Updates in Therapeutics® 2015:

The Pharmacotherapy Preparatory Review & Recertification Course

General Psychiatry

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Conflict of Interest Disclosures

Jacintha Cauffield has no conflicts of interest to disclose.

Learning Objectives

- For the following psychiatric disorders: depression, bipolar disorder, schizophrenia, anxiety disorders, insomnia and substance abuse:
- Describe pharmacotherapeutic options for management
- Describe the drugs used to treat these disorders with respect to unique pharmacologic properties, therapeutic uses, adverse effects, and cognitive and behavioral effects.
- Formulate a pharmacotherapeutic treatment plans

Overview

- Depression
- Bipolar Disorder
- Schizophrenia
- Anxiety Disorders
- Insomnia
- Substance Abuse

Diagnostic Criteria: DSM-V

- Core criteria-MUST have at least one of these:
  - Depressed mood
  - Anhedonia
- Always ask about suicidal ideation

Treatment Principles

- All antidepressants are equally efficacious
- Fit medication to patient
- First line:
  - SSRIs
  - SNRIs
  - Bupropion
  - Mirtazapine

Serotonin Specific Reuptake Inhibitors (SSRIs)

- Long half-life: fluoxetine
- Activating: fluoxetine, sertraline
- Sedating: paroxetine
- Neutral: citalopram
- 2D6 inhibitors: fluoxetine, paroxetine

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- Citalopram: QTc prolongation risk increases >40 mg
- Paroxetine: category D in pregnancy

Serotonin Norepinephrine Reuptake Inhibitors (SNRIs)

	Receptor Binding
Desvenlafaxine	Serotonin= norepinephrine
Duloxetine	Serotonin= norepinephrine
Levomilnacipran	Norepinephrine> serotonin
Venlafaxine	≤ 150 mg/day: SSRI >150 mg/day: SNRI

- Weight neutral
- Sleep neutral

Newer Mixed Serotonergic Agents

- Vilazodone
  - SSRI + partial agonist activity at 5HT1a
  - Sleep and weight neutral
  - Decrease dose when given with 3A4 inhibitors
  - Avoid with seizure disorders
- Vortioxetine
  - SSRI + additional specific serotonin receptor activities
  - Side effects: nausea, diarrhea, xerostomia
  - High incidence of sexual dysfunction
  - Decrease dose if given with 2D6 inhibitors

Miscellaneous Antidepressants

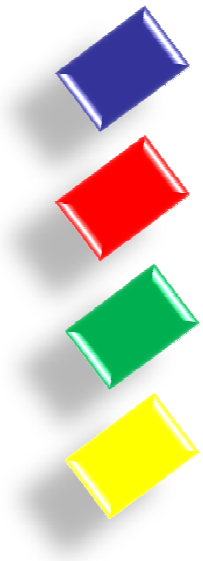
- Bupropion
  - Weight loss
  - Insomnia
  - Sexual dysfunction: none
  - Can cause seizures
- Mirtazapine
  - Causes weight gain
  - Somnolence; can be activating at higher doses
  - No sexual dysfunction
  - Orthostatic hypotension

Antidepressant-Patient Matches

Symptom (patient has this symptom)	Antidepressant (to counteract the symptom)
Weight loss	Mirtazapine, paroxetine, TCAs
Weight gain	Bupropion, duloxetine, SSRIs (except paroxetine), venlafaxine
Insomnia	Mirtazapine, TCAs, paroxetine, trazodone
Hypersomnia	Bupropion, duloxetine, fluoxetine, sertraline, vilazodone
Suicidal ideation	NOT TCAs, avoid bupropion; use SSIRs
Neuropathic pain	Duloxetine, TCAs (amtitriptyline (?), desipramine, nortriptyline)
Sexual dysfunction	Bupropion, mirtazapine, nefazodone, vilazodone?
Pregnancy	Fluoxetine, sertraline, bupropion?

Depression: Drug Choice

A 65-year-old white man with expresses all the target symptoms of depression, including suicidal ideation. His concomitant medical conditions include diabetes with neuropathy and seizure disorder. Which medication would be most appropriate to initiate in this patient?



