

ANSWER KEY WITH EXPLANATIONS FOR CHAPTER 21

Skill Drill Answers

SD 21.1: Drug Class Matching

1. **A** — Albuterol is a SABA (short-acting beta-agonist)
 2. **D** — Tiotropium is a LAMA (long-acting muscarinic antagonist)
 3. **E** — Fluticasone is an inhaled corticosteroid
 4. **B** — Salmeterol is a LABA (long-acting beta-agonist)
 5. **F** — Montelukast is a leukotriene receptor antagonist
 6. **C** — Ipratropium is a SAMA (short-acting muscarinic antagonist)
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SD 21.2: True/False with Correction

1. **F** — LABAs must ALWAYS be combined with ICS in asthma; monotherapy increases mortality.
 2. **F** — Bronchodilators (LABA or LAMA) are first-line in COPD; ICS only added for frequent exacerbations with LABA.
 3. **F** — ESAs should target hemoglobin 10-11 g/dL; higher targets increase cardiovascular risk.
 4. **T** — Folate corrects the anemia of B12 deficiency while masking ongoing neurological damage.
 5. **F** — Tiotropium is a LONG-acting anticholinergic (LAMA); ipratropium is short-acting.
 6. **T** — Oral candidiasis (thrush) results from ICS depositing in the oropharynx.
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SD 21.3: Fill in the Blank

1. **cAMP**
2. **pneumonia**

3. **neuropsychiatric**
 4. **iron**
 5. **intrinsic factor**
 6. **neutrophils**
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SD 21.4: Asthma vs. COPD Comparison

1. **A** — Eosinophilic inflammation is characteristic of asthma
 2. **C** — Neutrophilic inflammation is characteristic of COPD
 3. **A** — Reversible airflow obstruction is characteristic of asthma
 4. **A** — ICS as cornerstone therapy applies to asthma
 5. **B** — LAMA reduces exacerbations in both but particularly in COPD
 6. **C** — Progressive irreversible decline is characteristic of COPD
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SD 21.5: Anemia Type Matching

1. **A** — Iron deficiency causes microcytic, hypochromic RBCs
 2. **B** — B12 deficiency causes megaloblastic anemia with neurological findings
 3. **C** — Folate deficiency causes megaloblastic anemia without neurological findings
 4. **A** — Low ferritin indicates iron deficiency
 5. **B** — Elevated methylmalonic acid (MMA) indicates B12 deficiency
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SD 21.6: Rapid Recall

1. **Albuterol**
 2. **Bone pain**
 3. **Thrush (candidiasis)**
 4. **Omalizumab**
 5. **Ferrous (sulfate)**
 6. **Tiotropium**
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SD 21.7: Complete the Sentence

1. **ICS (inhaled corticosteroids)**
 2. **pneumonia**
 3. **cardiovascular events (mortality)**
 4. **subacute combined**
 5. **5-lipoxygenase**
 6. **LAMA**
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SD 21.8: Biologic Agent Matching

1. **A** — Omalizumab targets IgE
 2. **B** — Mepolizumab targets IL-5
 3. **C** — Dupilumab targets IL-4/IL-13 receptor
 4. **D** — Tezepelumab targets TSLP
 5. **B** — Benralizumab targets IL-5 receptor
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SD 21.9: Drug Adverse Effect Matching

1. **C** — Fluticasone causes oral candidiasis
 2. **A** — Albuterol causes tremor and tachycardia
 3. **B** — Tiotropium causes dry mouth and urinary retention
 4. **D** — Montelukast has black box warning for neuropsychiatric events
 5. **E** — Epoetin alfa causes cardiovascular events when targeting high Hgb
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SD 21.10: Stepwise Asthma Therapy

2 — ICS-LABA combination (Step 3)

1 — As-needed SABA only (Step 1)

4 — ICS-LABA plus biologic therapy (Steps 5-6)

2 — Low-dose ICS daily (Step 2)

Correct order: SABA only (1) → Low-dose ICS (2) → ICS-LABA (3) → ICS-LABA + biologic (4)

SD 21.11: Clinical Indication Identification

1. **F** — Omalizumab targets IgE; it's for ALLERGIC asthma, not non-allergic eosinophilic asthma.
 2. **F** — High-dose oral B12 can be effective through passive diffusion, even without intrinsic factor.
 3. **T** — G-CSF reduces depth and duration of neutropenia, decreasing infection risk.
 4. **F** — ICS monotherapy is NEVER appropriate in COPD; always combine with at least LABA.
 5. **T** — ESAs require adequate iron stores; replete iron before starting or concurrently.
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SD 21.12: Clinical Scenario Drug Selection

1. **B** — Omalizumab targets IgE for allergic asthma with elevated IgE.
2. **B** — Add LAMA (tiotropium) for COPD with frequent exacerbations; ICS alone is not appropriate.
3. **B** — Correct iron deficiency first; ESAs cannot work without adequate iron stores.

