PHARMACOLOGY · STUDY GUIDE

Exam 2 Study Guide

This guide covers chapters 3 and 4. Chapter 3 is about drugs that turn the immune system down or up and drugs that kill dividing cells. Chapter 4 follows pain from the injured tissue to the brain, then works through every class that treats it and the substances and withdrawal syndromes that bring people into care. Work one chapter at a time. Read the "what to know" paragraphs, copy the tables by hand, then try each worked example with the steps covered. Finish each chapter with its ten self-test items. Any dose or number in a worked example is a practice calculation only, not dosing advice.

WHAT THIS GUIDE COVERS

- Chapter 3 · transplant and autoimmune immunosuppressants, infection risk, colony-stimulating factors, checkpoint inhibitors, vaccine types and live vaccine rules, the cell cycle, log kill, chemotherapy classes and their signature toxicities, myelosuppression, nausea, mucositis, extravasation and hazardous drug handling.
- Chapter 4 · the four steps of nociception, pain types and scales, the ceiling effect, acetaminophen and its antidote, NSAIDs and COX, opioid receptor types, sedation before respiratory depression, naloxone, tolerance and dependence, adjuvants, migraine drugs, and alcohol, opioid, sedative, stimulant and nicotine withdrawal.

CHAPTER 3

Immunomodulators and Antineoplastic Agents

Read it in full: **Chapter 3 in the textbook**. Practice it in the lab: **Immunosuppressants** and **Chemo Toxicities**.

What to know

We turn the immune system down in two situations: **transplant**, where the graft is not-self, and **autoimmune disease**, where the body attacks its own tissue. Every bit of immunity removed was also guarding against infection and cancer. Transplant regimens use brief, heavy **induction** (basiliximab or antithymocyte globulin) and lifelong **maintenance** with three classes at lower

doses: a calcineurin inhibitor, an antiproliferative and a corticosteroid, so the toxicities do not stack in one organ.

Calcineurin inhibitors (tacrolimus, cyclosporine) block IL-2 production so T cells cannot multiply. They have a narrow therapeutic index: troughs before the dose, nephrotoxicity, hypertension, tremor, hyperkalemia, hyperglycemia with tacrolimus and gum overgrowth with cyclosporine. Both use CYP3A4, so grapefruit juice, azoles and clarithromycin raise levels while rifampin, phenytoin and St. John's wort drop them toward rejection.

Antiproliferatives starve lymphocytes of purines. Mycophenolate is teratogenic. Azathioprine plus **allopurinol** can cause marrow failure, because allopurinol blocks xanthine oxidase, which clears azathioprine's active metabolite. **mTOR inhibitors** (sirolimus) spare the kidney but slow wound healing. Corticosteroids are tapered, never stopped abruptly. Low-dose **methotrexate** for rheumatoid arthritis is given **once weekly**; a daily order is a lethal error. **TNF inhibitors** (adalimumab, etanercept, infliximab) need latent TB and hepatitis B screening first.

Immunosuppressed patients **hide infection**. Steroids blunt fever and neutropenia removes pus, so a low-grade temperature, new cough, sore throat or "I don't feel right" is reported. Prophylaxis is standard: TMP-SMX for Pneumocystis, an antiviral for CMV. Live vaccines are contraindicated in significant immunosuppression; bring vaccines up to date before transplant or a biologic. Teach sun protection for skin cancer risk.

Immunostimulants turn the system up. Filgrastim and pegfilgrastim (G-CSF) rebuild neutrophils after chemotherapy, cause deep bone pain, and are given at least 24 hours after chemotherapy, never with it. Epoetin and darbepoetin raise hemoglobin but carry a boxed warning for thrombosis, stroke and shorter survival in some cancers. Interferons cause flu-like symptoms and depression. **Checkpoint inhibitors** (pembrolizumab, nivolumab, atezolizumab, ipilimumab) release the immune brake and can cause colitis, pneumonitis, hepatitis and thyroiditis; new diarrhea or cough is reported the same day and treated with steroids. Name decoder: -mab antibody, -cept fusion protein, -nib kinase inhibitor.

A vaccine gives **active** immunity: slow to build, lasting. Immune globulin gives **passive** immunity: immediate, temporary, no memory. **Live attenuated** vaccines (MMR, varicella,

rotavirus, intranasal influenza, yellow fever) are contraindicated in pregnancy and significant immunosuppression. Inactivated, subunit, toxoid, conjugate and mRNA vaccines are not live. Tdap is given in every pregnancy (27 to 36 weeks). Give the VIS, observe at least 15 minutes with epinephrine at hand, and document lot, expiration, site and route. A mild cold is not a contraindication; prior anaphylaxis to a component is. Household contacts of an immunosuppressed person are generally still vaccinated.

