

ANSWER KEY WITH EXPLANATIONS FOR CHAPTER 20

Skill Drill Answers

SD 20.1: Drug Class Matching

1. **A** — Tacrolimus is a calcineurin inhibitor
 2. **B** — Sirolimus is an mTOR inhibitor
 3. **C** — Basiliximab is an anti-IL-2 receptor antibody
 4. **D** — Thymoglobulin is a polyclonal anti-T-cell antibody
 5. **E** — Pembrolizumab is an anti-PD-1 checkpoint inhibitor
 6. **F** — Infliximab is a TNF- α inhibitor
 7. **A** — Cyclosporine is a calcineurin inhibitor
 8. **B** — Everolimus is an mTOR inhibitor
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SD 20.2: True/False with Correction

1. **T** — CNI nephrotoxicity is a major limitation.
 2. **F** — mTOR inhibitors do NOT cause nephrotoxicity (major advantage).
 3. **F** — Live vaccines are CONTRAINDICATED in immunocompromised patients.
 4. **T** — Checkpoint inhibitors cause immune-related adverse events.
 5. **F** — Passive immunization provides SHORT-TERM protection (weeks-months).
 6. **T** — Tacrolimus is 10-100 $\times$ more potent than cyclosporine.
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SD 20.3: Fill in the Blank

1. **NFAT (nuclear factor of activated T-cells)**
 2. **FKBP12**
 3. **NF- κ B**
 4. **cancer (melanoma, lung cancer, etc.)**
 5. **corticosteroid (prednisone)**
 6. **immunocompromised**
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SD 20.4: T-Cell Activation Signal Matching

1. **C** — Cyclosporine blocks IL-2 transcription (Signal 3 initiation)
 2. **C** — Basiliximab blocks IL-2 receptor (Signal 3)
 3. **B** — Belatacept blocks co-stimulation (Signal 2)
 4. **C** — Sirolimus blocks mTOR (Signal 3 downstream)
 5. **B** — Abatacept blocks co-stimulation (Signal 2)
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SD 20.5: Adverse Effect Identification

1. **A** — CNIs cause nephrotoxicity and tremor
 2. **B** — mTOR inhibitors cause hyperlipidemia and impaired wound healing
 3. **C** — Glucocorticoids cause osteoporosis and hyperglycemia
 4. **D** — Checkpoint inhibitors cause immune-related colitis and pneumonitis
 5. **E** — TNF- α inhibitors cause TB reactivation
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SD 20.6: Rapid Recall

1. **Tacrolimus**
2. **Live (attenuated)**
3. **PD-1**
4. **Trough level (drug level monitoring)**
5. **Pulse steroids (or thymoglobulin)**
6. **Rituximab**

SD 20.7: Complete the Sentence

1. **FKBP12**
2. **do not**
3. **enhance**
4. **immediate**
5. **pre-formed**
6. **tapered**

SD 20.8: Vaccine Classification

1. **L** — MMR is live attenuated
2. **I** — Hepatitis B is inactivated/subunit (recombinant)
3. **M** — Pfizer COVID-19 is mRNA
4. **L** — Varicella is live attenuated
5. **I** — Injectable influenza is inactivated
6. **L** — Yellow fever is live attenuated

SD 20.9: Transplant Rejection Matching

1. **A** — Hyperacute occurs within minutes
2. **B** — Acute occurs days to months
3. **C** — Chronic causes gradual fibrosis
4. **A** — Hyperacute prevented by crossmatch
5. **B** — Acute treated with steroids or thymoglobulin

SD 20.10: Immune Checkpoint Pathway Matching

1. **A** — Ipilimumab targets CTLA-4
2. **B** — Pembrolizumab targets PD-1
3. **C** — Atezolizumab targets PD-L1

4. **B** — Nivolumab targets PD-1
 5. **C** — Durvalumab targets PD-L1
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SD 20.11: Drug Interaction/Monitoring Identification

