Achievable

USMLE STEP 1 DUMP SHEET

Pharmacology principles

Pharmacokinetics

- $V_d = \text{dose}/C_p$: small stays in plasma; large in tissue
- $CL = \text{elimination rate}/C_p$; $t_{1/2} = 0.693\, V_d/CL$
- **Loading dose** $= V_d C_p/F$ (no clearance term); **maintenance rate** $= CL\, C_p/F$
- **Steady state:** 4—5 half-lives. **Weak acids:** alkalinize urine to excrete
- **First order:** constant fraction; most drugs. **Zero order:** constant amount: ethanol; phenytoin, aspirin at high doses
- **Phase II:** glucuronidation, slow in newborns (chloramphenicol)
- **Slow acetylators:** isoniazid, hydralazine, procainamide toxicity
- **Aging:** diazepam gains V_d and half-life; digoxin, gentamicin lose V_d
- **Therapeutic index** $= TD_{50}/ED_{50}$. Narrow: digoxin, lithium, phenytoin, theophylline, warfarin

Analgesic toxicity

- **Acetaminophen:** NAPQI exhausts glutathione: centrilobular necrosis
- **Aspirin overdose:** respiratory alkalosis, then metabolic acidosis
- **NSAIDs:** ulcers, renal failure. Celecoxib (COX-2): fewer ulcers, more MI

CYP450 interactions

Inhibitors (other drug rises)	Inducers (other drug falls)
Cimetidine, amiodarone, macrolides, ciprofloxacin, omeprazole, azoles, ritonavir, metronidazole, grapefruit juice	Carbamazepine, phenytoin, phenobarbital, rifampin, chronic alcohol, tobacco, steroids

Agonists and antagonists

- **Potency:** ED50. **Efficacy:** maximal effect
- **Partial agonists:** buprenorphine, pindolol, aripiprazole
- **Competitive:** surmountable; shifts right, potency falls
- **Noncompetitive:** efficacy falls (phenoxybenzamine)

Gout and bone

- **Acute gout:** NSAIDs, colchicine (blocks tubulin), steroids
- **Allopurinol, febuxostat:** xanthine oxidase; cut 6-MP dose
- **Probenecid:** blocks urate reabsorption (URAT1)
- **Rasburicase:** urate to allantoin; not in G6PD deficiency
- **Bisphosphonates:** esophagitis, jaw osteonecrosis
- **Denosumab:** anti-RANKL. **Teriparatide:** osteosarcoma in rats (boxed warning removed 2020)

Receptors

Receptor	G protein	Agonists	Antagonists
α1	Gq	Phenylephrine, norepinephrine	Prazosin, doxazosin; phenoxybenzamine (irreversible)
α2	Gi	Clonidine	Yohimbine
β1 / β2	Gs	Dobutamine / albuterol, terbutaline	β1: metoprolol, atenolol, esmolol. β1 and β2: propranolol
Muscarinic	M1, M3 Gq; M2 Gi	Bethanechol, carbachol	Atropine; also TCAs, quinidine, disopyramide
Dopamine	D1 Gs; D2 Gi	Bromocriptine, apomorphine	Haloperidol, metoclopramide (D2)
Opioid	Gi	Morphine, fentanyl; buprenorphine (partial)	Naloxone, naltrexone; methylnaltrexone (peripheral)
V1 / V2	Gq / Gs	Vasopressin	Conivaptan (V1, V2), tolvaptan (V2)

- **Also Gq:** H1, AT1, oxytocin, GnRH. **Gs:** β3, glucagon, PTH, CRH. **Gi:** GABA-B, melatonin. **Ion channels:** nicotinic, GABA-A, 5-HT3, NMDA

Antidotes

Toxin	Antidote
Acetaminophen	N-acetylcysteine
Opioids	Naloxone
Benzodiazepines	Flumazenil
Methanol, ethylene glycol	Fomepizole
Organophosphates	Atropine, pralidoxime
Anticholinergics	Physostigmine

Toxin	Antidote
Cyanide	Sodium thiosulfate
Heparin	Protamine
Warfarin	Vitamin K
Digoxin	Digoxin Fab
Isoniazid	Pyridoxine (B6)
Methotrexate	Leucovorin

Toxin	Antidote
β or Ca blockers	Glucagon, calcium
Arsenic, lead, mercury	Dimercaprol
Tricyclics	Bicarbonate (serum)
Salicylates	Bicarbonate (urine)