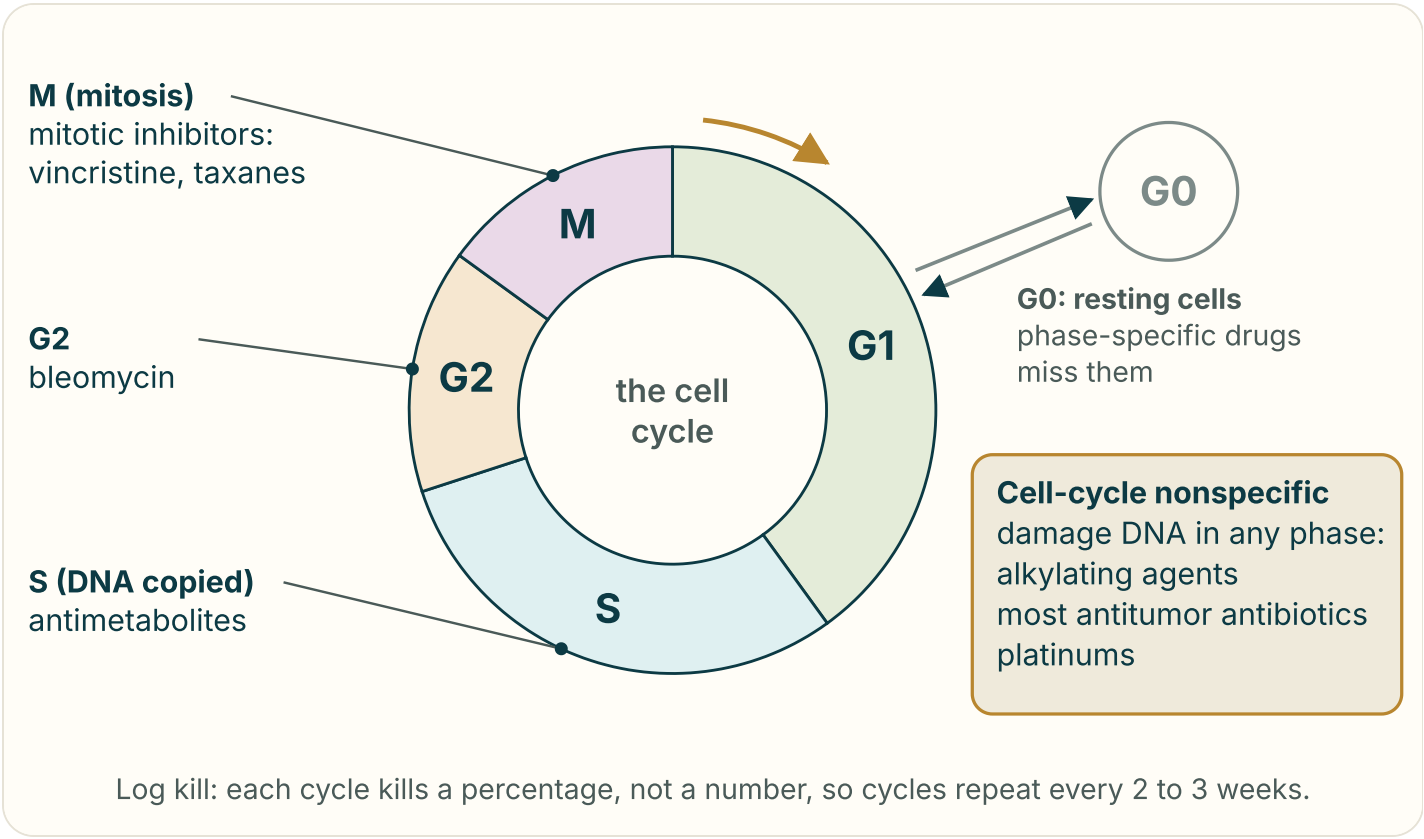
The cell cycle runs **G1, S, G2, M**, with **G0** as the resting hiding place. **Cell-cycle-specific** drugs hit one phase: antimetabolites in S, mitotic inhibitors in M, bleomycin in G2. **Nonspecific** drugs (alkylating agents, most antitumor antibiotics, platinums) damage DNA in any phase. The **log kill** hypothesis says each dose kills a percentage, not a number, so treatment comes in repeated cycles with 2 to 3 week rests that let marrow recover. Doses are by body surface area (mg/m^2); carboplatin by target AUC. Chemotherapy needs an independent double-check.

Chemotherapy cannot tell cancer from healthy tissue, only dividing from resting. Ask which normal tissues divide fastest and you predict the toxicities: marrow (myelosuppression, the dose-limiting effect), gut lining (mucositis, diarrhea), hair (alopecia), gonads (infertility, so discuss banking first), skin and nails, and a fetus (teratogenicity).

Signature toxicities: **cyclophosphamide**, hemorrhagic cystitis (hydrate, void often, mesna). **Cisplatin**, nephrotoxic, ototoxic and highly emetogenic. **Oxaliplatin**, cold-triggered neuropathy. **Doxorubicin**, cumulative irreversible cardiotoxicity (lifetime limit about 550 mg/m^2, baseline echo or MUGA, dexrazoxane), a vesicant, harmless red-orange urine. **Bleomycin**, pulmonary fibrosis with little marrow suppression. **Methotrexate** high dose, leucovorin rescue and no NSAIDs. **Vincristine**, neuropathy and constipation, and fatal if given intrathecally. **Taxanes**, hypersensitivity, so premedicate. Trastuzumab cardiotoxicity is usually reversible; rituximab needs hepatitis B screening; tamoxifen raises clot and endometrial cancer risk.

The **nadir** comes 7 to 14 days after a cycle. ANC under 1,000 is serious and under 500 severe. **Febrile neutropenia** (38.3°C once or 38.0°C for an hour) means cultures and broad antibiotics within one hour; no rectal temperatures, suppositories or enemas. Platelets under 50,000 bring bleeding precautions. Antiemetics are scheduled **before** chemotherapy; lorazepam helps anticipatory nausea. For extravasation, stop, leave the needle in, aspirate and notify: **cold** and

dexrazoxane for anthracyclines, **warm** and hyaluronidase for vincas. Handle chemotherapy as hazardous: double gloves, gown, and body fluid precautions at home for about 48 hours.