1. **T** — CYP3A4 inhibitors increase tacrolimus levels
 2. **T** — mTOR inhibitors require TDM
 3. **F** — Checkpoint inhibitors do NOT require routine drug level monitoring
 4. **T** — Short-term steroids can be stopped without taper
 5. **F** — CNIs have a NARROW therapeutic index
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SD 20.12: Clinical Scenario Drug Selection

1. **B** — Thymoglobulin for T-cell depletion induction
2. **B** — Pembrolizumab for metastatic melanoma
3. **B** — VZIG for immunocompromised varicella exposure

Case Study Answers

Case 20.1: Transplant Immunosuppression

Question 1. Two most likely causes: (1) **Tacrolimus toxicity**—level is 18 ng/mL (above target 8-12), and CNIs are nephrotoxic; (2) **Acute rejection**—always a concern in early post-transplant period. The elevated tacrolimus level suggests toxicity is more likely, but rejection cannot be excluded without biopsy.

Question 2. Tacrolimus causes nephrotoxicity through: (1) **Acute toxicity**: Vasoconstriction of afferent arterioles reduces renal blood flow; dose-related and reversible; (2) **Chronic toxicity**: Interstitial fibrosis and tubular atrophy; develops over months-years; irreversible. The elevated trough level indicates excessive drug exposure causing acute vasoconstriction.

Question 3. Reduce the tacrolimus dose and recheck the level in 2-3 days. Target trough is 8-12 ng/mL in most protocols. If creatinine doesn't improve after dose reduction, consider kidney biopsy to evaluate for rejection, which can coexist with CNI toxicity.

Question 4. Long-term complications to monitor: (1) **CNI toxicity**: Nephrotoxicity, hypertension, diabetes, hyperlipidemia; (2) **Infection**: Opportunistic infections (CMV, BK virus, PJP); (3) **Malignancy**: Skin cancer, PTLN (post-transplant lymphoproliferative disorder); (4) **Cardiovascular disease**:

Accelerated by immunosuppression-related metabolic effects; (5) **Bone disease**: Osteoporosis from steroids.

Case 20.2: Checkpoint Inhibitor Toxicity

Question 1. This is most likely **checkpoint inhibitor-induced pneumonitis** (immune-related adverse event). The clinical picture of dyspnea, dry cough, and bilateral ground-glass opacities on CT after 8 weeks of pembrolizumab—with negative infectious workup—is classic for this irAE.

Question 2. Checkpoint inhibitors block PD-1/PD-L1, releasing immune "brakes." This enhances T-cell activity against tumors but also unleashes autoimmune responses against normal tissues. In pneumonitis, activated T-cells infiltrate the lung interstitium, causing inflammation similar to autoimmune interstitial lung disease.

Question 3. Management: (1) **Hold pembrolizumab** immediately; (2) Start **high-dose corticosteroids** (prednisone 1-2 mg/kg/day or IV methylprednisolone if severe); (3) If no improvement in 48-72 hours, add **infliximab or mycophenolate**; (4) Slow steroid taper over 4-6 weeks after improvement; (5) Grade 3-4 pneumonitis usually requires permanent discontinuation of checkpoint inhibitor.

Question 4. Other irAEs to monitor: (1) **Colitis**: Diarrhea, bloody stools—can be life-threatening; (2) **Hepatitis**: Elevated transaminases; (3) **Endocrinopathies**: Thyroiditis, hypophysitis, adrenal insufficiency, type 1 diabetes; (4) **Dermatitis**: Rash, pruritus; (5) **Nephritis**: Rising creatinine; (6) **Myocarditis**: Rare but potentially fatal. Monitor symptoms, labs (TFTs, LFTs, glucose, creatinine), and vitals at each visit.

