



Updates in Therapeutics® 2013:

The Pharmacotherapy Preparatory Review & Recertification Course

Neurology

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Conflict of Interest Disclosures

Melody Ryan –no conflicts of interest to disclose

Learning Objectives

- Differentiate between various antiepileptic drugs based on use and adverse effects
- Develop a treatment strategy for status epilepticus
- Identify appropriate treatment strategies for primary and secondary stroke prevention
- Determine the appropriateness of treatment with tissue plasminogen activator for acute stroke
- Examine common adverse effects associated with treatment of Parkinson disease
- Differentiate between regimens for acute and prophylactic treatment of migraine, tension, and cluster headaches
- Identify common adverse effects of disease-modifying therapies for multiple sclerosis

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Patient Case # 1

TM is an 18-year-old new patient in the pharmacy where you work. He presents a prescription for carbamazepine 100 mg 1 PO BID with instructions to increase to 200 mg 1 PO TID. Currently, he does not take any medications and does not have any drug allergies. During your counseling session, TM tells you he must have blood drawn for a test in 3 weeks.

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Patient Case # 1

Which common potential adverse effect of carbamazepine is best assessed through a blood draw?

-  A. Leukopenia
-  B. Renal failure
-  C. Congestive heart failure
-  D. Hypercalcemia

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Carbamazepine Adverse Effects

- Rash
- SIADH
- Aplastic anemia
- Thrombocytopenia
- Anemia
- Leukopenia

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Patient Case # 2

One month later, TM returns to your pharmacy with a new prescription for lamotrigine 25 mg with instructions to take 1 tablet daily for 2 weeks, then 1 tablet PO BID for 2 weeks, then 2 tablets PO BID for 2 weeks, then 3 tablets PO BID thereafter. He tells you that he is discontinuing the carbamazepine because he developed a rash a few days ago.

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Patient Case # 2

Which is the best response?

-  A. The rash is likely caused by carbamazepine because carbamazepine rash often has delayed development
-  B. The rash is unlikely caused by carbamazepine because carbamazepine rash usually presents after the first dose
-  C. The rash is unlikely caused by carbamazepine; it is probably attributable to carbamazepine-induced liver failure
-  D. The rash is unlikely caused by carbamazepine; it is probably attributable to carbamazepine-induced renal failure

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Dermatologic Adverse Effects

- Dermatologic reactions to anticonvulsants occur after a delay of 2-8 weeks
- May include rash, Stevens-Johnson syndrome, anticonvulsant hypersensitivity syndrome
- Recommendation for testing for the HLA-B*1502 allele in patients of Asian, including South Asian Indians, ancestry have a 10-time increased risk of rash
- Patients with HLA-A*3101 (usually Caucasian) are also at increased risk for rash

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Patient Case # 3

TM wants to know why it is necessary to increase the dose of lamotrigine so slowly.

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Patient Case # 3

Which reply is best?

-  A. It causes dose-related psychomotor slowing
-  B. It causes dose-related renal stones
-  C. It causes dose-related paresthesias
-  D. It causes dose-related rash

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Lamotrigine Rash

- Related to starting dose
- Particular caution necessary in children
- Valproic acid inhibits lamotrigine metabolism and increases rash risk
- May be mild to serious in nature

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Patient Case # 4

JG is a 34-year-old patient who has been maintained on carbamazepine extended-release 400 mg orally 2 times/day for the past 2 years. She has had no seizures for the past 4 years. She presents to the emergency department in status epilepticus.

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Patient Case # 4

Which drug is best to use first?

-  A. Diazepam
-  B. Lorazepam
-  C. Phenytoin
-  D. Phenobarbital

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Status Epilepticus

- Always give an emergent medication to stop seizures immediately (benzodiazepine)
- Follow with an urgent medication to prevent recurrence of seizures (phenytoin, fosphenytoin, phenobarbital, valproic acid)
- All medications for status epilepticus should be given parenterally
- Do not use a neuromuscular blocker

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Status Epilepticus

- Lorazepam is the drug of choice for first line therapy
- Lorazepam is less lipophilic than diazepam
 - Stays in the CNS longer rather than being re-distributed to other areas of the body

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Patient Case # 5

SR is a 37-year-old patient who began taking phenytoin 100 mg 3 capsules PO QHS 6 months ago. He has experienced several seizures since that time; the most recent seizure occurred this past week. At that time, his phenytoin serum concentration was 8 mcg/mL. The treating physician increased his dose to phenytoin 100 mg 3 capsules PO BID.

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Patient Case # 5

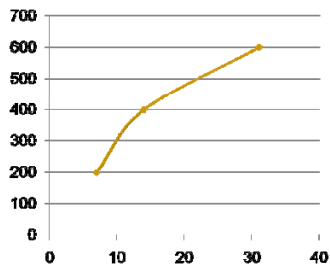
Today, which best represents his expected serum concentration?

-  A. 10 mcg/mL
-  B. 14 mcg/mL
-  C. 16 mcg/mL
-  D. 20 mcg/mL

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Phenytoin Pharmacokinetics

- Non-linear (Michaelis-Menton) kinetics
- Highly protein-bound



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Patient Case # 6

SS is a 22-year-old woman who has always had episodes of “zoning out.” Recently, one of these episodes occurred after an examination while she was driving home. She had a non-injury accident, but it prompted a visit to a neurologist. She is given a diagnosis of absence seizures.

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Patient Case # 6

Which drug is best to treat this type of epilepsy?

-  A. Phenytoin
-  B. Tiagabine
-  C. Carbamazepine
-  D. Ethosuximide

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Medications for Absence Seizures

- First-line
 - Ethosuximide
 - Valproic acid
- Second-line
 - Clonazepam
 - Lamotrigine

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Patient Case # 7

JB is a 25-year-old man with a history of seizure disorder. He has been treated with phenytoin 200 mg orally 2 times/day for 6 months and his current phenytoin concentration is 6.3 mcg/mL. His neurologist decides to increase his phenytoin dose to 300 mg 2 times/day.

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Patient Case # 7

Which adverse effect is JB most likely to experience related to the dose increase?

-  A. Drowsiness
-  B. Acne
-  C. Gingival hyperplasia
-  D. Rash

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Phenytoin Adverse Effects

Dose-related

- Nystagmus
- Ataxia
- Drowsiness
- Cognitive impairment

Non-Dose-related

- Gingival hyperplasia
- Hirsutism
- Acne
- Rash
- Hepatotoxicity
- Coarsening of facial features

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Patient Case # 8

MG is a 15-year-old male adolescent with a diagnosis of juvenile myoclonic epilepsy. He has been prescribed sodium divalproate.

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Patient Case # 8

On which adverse effect is it best to counsel MG?



A. Oligohidrosis



B. Renal stones



C. Alopecia



D. Word-finding difficulties

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Valproic Acid Adverse Effects

- Hepatotoxicity
- Nausea/vomiting
- Weight gain
- Interference with platelet aggregation
- Pancreatitis
- Alopecia

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Patient Case # 9

GZ, a 26-year-old woman, presents with a 6-month history of "spells." The spells are all the same, and all of them start with a feeling in the abdomen that is difficult for her to describe. This feeling rises toward the head. The patient believes that she will then lose awareness. After a neurologic work-up, she is given a diagnosis of focal seizures evolving to a bilateral, convulsive seizure. The neurologist is considering starting either carbamazepine or oxcarbazepine.