Phase-specific versus nonspecific chemotherapy. Drugs that hit one phase miss resting G0 cells; alkylating agents and platinums damage DNA whatever the phase.

LOCK THESE IN

- Transplant maintenance: calcineurin inhibitor + antiproliferative + corticosteroid.
- Tacrolimus and cyclosporine: troughs, nephrotoxicity, no grapefruit; inducers cause rejection.
- Methotrexate for RA is weekly. Azathioprine + allopurinol = marrow failure. TNF inhibitors: TB screen first.
- Live vaccines (MMR, varicella, rotavirus, LAIV, yellow fever): not in pregnancy or significant immunosuppression.
- Filgrastim: bone pain; at least 24 h after chemo. Checkpoint inhibitors: new diarrhea or cough is urgent.
- Log kill: a percentage per dose, so cycles matter even after a clear scan.
- Febrile neutropenia: cultures and antibiotics within 1 hour; no rectal anything.
- Extravasation: stop, leave needle, aspirate; cold for anthracyclines, warm for vincas. Vincristine is IV only.

Key terms and comparisons

Drug or group	Mechanism or type	Signature risk and nursing action
Tacrolimus, cyclosporine	Calcineurin inhibitors (block IL-2)	Troughs; kidney, K+, tremor; CYP3A4 interactions
Mycophenolate, azathioprine	Antiproliferatives	Leukopenia; mycophenolate teratogenic; azathioprine + allopurinol
Methotrexate (RA)	Low-dose folate antagonist	Weekly only; folic acid on other days; CBC, LFTs
Adalimumab, infliximab	TNF inhibitors	Latent TB and hepatitis B screen first
Filgrastim	G-CSF	Bone pain; at least 24 h after chemo
Pembrolizumab	Checkpoint inhibitor (anti-PD-1)	Immune colitis, pneumonitis; steroids, no delay
Live vs inactivated vaccine	Replicating vs killed	Live: not in pregnancy or immunosuppression
Active vs passive immunity	Vaccine vs immune globulin	Slow and lasting vs immediate and temporary
CCS vs CCNS	One phase vs any phase	Antimetabolites S, vincas and taxanes M, bleomycin G2

Chemotherapy signatures

Drug	Class	Signature toxicity	Prevention or response
cyclophosphamide	Alkylating	Hemorrhagic cystitis	Hydrate, void often, mesna
cisplatin	Platinum	Kidney, hearing, severe emesis	Pre-hydrate; creatinine; hearing
oxaliplatin	Platinum	Cold-triggered neuropathy	Avoid cold drinks, air, metal
doxorubicin	Anthracycline	Cumulative cardiotoxicity; vesicant	Lifetime dose, echo, dexrazoxane
bleomycin	Antitumor antibiotic (G2)	Pulmonary fibrosis	Baseline PFTs; report cough
methotrexate (high dose)	Antimetabolite (S)	Mucositis, marrow	Leucovorin rescue; no NSAIDs
vincristine	Vinca alkaloid (M)	Neuropathy, ileus; fatal intrathecal	IV only; bowel regimen
paclitaxel	Taxane (M)	Hypersensitivity	Steroid, antihistamine, H2 blocker; non-PVC tubing
irinotecan	Topoisomerase	Early and late diarrhea	Atropine early; loperamide late

Worked examples

WORKED EXAMPLE 1 · LOG KILL IN NUMBERS

A tumor holds 10^9 cells. Each cycle kills 99.9% of the cells present. How many cells remain after one, two and three cycles?

STEP 1 · FIND THE SURVIVORS PER CYCLE

Killing 99.9% leaves 0.1%, which is 1 in 1,000.

STEP 2 · APPLY IT THREE TIMES

Cycle 1: $10^9 \div 1{,}000 = 10^6$ (one million). Cycle 2: 10^3 (one thousand). Cycle 3: **about 1 cell**.

STEP 3 · CONNECT TO THE SCAN

A scan cannot see a million cells. A clear scan after two cycles still leaves about a thousand.

THE LESSON

Each dose kills a percentage, not a number. That is why the full schedule matters even when the patient feels well.

WORKED EXAMPLE 2 · CALCULATING AN ANC

A patient on chemotherapy has a WBC of 2,500/mm^3 with 15% segmented neutrophils and 5% bands. What is the ANC, and what does it mean?

STEP 1 · ADD THE NEUTROPHIL FORMS

15% + 5% = 20%.

STEP 2 · MULTIPLY

2,500 × 0.20 = **500/mm^3**.

STEP 3 · INTERPRET

Under 1,000 is serious; 500 sits at the edge of severe neutropenia. Neutropenic precautions apply.

IF A FEVER APPEARS

A temperature of 38.3°C once is febrile neutropenia: cultures and broad antibiotics within one hour.

WORKED EXAMPLE 3 · TRACKING A LIFETIME DOSE

The book gives a doxorubicin lifetime ceiling of roughly 550 mg/m^2. A practice patient has already received 300 mg/m^2. Each planned cycle is 60 mg/m^2. How many more cycles fit under the ceiling?

STEP 1 · FIND WHAT IS LEFT

550 − 300 = 250 mg/m^2.

STEP 2 · DIVIDE BY THE CYCLE DOSE

250 ÷ 60 = 4.17, so **4 full cycles**.

STEP 3 · CHECK

300 + (4 × 60) = 540 mg/m^2, which stays under 550. A fifth cycle would reach 600.

WHY IT MATTERS

The damage is cumulative and largely irreversible, and the total follows the patient across every admission.