A. Bupropion
B. Duloxetine
C. Nortriptyline
D. Sertraline

New Case; 1-559 to 1-562

Depression: Drug Choice

A. Bupropion

Lowers the seizure threshold.

B. Duloxetine

Relatively safe in overdose, and is also indicated for neuropathy.

C. Nortriptyline

Causes torsade de pointes and seizures in overdose.

D. Sertraline

Safe in overdose, but no efficacy for neuropathy.

New Case; 1-559 to 1-562

CYP450 Interactions

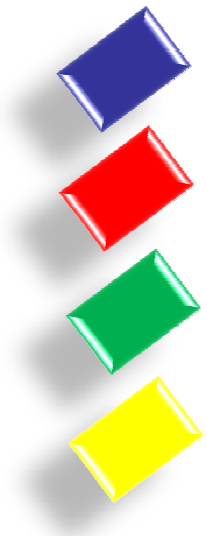
	1A2	2C9/19	2D6	3A4
Substrate	duloxetine	citalopram escitalopram fluoxetine imipramine	amitriptyline desipramine duloxetine fluoxetine imipramine nefazodone nortriptyline venlafaxine vortioxetine	citalopram escitalopram levomilnacipran nefazodone trazodone venlafaxine vilazodone vortioxetine
Inhibitor	fluoxetine **fluvoxamine**	sertraline	**bupropion*** duloxetine **fluoxetine** **paroxetine** sertraline	fluvoxamine **nefazodone**

*metabolized by CYP2B6; **bold**=strong inhibitor

Additional Material; 1-557 to 1-562

Antidepressant Choice

A.Z. is a 45-year-old woman newly diagnosed depression. She is currently taking carvedilol, lisinopril, codeine/acetaminophen, and aspirin. You decide that A.Z. should receive an antidepressant in the selective serotonin reuptake inhibitor (SSRI) class to treat her depressive symptoms. Which SSRI would most likely interact with her current medications?



A. Citalopram

B. Fluvoxamine

C. Paroxetine

D. Sertraline

Antidepressant Choice

A. Citalopram

Metabolized by 3A4, not a CYP450 inhibitor.

B. Fluvoxamine

Strongly inhibits 1A2; no interactions with her medications.

C. Paroxetine

Strong 2D6 inhibitor, thus will decrease the metabolism of codeine and thus its efficacy. Carvedilol is also metabolized by 2D6.

D. Sertraline

Not a strong inhibitor of any CYP450 enzymes.

Overview

- Depression
- Bipolar Disorder
- Schizophrenia
- Anxiety Disorders
- Insomnia
- Substance Abuse

Bipolar Disorder In a Nutshell

- Some form of elevated mood AND an increase in goal directed activity must be present

	Mania	Hypomania
Diagnosis	Bipolar Disorder Type I	Bipolar Disorder Type II
Major Depression?	Not necessarily	Yes-Hallmark
Duration	>1 week	≥ 4 days
Severity	Marked impairment Hospitalization Psychosis possible	Impairment, if present, is mild Noticed by others
Identification	Hallmark	Can be missed

Mania Treatment

- Hypomania often doesn't need treatment
- Mood stabilizers are the cornerstones of treatment
  - Lithium ("Gold standard")
  - Anticonvulsants (divalproex, carbamazepine)
- Atypical antipsychotics
  - Acute and chronic treatment

Lithium

- Still first-line treatment for bipolar type I
- Effective for euphoric mania
- Takes time to work
  - Some effect in 5-7 days
  - Antimanic effects: 10-21 days
  - Antidepressant effects: 6-8 weeks
- High rate of side effects
  - High d/c rate
  - Resistance develops with repeated d/c's

