: Complete the Sentence

1. **shorter**
 2. **contraindicated**
 3. **reversible**
 4. **Xa**
 5. **increase**
 6. **lifetime**
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SD 18.8: Lipid Drug Mechanism Matching

1. **A** — Atorvastatin: HMG-CoA reductase inhibitor
 2. **B** — Ezetimibe: cholesterol absorption inhibitor
 3. **C** — Evolocumab: PCSK9 inhibitor
 4. **D** — Fenofibrate: PPAR- α agonist
 5. **E** — Bempedoic acid: ATP-citrate lyase inhibitor
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SD 18.9: Reversal Agent Matching

1. **A** — UFH: Protamine sulfate
 2. **B** — Warfarin: Vitamin K
 3. **C** — Dabigatran: Idarucizumab
 4. **D** — Rivaroxaban: Andexanet alfa or PCC
 5. **E** — Fondaparinux: No specific reversal
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SD 18.10: Drug Interaction Identification

1. **T** — Vitamin K competes with warfarin
 2. **F** — CYP2C19 INHIBITORS DECREASE clopidogrel effect (blocks activation)
 3. **T** — CYP3A4 inhibitors increase statin levels
 4. **T** — Gemfibrozil inhibits statin metabolism
 5. **T** — PPIs reduce dabigatran absorption (needs acid)
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SD 18.11: Clinical Indication Matching

1. **D** — tPA for acute ischemic stroke
 2. **B** — Apixaban for non-valvular AFib
 3. **C** — DAPT after stent
 4. **A** — Warfarin for mechanical valve
 5. **E** — High-intensity statin for secondary prevention
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SD 18.12: Clinical Scenario Drug Selection

1. **B** — Apixaban (or other DOAC) for AFib
2. **C** — Argatroban for HIT (non-heparin anticoagulant)
3. **B** — Add ezetimibe for additional LDL lowering

Case Study Answers

Case 18.1: Anticoagulation for Atrial Fibrillation

Question 1. Options include: (1) DOACs—apixaban, rivaroxaban, dabigatran, edoxaban; (2) Warfarin. With a CHA₂DS₂-VASc score of 3, he has significant stroke risk and anticoagulation is indicated. Aspirin alone is insufficient. Given non-valvular AFib, either DOACs or warfarin is appropriate.

Question 2. DOAC advantages: (1) No routine INR monitoring, (2) Fewer drug and food interactions, (3) Rapid onset (hours vs. days), (4) Lower intracranial hemorrhage risk, (5) Fixed dosing without titration, (6) Specific reversal agents available. DOACs are now preferred over warfarin for non-valvular AFib in guidelines.

Question 3. All DOACs are renally cleared to varying degrees and require dose adjustment in renal impairment. With CrCl 55 mL/min, he can use most DOACs at standard or reduced doses. Apixaban has the least renal dependence (27%) and may be preferred in borderline renal function. Dabigatran requires most caution (80% renal).

Question 4. Yes—mechanical heart valves require warfarin. DOACs are contraindicated with mechanical valves (RE-ALIGN trial showed increased thrombosis and bleeding with dabigatran). Warfarin with target INR 2.5-3.5 (depending on valve position) is the only appropriate anticoagulant.

Case 18.2: Statin Intolerance

Question 1. True statin intolerance is rare. Steps: (1) Confirm symptoms are statin-related (symptoms should resolve off statin, recur on rechallenge), (2) Rule out other causes (hypothyroidism, vitamin D deficiency, drug interactions), (3) Try a different statin (hydrophilic like pravastatin may be better tolerated), (4) Try lower dose or every-other-day dosing, (5) Her normal CK suggests myalgia without myopathy—she may tolerate lower-intensity therapy.

Question 2. She has established ASCVD (prior MI), placing her at very high risk for recurrent events. Guidelines recommend LDL <70 mg/dL for secondary prevention. High-intensity statin reduces events by ~30%. Every 39 mg/dL LDL reduction decreases cardiovascular events by ~22%. Her current LDL of 142 doubles her risk compared to goal.

Question 3. Non-statin options: (1) Ezetimibe—adds 15-20% LDL reduction, well-tolerated; (2) PCSK9 inhibitors (evolocumab, alirocumab)—reduce LDL 50-60%, proven outcomes benefit, injectable, expensive; (3) Bempedoic acid—reduces LDL ~18%, activated only in liver (may have less myopathy); (4) Inclisiran—siRNA targeting PCSK9, twice-yearly injection.