WORKED EXAMPLE 4 · A LEAKING VESICANT

Mrs. Lindqvist is receiving doxorubicin through a peripheral IV. She says the site burns; you see swelling and get no blood return. What do you do?

STEP 1 · STOP

Stop the infusion immediately. Leave the needle in.

STEP 2 · REMOVE WHAT YOU CAN

Disconnect the tubing and aspirate residual drug through the catheter.

STEP 3 · NOTIFY AND DOCUMENT

Notify the provider; mark and photograph the area; elevate the limb.

STEP 4 · APPLY THE RIGHT TEMPERATURE

Doxorubicin is an anthracycline: apply **cold** and expect dexrazoxane or topical DMSO. If it were vincristine, apply **warm** and give hyaluronidase.

TRAPS PEOPLE FALL INTO

- **Treating a low-grade fever casually in a transplant patient.** Fever may be the only sign of systemic infection. Report it.
- **Transcribing weekly methotrexate as daily.** Daily dosing has killed patients. Clarify any daily order for RA.
- **Giving filgrastim alongside chemotherapy.** Wait at least 24 hours after chemotherapy.
- **Refusing to vaccinate a household contact.** Contacts of an immunosuppressed person are generally vaccinated; the live vaccine rule is about the patient.
- **Swapping cold and warm for extravasation.** Cold for anthracyclines, warm for vincas. Reversing them worsens the injury.
- **Giving antiemetics only after vomiting starts.** Schedule them before chemotherapy.
- **Confusing doxorubicin urine with cyclophosphamide urine.** Red-orange urine after doxorubicin is harmless; pink urine on cyclophosphamide is cystitis.

Chapter 3 self-test · ten items

1. Why do transplant regimens combine three drug classes at lower doses?

A. Only combinations are absorbed well from the gut
B. Three mechanisms spread the toxicity across organs
C. One drug at a high dose always costs far more
D. The three drugs cancel out each other's side effects

B. Three mechanisms spread the toxicity across organs Three mechanisms at modest doses control rejection while keeping any one organ from taking the whole toxic load.

2. A patient on tacrolimus begins drinking grapefruit juice daily. What should the nurse expect?

A. Lower tacrolimus levels and graft rejection
B. No change because the juice is a food
C. Higher tacrolimus levels and kidney injury risk
D. Lower levels because juice speeds excretion

C. Higher tacrolimus levels and kidney injury risk Grapefruit juice inhibits CYP3A4, so tacrolimus levels rise toward nephrotoxicity, tremor and hyperkalemia.

3. Which combination can cause severe marrow failure?

A. Azathioprine with allopurinol
B. Mycophenolate with prednisone
C. Filgrastim with acetaminophen
D. Tacrolimus with folic acid

A. Azathioprine with allopurinol Allopurinol blocks xanthine oxidase, which clears azathioprine's active metabolite, so levels climb dangerously.

4. What must be done before a first dose of infliximab?

A. Start a daily folic acid tablet
B. Draw a digoxin level
C. Give a live varicella vaccine
D. Screen for latent tuberculosis

D. Screen for latent tuberculosis Blocking TNF lets walled-off TB reactivate. Hepatitis B is screened too. Live vaccines should be given before, not during, therapy.

5. Which vaccine should NOT be given to a patient on high-dose prednisone?

A. Hep B
B. MMR
C. Td
D. IPV

B. MMR MMR is live attenuated and can cause disease in significant immunosuppression. The others are not live.

6. A patient on pembrolizumab reports six watery stools a day. What is the concern?

A. Immune-related colitis needing prompt steroids
B. Opioid withdrawal from several missed doses
C. An allergy to the plastic infusion bag itself
D. Expected mild diarrhea that will soon pass

A. Immune-related colitis needing prompt steroids Checkpoint inhibitors can turn the immune system on the bowel. Delay risks perforation, so it is reported the same day.

7. Which drug class works mainly in the S phase of the cell cycle?

A. Alkylating agents
B. Taxanes
C. Vinca alkaloids
D. Antimetabolites

D. Antimetabolites Antimetabolites mimic DNA building blocks and act during synthesis. Vincas and taxanes act in M; alkylating agents are nonspecific.

8. A patient receiving cyclophosphamide reports pink urine. What is happening?

A. Expected rifampin-like discoloration
B. Harmless dye from the drug
C. Hemorrhagic cystitis from acrolein
D. Normal concentration of the urine

C. Hemorrhagic cystitis from acrolein Acrolein burns the bladder. Prevention is hydration, frequent voiding and mesna. Harmless red-orange urine belongs to doxorubicin.

9. A neutropenic patient has an oral temperature of 38.4°C. What is the time goal for antibiotics?

A. Within 72 hours
B. Within 6 hours
C. Within 24 hours
D. Within 1 hour

D. Within 1 hour Febrile neutropenia is an emergency. Cultures are drawn and broad antibiotics started within one hour.

10. Which order on a vincristine label is absolute?

A. For intravenous use only
B. For intramuscular use only
C. For intrathecal use only
D. For oral use with a meal

A. For intravenous use only Intrathecal vincristine causes ascending paralysis and death. It is dispensed in a minibag to prevent that error.

CHAPTER 4

Pain and Substance Use

Read it in full: **Chapter 4 in the textbook**. Practice it in the lab: **The Ceiling and the Limit** and **Opioids**.