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Patient Case # 9

Which is the most accurate comparison of carbamazepine and oxcarbazepine?



A. Oxcarbazepine causes more liver enzyme induction than carbamazepine



B. Oxcarbazepine does not cause rash



C. Oxcarbazepine does not cause hyponatremia



D. Oxcarbazepine does not form an epoxide intermediate in its metabolism

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Oxcarbazepine

- Does not form an epoxide intermediate in its metabolism
- Enzyme inducer, but no autoinduction
- Hyponatremia more common than with carbamazepine
- Blood dyscrasias less common than with carbamazepine

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Patient Case # 10

When you see GZ 6 months later for follow-up, she tells you that she is about 6 weeks pregnant. She has had no seizures since beginning drug therapy.

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Patient Case # 10

Which is the best strategy for GZ?

-  A. Immediately discontinue her antiepileptic drug
-  B. Immediately discontinue her antiepileptic drug and give folic acid
-  C. Continue her antiepileptic drug
-  D. Change her antiepileptic drug to phenobarbital

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Pregnancy Recommendations

- Women of childbearing potential
 - Have the best medication for their seizure type
 - Be treated with monotherapy, if possible
 - Discuss the possible decrease in oral contraceptive effectiveness with enzyme-inducing antiepileptic medicines
 - 50 mcg of ethinyl estradiol or mestranol
 - Folic acid supplementation of at least 0.4 mg/day

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Pregnancy Recommendations

- During/after pregnancy
 - Medications optimized before conception
 - Withdrawals accomplished at least 6 months before
 - Avoid valproic acid
 - Avoid polytherapy, if possible
 - Allow breastfeeding
 - Monitor serum concentrations
 - Before, at the beginning of each trimester, last month, during first 8 weeks post-partum
 - Lamotrigine, carbamazepine, phenytoin, levetiracetam, oxcarbazepine

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Patient Case # 11

LR is a 78-year-old man who presents to the emergency department for symptoms of right-sided paralysis. He states these symptoms began about 5 hours ago and have not improved since then. He also has hypertension, benign prostatic hypertrophy, diabetes mellitus, erectile dysfunction, and osteoarthritis.

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Patient Case # 11

Which is the most accurate assessment of LR's risk factors for stroke?

-  A. Erectile dysfunction, age, osteoarthritis
-  B. Sex, diabetes mellitus, osteoarthritis
-  C. Benign prostatic hypertrophy, diabetes mellitus, age, sex
-  D. Age, diabetes mellitus, sex, hypertension

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Stroke Risk Factors

Non-modifiable

- Age
- Race
- Male sex
- Low birth weight
- Family history

Somewhat modifiable

- Diabetes mellitus

Modifiable

- Hypertension
- Smoking
- Estrogens
- Atrial fibrillation
- Coronary artery disease
- Carotid stenosis
- Dyslipidemia
- Obesity
- Physical inactivity
- Sickle cell anemia

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Stroke Risk Factors

Modifiable

- Peripheral artery disease
- Pregnancy
- Patent foramen ovale
- Depression

Less well documented

- Alcohol abuse
- Hyperhomocysteinemia
- Drug abuse
- Hypercoagulability
- Periodontal disease
- Acute systemic inflammation and infection
- Sleep disordered breathing
- Metabolic syndrome
- Migraine with aura

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Patient Case # 12

Is LR a candidate for tissue plasminogen activator for treatment of stroke?

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Patient Case # 12

Which option is the best response?

-  A. Yes
-  B. No, he is too old
-  C. No, his stroke symptoms began too long ago
-  D. No, his diabetes mellitus is a contraindication for tissue plasminogen activator

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Tissue Plasminogen Activator

- Within 3 hours of symptoms
- 3 month outcome significantly improved
- Intracerebral hemorrhage increased, but no increase in mortality or disability
- Dose 0.9 mg/kg IV (max 90 mg with 10% as a bolus, remainder over 1 hr)

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TPA Exclusion Criteria

- Intracranial or subarachnoid bleeding or hx
- Other active internal bleeding
- Recent intracranial surgery, head trauma, stroke
- Blood pressure > 185/110 mm Hg
- Seizure at stroke onset
- Intracranial neoplasm, AV malformation, aneurysm
- Active treatment with warfarin, heparin, platelets < 100,000

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Time Window for TPA

- Expanded to 4.5 hours with additional exclusion criteria
 - Taking any oral anticoagulant
 - Baseline NIHSS score greater than 25
 - Previous stroke combined with diabetes
 - Age older than 80

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Patient Case # 13

He was previously taking no drugs at home.

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Patient Case # 13

Which choice is the best secondary stroke prevention therapy for this patient?

-  A. Sildenafil
-  B. Celecoxib
-  C. Aspirin
-  D. Warfarin

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Secondary Stroke Prevention

- Reduction of risk factors
- Carotid endarterectomy
- Aspirin
- Aspirin/dipyridamole
- Ticlopidine
- Clopidogrel
- Cilostazol
- Warfarin

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Patient Case # 14

You are the pharmacist at a community pharmacy and receive a call from MW, a 64-year-old man recently given a diagnosis of atrial fibrillation. He is concerned about his risk for having a stroke because his friend, who also has atrial fibrillation, asked him what dose of warfarin he is taking. MW called you because he is not taking warfarin and he wants to know if he should. He has no other medical conditions and takes atenolol 50 mg/day orally for ventricular rate control.

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Patient Case # 14

After encouraging him to discuss this with his doctor, which choice best describes what you should tell him?

-  A. You need warfarin treatment to prevent a stroke
-  B. You do not need warfarin, but you should take aspirin and clopidogrel
-  C. You do not need drug therapy at this time
-  D. Because you have atrial fibrillation, nothing can reduce your risk of stroke

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CHADS₂ Score

Congestive heart failure, hypertension, age >75 years, diabetes mellitus, and prior stroke or transient ischemic attack stratification scheme

- Assign 1 point each for CHF, HTN, age ≥ 75 years, or diabetes
- Assign 2 points for previous stroke or TIA
- If total=0, no therapy or aspirin 75-325 mg/day
- If total≥1, give oral anticoagulant (alternative aspirin 75-325 mg/day and clopidogrel 75 mg BID)
- Dabigatran 150 mg BID recommended over warfarin

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CHADS₂ Score

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Patient Case # 15

L.S. is a 72-year-old woman with a medical history of hypertension, type 2 diabetes mellitus, renal failure, and atrial fibrillation. She presents to the anticoagulation clinic for her initial visit.

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Patient Case # 15

Which best reflects her target INR?

-  A. 1.5
-  B. 2.0
-  C. 2.5
-  D. 3.0

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Patient Case # 16

You work as the clinical pharmacist in a small hospital. Several of the physicians with whom you work want to use aspirin and clopidogrel together after stroke, similar to what they are doing for MI. You access the MATCH study and obtain the following results:

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Patient Case # 16

	ASA + Clopidogrel (n)	Placebo + Clopidogrel (n)	RRR (95% CI)
Primary outcome	596	636	6.4% (-4.6-6.3)
Secondary outcomes			
MI	73	68	-7.7% (-8.5-20.4)
Ischemic stroke	309	333	7.1% (-8.5-20.4)
Death, all cause	201	201	0.1% (-21.5-17.8)

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Patient Case # 16

Which is the best interpretation of this information?

