

ANSWER KEY WITH EXPLANATIONS FOR CHAPTER 19

Skill Drill Answers

SD 19.1: Drug Class Matching

1. **A** — Ibuprofen is a non-selective NSAID
 2. **B** — Celecoxib is COX-2 selective
 3. **C** — Allopurinol is a xanthine oxidase inhibitor
 4. **F** — Methotrexate is a conventional DMARD
 5. **E** — Adalimumab is a TNF inhibitor
 6. **D** — Probenecid is a uricosuric
 7. **A** — Indomethacin is a non-selective NSAID
 8. **C** — Febuxostat is a xanthine oxidase inhibitor
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SD 19.2: True/False with Correction

1. **F** — COX-2 is the inducible isoform; COX-1 is constitutive.
 2. **T** — COX-2 inhibitors increase MI and stroke risk.
 3. **F** — Acetaminophen has MINIMAL anti-inflammatory activity.
 4. **F** — Colchicine inhibits MICROTUBULE polymerization, not xanthine oxidase.
 5. **F** — First-generation antihistamines ARE sedating; second-generation are non-sedating.
 6. **T** — Daily methotrexate dosing causes fatal toxicity.
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SD 19.3: Fill in the Blank

1. **phospholipase A2 (PLA2)**

2. **NAPQI (N-acetyl-p-benzoquinone imine)**
 3. **N-acetylcysteine (NAC)**
 4. **microtubule**
 5. **tuberculosis (TB)**
 6. **bradykinin**
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SD 19.4: COX Isoform Function Matching

1. **A** — COX-1 provides gastric protection
 2. **B** — COX-2 produces inflammatory prostaglandins
 3. **A** — COX-1 produces platelet TXA₂
 4. **C** — Both contribute to renal prostaglandins
 5. **B** — COX-2 primarily mediates fever and inflammatory pain
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SD 19.5: NSAID Adverse Effect Matching

1. **A** — GI toxicity from COX-1 inhibition in stomach
 2. **B** — CV events from COX-2 inhibition (decreased PGI₂)
 3. **C** — AKI from prostaglandin inhibition in kidney
 4. **D** — AERD from leukotriene shunting
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SD 19.6: Rapid Recall

1. **Xanthine oxidase**
 2. **Methotrexate**
 3. **First-generation**
 4. **Aspirin**
 5. **Folic acid**
 6. **4 grams (4 g)**
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SD 19.7: Complete the Sentence

1. **less**
 2. **liver**
 3. **non-sedating**
 4. **increase**
 5. **increase**
 6. **irreversible**
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SD 19.8: Antihistamine Classification

1. **First-generation** — Diphenhydramine
 2. **Second-generation** — Loratadine
 3. **Second-generation** — Cetirizine
 4. **First-generation** — Chlorpheniramine
 5. **Second-generation** — Fexofenadine
 6. **First-generation** — Hydroxyzine
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SD 19.9: Gout Drug Mechanism Matching

1. **B** — Allopurinol inhibits xanthine oxidase
 2. **A** — Colchicine inhibits microtubule polymerization
 3. **C** — Probenecid inhibits urate reabsorption
 4. **E** — Indomethacin inhibits COX
 5. **D** — Pegloticase enzymatically degrades uric acid
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SD 19.10: DMARD Adverse Effect Identification

1. **B** — Hydroxychloroquine causes retinal toxicity
2. **C** — TNF- α inhibitors cause TB reactivation
3. **A** — Methotrexate causes hepatotoxicity and bone marrow suppression
4. **E** — JAK inhibitors increase VTE risk
5. **D** — Leflunomide requires cholestyramine washout due to teratogenicity

SD 19.11: Drug Interaction/Contraindication Identification

1. **T** — NSAIDs + ACE inhibitors increase AKI risk
 2. **F** — Probenecid is **INEFFECTIVE** in severe renal impairment
 3. **F** — Colchicine has a **NARROW** therapeutic index
 4. **F** — Methotrexate is **TERATOGENIC** and contraindicated in pregnancy
 5. **F** — Do **NOT** start allopurinol during acute flare (wait until resolved)
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SD 19.12: Clinical Scenario Drug Selection

1. **B** — Low-dose colchicine (or corticosteroids) for acute gout with CKD
2. **B** — Add TNF inhibitor for methotrexate failure
3. **C** — Fexofenadine (non-sedating for driving)

Case Study Answers

Case 19.1: NSAID-Induced Adverse Effects

Question 1. His GI bleeding is caused by chronic NSAID use. NSAIDs inhibit COX-1 in gastric mucosa, reducing protective prostaglandins (PGE₂, PGI₂) that maintain mucus production, bicarbonate secretion, and mucosal blood flow. This leads to peptic ulceration and bleeding. His dark stools (melena) and anemia indicate significant upper GI hemorrhage.

Question 2. His creatinine increase indicates NSAID-induced acute kidney injury. Prostaglandins maintain renal blood flow, particularly when perfusion is compromised. NSAIDs block renal prostaglandin production, causing vasoconstriction. Lisinopril (ACE inhibitor) blocks angiotensin II, which maintains GFR via efferent arteriolar constriction. Together ("double whammy"), they severely compromise renal perfusion.

Question 3. GI risk could have been reduced by: (1) Co-prescribing a PPI (omeprazole, esomeprazole), (2) Using misoprostol (PGE₁ analog that replaces protective prostaglandins), (3) Using a COX-2 selective inhibitor (celecoxib) which has lower GI risk, (4) Using the lowest effective NSAID dose for shortest duration, (5) Considering topical diclofenac for localized pain.