What to know

Nociception has four steps, and each analgesic class interrupts a different one. **Transduction**: injured tissue releases prostaglandins and other mediators that lower the nociceptor threshold; NSAIDs act here. **Transmission**: A-delta fibers carry fast, sharp, localized pain; C fibers carry slow, dull, burning pain to the dorsal horn, where substance P and glutamate pass the signal up the spinothalamic tract; opioids act mostly here and above. **Perception** happens in the cortex and limbic system, which is why fear and exhaustion make pain worse. **Modulation** is the descending brake using serotonin, norepinephrine and endorphins; antidepressant adjuvants strengthen it.

Acute pain has a cause and an end and often a sympathetic surge. **Chronic** pain lasts past healing, about three months, and the sympathetic signs fade, so normal vital signs do not disprove pain. **Nociceptive** pain comes from tissue damage (somatic or visceral) and responds to classic analgesics. **Neuropathic** pain (burning, shooting, electric) comes from damaged nerves and responds poorly to opioids and NSAIDs but well to adjuvants.

Self-report is the gold standard. Match the scale to the patient: numeric 0 to 10 for verbal adults, Wong-Baker FACES for children about 3 and up, FLACC for nonverbal children and patients,

CRIES for neonates, PAINAD for advanced dementia, CPOT or BPS for intubated patients. Reassess about 15 to 30 minutes after an IV dose and about 60 minutes after an oral dose. **Multimodal** analgesia stacks mechanisms so each works at a lower dose.

Non-opioids have a **ceiling effect**: past a dose, relief stops rising but toxicity keeps climbing. The fix is a different mechanism, not more milligrams. They do not depress breathing or cause dependence, and scheduled acetaminophen spares opioids.

Acetaminophen relieves pain and fever with no anti-inflammatory or antiplatelet effect, so it suits patients who cannot take NSAIDs, including in pregnancy. A small fraction becomes **NAPQI**, which glutathione neutralizes; in overdose or with depleted glutathione (alcohol, fasting) it destroys hepatocytes. It hides in combination products. The book gives a healthy adult maximum of 4 g in 24 hours, many teach 3 g, and 2 g or less in liver disease, heavy alcohol use or frailty. The antidote is **acetylcysteine**, best within 8 to 10 hours, guided by a 4 hour level on the Rumack-Matthew nomogram.

NSAIDs block COX, giving analgesic, anti-inflammatory and antipyretic effects. Blocking **COX-1** explains the toxicities: GI ulcer and painless bleeding, acute kidney injury (the "triple whammy" with an ACE inhibitor or ARB plus a diuretic), MI and stroke risk, fluid retention, platelet impairment and bronchospasm in aspirin-exacerbated respiratory disease. Avoid from 20 weeks of pregnancy and treat as contraindicated in the third trimester. Celecoxib is COX-2 selective and a sulfonamide. Ketorolac is limited to 5 days total. Aspirin is irreversible (platelet life 7 to 10 days), causes Reye syndrome in children with viral illness, and tinnitus signals toxicity.

The **mu** receptor gives analgesia and respiratory depression together, plus euphoria, sedation, constipation, miosis and dependence. Full agonists (morphine, hydromorphone, fentanyl, oxycodone, methadone, codeine, tramadol) have no ceiling. Buprenorphine is a partial agonist with a ceiling on respiratory depression that can precipitate withdrawal. Nalbuphine and butorphanol are agonist-antagonists. Naloxone is the antagonist; methylnaltrexone and naloxegol block only gut receptors.

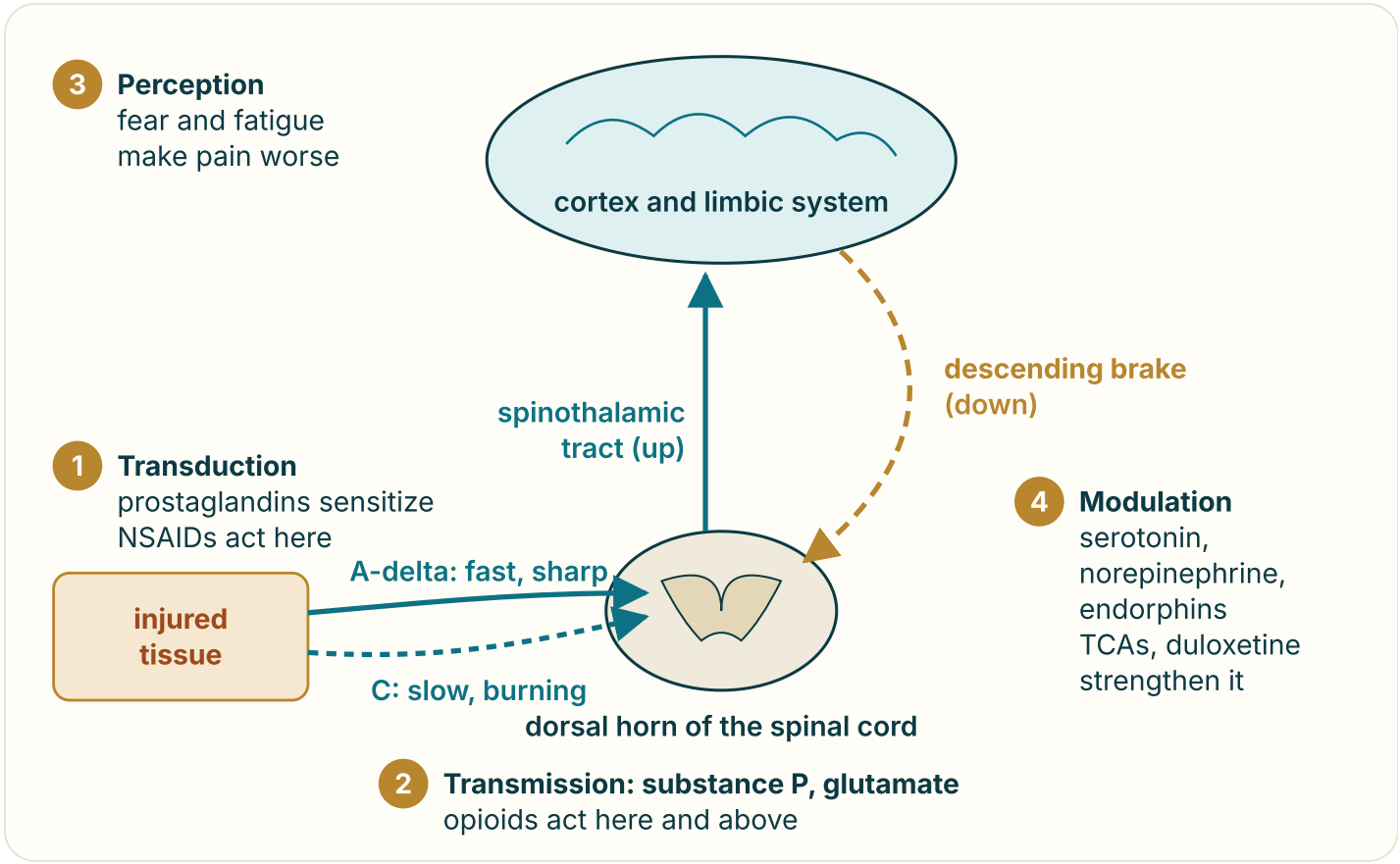
Sedation comes before respiratory depression. Assess sedation with POSS on every check; a difficult-to-arouse patient gets the next dose held even if the rate is still normal. The overdose