Question 4. If completely statin intolerant: Start ezetimibe (15-20% reduction) → If LDL still above goal, add PCSK9 inhibitor or bempedoic acid. Given her very high risk (prior MI), PCSK9 inhibitors would provide greatest additional LDL reduction and have proven cardiovascular benefit (FOURIER, ODYSSEY trials). Cost and injection requirement are limitations.

Diagram/Table Exercise Answers

DT 18.1: Coagulation Cascade and Drug Targets

1. Heparins enhance **antithrombin III** to inhibit Xa and IIa.
2. Warfarin blocks synthesis of factors: **II, VII, IX, X**
3. Factor Xa inhibitors directly inhibit: **Factor Xa**
4. Dabigatran directly inhibits: **Factor IIa (thrombin)**

DT 18.2: Antiplatelet Drug Mechanisms

1. Aspirin inhibits **cyclooxygenase (COX)**, blocking TXA₂ synthesis.
 2. Clopidogrel and ticagrelor block the **P2Y₁₂** receptor.
 3. Abciximab blocks the **GP IIb/IIIa** receptor.
 4. DAPT typically combines: **Aspirin + P2Y₁₂ inhibitor (clopidogrel/ticagrelor/prasugrel)**
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DT 18.3: Anticoagulant Comparison Table

Drug	Mechanism	Monitoring	Reversal	Key Consideration
UFH	Enhances ATIII (IIa, Xa)	aPTT	Protamine	HIT risk, short half-life
LMWH	Enhances ATIII (mainly Xa)	Anti-Xa needed) (if	Protamine (partial)	Predictable dosing
Warfarin	Blocks vit K factors	PT/INR	Vitamin K, PCC, FFP	Many drug interactions
Apixaban	Direct Xa inhibitor	None routine	Andexanet alfa/PCC	Renal dose adjustment
Dabigatran	Direct IIa inhibitor	None routine	Idarucizumab	GI side effects, needs acid for absorption

DT 18.4: Lipid-Lowering Drug Comparison Table

Drug Class	Mechanism	LDL Effect	Primary Use
Statins	HMG-CoA reductase inhibition	↓ 30-50%	First-line for ASCVD prevention
Ezetimibe	Blocks intestinal absorption	↓ 15-20%	Add-on to statin
PCSK9 inhibitors	↑ LDL receptor expression	↓ 50-60%	High-risk patients, FH
Fibrates	PPAR- α activation	↓ 10-20%	Hypertriglyceridemia
Bempedoic acid	ATP-citrate lyase inhibition	↓ 18%	Statin intolerance

Multiple-Choice Question Answers

Question 1. Answer: C

Warfarin inhibits vitamin K epoxide reductase, blocking synthesis of vitamin K-dependent factors.

Question 2. Answer: B

INR (PT) monitors the extrinsic pathway, which includes vitamin K-dependent factors blocked by warfarin.

Question 3. Answer: C

Aspirin irreversibly inhibits cyclooxygenase, preventing thromboxane A₂ synthesis.

Question 4. Answer: B

Statins inhibit HMG-CoA reductase, reducing hepatic cholesterol and upregulating LDL receptors.

Question 5. Answer: B

Protamine sulfate binds and neutralizes heparin.

Question 6. Answer: B

For INR >9 without bleeding, hold warfarin, give oral vitamin K, and resume at reduced dose.

Question 7. Answer: B

HIT causes paradoxical thrombosis (not bleeding) due to platelet activation by antibodies.

Question 8. Answer: C

Idarucizumab specifically reverses dabigatran by binding it with high affinity.

Question 9. Answer: B

Clopidogrel requires CYP2C19 activation to become active.

Question 10. Answer: B

Prostaglandin-mediated flushing is the major tolerability issue with niacin.

Question 11. Answer: B

DOACs have predictable pharmacokinetics, fewer interactions, and no routine monitoring requirement.

Question 12. Answer: C

IV alteplase within 4.5 hours (ideally <3 hours) is indicated for acute ischemic stroke.

Question 13. Answer: C

Mechanical valves require warfarin; DOACs are contraindicated (RE-ALIGN trial).

Question 14. Answer: C

CK >10× ULN indicates rhabdomyolysis—stop statin immediately to prevent renal failure.

Question 15. Answer: B

PCSK9 normally degrades LDL receptors; inhibiting PCSK9 increases LDL receptor expression.

Question 16. Answer: B

Fondaparinux does not cause HIT and can be used in patients with HIT history.