Diagram/Table Exercise Answers

DT 20.1: T-Cell Activation and Immunosuppressant Targets

1. Calcineurin inhibitors block **IL-2** transcription by inhibiting NFAT.
 2. Basiliximab blocks the **IL-2 (CD25)** receptor.
 3. mTOR inhibitors block T-cell **proliferation** in response to IL-2.
 4. Belatacept blocks Signal 2 by preventing **CD28-B7 (co-stimulation)** interaction.
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DT 20.2: Checkpoint Inhibitor Mechanism

1. Tumors express **PD-L1** to evade immune detection.
2. PD-1 on T-cells binding PD-L1 causes T-cell **exhaustion (inactivation)**.

3. Pembrolizumab blocks **PD-1**, preventing tumor escape.
4. Unleashed T-cell activity can cause **immune-related (autoimmune)** adverse events.

DT 20.3: Immunosuppressant Comparison Table

Drug	Mechanism	Major Toxicities	Monitoring
Tacrolimus	Calcineurin inhibition	Nephrotoxicity, diabetes, neurotoxicity	Trough drug levels
Sirolimus	mTOR inhibition	Hyperlipidemia, impaired wound healing, myelosuppression	Drug levels
Mycophenolate	IMPDH inhibition	GI toxicity, bone marrow suppression	CBC
Prednisone	Multiple (NF- κ B, etc.)	Hyperglycemia, osteoporosis, infection	Glucose, bone density
Thymoglobulin	T-cell depletion	Cytokine release, profound immunosuppression	CBC, infection signs

DT 20.4: Active vs. Passive Immunization Table

Feature	Active Immunization (Vaccines)	Passive Immunization (Ig)
Onset of protection	Slow (weeks)	Immediate
Duration	Long-lasting (years)	Short (weeks-months)
Immune memory	Yes	No
Use in immunocompromised	Live vaccines contraindicated	Safe and indicated
Example	MMR vaccine	IVIG, VZIG, RhoGAM

Multiple-Choice Question Answers

Question 1. Answer: C

Calcineurin inhibitors block IL-2 gene transcription by preventing NFAT nuclear translocation.

Question 2. Answer: C

Sirolimus (mTOR inhibitor) does not cause nephrotoxicity—a major advantage over CNIs.

Question 3. Answer: B

Live vaccines can cause disease in immunocompromised patients who cannot control attenuated organisms.

Question 4. Answer: B

Pembrolizumab blocks PD-1, preventing T-cell exhaustion and enhancing anti-tumor immunity.

Question 5. Answer: D

Thymoglobulin is used for induction, not maintenance therapy.

Question 6. Answer: B

Level of 22 ng/mL is above target (8-12); tremor and elevated creatinine are classic tacrolimus toxicity.

Question 7. Answer: B

Thymoglobulin is a polyclonal antibody that profoundly depletes T-cells.

Question 8. Answer: C

Checkpoint inhibitor colitis is an irAE treated with high-dose corticosteroids (and infliximab if refractory).

Question 9. Answer: B

Gingival hyperplasia and hirsutism are specific to cyclosporine.

Question 10. Answer: B

Passive immunization provides immediate protection when there's no time for vaccine response.

Question 11. Answer: B

mTOR inhibitors allow CNI dose reduction, minimizing nephrotoxicity while maintaining immunosuppression.

Question 12. Answer: B

Hyperacute rejection is caused by pre-formed antibodies (ABO or HLA) attacking donor antigens immediately.

Question 13. Answer: B

Checkpoint inhibitors can unleash autoimmune destruction of pancreatic beta cells, causing type 1 diabetes.

Question 14. Answer: B

Belatacept allows CNI-free or CNI-minimization protocols, avoiding CNI nephrotoxicity.

Question 15. Answer: B

BK virus nephropathy results from over-immunosuppression; treatment is reduction of immunosuppression.

Question 16. Answer: B

Tocilizumab blocks IL-6 receptor. Rituximab blocks CD20, infliximab blocks TNF- α , basiliximab blocks IL-2R.