triad is depressed consciousness, pinpoint pupils and slow breathing. **Naloxone** works in 1 to 2 minutes IV but lasts only 30 to 90 minutes, shorter than most opioids, so titrate to breathing and keep monitoring for re-sedation. Tolerance does not develop to **constipation**; start senna with the first order. Morphine's metabolite builds up in kidney failure; codeine and tramadol are CYP2D6 prodrugs, contraindicated under 12; methadone prolongs QT; fentanyl patches are for opioid-tolerant patients only and heat speeds absorption. Only the patient presses the PCA button.

Tolerance (less effect from the same dose) and **physical dependence** (withdrawal on stopping) are expected pharmacology, not addiction. **Opioid use disorder** is compulsive use despite harm. Use people-first language: a person with a substance use disorder, a positive toxicology screen.

Adjuvants are first-line for neuropathic pain. Gabapentin and pregabalin calm firing nerves; they are renally cleared, cause dizziness and falls, are tapered, and add respiratory depression with opioids. TCAs and duloxetine strengthen the descending brake and take days to weeks. Carbamazepine treats trigeminal neuralgia; lidocaine 5% patches treat postherpetic neuralgia. **Triptans** (sumatriptan) abort migraine at the first sign and are contraindicated in coronary disease, prior MI or stroke and uncontrolled hypertension; no ergot within 24 hours. Gepants and lasmiditan avoid vasoconstriction. Preventives are daily and judged over 8 to 12 weeks. Acute drugs used more than about 10 to 15 days a month cause medication overuse headache.

Alcohol withdrawal can kill: tremor at 6 to 24 hours, hallucinosis 12 to 24, seizures 12 to 48, delirium tremens 48 to 96. Treat with benzodiazepines guided by CIWA-Ar and give **thiamine before glucose**. Long term: naltrexone, acamprosate, disulfiram (no alcohol in anything for 14 days after). **Opioid withdrawal** (yawning, tearing, dilated pupils, gooseflesh, diarrhea) is rarely fatal but drives relapse; buprenorphine waits for moderate withdrawal on COWS. **Benzodiazepine** withdrawal can kill; always taper. Stimulant withdrawal brings depression and suicide risk. Nicotine: patch plus short-acting NRT, varenicline, bupropion (not with seizure or eating disorders).



Four steps, four kinds of analgesic. NSAIDs stop sensitization in the tissue, opioids damp transmission in the cord and brain, and antidepressant adjuvants strengthen the descending brake.

LOCK THESE IN

- Transduction (NSAIDs), transmission and perception (opioids), modulation (antidepressant adjuvants).
- Neuropathic pain: adjuvants first, not more opioid.
- Non-opioid ceiling: add a mechanism, not milligrams. Acetaminophen 4 g/day healthy adult max; antidote acetylcysteine.
- NSAIDs: COX-1 explains GI bleed, AKI, platelets; triple whammy; avoid from 20 weeks of pregnancy.
- Sedation precedes respiratory depression. Naloxone lasts 30 to 90 min: watch for re-sedation.
- Constipation never gets tolerance: laxative with the first opioid order.
- Tolerance and dependence are not addiction.
- Alcohol: seizures 12 to 48 h, DTs 48 to 96 h; benzodiazepines; thiamine before glucose.