Lithium

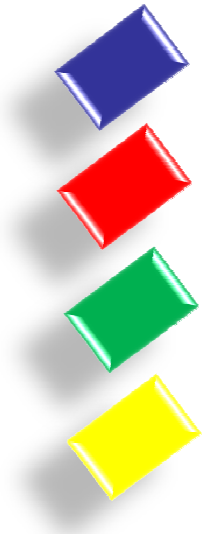
- Renally eliminated
- Serum concentrations:
  - Acute: 0.8-1.2 mEq/dL
  - Maintenance: 0.6-1.0 mEq/dL
- Obtain serum concentration 12 hours post-dose
- Achieves steady state in 5-7 days
- Perform serum creatinine, thyroid function tests and urinalysis every 6-12 months

Lithium Concentrations

- Increase:
  - ACE inhibitors
  - ARBs
  - Decreased renal function
  - Dehydration
  - Nondihydropuridine calcium channel blockers
  - NSAIDs
  - Thiazide diuretics
- Decrease:
  - Excess salt intake
  - Caffeine

Lithium: Drug Interactions

J.L. is a patient with bipolar disorder type I who has been stable on lithium 900 mg/day. During a clinic visit, you find that he is confused and slurring his words. His other medications include lisinopril, ibuprofen, atorvastatin, and zolpidem. Which is the best recommendation?



A. Discontinue lisinopril

B. Discontinue zolpidem

C. Obtain a lithium level

D. Discontinue ibuprofen

Lithium: Drug Interactions

A. Discontinue lisinopril

Lisinopril elevates lithium concentrations, but should not be d/c'ed if the patient is stable.

B. Discontinue zolpidem

Zolpidem can be used with lithium.

C. Obtain a lithium level

This should be done before making any changes in medications.

D. Discontinue ibuprofen

Once the lithium level is obtained, this should be the first focus of a drug history.

Anticonvulsants

- Take time to work
- Valproate
  - Also a first line treatment for mania
  - More effective for:
    - Rapid cyclers
    - Mixed episodes
    - Dysphoric mania
    - Comorbid substance abuse
- Carbamazepine
  - Not first line therapy
  - Effective; reasonable choice if s/p head injury

Antipsychotics

- Useful for acute symptom treatment
  - PO: quetiapine, olanzapine, risperidone
  - IM: aripiprazole, olanzapine
    - As effective as IM lorazepam
    - Haloperidol/benztropine can also be used
- Maintenance:
  - Approved: aripiprazole, olanzapine, quetiapine, risperidone
  - Data for typical (FGA) antipsychotics not as supportive

Acute Mania: Mood Stabilizer

C.Z. is a 25 yo man with h/o bipolar DO presents to your facility in acute dysphoric mania. He is aggressive, irritated, combative and attacking staff. His urine is positive for cocaine. Which mood stabilizer is best?

A. Carbamazepine

B. Divalproex

C. Haloperidol

D. Lithium

New Case; 1-565 to 1-568

Acute Mania: Mood Stabilizer

A. Carbamazepine

Not a first line mood stabilizer.

B. Divalproex

The preferred agent for dysphoria and substance abuse.

C. Haloperidol

Data don't support the use of FGAs as mood stabilizers.

D. Lithium

Not the first choice for substance abuse or dysphoria.

New Case; 1-565 to 1-568

Acute Mania: Antipsychotic

C.Z. is a 25 yo man with h/o bipolar DO presents to your facility in acute dysphoric mania. He is aggressive, irritated, combative and attacking staff. His urine is positive for cocaine. Which antipsychotic would be the best choice?

A. Aripiprazole PO

B. Haloperidol/benztropine IM

C. quetiapine PO

D. risperidone IM

Acute Mania: Antipsychotic

A. Aripiprazole PO

He is physically threatening staff. He needs parenteral treatment.

B. Haloperidol/benztropine IM

The most appropriate choice here in a physically aggressive patient.

C. Quetiapine PO

Parenteral is preferred.

D. Risperidone PO

Reasonable alternative if the dispersible tablet is given…if they can get it in his mouth.

