

# In the name of God

## How to learn and retain pharmacology the BEST way?

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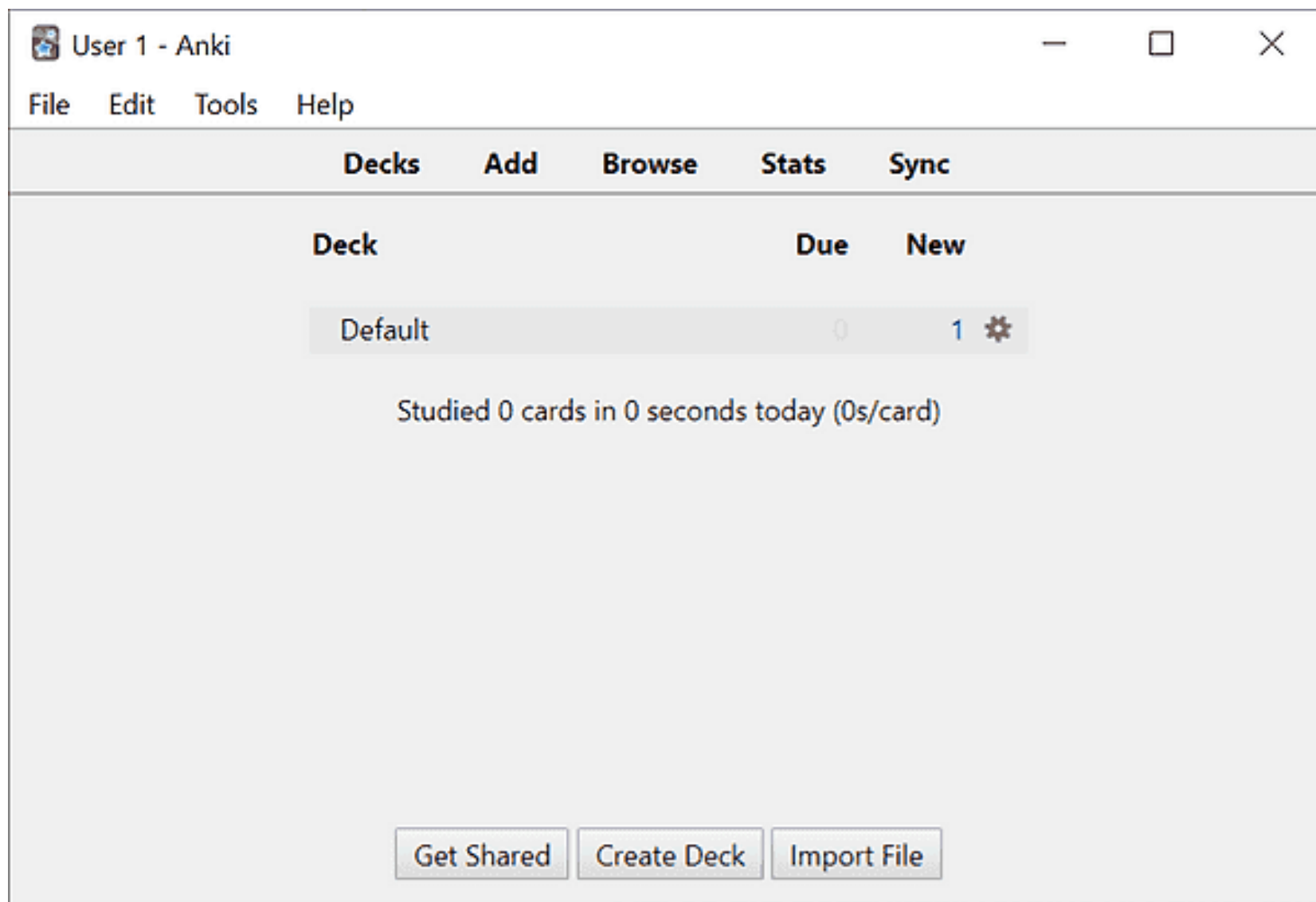


# Basics

- Before everything, we need to understand the basics of learning.
- Write questions for yourself as long as you study and understand material. (One of the best ways for doing it is writing questions in ANKI)
- Review those questions you've written for yourself in a sufficient long period of time.
- Use question banks and do as many questions as you can find.
- Test your understanding about each chapter, topic etc by reviewing your own questions and question banks.
- Do the previous step for a sufficient long period of time.
- These steps are evidence based and they are called active recall plus spaced repetition. **\*\* Mix your practice and revisions\*\***

# Basics

- Learning is misunderstood, it is effective when it feels effortful.
- Embrace difficulties.
- To learn, retrieve.
- Mix up your practice.
- Use interleaving, spacing your repetitions.
- Test yourself in one way or the other!
- All of these tests will lead you to big picture of that chapter, like solving a puzzle.