-  A. Aspirin plus clopidogrel is more effective than placebo plus clopidogrel only for the primary outcome
-  B. Aspirin plus clopidogrel is more effective than placebo plus clopidogrel for all the secondary outcomes.
-  C. Aspirin plus clopidogrel is more effective than placebo plus clopidogrel for prevention of myocardial infarction.
-  D. Aspirin plus clopidogrel is no more effective than placebo plus clopidogrel for any of the listed outcomes.

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Relative Risk Reduction

- RRR of 1 indicates no difference between groups
- The 95% CI also cannot contain 1

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Patient Case # 17

LS is taking levodopa/carbidopa 25 mg/100 mg orally 4 times/day and trihexyphenidyl 2 mg orally 3 times/day for his Parkinson disease. LS's wife reports that he is often confused and experiences constipation; he has trouble talking because of his dry mouth.

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Patient Case # 17

Which change is best to resolve these symptoms?

-  A. Increase carbidopa/levodopa
-  B. Increase trihexyphenidyl
-  C. Decrease carbidopa/levodopa
-  D. Decrease trihexyphenidyl

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Anti-Parkinson Adverse Effects

- Dopaminergic
 - Nausea/vomiting
 - Orthostatic hypotension
 - Hallucinations
- Anticholinergic
 - Dry mouth
 - Urinary retention
 - Dry eyes
 - Constipation
 - Confusion

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Patient Case # 18

Six months later, LS returns to the clinic concerned that his levodopa/carbidopa dose is wearing off before his next dose is due.

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Patient Case # 18

Which is best to suggest?

- 
- A. Increase the dose of carbidopa/levodopa
 - B. Decrease the dose of carbidopa/levodopa
 - C. Increase the dosing interval
 - D. Decrease the dosing interval

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Anti-Parkinson Adverse Effects

- Levodopa/carbidopa
 - Wearing off
 - Use controlled release formulation
 - Give doses more frequently
 - Add COMT inhibitor
 - Add dopamine agonist
 - On-off
 - Add COMT inhibitor, selegiline, rasagiline, pramipexole, ropinirole, apomorphine
 - Redistribute dietary protein

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Patient Case # 19

PJ is a 57-year-old man with an 8-year history of Parkinson disease. His current drugs include carbidopa/levodopa 50/200 orally 4 times/day, entacapone 200 mg orally 4 times/day, and amantadine 100 mg orally 3 times/day. He presents to the clinic with a reddish blue discoloration on his lower arms and legs.

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Patient Case # 19

Which, if any, of his drugs is the most likely cause of this condition?

- 
- A. Carbidopa/levodopa
 - B. Entacapone
 - C. Amantadine
 - D. None; likely represents venous stasis

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Anti-Parkinson Adverse Effects

- Dopamine agonists
 - Ergot derived agents (bromocriptine and pergolide) rarely have retroperitoneal, pleuropulmonary, or cardiac fibrosis
 - Pergolide is associated with valvular heart disease
- Amantadine
 - Livedo reticularis
- COMT inhibitors
 - Diarrhea
 - Urine discoloration (entacapone)

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Patient Case # 20

LL is a 47-year-old man with Parkinson disease. He takes carbidopa/levodopa 50/200 orally 4 times/day. He recently noticed an involuntary twitching movement of his left foot.

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Patient Case # 20

Which is the best therapy to treat LL's dyskinesia?

- 
- A. Add ropinirole
 - B. Add selegiline
 - C. Increase carbidopa/levodopa
 - D. Decrease carbidopa/levodopa

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Anti-Parkinson Adverse Effects

- Levodopa/carbidopa
 - Dyskinesias
 - Decrease dopaminergics
 - Add amantadine

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Patient Case # 21

CA, a 57-year-old white man who just retired from the NYC Fire Department, has been experiencing tremors in his right hand that have become progressively worse for the past 6 months. He has difficulty walking. He also has backaches and no longer plays golf. In addition, he is losing his sense of taste. He is given a diagnosis of Parkinson disease.

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Patient Case # 21

Which is the best treatment for this man?

- 
- A. Trihexyphenidyl
 - B. Entacapone
 - C. Apomorphine
 - D. Ropinirole

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Treatment Choice in Parkinson Disease

- Anticholinergics work best for tremor
- COMT inhibitors currently available do not cross the blood-brain barrier and must be given with carbidopa/levodopa
- Apomorphine is only for severe on-off symptoms

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Patient Case # 22

MR, a 34-year-old pharmacist, has throbbing right-sided headache. She experiences nausea, sonophobia, and photophobia with these headaches, but no aura. She usually has headaches 2 times/month. She is hypertensive and morbidly obese. She takes an ethinyl estradiol/progestin combination oral contraceptive daily and hydrochlorothiazide 25 mg/day orally. She has a diagnosis of migraine headaches.

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Patient Case # 22

Which medication is best for prophylaxis of her headaches?



- A. Propranolol
- B. Valproic acid
- C. Amitriptyline
- D. Lithium

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When to Use Prophylactic Agents

- Recurrent migraines that interfere with daily routine
- Frequent migraines
- Inefficacy or inability to use acute therapy
- Patient preference
- Cost of acute medications problematic
- Adverse effects with acute therapies
- Uncommon migraine presentation

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Prophylactic Agents

- Use lowest effective dose
- Give adequate trial (2-3 months)
- Consider other disease states
 - Additional treatment
 - Contraindications

Page Number 1-221

Migraine Treatment

- Prophylaxis page 1-221-222
 - Frovatriptan (for menstrually associated migraine, short-term prophylaxis only)
 - Metoprolol
 - Petasites (butterbur extract)
 - Propranolol
 - Timolol
 - Valproic acid
 - Topiramate
- Acute treatment pages 1-223-224

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Patient Case # 23

SR is a 54-year-old female homemaker with squeezing, bandlike headaches that occur 3 or 4 times/week. She rates the pain of these headaches as 7 of 10 and finds acetaminophen, aspirin, ibuprofen, naproxen, ketoprofen, and piroxicam only partly effective. She wishes to take a prophylactic medication to prevent these tension headaches.

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Patient Case # 23

Which is best for prophylaxis of her headaches?

- 
- A. Propranolol
 - B. Valproic acid
 - C. Amitriptyline
 - D. Lithium

Page Number 1-224

Tension Headache Treatment

- Prophylaxis
 - Tricyclic antidepressants
 - Botulinum toxin
- Acute treatment
 - Acetaminophen
 - NSAIDs

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Patient Case # 24

DS is a 49-year-old male computer programmer who describes lancinating right eye pain and tearing several times a day for 2-3 days in a row. He will then have no episodes for 2-3 weeks but then will have recurrent episodes. In the office, he receives oxygen by nasal cannula during an episode, and his pain is relieved. He has a diagnosis of cluster headaches.

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Patient Case # 24

Which drug is best for prophylaxis of his headaches?

- 
- A. Propranolol
 - B. Valproic acid
 - C. Amitriptyline
 - D. Lithium

Page Number 1-224

Cluster Headache Treatment

- | | |
|---|------------------------|
| ■ Prophylaxis | ■ Acute Treatment |
| □ Verapamil | □ Triptans |
| □ Melatonin | □ Oxygen |
| □ Suboccipital injection of betamethasone | □ Intranasal lidocaine |
| □ Lithium | |

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Patient Case # 25

MK is a 44-year-old woman with right-sided headaches of moderate intensity that are accompanied by severe nausea and vomiting.