Bipolar Disorder Depression

- Mood stabilizers are first line
  - Not antidepressants
- Lithium has some antidepressant effects
- Lamotrigine
- SGA antipsychotics: quetiapine and lurasidone
- Some antidepressants can be given with:
  - SGA antipsychotic (fluoxetine + olanzapine)
  - Lithium, divalproex, or lamotrigine

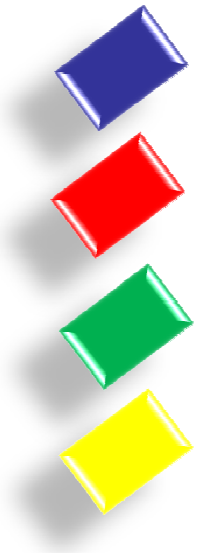
ISBD Antidepressant Guidelines

- Concern for “switching”
- Data for antidepressant efficacy is weak
- Appropriate if:
  - h/o response
  - Relapses off of an antidepressant
- Avoid:
  - Monotherapy, particularly in Type I
  - If h/o switching on antidepressant
- Worse with TCAs, SNRIs?
- Bupropion, fluoxetine, paroxetine may be better choices

Page 1-569; *Am J Psychiatry* 2013;170(11):1249-62.

Treatment of Bipolar Depression

A patient has been receiving lithium for his bipolar disorder for the past 2 years. He is now actively depressed. Which medication would be the most appropriate treatment for his depressive symptoms?



A. Aripiprazole

B. Divalproex

C. Fluoxetine

D. Lurasidone

New Case; 1-567 to 1-569

Treatment of Bipolar Depression

A. Aripiprazole

Indicated for treatment-resistant depression, but data for use in bipolar depression is not robust.

B. Divalproex

More efficacious for mania.

C. Fluoxetine

Could be considered if patient is refractory to mood stabilizers and SGA antipsychotics.

D. Lurasidone

Indicated for bipolar depression.

New Case; 1-567 to 1-569

Overview

- Depression
- Bipolar Disorder
- Schizophrenia
- Anxiety Disorders
- Insomnia
- Substance Abuse

Schizophrenia: Diagnosis

- Major symptoms (≥ 2 for at least 1 month)
  - Delusions
  - Hallucinations
  - Disorganized speech
  - Grossly disorganized or catatonic behavior
  - Negative symptoms

Must have at least one of these three symptoms

Schizophrenia: Symptoms

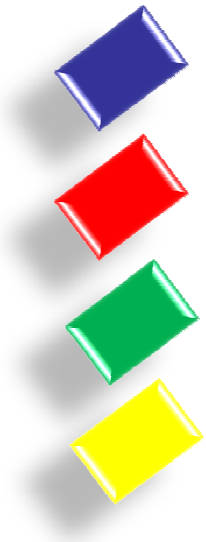
Positive	Negative	Cognitive
Hallucinations	Blunted/Flat Affect	Poor executive function
Delusions	Social Withdrawal (passive-apathetic)	Impaired attention
Paranoia/Suspiciousness	Lack of personal hygiene	Impaired working memory (fail to learn from mistakes)
Conceptual Disorganization	Prolonged time to respond	

Antipsychotics

- 2 classes
  - Typical antipsychotics (first generation antipsychotics, FGA)
    - e.g. Chlorpromazine, haloperidol
  - Atypical antipsychotics (second generation antipsychotics, SGA)
- Controversies
  - Are SGAs more effective than FGAs against negative symptoms?
  - Is the side effect profile of SGAs more favorable than FGAs?

Antipsychotic Choice

Despite therapeutic trials with haloperidol and quetiapine, LX continues to be socially withdrawn and unable to care for herself. She also has terrifying hallucinations. Which antipsychotic would be most appropriate to consider at this time?



A. Aripiprazole

B. Clozapine

C. Haloperidol

D. Perphenazine

Antipsychotic Choice

A. Aripiprazole

SGA; might help negative symptoms, but not agent of choice for treatment resistant schizophrenia.

B. Clozapine

Agent of choice for treatment-resistant schizophrenia.

C. Perphenazine

FGA; might have efficacy against positive symptoms, effects on negative symptoms may be less.

D. Risperidone

SGA; also not agent of choice for treatment-resistant schizophrenia.