Case Study Answers

Case 21.1: Asthma Step-Up Therapy

Question 1. This patient has **mild persistent asthma** (Step 2). Symptoms >2 days/week (4-5 times weekly albuterol) and nighttime awakening >2 times/month (twice monthly) indicate persistent disease requiring daily controller therapy. Treatment is **low-dose ICS** (such as fluticasone or budesonide) plus as-needed SABA for rescue.

Question 2. Asthma is fundamentally an **inflammatory disease**. SABA provides only symptom relief through bronchodilation without addressing underlying airway inflammation. Without anti-inflammatory therapy, inflammation persists, airway hyperresponsiveness continues, and the disease may worsen with airway remodeling. ICS reduce eosinophilic inflammation, decrease exacerbation risk, and improve long-term outcomes.

Question 3. Instructions for ICS use: (1) Use daily even when feeling well—it's a controller, not rescue medication; (2) Use a spacer device with MDI to improve drug delivery and reduce oropharyngeal deposition; (3) Rinse mouth and spit after each use to prevent oral candidiasis; (4) Do not expect immediate relief—full benefit takes days to weeks; (5) Continue SABA for acute symptoms but contact provider if using SABA more than twice weekly.

Question 4. If uncontrolled on low-dose ICS after 3 months, **step up to ICS-LABA combination** (Step 3). Options include fluticasone-salmeterol (Advair), budesonide-formoterol (Symbicort), or mometasone-

formoterol (Dulera). This provides both enhanced anti-inflammatory effect and long-acting bronchodilation. Never add LABA without ICS.

Case 21.2: Anemia Workup

Question 1. This patient has **two causes of anemia**: (1) Anemia of CKD from reduced erythropoietin production, and (2) Iron deficiency, indicated by low ferritin (15 ng/mL), low TSAT (12%), and microcytic RBCs (MCV 78 fL). The microcytosis suggests iron deficiency is significant—CKD anemia alone typically causes normocytic anemia. Both must be addressed.

Question 2. No—do not start ESA immediately. Iron deficiency must be corrected first or concurrently. ESAs stimulate erythropoiesis, which requires adequate iron for hemoglobin synthesis. Starting ESA without iron repletion results in poor response (functional iron deficiency) and wastes medication. Replete iron stores first, then reassess hemoglobin and consider ESA if still below target.

Question 3. Target hemoglobin is **10-11 g/dL**, not higher. Clinical trials (CHOIR, CREATE, TREAT) demonstrated that targeting hemoglobin >11-12 g/dL with ESAs increased cardiovascular events, stroke, and mortality without quality-of-life benefit. Black box warnings require using the lowest ESA dose necessary to avoid transfusion. Normalizing hemoglobin is not the goal.

Question 4. In CKD stage 4, **IV iron is preferred** over oral iron. CKD patients have impaired oral iron absorption due to elevated hepcidin from chronic inflammation. IV iron (iron sucrose, ferric gluconate, or ferric carboxymaltose) provides more reliable repletion, faster response, and better ESA effectiveness. Oral iron can be tried but often fails in CKD. Monitor ferritin and TSAT to guide ongoing supplementation.

Diagram/Table Exercise Answers

DT 21.1: Bronchodilator Mechanisms

1. Beta-2 agonists increase **cAMP** in smooth muscle cells.
 2. Anticholinergics block **M3 (muscarinic)** receptors.
 3. Both mechanisms result in airway smooth muscle **relaxation (bronchodilation)**.
 4. The short-acting beta-agonist used for rescue is **albuterol**.
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DT 21.2: Hematopoietic Growth Factors

1. Erythropoietin stimulates **red blood cell (erythrocyte)** production.
2. G-CSF (filgrastim) stimulates **neutrophil** production.

3. Thrombopoietin receptor agonists stimulate **platelet** production.
4. ESAs require adequate **iron** for effectiveness.