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Patient Case # 25

Which triptan is best to treat MK's migraine headaches?

-  A. Almotriptan
-  B. Naratriptan
-  C. Rizatriptan
-  D. Sumatriptan

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Patient Case # 26

One of the neurologists you work with recently read a meta-analysis of migraine treatments. He is most interested in the outcome of sustained relief at 24 hours, but he is confused by the number needed to treat analyses. He shows you the following table:

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Patient Case # 26

Drug	NNT
■ Ergotamine + caffeine	6.6
■ Eletriptan 80 mg	2.8
■ Rizatriptan 10 mg	5.6
■ Sumatriptan 50 mg	6.0

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Patient Case # 26

Which is the best interpretation of these data?

-  A. Eletriptan 80 mg is the most effective agent
-  B. Ergotamine plus caffeine is the most effective drug
-  C. Eletriptan has the most adverse effects
-  D. Ergotamine plus caffeine has the most adverse effects

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Number Needed to Treat

- Way to express the number of patients it would be necessary to treat to have one patient with benefit/adverse effect

$$\text{NNT} = \frac{1}{\% \text{ improved on active therapy} - \% \text{ improved on placebo}}$$

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Patient Case # 27

SF is a 33-year-old African American woman of Cuban descent living in the Miami area. This morning, her right leg became progressively weaker over about 3 hours. She was previously healthy except for a broken radius when she was 13 years old and a case of optic neuritis when she was 25 years old.

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Patient Case # 27

Which is the best method for treating SF's exacerbation?

- 
- A. Interferon beta-1a
 - B. Glatiramer acetate
 - C. Mitoxantrone
 - D. Methylprednisolone

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Treatment of Acute Relapses

- Intravenous methylprednisolone: The usual dose is 1 g/day as one or divided doses for 3–5 days
- Oral prednisone: The usual dose is 1250 mg/day given every other day for five doses
- Intravenous adrenocorticotrophic hormone
- Neurologic recovery is the same with or without an oral prednisone taper

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Patient Case # 28

Which therapy is best for SF to prevent further exacerbations?

- 
- A. Interferon beta-1a
 - B. Interferon beta-1b
 - C. Glatiramer acetate
 - D. Any of the above

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Patient Case # 29

S.F. elects to start beta interferon-1b and wants to know whether there is any way she can prevent or minimize some of the adverse effects.

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Patient Case # 29

Which is the best advice?

- 
- A. Always give the injection at the same time of day
 - B. Lie down for 2 hours after the injection
 - C. Rotate injection sites
 - D. Use a heating pad on the injection sites

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Injection Site Reactions

- More common with subcutaneous products
- Bring medication to room temperature before injection
- Ice injection site
- Rotate injection sites

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Updates in Therapeutics® 2013:

The Pharmacotherapy Preparatory Review & Recertification Course

General Psychiatry

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Conflict of Interest Disclosures

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Learning Objectives and/or Agenda

1. Describe pharmacotherapeutic options for managing the following psychiatric disorders: major depression, bipolar disorder, schizophrenia, anxiety disorders, insomnia, and alcohol withdrawal/dependence.
2. Describe the drugs used to treat the above disorders with respect to unique pharmacologic properties, therapeutic uses, adverse effects, and cognitive and behavioral effects.
3. Formulate a pharmacotherapeutic treatment plan when presented with a patient having depression, bipolar disorder, schizophrenia, anxiety disorder, insomnia, and alcohol withdrawal/dependence.

Major Depression

Patient Case Page 1-242

- A.Z. is a 45-year-old woman with sleep apnea, hypertension, diabetes mellitus type 2, and chronic pain.
- She endorses sad mood, poor appetite (lost 15 lb), poor concentration, and feelings of hopelessness and worthlessness for the past 3 weeks.

Major Depression

Patient Case Page 1-242

- Also stopped going to her book club due to lack of motivation to get out of the house, and has frequent mid-nocturnal awakening.
- Denies SI/HI, ETOH, tobacco, or illicit drugs.
- Currently taking HCTZ, metformin, hydrocodone/acetaminophen, and aspirin. You decide that A.Z. should receive a selective serotonin reuptake inhibitor (SSRI) to treat her depressive symptoms.

DSM-IV Diagnostic Criteria

- **Depressed mood** or **anhedonia** (loss of interest or pleasure) and four (4) or more target symptoms (below) for at least two (2) weeks
- Weight change (loss or gain)
- Sleep disturbance (insomnia or hypersomnia)
- Decreased energy
- Feelings of worthlessness or guilt
- Decreased concentration
- Psychomotor agitation or retardation
- Recurrent thoughts of death or suicide





DSM-IV Diagnostic Criteria

- Rule out medical conditions or medications that could contribute to symptoms
 - Medical conditions
 - Hypothyroidism, Cushing's disease, pregnancy/postpartum, diabetes mellitus, Parkinson's, MS, Alzheimer's disease, CVA, MI, CHF, AIDS, menopause, RA, FM, IBS
 - Medications
 - High probability: Benzodiazepines, barbiturates, ETOH, corticosteroids, contraceptive implants, interferon alpha, interleukin-2, mefloquine, GnRHA, stimulant withdrawal
 - Low probability/uncertain: Reserpine, BB (propranolol), interferon beta, tamoxifen, digitalis

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Patient Case # 1

Which SSRI would most likely interact with her current medications?

-  **A. Citalopram.**
-  **B. Fluvoxamine.**
-  **C. Paroxetine.**
-  **D. Sertraline.**





Handout Page 1-242 ; Answer Page 1-278

Table 1. Antidepressants and the CYP System, Page 1-244

CYP Enzyme	Inhibition Potential
1A2	Fluvoxamine: high Fluoxetine: moderate
2C	Fluoxetine, fluvoxamine, sertraline: low
2D6	Bupropion, citalopram, escitalopram, sertraline: very low Duloxetine: moderate Fluoxetine, paroxetine: very high
3A4	Sertraline: very low Fluoxetine: low Fluvoxamine: moderate Nefazodone: very high
Minimal	Venlafaxine, desvenlafaxine, mirtazapine

Patient Case # 2

Which antidepressant would be most appropriate for A.Z.'s depressive symptoms?