Extrapyramidal Symptoms

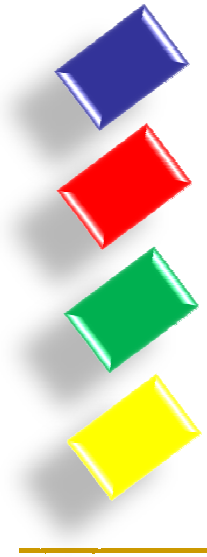
- More common with FGAs
- Acute Dystonias-FGAs
  - Spontaneous, prolonged tonus: Oculogyric crisis, torticollis, laryngospasm, opisthotonos
  - Acutely treated with anticholinergics
  - NO advantage to “loading” antipsychotics
- Pseudo-Parkinsonism
  - Cogwheel rigidity, tremor, bradykinesia, rigidity
  - Anticholinergics (benztropine, diphenhydramine, trihexylphenidyl) and/or switch agents

Extrapyramidal Symptoms

- Tardive dyskinesia-FGAs
  - Abnormal involuntary movements
  - Delayed development after starting antipsychotics
  - Occurs significantly more in FGAs, low to nonexistent in SGAs (depending on agent)
  - MAY be reversible if discovered early
- Akathisia-also occurs with SGAs (aripiprazole)
  - Somatic restlessness and inability to stay still
  - Lipophilic beta blockers are the treatment of choice (e.g. propranolol)
  - Rate lowest with quetiapine

EPS Symptoms

K.C. has been stable on low dose haloperidol for 5 years. She has developed involuntary chewing motions of her mouth and eyebrow lifting. She is concerned and would like to do something about it. Which is the most appropriate?



A. Give benztropine.

B. Increase haloperidol.

C. Start propranolol.

D. Switch to quetiapine.

EPS Symptoms

A. Give benztropine.

Anticholinergics are ineffective against tardive dyskinesia.

B. Increase haloperidol.

This may make symptoms disappear temporarily, but they will return and amplify.

C. Start propranolol.

First line for akathisia.

D. Switch to quetiapine.

Switching to an SGA should help decrease symptoms, and quetiapine has a low incidence.

SGAs: Metabolic Syndrome

- SGAs are low in EPS, but have their own drawbacks…
- Diabetes, Dyslipidemia
  - Highest with clozapine, olanzapine
- Weight Gain
  - Highest in clozapine, olanzapine
  - Moderate with quetiapine, iloperidone
  - Low with most others (aripiprazole, lurasidone, ziprasidone, asenapine, paliperidone)

SGAs: Sedation

High	Low
Clozapine Olanzapine Quetiapine	Aripiprazole Asenapine Iloperidone Lurasidone (Moderate) Paliperidone Risperidone Ziprasidone

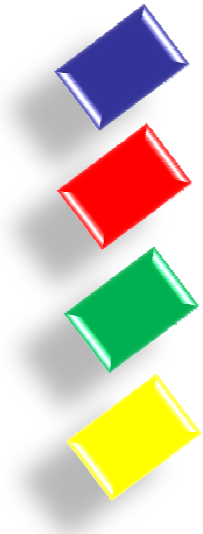
SGAs: Distinguishing Factors

- Ziprasidone: QTc prolongation
  - Iloperidone
  - FGAs-thioridazine
- Risperidone: EPS, Hyperprolactinemia
  - Particularly >6 mg/day
- Clozapine: agranulocytosis, seizures
- Aripiprazole, asenapine, lurasidone: akathisia
  - Asenapine, lurasidone associated with pseudo-Parkinsonism

Antipsychotic Choice

GH is a 32 yo man with schizophrenia and diabetes who is intolerant of his haloperidol due to gynecomastia and impotence. He has long QT syndrome and h/o akathisia on asenapine.

Which is the most appropriate?



A. Aripiprazole.

B. Quetiapine.

C. Risperidone.

D. Ziprasidone.

Antipsychotic Choice

A. Aripiprazole.

Has a high incidence of akathisia.

B. Quetiapine.

Some risk of weight gain, but not associated with hyperprolactinemia, akathisia or prolonged QT interval.