Voriconazole is similar to itraconazole in its spectrum of action, having excellent activity against *Candida* sp (including some fluconazole-resistant species such as *Candida krusei*) and the dimorphic fungi. Voriconazole is less toxic than amphotericin B and is the treatment of choice for invasive aspergillosis and some environmental molds (see Box: Iatrogenic Fungal Meningitis). Measurement of voriconazole levels may predict toxicity and clinical efficacy, especially in immunocompromised patients. Therapeutic trough levels should be between 1 and 5 mcg/mL.

## POSACONAZOLE

Posaconazole was originally available only in a liquid oral formulation and is used at a dosage of 800 mg/d, divided into two or four doses. Absorption is improved when taken with meals high in fat. An intravenous form of posaconazole and a sustained acting tablet form with higher bioavailability are now available. Posaconazole is rapidly distributed to the tissues, resulting in high tissue levels but relatively low blood levels. Measurement of posaconazole

## ECHINOCANDINS

### Chemistry & Pharmacokinetics

Echinocandins are the newest class of antifungal agents to be developed. They are large cyclic peptides linked to a long-chain fatty acid. **Caspofungin**, **micalfungin**, and **anidulafungin** are the only licensed agents in this category of antifungals, although other drugs are under active investigation. These agents are active against *Candida* and *Aspergillus*, but not *C. neoformans* or the agents of zygomycosis and mucormycosis.

Echinocandins are available only in intravenous formulations. Caspofungin is administered as a single loading dose of 70 mg, followed by a daily dose of 50 mg. Caspofungin is water soluble and highly protein-bound. The half-life is 9–11 hours, and the metabolites are excreted by the kidneys and gastrointestinal tract. Dosage adjustments are required only in the presence of severe hepatic insufficiency. Micalfungin displays similar properties with a half-life of 11–15 hours and is used at a dose of 150 mg/d for treatment of esophageal candidiasis, 100 mg/d for treatment of candidemia, and 50 mg/d for prophylaxis of fungal infections.



## Iatrogenic Fungal Meningitis

In September 2012, the U.S. Centers for Disease Control and Prevention (CDC) in Atlanta received reports of a number of cases of fungal meningitis in patients who had received injections with the corticosteroid methylprednisolone. An investigation revealed a multistate outbreak of septic arthritis, paraspinal infections, and meningitis due to environmental molds, with the black mold *Exserohilum rostratum* being the most commonly isolated species. The outbreak was traced to the injection of methylprednisolone that was contaminated during its preparation by a compounding pharmacy facility in New England. Methylprednisolone injections are commonly given to patients with joint or back arthritis, and in the affected cases the patients were not only inadvertently injected with spores of environmental molds, but the normal immune response to this infection was inhibited by the potent immunosuppressive effect of the corticosteroid. As of November 2013 more than 750 cases of fungal infection had been identified in 20 states, with over 60 deaths. Treatment of

levels is recommended in patients with serious invasive fungal infections (especially mold infections); steady-state posaconazole levels should be between 0.5 and 1.5 mcg/mL. Drug interactions with increased levels of CYP3A4 substrates such as tacrolimus and cyclosporine have been documented.

Posaconazole is the broadest-spectrum member of the azole family, with activity against most species of *Candida* and *Aspergillus*. It is the first azole with significant activity against the agents of mucormycosis. It is currently licensed for salvage therapy in invasive aspergillosis, as well as prophylaxis of fungal infections during induction chemotherapy for leukemia, and for allogeneic bone marrow transplant patients with graft-versus-host disease.