-  **A. Bupropion.**
-  **B. Fluoxetine.**
-  **C. Mirtazapine.**
-  **D. Venlafaxine.**

Handout Page 1-242; Answer Page 1-278

Selecting an Antidepressant

- Indication
- Previous response or familial response
- Severity and type of depression and symptoms
- Patient preference
- Financial consideration
- Side effect profile
- Suicidal ideation or risk of overdose
- Comorbidities (medical/psychiatric disorders, substance abuse history)
- Demographics: age, ethnicity

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Adverse Effects*

- **CNS Effects**
 - Insomnia/Sedation: Fluvox, parox – most sedating, fluox most activating
 - Headaches, vivid dreams/nightmares
- **GI Effects**
 - N/V/D/constipation (parox associated with most nausea/vomiting, CR formulation may help)
- **Anticholinergic effects**
 - Parox appears to be worst due to slight M₁ binding property (dry mouth, constipation, etc)
- **Bleeding/anemia: due to platelet serotonin depletion**

*See Table 79-12 in Applied Therapeutics, Table 77-4 in Pharmacotherapy

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Adverse Effects

- Sexual dysfunction: ~30-73% of patients on SSRI
 - Stimulate 5HT_{2A} receptor
 - fluox ≥ sert, cital, escital > fluvox
 - Type of sexual dysfunction: delayed ejaculation, anorgasmia, impaired libido, erectile dysfunction can occur but less common
- QT prolongation (8/24/11)
 - Citalopram >40mg/day
- Withdrawal syndrome
 - Paroxetine
- Others: Sweating, bruxism, EPS, SIADH, weight gain, hyponatremia, ↓ bone mineral density

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Patient Case # 3

It has been 4 weeks since AZ's initial visit with you and she has been treated with citalopram 20mg/day QAM. Still has sad mood, but her insomnia, concentration and appetite have improved. Still has feelings of hopelessness and worthlessness, lack of motivation, and anhedonia. At this point, which is the best recommendation to optimize her therapy?



- A. Continue at current dose of 20 mg/day.
- B. Increase the current dose to 40 mg/day.
- C. Add bupropion 150 mg twice daily.
- D. Switch to a different SSRI.

Handout Page 1-242; Answer Page 1-278

Table 3. Antidepressant Dosing Page 1-246

Characteristic	Fluoxetine	Sertraline	Paroxetine	Fluvoxamine ^a	Citalopram	Escitalopram	Vilazodone
Half-life	1-4 days	26 hours	21 hours	15 hours	32 hours	27-32 hours	25 hours
Active metabolite	Yes ^b	No	No	No	No	No	No
Usual dose (mg/day)	20-60	50-200	10-60	50-300	20-40	10-20	40
Maximal daily dose (mg)	80	200	50 (depression) 60 (anxiety)	300	40	20	40

^aIndicated only for obsessive-compulsive disorder, seldom used for depression.
^bNorfluoxetine.

What to do when patients don't respond?

- Wait and see
- Increase the dose
- Switch within class
- Switch to another class
- Add another antidepressant
- Add a non-antidepressant

Major Depression Clinical Pearls

- Antidepressant are equally efficacious
- Selection is dependent on multiple patient and drug-related factors (next slide)
- Remission is primary goal of therapy
- Pharmacotherapy and psychotherapy produce best outcomes
- Onset of effect may take 4-6 weeks
- Single episode requires at least 7-12 months of antidepressant treatment

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Patient Case # 4

Six months later, AZ reports that although her depression symptoms have improved, she has "trouble" during intercourse, which is quite disturbing to her. You determine that she has anorgasmia caused by citalopram treatment. Which is the most appropriate recommendation at this time?



- A. Discontinue citalopram
- B. Add bupropion to treat anorgasmia
- C. Switch to a different SSRI
- D. Switch to mirtazapine

Handout Page 1-242; Answer Page 1-278

Bipolar Disorder

Patient Case Page 1-251

- J.L. is a 26-year-old man with bipolar disorder I, who presents with delusions that the FBI is tracking his movements and that his thoughts are being recorded in a secret governmental database. He believes he has special powers to hide from the FBI by making himself invisible.
- He is hyperverbal and has not slept in the past 48 hours. He is placed on a 72-hour hold for control of his manic symptoms..

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Bipolar Disorder

Patient Case Page 1-251

- He has a history of nonadherence to medications and is currently not taking any medications. J.L.'s last hospitalization was 2 months ago, when he had significant depressive symptoms and suicidal ideation.
- He has 3-4 hospitalizations per year, and his medication trials include carbamazepine, olanzapine, and lamotrigine (may be helpful but uncertain because of nonadherence). He has also received a diagnosis of hepatitis C.

Patient Case # 5

Which statement is most applicable regarding selecting J.L.'s mood stabilizer at this time?

-  A. Carbamazepine should be tried again because it is effective for preventing rehospitalization.
-  B. Divalproex should be tried because it is good for maintenance treatment.
-  C. Lithium should be tried because it can effectively treat the manic phase and prevent future episodes.
-  D. Lamotrigine should be tried again because it is effective for bipolar maintenance.

Handout Page 1-251; Answer Page 1-278

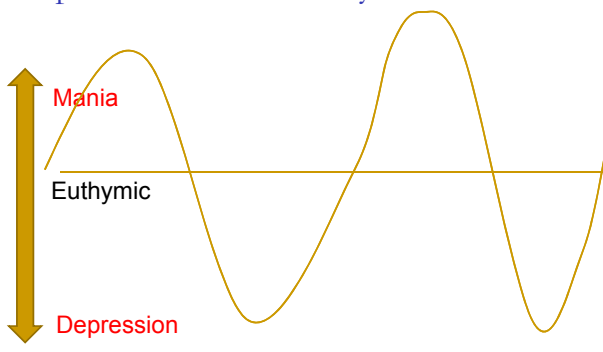
DSM-IV Diagnostic Criteria

- Manic episode
 - Distinct period of abnormally and persistently elevated, expansive or irritable mood, lasting at least **1 week** (or any duration if hospitalization necessary)
 - **Three or more*** of following sx during mood disturbance: 1) inflated self-esteem or grandiosity, 2) decreased need for sleep, 3) more talkative than usual or pressured speech, 4) flight of ideas or racing thoughts (subjective), 5) distractibility, 6) increase in goal-directed activity (either socially, occupationally, sexually) or psychomotor agitation, 7) excessive involvement in pleasurable activities that have negative consequences (gambling, spending \$\$, sexual activity)

*Four or more sx required if only irritable mood

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Bipolar Disorder Life Cycle



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Mood Stabilizers: Uses

- Lithium
- Valproic acid
- Lamotrigine
- Carbamazepine
- Oxcarbazepine
- Antipsychotics
- Mania, depression, maintenance
- Mania, maintenance
- Maintenance, depression
- Mania, maintenance
- Mania, maintenance
- Olanz: mania, maintenance
- Quet: mania, depression, maint*
- Aripip: mania, maintenance
- Risp, zipras, asenapine: mania

*As adjunct

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Mood Stabilizers





Therapeutic Efficacy

- Lithium ■ 1-2 weeks
- Valproic acid ■ 3-5 days
- Lamotrigine ■ 5 weeks to reach target dose
- Carbamazepine ■ 4 weeks for autoinduction
- Oxcarbazepine ■ 1-2 weeks
- Antipsychotics ■ Few days

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Patient Case # 6

Which adverse effect would be of most concern and would require immediate evaluation if J.L. were prescribed lithium?