C. Risperidone.

High incidence of hyperprolactinemia.

D. Ziprasidone.

Can prolong the QTc.

Overview

- Depression
- Bipolar Disorder
- Schizophrenia
- Anxiety Disorders
- Insomnia
- Substance Abuse

Anxiety Disorders: DSM-V Classification

- Generalized Anxiety Disorder (GAD)
- Panic Disorder
- Agoraphobia
- Social Anxiety Disorder
- Specific Phobia: nonpharmacologic
- Post-Traumatic Stress Disorder (PTSD)
  - Moved to Trauma- and Stressor-Related Disorders
- Obsessive-Compulsive Disorder (OCD)
  - moved into a new chapter

General Treatment Principles

- Psychotherapy integral to treatment
  - Cognitive behavioral therapy (CBT) has best evidence
- Remission rates low
- Once remission reached, treat for 12 months
  - Varies for specific disorder
  - Most disorders have waxing and waning pattern
- High comorbidity with depression, substance abuse

Anxiety Disorders: DSM-V Classification

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Benzodiazepines in Moderation

- Treat somatic and autonomic symptoms
  - Relief rapid
  - Relieve severe symptoms until antidepressant activity occurs
- Not as effective against cognitive and behavioral symptoms
- Limit use to 2-4 weeks
- Do not discontinue abruptly
- Not effective against PTSD, OCD

Benzodiazepines: Frequently Used

Agent	Half-life (hours)	Dose (mg)
Alprazolam (Xanax)	6–12	0.5
Chlordiazepoxide (Librium)	5–30 (act. met.)	25
Clonazepam (Klonopin)	20–50	0.5
Diazepam (Valium)	20–100 (act. met.)	10
Lorazepam (Ativan)	10–18	1

Antidepressants: First Line

- SSRIs
  - Panic DO: responds to all SSRIs
  - Paroxetine: wide spectrum (all diagnoses)
  - Sertraline: wide spectrum (all diagnoses)
  - Spectrum narrower for fluoxetine, citalopram and escitalopram
- Selected SNRIs
  - Venlafaxine (all anxiety disorders, PTSD, not OCD)
  - Duloxetine (GAD)
- TCAs: efficacious, not first line
  - Side effect profile

Antidepressants: First Line

- At initiation
  - Increased sensitivity to serotonergic effects
  - Particularly in GAD and panic disorder
  - Start with ¼- ½ antidepressant dose
- Takes 2-4 weeks to see effects
- Therapeutic trial: 4-6 weeks
  - Longer for Social Anxiety Disorder

Buspirone

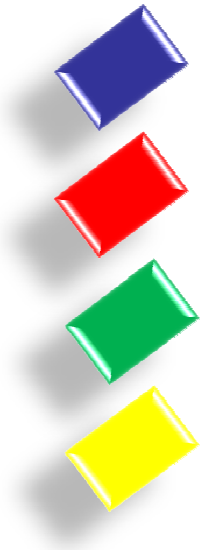
- Nonbenzodiazepine:5-HT_{1A} partial agonist
- Not for acute treatment-Takes 2-4 weeks
- Effective only against GAD
- Improves cognitive and behavioral symptoms before somatic and autonomic
- Not effective for comorbid depression

Pregabalin

- GABA analog, but no effect on GABA receptors
  - Bind to the voltage gated CA+ channel
  - Decreases release of glutamate
- Considered 1st or 2nd line therapy for GAD, depending on guidelines
- Reserve for use after antidepressants
- Comparable to venlafaxine, benzodiazepines

Panic Disorder

- A.X. is a 32-year-old woman with newly diagnosed panic disorder. She currently takes tamoxifen and propranolol. Which medication would be most appropriate to initiate for maintenance therapy?



A. Buspirone.

B. Clonazepam.

C. Fluoxetine.

D. Venlafaxine.

Panic Disorder

A. Buspirone.

Effective only for GAD.

B. Clonazepam.

Long term benzodiazepine therapy is not recommended.

C. Fluoxetine.

Interacts with her tamoxifen, decreasing its efficacy.