## ISAVUCONAZOLE (ISAVUCONAZONIUM SULFATE)

Isavuconazonium sulfate is a prodrug of the newest triazole, isavuconazole; 186 mg of the water-soluble prodrug is equivalent to 100 mg of isavuconazole. It is available as highly bioavail-

<b><math>\alpha</math> BLOCKERS</b>				
<ul style="list-style-type: none"> <li>• Prazosin</li> <li>• Terazosin</li> <li>• Doxazosin</li> </ul>	Selectively block $\alpha_1$ adrenoceptors	Prevent sympathetic vasoconstriction • reduce prostatic smooth muscle tone	Hypertension • benign prostatic hyperplasia	Oral • <i>Toxicity</i> : Orthostatic hypotension
<b><math>\beta</math> BLOCKERS</b>				
<ul style="list-style-type: none"> <li>• Metoprolol, others</li> <li>• Carvedilol</li> <li>• Nebivolol</li> </ul>	Block $\beta_1$ receptors; carvedilol also blocks $\alpha$ receptors; nebivolol also releases nitric oxide	Prevent sympathetic cardiac stimulation • reduce renin secretion	Hypertension • heart failure • coronary disease	See Chapter 10
<ul style="list-style-type: none"> <li>• <i>Propranolol</i>: Nonselective prototype <math>\beta</math> blocker</li> <li>• <i>Metoprolol and atenolol</i>: Very widely used <math>\beta_1</math>-selective blockers</li> </ul>				
<b>VASODILATORS</b>				
<ul style="list-style-type: none"> <li>• Verapamil</li> <li>• Diltiazem</li> </ul>	Nonselective block of L-type calcium channels	Reduce cardiac rate and output • reduce vascular resistance	Hypertension, angina, arrhythmias	See Chapter 12
<ul style="list-style-type: none"> <li>• Nifedipine, amlodipine, other dihydropyridines</li> </ul>	Block vascular calcium channels > cardiac calcium channels	Reduce vascular resistance	Hypertension, angina	See Chapter 12
<ul style="list-style-type: none"> <li>• Hydralazine</li> <li>• Minoxidil</li> </ul>	Causes nitric oxide release Metabolite opens K channels in vascular smooth muscle	Vasodilation • reduces vascular resistance • arterioles more sensitive than veins • reflex tachycardia	Hypertension • minoxidil also used to treat hair loss	Oral • <i>Toxicity</i> : Angina, tachycardia • Hydralazine: Lupus-like syndrome • Minoxidil: Hypertrichosis



Subclass, Drug	Mechanism of Action	Effects	Clinical Applications	Pharmacokinetics, Toxicities, Interactions	
<b>DIURETICS</b>					
<ul style="list-style-type: none"><li>• Thiazides: Hydrochlorothiazide, chlorthalidone</li><li>• Loop diuretics: Furosemide</li><li>• Spironolactone, eplerenone</li></ul>	<p>Block Na/Cl transporter in renal distal convoluted tubule</p> <p>Block Na/K/2Cl transporter in renal loop of Henle</p> <p>Block aldosterone receptor in renal collecting tubule</p>	<p>Reduce blood volume and poorly understood vascular effects</p> <p>Like thiazides • greater efficacy</p> <p>Increase Na and decrease K excretion • poorly understood reduction in heart failure mortality</p>	<p>Hypertension, mild heart failure</p> <p>Severe hypertension, heart failure</p> <p>Aldosteronism, heart failure, hypertension</p>	See Chapter 15	
<b>SYMPATHOPLEGICS, CENTRALLY ACTING</b>					
<ul style="list-style-type: none"><li>• Clonidine, methyldopa</li></ul>	Activate $\alpha_2$ adrenoceptors	Reduce central sympathetic outflow • reduce norepinephrine release from noradrenergic nerve endings	Hypertension • clonidine also used in withdrawal from abused drugs		Oral • clonidine also as patch • Toxicity: sedation • methyldopa hemolytic anemia
<b>SYMPATHETIC NERVE TERMINAL BLOCKERS</b>					
<ul style="list-style-type: none"><li>• Reserpine</li><li>• Guanethidine, guanadrel</li></ul>	<p>Blocks vesicular amine transporter in noradrenergic nerves and depletes transmitter stores</p> <p>Interferes with amine release and replaces norepinephrine in vesicles</p>	<p>Reduces all sympathetic effects, especially cardiovascular, and reduce blood pressure</p> <p>Same as reserpine</p>	<p>Hypertension but rarely used</p> <p>Same as reserpine</p>	<p>Oral • long duration (days) • Toxicity: psychiatric depression, gastrointestinal disturbances</p> <p>Severe orthostatic hypotension • sexual dysfunction • availability limited</p>	