-  **A. Hyperthyroidism.**
-  **B. Coarse tremor.**
-  **C. Severe acne.**
-  **D. Weight gain.**

Handout Page 1-251; Answer Page 1-278

Bipolar Disorder

- Lithium
 - Excreted 95% unchanged by glomerular filtration
 - Initial workup: CBC, electrolytes, renal function
 - Serum concentration:
 - 0.8-1.2 mEq/L (acute mania)
 - 0.6-1.0 mEq/L (maintenance)
 - Other labs: thyroid function, urinalysis, poss. EKG, pregnancy test





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Table 4. Lithium Adverse Effects Page 1-252

Problem	Potential Interventions
Rash or ↑ psoriasis	Discontinue the drug temporarily or permanently
Tremor	Reduce dose (Cp); add β-blocker
CNS toxicity (e.g., agitation, confusion)	Reduce dose (Cp)
GI (nausea/vomiting, diarrhea)	Reduce dose; try extended-release product
Hypothyroidism	Discontinue Li or give levothyroxine
Polydipsia/polyuria	Reduce dose, manage intake, and try amiloride or HCTZ, but know that HCTZ will ↑ Li Cp; single HS dosing helps
Interstitial fibrosis, glomerulosclerosis	Controversial! Keep dose at lowest effective concentration
Teratogenicity	Avoid during first trimester if possible

Patient Case # 7

J.L. has been stable on lithium 900 mg/day x 3mo. During a clinic visit, J.L. is confused and slurring his words. His other medications include lisinopril, ibuprofen, atorvastatin, and zolpidem. Which is best to recommend immediately?

-  **A. Discontinue lisinopril because it interacts with lithium.**
-  **B. Discontinue zolpidem because it may increase confusion.**
-  **C. Obtain a lithium level because J.L. may have supratherapeutic levels.**
-  **D. Discontinue ibuprofen because it interacts with lithium.**

Handout Page 1-251; Answer Page 1-278

Table 5. Situations to Consider During Lithium Therapy, Page 1-253

Situation	Factors	Results
Drug Interactions	Diuretics	
	Thiazides	↑ Li Cp; avoid use to reduce toxicity
	Furosemide	Little effect
	Amiloride	Little effect
	NSAIDs	↑ Li Cp; avoid use to reduce toxicity
	Theophylline	↓ Li Cp
	ACEIs	↑ Li Cp; avoid use to reduce toxicity
	Neuromuscular blockers	Li prolongs action
	Neuroleptics	Li may potentiate EPS
	Carbamazepine	↑ CNS toxicity

Table 5. Situations to Consider During Lithium Therapy, Page 1-253

Situation	Factors	Results
Thyroid	Li ↓ synthesis and release of thyroid hormone	Hypothyroidism
Pregnancy	↑ GFR	↓ Li Cp
Aging	↓ GFR	↓ Li Requirements
	↑ Sensitivity to ADRs	Li toxicity
↓ Renal function	↓ GFR, ↑ Cr and BUN	↑ Li Cp
Dehydration, salt restriction, and extrarenal salt loss	↑ Na reabsorption	↑ Li Cp

Bipolar Disorder Clinical Pearls

- Selection of treatment depends on acute phase vs maintenance phase
- Mood stabilizers are not equally efficacious
- Selection is dependent on efficacy and drug-related factors
- Euthymic state and avoidance of hospitalization are goal of therapy
- Onset of effect may occur within 1-2 weeks
- Patients may need life-long treatment

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Schizophrenia

Patient Case Page 1-255

- L.M. is a 25-year-old man recently given a diagnosis of schizophrenia, paranoid type. He often hears voices telling him that he is “stupid and worthless” and that he should “just jump off his apartment building.” His parents became very concerned over his isolative behavior and brought him to the hospital.

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Schizophrenia

Patient Case Page 1-255

- He was given haloperidol in the psychiatry unit and now presents with neck stiffness and feelings of extreme restlessness.
- Until now, he has not taken medications because he felt that he could control his symptoms on his own with vitamins and Red Bull drinks.

Patient Case # 8

Which is the most appropriate treatment of L.M.’s symptoms at this time?

-  **A. Benztropine.**
-  **B. Haloperidol.**
-  **C. Olanzapine.**
-  **D. Quetiapine.**

Handout Page 1-255; Answer Page 1-278

Antipsychotic Agents

- Conventional “first generation”, “typical”
 - Block postsynaptic D₂ receptors (mainly), α1, M1, H1
 - Alleviate **positive symptoms** of schizophrenia
 - Blockade of DA in nigrostriatal tract → movement d/o
 - Blockade of DA in tuberoinfundibular tract → ↑prolactin
- Atypical (“novel”, “second generation”)
 - Block D₂ and 5HT₂, α1, M1, H1 receptors
 - Alleviate **positive** and **negative** symptoms, cognitive dysfunction
 - Minimal ↑ in serum prolactin, minimal risk of EPS, TD
- In each class, efficacy most likely similar for first episode schizophrenia; exception: clozapine

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Table 8. First Generation Antipsychotics, Page 1-258

Generic Name	Trade Name	Chemical Class	Dose Equivalence
Low Potency			
Chlorpromazine	Thorazine	Aliphatic phenothiazine	100
Thioridazine	Mellaril	Piperidine phenothiazine	100
Mid-Potency			
Perphenazine	Trilafon	Piperazine phenothiazine	10
Loxapine	Loxiltane	Dibenzoxazepines	10
High Potency			
Haloperidol	Haldol	Butyrophenone	2
Fluphenazine	Prolixin	Piperazine phenothiazine	2
Thiothixene	Navane	Thioxanthenes	4

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Second Generation Antipsychotics

Generic Name	Trade Name	Chemical Class	Dose Equivalence*
Clozapine	Clozaril	Dibenzodiazepine	50
Risperidone	Risperdal	Benzisoxazole	2
Olanzapine	Zyprexa	Thienobenzodiazepine	5
Quetiapine	Seroquel	Dibenzothiazepine	75
Ziprasidone	Geodon	Benzohizolylpiperazine	60
Aripiprazole	Abilify	Quinolone derivative	7.5
Paliperidone	Invega	Benzisoxazole	--
Asenapine	Saphris	Dibenzo-oxepino pyrroles	--
Iloperidone	Fanapt	Piperidinyl-benzisoxazole	--
Lurasidone	Latuda	Benzoisothiazole	--

*Woods SW. Chlorpromazine equivalent doses for the newer atypical antipsychotics. J Clin Psychiatry 2003;64(6):663-7

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Extrapyramidal Symptoms

- Extrapyramidal symptoms
 - Typical: High potency >> mid/low potency
 - Atypical: Risp*, palip, luras > cloz, olan**, quet, zipras, aripip, asenap, ilop
- Due to blockade of dopamine receptors in nigrostriatal tract & extrapyramidal system; three types of EPS

*Lower risk at doses <8mg/day; **lower risk at doses<20mg/day

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Extrapyramidal Symptoms (EPS)

- Dystonic reactions
 - Involuntary muscle contraction involving neck trunk and other muscles
- Akathisia
 - Subjective feelings of anxiety and jitteriness
- Parkinsonism
 - Symptoms similar to Parkinson's disease including
 - Tremor, rigidity, bradykinesia, stoop gait

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Extrapyramidal Symptoms

- Treatment
 - Dystonia: ↓ dose or give anticholinergic agents (e.g. IM benztropine, diphenhydramine), BZD (if anticholinergics are contraindicated)
 - Akathisia: ↓ dose or give propranolol, clonidine, BZD, anticholinergics
 - Parkinsonism: ↓ dose or anticholinergic agent, amantadine
 - See Agents Used to Treat Extrapyramidal Symptoms Table

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Patient Case # 9

You and the psychiatric team decide to recommend risperidone for L.M. Which is the most likely reason for this selection?