D. Venlafaxine.

Effective for treating panic disorder. It has both anti-anxiety and antipanic effects.

Anxiety Disorders: DSM-V Classification

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  - moved into a new chapter

PTSD: Treatment

- CBT focused on trauma and exposure
- Antidepressants: effective for "numbing" sxs
  - Selected SSRIs (fluoxetine, paroxetine, sertraline)
  - Venlafaxine
  - Mirtazapine and TCAs also used, but not 1st line
- Augmentation:
  - Prazosin: nightmares and sleep disturbances
  - Lamotrigine: impulsive anger
  - Atypical Antipsychotics
    - Intrusive thoughts
    - Hypervigilence
    - Psychosis

Treatment of PTSD

C.P. is a recent Iraq war veteran who is taking paroxetine for his major depression and PTSD. He still has a “short fuse” and reacts quickly by yelling when he doesn’t mean to. Which adjunctive medication is most appropriate in this patient?

A. Buspirone.

B. Clonazepam.

C. Lamotrigine.

D. Risperidone.

Treatment of PTSD

A. Citalopram.

Useful for the “numbing” or negative emotions and emotional withdrawal associated with PTSD.

B. Clonazepam.

Benzodiazepines are not efficacious for PTSD, and carry a high risk for dependence.

C. Lamotrigine.

Anticonvulsants can be effective against impulsive anger.

D. Risperidone.

SGAs are more effective against psychotic sxs.

New Case; 1-584

Anxiety Disorders: DSM-V Classification

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OCD: Treatment

- CBT is the cornerstone of therapy
- Serotonergic reuptake activity appears necessary for efficacy
  - SSRIs (fluoxetine, fluvoxamine, paroxetine, sertraline)
  - Clomipramine
  - High doses often needed
- Response is often slow and partial
- Adjunctive antipsychotic therapy can be considered after unsuccessful trials with 3 different antidepressants, including clomipramine

Treatment of Obsessive-Compulsive Disorder

C.D. has both depression and obsessive-compulsive disorder (OCD). What agent treats both conditions?

A. Citalopram

B. Clomipramine

C. Fluoxetine

D. Venlafaxine

New Case; 1-583

Treatment of OCD

A. Citalopram.

Effective for depression, but not OCD.

B. Clomipramine

Effective for OCD, but not depression.

C. Fluoxetine

Effective for both depression and OCD.

D. Venlafaxine

Effective for depression, but not OCD.

Overview

- Depression
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Benzodiazepines

Drug	Half-Life (hours)	Duration
Triazolam	2-6	Short
Temazepam	8-20	Intermediate
Estazolam	8-24	Intermediate
Flurazepam	48-120	Long
Quazepam	48-120	Long

- Tolerance
- Dependence
- “Hangover effect”
- Rebound effect
- Anterograde amnesia

FDA-Approved Nonbenzodiazepines

- "Z" Drugs: $GABA_A$ Receptor Agonist
  - Eszopiclone
  - Zaleplon
  - Zolpidem
- Orexin receptor antagonist: Suroxevant
- Tricyclic antidepressant: Doxepin
- Melatonin receptor agonist: Ramelteon

$GABA_A$ Receptor Agonists

- Abnormal thinking and complex behavior
  - Hallucinations
  - Phone calls
  - Sleep-eating, sleep-driving
- Eszopiclone: Multiple effects on sleep
  - Decreases sleep latency
  - Decreases wake time after falling asleep
  - Decreases number of awakenings
  - Increases sleep time and sleep quality
- Zaleplon: short half-life

Zolpidem

- New dosing recommendations due to next-morning impairment

Dosage Form	Name	Dosing (Daily) Women	Men
Delayed release tablet	Ambien CR®	6.25 mg	6.25-12.5 mg
Immediate release tablet	Ambien®, generic	5 mg	5-10 mg
Oral Spray	Zolpmist®	5 mg	5-10 mg
Sublingual tablet	Edluar®, Intermezzo®*	5 mg 1.75 mg	10 mg 1.75-3.5 mg