Key terms and comparisons

Item	Fact	Nursing meaning
Acetaminophen	Central COX; no anti-inflammatory or antiplatelet effect	Add every source; antidote acetylcysteine within 8 to 10 h
Ibuprofen, naproxen	Nonselective NSAIDs	Food, GI bleed, creatinine, BP
Ketorolac	Potent injectable NSAID	5 day total limit, all routes
Celecoxib	COX-2 selective	Sulfa allergy; CV and renal risk remain
Aspirin	Irreversible COX	Reye syndrome; tinnitus means toxicity
Morphine	Full mu agonist	Metabolite builds in renal failure
Fentanyl patch	Potent full agonist	Opioid-tolerant only; heat raises absorption
Buprenorphine	Partial agonist	Wait for moderate withdrawal (COWS)
Naloxone	Antagonist	Onset 1 to 2 min IV; lasts 30 to 90 min
Gabapentin, pregabalin	Alpha-2-delta calcium channel	Renal dosing, falls, taper
Sumatriptan	5-HT1B/1D agonist	First sign; not with CAD or uncontrolled HTN

Pain scales and withdrawal timelines

Item	Use or timing	Note
Numeric 0 to 10	Verbal adults	Ask the acceptable goal too
FACES / FLACC / CRIES	Children 3+ / nonverbal 2 mo to 7 yr / neonates	Patient picks the face
PAINAD / CPOT	Advanced dementia / intubated	Observe behavior, not vitals alone
Alcohol tremor	6 to 24 h	Anxiety, sweating, tachycardia
Alcohol seizures	12 to 48 h	Generalized tonic-clonic
Delirium tremens	48 to 96 h	Confusion, fever, autonomic storm
Opioid withdrawal	Score with COWS	Miserable, rarely fatal; relapse risk
Benzodiazepine withdrawal	Can be fatal	Always taper

Worked examples

WORKED EXAMPLE 1 · ADDING UP HIDDEN ACETAMINOPHEN

Mr. Brennan takes oxycodone/acetaminophen tablets containing 325 mg acetaminophen each, two tablets every 6 hours, plus one dose of a nighttime cold remedy labeled 650 mg acetaminophen, plus two 500 mg tablets for a headache. What is his 24 hour total? (Practice numbers from labels.)

STEP 1 · COUNT THE COMBINATION TABLETS

Every 6 hours is 4 times a day: 2 × 4 = 8 tablets. 8 × 325 = 2,600 mg.

STEP 2 · ADD THE OTHER SOURCES

Cold remedy 650 mg. Headache tablets 2 × 500 = 1,000 mg.

STEP 3 · TOTAL

2,600 + 650 + 1,000 = **4,250 mg**.

STEP 4 · COMPARE

That passes the 4 g healthy adult maximum the book gives, and far passes 2 g if he drinks heavily or has liver disease.

ACTION

Notify the prescriber, teach him to read every label, and count the sources out loud with him.

WORKED EXAMPLE 2 · SEDATION BEFORE THE RATE FALLS

Ms. Achebe, opioid-naive, is on IV morphine after surgery. She drifts off mid-sentence and needs a shake to answer. Her respiratory rate is 14. What do you do?

STEP 1 · READ THE SIGN

Sedation comes before respiratory depression. A normal rate is what you expect to see before it falls.

STEP 2 · ACT ON SEDATION

Hold the next dose. Stimulate her, apply oxygen and continuous monitoring.

STEP 3 · ESCALATE

Score sedation (POSS), notify the provider, and have naloxone and a bag-valve mask ready.

STEP 4 · FIND CONTRIBUTORS

Check for other CNS depressants, sleep apnea and kidney function.

WORKED EXAMPLE 3 · WHEN DOES NALOXONE WEAR OFF?

At 1400 a patient found unresponsive with pinpoint pupils wakes after IV naloxone. Naloxone lasts about 30 to 90 minutes. During what window can he re-sedate?

STEP 1 · ADD THE DURATION

1400 + 30 min = 1430. 1400 + 90 min = 1530.

STEP 2 · STATE THE WINDOW

From **about 1430 to 1530** the naloxone fades while long-acting opioid may still be bound.

STEP 3 · PLAN

Keep him monitored, be ready to repeat the dose or start an infusion, and titrate to breathing rather than full alertness.

WORKED EXAMPLE 4 · MAPPING AN ALCOHOL WITHDRAWAL TIMELINE

A patient's last drink was Saturday at 2200. Using the book's windows, when is the seizure risk highest, and when could delirium tremens appear?

STEP 1 · SEIZURES 12 TO 48 H

2200 Saturday + 12 h = 1000 Sunday. + 48 h = 2200 Monday. Window: **Sunday 1000 to Monday 2200**.

STEP 2 · DTS 48 TO 96 H

+ 48 h = 2200 Monday. + 96 h = 2200 Wednesday. Window: **Monday 2200 to Wednesday 2200**.

STEP 3 · TREAT AHEAD

Symptom-triggered benzodiazepines with CIWA-Ar, thiamine before glucose, folate and magnesium.

TRAPS PEOPLE FALL INTO

- **Using vital signs as a lie detector.** Chronic pain often has normal vitals. Believe the report.
- **Taking more ibuprofen when relief is poor.** The ceiling effect means more drug adds harm, not relief.
- **Waiting for the respiratory rate to fall.** Sedation is the early sign. Act on it.
- **Giving naloxone as one big push to an alert patient in pain.** Titrate to breathing; a full dose can cause severe withdrawal and pain.
- **Calling dependence addiction.** Tolerance and dependence are expected; use disorder is compulsive use despite harm.
- **Glucose before thiamine in alcohol withdrawal.** Thiamine first, or Wernicke encephalopathy can follow.
- **Taking a migraine preventive during an attack.** Preventives are daily; triptans abort at the first sign.