-  **A. Risperidone has less risk of causing EPS than haloperidol.**
-  **B. Risperidone is available in a long-acting injection for increasing adherence.**
-  **C. Risperidone is effective for decreasing L.M.'s negative symptoms.**
-  **D. Risperidone can be dosed once daily after titration to target dose.**

Handout Page 1-255 ; Answer Page 1-278





Risperdal® Consta™

- First long-acting atypical antipsychotic
- Delayed-release injection using Medisorb® drug delivery system (polymeric microspheres that degrade slowly and release med at controlled rate)
- Main release of drug occurs at **3 weeks** and maintained for 4-6 weeks
- Dose: 25mg IM every 2 weeks, maximum dose of 50mg IM every 2 weeks. Dosage adjustment should not be made more frequently than Q4 weeks
- Oral risperidone (or other antipsychotic) should be administered with initial injection and continued for 3 weeks (then D/C'd) due to delayed release phase

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Patient Case # 10

Which adverse effect of risperidone would be of most concern in L.M.?

-  **A. Sedation**
-  **B. Anticholinergic effects.**
-  **C. EPS.**
-  **D. Correct QT (QTc) prolongation**

Handout Page 1-255; Answer Page 1-278

Table 9. Antipsychotics Adverse Effects, Page 1-263





	Anticholinergic	Sedation	EPS	Orthostasis
Clozapine	4	4	1	4
Risperidone	1	2	2-3	3
Olanzapine	3	3	1	1
Quetiapine	1	3	1	3
Ziprasidone	1	1	1	1
Aripiprazole	1	1	1	1
Paliperidone	1	1	2-3	1
Asenapine	2	4	1	4
lloperidone	1	1	1	4
Lurasidone	1	1	1	1

1=none to minimal, 4=high; EPS=extrapyramidal symptoms

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Patient Case # 11

One year later, L.M. is no longer responding to risperidone, and you decide to switch him to another medication. He is only interested in oral medications. Which one of the following agents is most appropriate at this time?

-  **A. Clozapine.**
-  **B. Fluphenazine.**
-  **C. Olanzapine.**
-  **D. Quetiapine.**

Handout Page 1-255; Answer Page 1-278-279

Schizophrenia Clinical Pearls

- All antipsychotics are equally efficacious except clozapine
- Second generation antipsychotics have better negative symptom control and less EPS
- Selection is dependent on multiple patient and drug-related factors
- Remission may never be achieved and primary goal is to control symptoms and minimize adverse effects

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Schizophrenia Clinical Pearls

- Positive and negative symptoms, functional outcomes and cognitive impairment are key target areas for treatment
- Avoidance of hospitalization is critical
- Onset of effect may take 4-6 weeks
- Most patients require life-long treatment

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Anxiety Disorders

Patient Case Page 1-265

- C.P. is a recent Iraq war veteran who has been treated successfully with paroxetine for his major depression for the past 3 weeks. He presents to the clinic with nightmares, “feeling on edge all the time,” and flashbacks of his time in the war. He is evaluated and given a diagnosis of posttraumatic stress disorder (PTSD). He has no history of substance dependence and has no significant medical history.

Patient Case # 12

Which recommendations is most appropriate at this time?

-  **A. Continue paroxetine because it treats both PTSD and major depression.**
-  **B. Discontinue paroxetine and initiate sertraline, which treats both PTSD and major depression.**
-  **C. Continue paroxetine and add lorazepam for the anxiety symptoms.**
-  **D. Discontinue paroxetine and start buspirone for the anxiety symptoms.**

Handout Page 1-265; Answer Page 1-279

Guess the Anxiety Disorder

- Patient who is often labeled as a worrywart
- Patient who spends 2 hours every day making sure her towels are neatly folded
- Patient who startles easily and complains of nightmares about her time in combat
- Patient who has moments where she feels like she's dying and afraid to drive
- Patient who is afraid of snakes and can't go to the zoo





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Anxiolytics and Indications

Anxiety Disorder	FDA Approved Agents
Panic Disorder	Benzodiazepines (alprazolam, clonazepam) Fluoxetine, Paroxetine, Paroxetine CR, Sertraline, venlafaxine
GAD	Paroxetine, escitalopram, venlafaxine, duloxetine, buspirone
OCD	First Line: Fluoxetine, Fluvoxamine, Paroxetine, Sertraline Second line: TCA (clomipramine)
PTSD	Paroxetine, Sertraline
SAD	Paroxetine, Paroxetine CR, Sertraline, Venlafaxine

Patient Case # 13

C.P. has been adherent to the medication you recommended earlier, but he still feels very irritable and has been aggressive at times at work toward others. Which adjunctive medication is most appropriate in this patient?

-  **A. Buspirone.**
-  **B. Clonazepam.**
-  **C. Divalproex.**
-  **D. Lithium.**





Handout Page 1-265; Answer Page 1-279

Adjunctive Agents for PTSD

- Lithium, CBZ, VPA for mood lability and aggression
- Propranolol for countering hyperarousal
- Prazosin for nightmares
- Nefazodone indicated for PTSD but hepatotoxicity, trazodone for sleep (not well-studied as SSRIs)
- Antipsychotics for psychotic symptoms, not effective for core symptoms
Benzodiazepines are of limited value

Patient Case # 14

After 8 months of treatment, C.P. is not responding to the medication you recommended. Having heard a lot about buspirone, he wonders whether this medication might be helpful for his conditions. Which is the most accurate statement for this patient?

-  **A. Buspirone may be helpful for the nightmares.**
-  **B. Buspirone may work as quickly as 3 days.**
-  **C. Buspirone is convenient because of its once-daily dosing.**
-  **D. Buspirone does not have much dependence potential.**

Handout Page 1-265 ; Answer Page 279

Buspirone

- 5HT_{1A} partial agonist
- No significant sedation, cognitive impairment, motor impairment or respiratory depression
- Common side effects: dizziness, nausea/diarrhea, HA, nervousness, jitteriness, restlessness, numbness, paresthesia, diaphoresis

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Buspirone

- Useful for GAD only
- Takes 2 weeks for onset of effect; may need to bridge therapy with benzodiazepines if symptoms are severe
 - Good for benzodiazepine naïve patients
 - No dependence, withdrawal, abuse potential
- Dose
 - Initiate 5mg PO TID, increase by 5mg/day every 2-3 days, up to maximum of 20mg TID (60mg/day)

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Patient Case # 15

C.P. returns to the clinic and states that his depressive and anxiety symptoms have much improved. However, he is concerned that his girlfriend, who has obsessive-compulsive disorder, is not doing well on her treatment with lorazepam. If you were also treating the girlfriend, which one of the following would be the most appropriate medication you would initiate?

-  **A. Clomipramine.**
-  **B. Amitriptyline.**
-  **C. Imipramine.**
-  **D. Nortriptyline.**

Handout Page 1-265 ; Answer Page 1-279

Anxiolytics and Indications

Anxiety Disorder	FDA Approved Agents
Panic Disorder	Benzodiazepines (alprazolam, clonazepam) Fluoxetine, Paroxetine, Paroxetine CR, Sertraline, venlafaxine
GAD	Paroxetine, escitalopram, venlafaxine, duloxetine, buspirone
OCD	First Line: Fluoxetine, Fluvoxamine, Paroxetine, Sertraline Second line: TCA (clomipramine)
PTSD	Paroxetine, Sertraline
SAD	Paroxetine, Paroxetine CR, Sertraline, Venlafaxine

Insomnia

Patient Case Page 1-268

- C.D. is a 38-year-old kindergarten teacher who presents to clinic today with noticeable dark circles under her eyes. She has difficulty with sleep, mainly with staying asleep. It takes her about 20 minutes to fall asleep, but after about 2 hours, she wakes up and cannot fall asleep again for several hours. This pattern has taken a toll on her job, and she feels tired all the time.