# Pharmacological classification

- Atenolol, metoprolol, carvedilol, nebivolol ... beta blocker
- Warfarin, heparin, enoxaparin ... anti-coagulant
- Risperidone, ziprasidone, paliperidone, clozapine, olanzapine ... neuroleptics
- Ciprofloxacin, moxifloxacin, gefloxacin ... fluoroquinolone
- Prazosin, terazosin, doxazosin ... alpha-1 blockers
- Sinagliptin, saxagliptin ... DPP-4 inhibitor
- **Question: What pharmacological classification does prazosin belong to ?**
- **Answer: Alpha-1 blockers**

# Pharmacodynamic information

- **Mechanism of action**
- Haloperidol, trifluoperazine and fluphenazine ... D2 blocker (high potency)
- Betanechol (M1&M3 agonist), metacholine (M3 agonist), pilocarpine (M3 agonist)
- Imatinib, dasatinib ... tyrosine kinase inhibitor
- G protein ... Which G protein does alpha-1 receptor act with ? Gq
- Which G protein does M2 act with ? Gi

# Pharmacokinetic information

- ADME (LADMER)
- Ketoconazole ... potent Cyp450 inhibitor ---> A lot of interactions
- Fluconazole ... less interactions (Cyp2C9 inhibitor)
- Half life ... zaleplon (less half life) – diazepam (longer half life because of active metabolites)
- Onset of action for diazepam is very fast, but for oxazepam is slow
- Bupivacaine has longer half life than procaine
- Which one has less sedative effects tomorrow of the day you consume? Zaleplon or diazepam?
- Zaleplon because of less half life than diazepam's

# Adverse effects and toxicities

- Different organs, different adverse effects
- Maybe you can relate it to MOA and classification(very important)
- What is adverse effect of bevacizumab in GI? GI perforation
- What is adverse effect of bevacizumab on blood and circulation?  
Dysregulated blood clotting (thrombosis, bleeding)
- What is adverse effect of cimetidine in male patients? (long term use)  
gynecomastia
- What is effect of rifampin on color of body fluids? Making them  
red,orange



# Indications (DOC) and dosings

- Clinical applications and clinical effects
- What is DOC for MRSA? Vancomycin (dapto, linezolid and D/Q last)
- What is first line treatment for essential tremor, migraine prophylaxis? Non selective beta blockers like propranolol
- What is first line treatment for rheumatoid arthritis? MTX
- What is normal dosing for isotretinoin ? 0.5-1 mg/kg/day
- What is normal loading dose for leflunomide in RA ? 100 mg
- What is first line treatment for high triglyceride ? fibrates
- What is effect of niacin on HDL ? increases

# Interactions (Food and drug)

- Inducers and inhibitors of CYP (RIF.PHE.CBZ, ketoconazole, cyclosporine)
- Substrates for CYP (OCP)
- P-glycoprotein inhibitors (verapamil, cyclosporine)
- Foods like Ca,Mg,K (electrolyte emphasized interactions like digoxin)
- Before or after food? Some of them before, many after food
- Iron supplements, rifampin ----> some of the most important examples

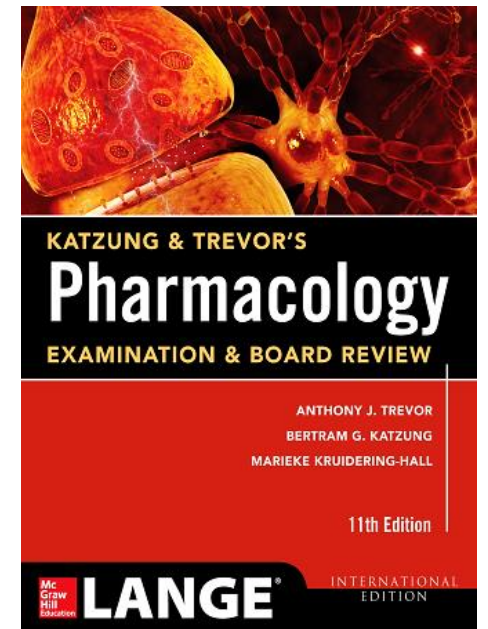
# What parts of Katzung should we focus on more? (in each chapter)