Chapter 4 self-test · ten items

1. Ibuprofen lowers the sensitivity of nerve endings at an injured ankle. Which nociception step is that?

A. Transmission
B. Perception
C. Transduction
D. Modulation

C. Transduction NSAIDs block prostaglandins that sensitize nociceptors at the site of injury, the transduction step.

2. Which description points to neuropathic pain?

A. Sharp pain at a fresh surgical incision
B. Burning and electric shooting in both feet
C. Cramping, squeezing pain from a blocked bowel
D. Throbbing ache over a broken wrist bone

B. Burning and electric shooting in both feet Burning, shooting and electric sensations suggest damaged nerves, which respond best to adjuvants.

3. Which scale fits an intubated, sedated ICU patient?

A. NRS
B. CRIES
C. FACES
D. CPOT

D. CPOT CPOT and BPS score behavior in critically ill patients who cannot self-report. CRIES is for neonates.

4. What is the antidote for acetaminophen overdose?

A. Acetylcysteine
B. Methylnaltrexone
C. Protamine sulfate
D. Flumazenil

A. Acetylcysteine Acetylcysteine restores glutathione so NAPQI is neutralized. It works best within 8 to 10 hours.

5. A patient takes lisinopril, furosemide and now daily ibuprofen. What is the main risk?

A. Low blood glucose
B. Acute kidney injury
C. Serotonin syndrome
D. Opioid toxicity

B. Acute kidney injury An ACE inhibitor plus a diuretic plus an NSAID is the triple whammy that drops glomerular filtration.

6. A parent asks why the clinic said no aspirin for a 12-year-old who has the flu. What risk is the nurse explaining?

A. Risk of Reye syndrome
B. Risk of tendon rupture
C. Risk of tooth staining
D. Risk of opioid withdrawal

A. Risk of Reye syndrome Aspirin in children and teens with a viral illness is linked to Reye syndrome, an encephalopathy with fatty liver.

7. Which opioid effect does not develop tolerance?

A. Drowsiness
B. Nausea and vomiting
C. Constipation
D. Pruritus

C. Constipation The bowel does not adapt, so a stimulant laxative starts with the first opioid order.

8. Why can a patient re-sedate after naloxone works?

A. Naloxone blocks only kappa receptors
B. Naloxone slowly turns into an opioid
C. Naloxone raises opioid absorption
D. Naloxone wears off before most opioids

D. Naloxone wears off before most opioids Naloxone lasts about 30 to 90 minutes. Long-acting opioid still on board can rebind as it fades.

9. A patient with coronary artery disease asks about sumatriptan. What is the concern?

A. It must be taken daily to work at all
B. It causes severe drowsiness for a day
C. It interacts with acetaminophen in the liver
D. It constricts vessels and is contraindicated

D. It constricts vessels and is contraindicated Triptans are vasoconstrictors and are contraindicated in coronary disease, prior MI or stroke and uncontrolled hypertension. Gepants are an option.

10. A patient in alcohol withdrawal needs IV dextrose. What is given first?

A. Thiamine
B. Folic acid
C. Naloxone
D. Potassium

A. Thiamine Glucose given to a thiamine-depleted brain can trigger Wernicke encephalopathy, so thiamine goes first.

Cram sheet

Everything from chapters 3 and 4 in one place. Cover the right column and see if you can rebuild each row.

Immunity and chemotherapy

Item	Fact	Note
Transplant maintenance	CNI + antiproliferative + steroid	Lower doses, spread toxicity
Calcineurin inhibitors	Troughs; no grapefruit	Inducers cause rejection
Methotrexate (RA)	Weekly	Folic acid other days
Azathioprine	Not with allopurinol	Marrow failure
TNF inhibitors	TB and hepatitis B screen	Hold in active infection
Filgrastim	Bone pain	At least 24 h after chemo
Checkpoint inhibitors	Colitis, pneumonitis, thyroiditis	Steroids; report same day
Live vaccines	MMR, varicella, rotavirus, LAIV, yellow fever	Not in pregnancy or immunosuppression
Tdap	Every pregnancy, 27 to 36 weeks	Td booster every 10 years
Log kill	Percentage per dose	Finish the cycles
Nadir	7 to 14 days	ANC under 500 is severe
Febrile neutropenia	38.3°C once or 38.0°C for 1 h	Antibiotics within 1 h
Platelets	Under 50,000 bleeding; under 20,000 spontaneous	Soft brush, electric razor, no IM
Extravasation	Cold for anthracyclines; warm for vincas	Leave needle in, aspirate
Home precautions	About 48 h	Gloves, flush twice, wash laundry separately

Pain and substance use

Item	Fact	Note
Nociception	Transduction, transmission, perception, modulation	NSAIDs, opioids, adjuvants
Reassess	15 to 30 min IV; about 60 min oral	Chart it
Acetaminophen	4 g/day healthy adult; 2 g or less with liver risk	Acetylcysteine within 8 to 10 h
NSAIDs	GI, kidney, CV, platelets	Avoid from 20 weeks of pregnancy
Ketorolac	5 days total	All routes
Opioids	Sedation before respiratory depression	POSS; triad: LOC, pupils, breathing
Naloxone	1 to 2 min onset; 30 to 90 min duration	Titrate; watch re-sedation
Codeine, tramadol	CYP2D6 prodrugs	Contraindicated under 12
Adjuvants	Gabapentinoids, TCAs, duloxetine, lidocaine patch	First-line for neuropathic pain
Migraine	Triptan at first sign; preventive daily	Overuse: more than 10 to 15 days/month
Alcohol withdrawal	Benzodiazepines, CIWA-Ar	Thiamine before glucose
Opioid use disorder	Buprenorphine, methadone, naltrexone	Take-home naloxone
Disulfiram	No alcohol in anything	14 days after last dose

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