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Insomnia

Patient Case Page 1-268

- She once took diphenhydramine for sleep but had to miss work because of extreme drowsiness in the morning. She wonders whether there are any other medications that she can take. Her other medical problems include hypothyroidism (levothyroxine 125 mcg at bedtime), hypertension (HCTZ 25 mg in the morning), chronic back pain (ibuprofen 800 mg 3 times/day), and MDD (citalopram 20 mg in the morning).

Patient Case # 16

Which agent is most likely contributing to C.D.'s insomnia?

-  **A. Citalopram.**
-  **B. Hydrochlorothiazide**
-  **C. Ibuprofen.**
-  **D. Levothyroxine.**

Handout Page 1-268; Answer Page 1-279





Secondary Etiologies

- **Medications**
 - Fluoxetine
 - Bupropion
 - MAOI
 - Thyroid supplements
 - CNS stimulants
 - Calcium channel blockers
 - Beta blockers
 - Decongestants
 - Dopamine agonists
 - Corticosteroids
 - Theophylline
- **Substance Use/Abuse**
 - Caffeine
 - Nicotine
 - Alcohol
 - Alcohol withdrawal
 - Benzodiazepine withdrawal
 - Narcotic withdrawal
 - Stimulant intoxication/withdrawal

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Patient Case # 17

Which medication used for insomnia is most appropriate to recommend for C.D.?

-  **A. Eszopiclone.**
-  **B. Trazodone.**
-  **C. Temazepam.**
-  **D. Zaleplon.**

Handout Page 1-268; Answer Page 1-279

Table 14. Insomnia Classification

Page 1-270

Type	Duration	Likely Causes
Transient	<1 week	Acute situational or environmental stressors
Short term	< 4 weeks	Continued personal stress
Chronic	> 4 weeks	Psychiatric illness, substance abuse
		Behavioral causes (poor sleep hygiene)
		Medical causes, primary sleep disorder (e.g. sleep apnea, restless legs syndrome)

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Insomnia

- Sedative hypnotics are differentiated by
 - Pharmacokinetic properties
 - Efficacy in onset and duration
 - Adverse effects
 - Drug interactions
 - Abuse potential
 - Cost

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Table 15. Sedative-Hypnotics, 1-272

Drug	Usual Dose (mg)	Half-life (hrs)	Duration
Triazolam	0.125-0.25	2-6	Short
Temazepam	15-30	8-20	Intermediate
Estazolam	1-2	8-24	Intermediate
Flurazepam	15-30	48-120	Long
Quazepam	7.5-15	48-120	Long
Zolpidem	5-10	1.5-4.0	Short
Zaleplon	5-10	1	Very Short
Eszopiclone	2-3	6	Short
Ramelteon	8	1-3	Short

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Patient Case # 18

Which adverse effect should C.D. be most concerned about when using zolpidem?

-  **A. Orthostasis.**
-  **B. Disorientation.**
-  **C. Abnormal behaviors while asleep.**
-  **D. Seizures at high doses of the drug.**

Handout Page 1-268; Answer Page 1-279

Complex Sleep Behaviors (CSB)

- FDA issued Black Box Warning for all insomnia agents
 - Angioedema
 - Complex sleep behaviors
- CSB may include walking, eating, having sex while asleep
- Incidence
- Risk Factors

Substance Abuse – Alcohol

Patient Case Page 1-273

- L.M. is a 50-year-old man with a 25-year history of alcohol dependence who was found unconscious after his last drinking binge. He was first admitted to the medical unit for alcohol withdrawal symptoms before being transferred to the substance dependence unit. His last drink was 6 hours ago, and fluids have been started.

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Substance Abuse – Alcohol

Patient Case Page 1-273

- He has had three alcohol-withdrawal seizures in the past and an episode of delirium tremens.
- He also has significant hepatitis, and liver function tests show aspartate aminotransferase (AST) of 220 and alanine aminotransferase (ALT) of 200.

Patient Case # 19

Which symptom are you most likely to observe in the medical unit?

-  **A. Alcohol craving.**
-  **B. Delirium tremens.**
-  **C. Increased heart rate.**
-  **D. Seizures.**

Handout Page 1-273; Answer Page 1-279

Substance Abuse – Alcohol Management

- Labs: tox screen, renal and liver function, folate, thiamine, B12 levels, electrolytes
- Nutrition: thiamine, magnesium, vitamins, fluid
- Seizures: benzodiazepines, other antiepileptics not as effective
- Hallucinations: benzodiazepines, haloperidol (caution with seizures)

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Table 15. Substance Abuse – Alcohol Page 1-274

Stage	Onset	Symptoms
1	0-8 hrs	Mild tremors, nervousness, tachycardia, nausea
2	12-24 hrs	Marked tremors, hyperactivity, tachycardia, insomnia, nightmares, illusions, alcohol craving
3	12-48 hrs	More severe symptoms than during stage 2, seizures may occur
4	3-5 days	Delirium tremens, confusion, agitation, tremor, insomnia, tachycardia, sweating, hyperpyrexia

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Patient Case # 20

Which agent is best for alcohol withdrawal symptoms in L.M. for intramuscular administration?

-  **A. Chlordiazepoxide.**
-  **B. Clonazepam.**
-  **C. Diazepam.**
-  **D. Lorazepam.**

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Table 16. Substance Abuse – Alcohol Page 1-275

Drug	Dose	Comments
Lorazepam	1-2 mg PO/IV/IM	Can use with liver disease
Diazepam	5-20 mg PO	Use lower dose with liver disease, can use loading-dose strategy
Chlordiazepoxide	25-100 mg PO/IV	Long acting; caution with liver disease

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Patient Case # 21

Before administering fluids with glucose, which agent is most important to administer?

-  **A. Folate.**
-  **B. Multivitamin supplement (MVI).**
-  **C. B12.**
-  **D. Thiamine.**

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Wernicke-Encephalopathy

- Due to severe thiamine deficiency and malnutrition
- 10-20% mortality, medical emergency
- Abrupt onset, gradual symptoms over several days
- Sx: confusion, ataxia, paralysis of ocular muscle, confusion, hypothermia, hypotension, polyneuropathy
- Korsakoff's psychosis
 - 80% of Wernicke's progress to Korsakoff's
 - Sx: Psychosis, amnesia (retro, antero), hallucinations

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Patient Case # 22

Which medication is best to use in L.M. for alcohol dependence?

-  **A. Acamprosate.**
-  **B. Diazepam.**
-  **C. Disulfiram.**
-  **D. Naltrexone.**

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Treatment of Alcohol Dependence

- Disulfiram (Antabuse)  
 - Inhibits aldehyde dehydrogenase
- Naltrexone (Revia, Vivitrol)  
 - Opioid antagonist
- Acamprosate (Campral)  
 - Inhibits Glutamatergic activity
 - Enhances GABA activity

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Questions?

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