DT 21.3: Asthma Medications Comparison Table

Drug Class	Example	Mechanism	Role in Therapy
SABA	Albuterol	β_2 agonist $\rightarrow$ bronchodilation	Rescue/reliever
ICS	Fluticasone	Anti-inflammatory	Controller (foundation)
LABA	Salmeterol	β_2 agonist $\rightarrow$ bronchodilation	Controller (with ICS)
LAMA	Tiotropium	M3 blockade	Add-on for severe asthma/COPD
LTRA	Montelukast	Blocks CysLT1 receptor	Add-on/alternative (AERD, rhinitis)

DT 21.4: Anemia Treatment Comparison Table

Deficiency	Lab Findings	Treatment	Key Consideration
Iron	Low ferritin, low MCV	Oral or IV iron	GI side effects limit oral adherence
B12	Megaloblastic, $\uparrow$ MMA	Parenteral (or high-dose oral) B12	Neurological damage if delayed
Folate	Megaloblastic, normal MMA	Oral folic acid	Check B12 first—can mask deficiency
CKD anemia	Low EPO, normocytic	ESA + iron	Target Hgb 10-11, not higher

Multiple-Choice Question Answers

Question 1. Answer: B

Albuterol activates β_2 adrenergic receptors on airway smooth muscle, stimulating adenylyl cyclase and increasing intracellular cAMP, which causes smooth muscle relaxation and bronchodilation.

Question 2. Answer: B

LABAs must always be combined with ICS in asthma. LABA monotherapy increases mortality risk and carries an FDA black box warning. Combination ICS-LABA inhalers help ensure appropriate use.

Question 3. Answer: B

Oral candidiasis (thrush) is the most common local adverse effect of ICS, caused by drug depositing in the oropharynx. Using a spacer and rinsing the mouth after use reduces this risk.

Question 4. Answer: C

Clinical trials showed that targeting hemoglobin >11-12 g/dL with ESAs increased cardiovascular events, stroke, and mortality. Current guidelines recommend targeting 10-11 g/dL, using the lowest dose to avoid transfusion.

Question 5. Answer: B

B12 deficiency causes neurological manifestations (peripheral neuropathy, subacute combined degeneration of spinal cord) that folate deficiency does not. Both cause megaloblastic anemia, but only B12 deficiency affects the nervous system.

Question 6. Answer: B

In COPD with frequent exacerbations, adding LAMA to LABA provides additive bronchodilation and superior exacerbation reduction. ICS should not be used as monotherapy in COPD (increases pneumonia risk without bronchodilation).

Question 7. Answer: B

The FDA added a black box warning to montelukast for neuropsychiatric events including agitation, depression, sleep disturbances, and suicidal ideation. Patients should be counseled about these risks.

Question 8. Answer: B

Mepolizumab targets IL-5, which is critical for eosinophil development and survival. It reduces blood eosinophil counts and is used for severe eosinophilic asthma.

Question 9. Answer: C

Iron deficiency anemia is characterized by low MCV (microcytic), low ferritin (depleted iron stores), and low TSAT. Macrocytic anemia with elevated MMA suggests B12 deficiency.

Question 10. Answer: B

G-CSF (filgrastim, pegfilgrastim) stimulates neutrophil production and is used to reduce the depth and duration of chemotherapy-induced neutropenia, thereby decreasing infection risk.

Question 11. Answer: B

ICS increase pneumonia risk primarily in COPD patients, not asthma patients. This is why ICS are not first-line in COPD and should only be used in combination with LABA for patients with frequent exacerbations.

Question 12. Answer: B

Pernicious anemia (autoimmune destruction of parietal cells) causes B12 deficiency. Neurological symptoms require prompt parenteral B12 to prevent permanent damage. Oral folic acid would worsen neurological damage by masking the anemia.

Question 13. Answer: B

LABA monotherapy is contraindicated in asthma. It increases mortality risk compared to placebo and carries an FDA black box warning. LABAs must always be combined with ICS.

Question 14. Answer: B

Omalizumab binds free IgE and is indicated for moderate-to-severe allergic asthma with elevated IgE levels and demonstrated sensitivity to perennial allergens. It is not appropriate for low-IgE or non-allergic asthma.

Question 15. Answer: B

Folate can correct the megaloblastic anemia of B12 deficiency while neurological damage from B12 deficiency continues to progress silently. Always check B12 before treating megaloblastic anemia with folate to avoid this dangerous scenario.

Question 16. Answer: B

Triple therapy in COPD consists of ICS + LABA + LAMA (three different drug classes). This combination is reserved for severe COPD with persistent exacerbations despite dual bronchodilator therapy.