Question 4. Alternative strategies include: (1) Acetaminophen (no GI toxicity, but limited efficacy for OA), (2) Topical NSAIDs (less systemic absorption), (3) Physical therapy and exercise, (4) Weight loss if

overweight, (5) Intra-articular corticosteroid injections, (6) Duloxetine (FDA-approved for OA pain), (7) Consider joint replacement if severe. Avoid systemic NSAIDs given his bleeding and renal injury.

Case 19.2: Gout Management

Question 1. With CKD stage 3, NSAIDs should be avoided due to renal toxicity risk. Options include: (1) Low-dose colchicine (1.2 mg, then 0.6 mg one hour later—dose-adjusted for renal function), (2) Corticosteroids (oral prednisone, intra-articular injection, or IM triamcinolone). Corticosteroids are often preferred with renal impairment as they don't require dose adjustment and are highly effective.

Question 2. Yes, urate-lowering therapy is indicated. He has had ≥ 2 flares per year (three this year) and hyperuricemia (uric acid 9.8). Guidelines recommend ULT after ≥ 2 flares annually, presence of tophi, or evidence of urate arthropathy. ULT should be started after the acute flare resolves, not during the acute attack.

Question 3. Allopurinol is first-line. With CrCl 45 mL/min, he needs dose adjustment—start at 100 mg daily (or lower) and titrate based on uric acid levels. Important precautions: (1) Consider HLA-B*5801 testing, especially if Asian descent (high risk of severe hypersensitivity), (2) Start low and increase gradually, (3) Provide flare prophylaxis, (4) Target serum urate < 6 mg/dL.

Question 4. When ULT lowers serum urate, crystals deposited in tissues begin to dissolve and mobilize. This paradoxically triggers inflammation and acute gout flares. Prophylaxis with low-dose colchicine (0.6 mg daily or BID) or low-dose NSAID for 3-6 months prevents these mobilization flares. This is why patients should be warned that flares may occur initially and prophylaxis is essential.

Diagram/Table Exercise Answers

DT 19.1: Arachidonic Acid Metabolism

1. Phospholipase A2 releases **arachidonic acid** from membrane phospholipids.
 2. The COX pathway produces **prostaglandins** and **thromboxanes**.
 3. NSAIDs block the **cyclooxygenase (COX)** enzyme.
 4. The lipoxygenase pathway produces **leukotrienes**, which are blocked by zileuton.
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DT 19.2: COX-1 vs. COX-2 Selectivity

1. COX-1 is responsible for gastric protection, platelet function, and **renal** blood flow.
2. COX-2 is primarily induced during **inflammation**.

3. Blocking COX-1 increases risk of **GI ulceration/bleeding**.
4. Blocking COX-2 selectively increases risk of **cardiovascular events (MI, stroke)**.

DT 19.3: NSAID Comparison Table

Drug	COX Selectivity	Half-Life	Special Characteristics
Aspirin	Non-selective	Short	Irreversible COX inhibition; antiplatelet
Ibuprofen	Non-selective	Short (2-4 h)	Good safety profile, OTC
Naproxen	Non-selective	Long (12-17 h)	Possibly better CV safety
Celecoxib	COX-2 selective	Long	Less GI toxicity; increased CV risk
Ketorolac	Non-selective	Short	Potent analgesic; limit 5 days use

DT 19.4: Gout Drug Comparison Table

Drug	Mechanism	Use	Key Consideration
Colchicine	Inhibits microtubule polymerization	Acute flare, prophylaxis	Narrow therapeutic index; GI toxicity
Allopurinol	Inhibits xanthine oxidase	Chronic ULT (first-line)	HLA-B*5801 hypersensitivity
Probenecid	Increases urate excretion	Chronic ULT	Requires CrCl >50; avoid with kidney stones
Febuxostat	Xanthine oxidase inhibitor	Chronic ULT	CV mortality black box warning
Pegloticase	Enzymatic degradation of urate	Refractory gout	Infusion reactions

Multiple-Choice Question Answers

Question 1. Answer: B

NSAIDs inhibit cyclooxygenase (COX), reducing prostaglandin synthesis.

Question 2. Answer: C

NAPQI is normally conjugated with glutathione; overdose depletes glutathione.

Question 3. Answer: C

Fexofenadine is a second-generation antihistamine with minimal CNS penetration.

Question 4. Answer: B

Allopurinol inhibits xanthine oxidase, blocking uric acid production.

Question 5. Answer: B

Methotrexate is the anchor DMARD for RA; other agents are added to it.

Question 6. Answer: B

Prostaglandins maintain renal blood flow; NSAIDs block this protective mechanism.

Question 7. Answer: B

COX-2 inhibitors block endothelial PGI₂ (antiplatelet, vasodilator) while platelet TXA₂ (via COX-1) is preserved, creating a prothrombotic imbalance.

Question 8. Answer: B

N-acetylcysteine replenishes glutathione and is most effective within 8-10 hours but should be given regardless of timing.

Question 9. Answer: B

Lowering urate mobilizes tissue crystal deposits, triggering inflammatory flares.

Question 10. Answer: B

First-generation antihistamines cross the BBB and block central H₁ receptors involved in wakefulness.

Question 11. Answer: B

TNF- α is essential for TB granuloma maintenance; TNF inhibitors can reactivate latent TB.

Question 12. Answer: B

COX inhibition shunts arachidonic acid to the lipoxygenase pathway, increasing bronchoconstricting leukotrienes.

Question 13. Answer: C

Naproxen has the most favorable CV profile among NSAIDs based on available evidence.

Question 14. Answer: B

Methotrexate inhibits DHFR, causing folate deficiency and pancytopenia; folic acid supplementation reduces this risk.

Question 15. Answer: C

Probenecid requires adequate renal function to promote urate excretion; it's ineffective with low GFR.

Question 16. Answer: D

JAK inhibitors have black box warnings for infections, malignancy, and thrombosis—not hepatic failure.