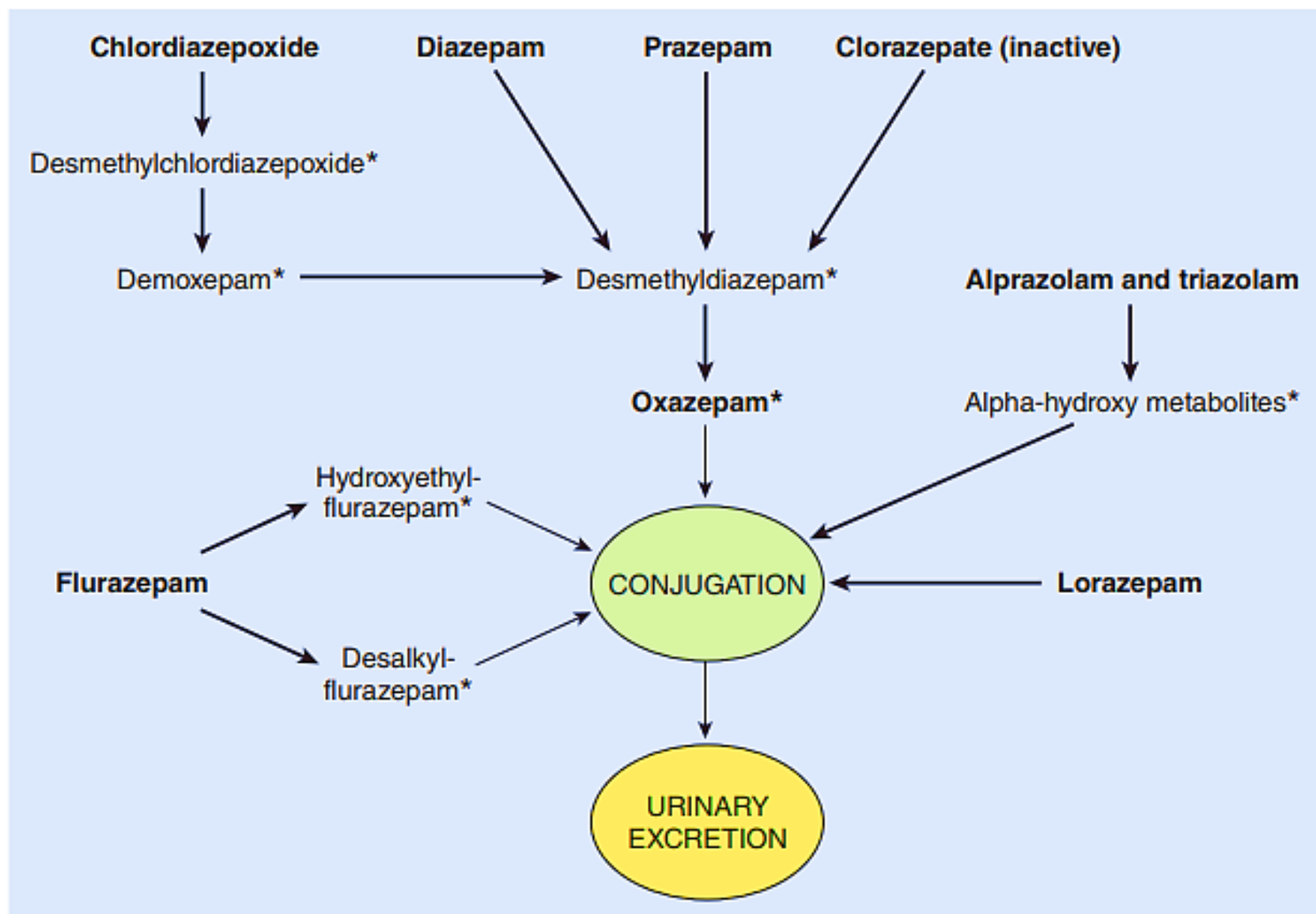
**TABLE 22-1** Pharmacokinetic properties of some benzodiazepines and newer hypnotics in humans.

Drug	Tmax (hours) <sup>1</sup>	t <sub>1/2</sub> (hours) <sup>2</sup>	Comments
Alprazolam	1–2	12–15	Rapid oral absorption
Chlordiazepoxide	2–4	15–40	Active metabolites; erratic bioavailability from IM injection
Clorazepate	1–2 (nordiazepam)	50–100	Prodrug; hydrolyzed to active form in stomach
Diazepam	1–2	20–80	Active metabolites; erratic bioavailability from IM injection
Eszopiclone	1	6	Minor active metabolites
Flurazepam	1–2	40–100	Active metabolites with long half-lives
Lorazepam	1–6	10–20	No active metabolites
Oxazepam	2–4	10–20	No active metabolites
Temazepam	2–3	10–40	Slow oral absorption
Triazolam	1	2–3	Rapid onset; short duration of action
Zaleplon	< 1	1–2	Metabolized via aldehyde dehydrogenase
Zolpidem	1–3	1.5–3.5	No active metabolites

<sup>1</sup>Time to peak blood level.

<sup>2</sup>Includes half-lives of major metabolites.





**TABLE 39–1** Some commonly used natural and synthetic corticosteroids for general use. See Table 61–2 for dermatologic corticosteroids.

Agent	Activity <sup>1</sup>			Equivalent Oral Dose (mg)	Forms Available
	Anti-Inflammatory	Topical	Salt-Retaining		
Short- to medium-acting glucocorticoids					
Hydrocortisone (cortisol)	1	1	1	20	Oral, injectable, topical
Cortisone	0.8	0	0.8	25	Oral
Prednisone	4	0	0.3	5	Oral
Prednisolone	5	4	0.3	5	Oral, injectable
Methylprednisolone	5	5	0.25	4	Oral, injectable
Meprednisone <sup>2</sup>	5		0	4	Oral, injectable
Intermediate-acting glucocorticoids					
Triamcinolone	5	5 <sup>3</sup>	0	4	Oral, injectable, topical
Paramethasone <sup>2</sup>	10		0	2	Oral, injectable
Fluprednisolone <sup>2</sup>	15	7	0	1.5	Oral
Long-acting glucocorticoids					
Betamethasone	25–40	10	0	0.6	Oral, injectable, topical
Dexamethasone	30	10	0	0.75	Oral, injectable, topical
Mineralocorticoids					
Fludrocortisone	10	0	250	2	Oral
Desoxycorticosterone acetate <sup>2</sup>	0	0	20		Injectable, pellets

<sup>1</sup>Potency relative to hydrocortisone.

<sup>2</sup>Outside United States.

<sup>3</sup>Triamcinolone acetonide: Up to 100.



# Project and how to get most out of this course?

۱. یکی از فصل های فارماکولوژی را انتخاب کنید به دلخواه خودتان
۲. از ایده هایی که در طول این دوره با هم مرور کردیم، در مطالعه اون فصل اعمال کنید
۳. در بخش هایی که به مشکل بر میخورین، حتما در کامنت ها بنویسین و سوالاتتون رو بپرسین
۴. تفاوتی که در میزان یاد گیری تون بعد استفاده از این دوره اتفاق افتاده، در بخش نظرات بنویسید
۵. در صورتی که نتیجه تون بطور واضحی بهتر شده، فصل های دیگه رو هم با این روش مطالعه کنید و بهم فیدبک بدین لطفا

# Contact with me

- Comments section in my website amirmahdiimanzadeh.com
- [Youtube.com/@amirmahdiimanzadeh2211](https://www.youtube.com/@amirmahdiimanzadeh2211)
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- [Imanzadeh.blogsky.com](https://imanzadeh.blogsky.com)

# References and more to read

- Make it stick book
- Katzung pharmacology
- Katzung and Trevor's pharmacology, board examination review
- Question banks, ETC books