*Only take if ≥ 4 hours of sleep remain

Ramelteon

- Melatonin analog
- Helps regulate circadian rhythm
- May help patients with blindness
- Half-life=2-5 hours

Suvorexant: Orexin Receptor Antagonist

- Approved August 2014
- Orexin promotes wakefulness
- Decreased sleep latency
- Promotes sleep maintenance
- Metabolized by 3A4

Choose Agent Based Upon Sleep Disturbance

- Delayed sleep onset
- Poor sleep maintenance
- Short term vs. chronic

Agent Classification

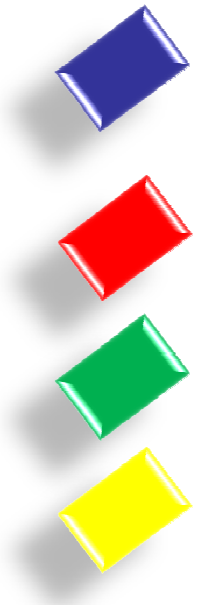
Agent	Sleep Onset	Sleep Maintenance	Chronic Therapy
Doxepin		X	
Eszopiclone	X	X	X
Ramelteon	X		X
Suroxevant	X	X	
Zaleplon	X		
Zolpidem	X	X (CR only)	

Miscellaneous Agents

- OTC antihistamines (diphenhydramine, doxylamine)
  - Tolerance builds rapidly
  - hangover effect
- Trazodone (unlabeled): 25-100 mg
- TCAs (amitriptyline)
- Melatonin
- Mirtazapine (unlabeled)

Sedative-Hypnotic Choice

- C.D. is a 38-year-old kindergarten who has difficulty staying asleep. She awakens after 2 hours and can't sleep for several hours. She took diphenhydramine once, but had to miss work due to hangover effect. Which medication used for insomnia is most appropriate to recommend for C.D.?



A. Eszopiclone

B. Trazodone

C. Temazepam

D. Zaleplon

Sedative-Hypnotic Choices

A. Eszopiclone

Will help her sleep through the night.

B. Trazodone

Not indicated for insomnia. May also give hangover effect.

C. Temazepam

Benzodiazepines are not preferred treatment. It might also cause hangover effect.

D. Zaleplon

The short half-life will not help sleep maintenance.

Overview

- Depression
- Bipolar Disorder
- Schizophrenia
- Anxiety Disorders
- Insomnia
- Substance Abuse

Benzodiazepines

- Alcohol Withdrawal: Standard of Care
- Most effective agent for seizures
- Long-Acting: Patients at Risk for Seizures
  - Chlordiazepoxide: “Gold Standard” (PO/IV)
    - Not more effective
  - Diazepam: used in loading dose protocols (PO/IV)
- Short-Acting: for liver disease
  - Lorazepam: no active metabolites; PO/IV/IM

Acute Alcohol Detoxification

L.M. is a 50-year-old patient admitted to the medical unit because he stopped drinking 3 days ago and is now experiencing delirium tremens. He has cirrhosis.

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

A. Chlordiazepoxide.

B. Clonazepam.

C. Diazepam.

D. Lorazepam.

Acute Alcohol Detoxification

A. Chlordiazepoxide.

Long acting, hepatically metabolized.

B. Clonazepam.

Not used to alcohol withdrawal, only available PO.

C. Diazepam.

Long acting, hepatically metabolized.

D. Lorazepam.

Short acting, not hepatically metabolized.

Chronic Treatment-3 Agents

- Disulfiram:
  - Adherence critical
  - Contraindicated with liver disease (hepatotoxicity)
- Naltrexone
  - Opioid free
  - Dose dependent hepatotoxicity
- Acamprosate
  - Renally eliminated; don't use if CrCL < 30 mL/min
  - Dosed tid

Alcohol Abstinence

L.M. is being transferred to a substance abuse unit.

Which medication is best to treat his alcohol dependence?

A. Acamprosate

B. Diazepam

C. Disulfiram

D. Naltrexone

Alcohol Abstinence

A. Acamprosate

Renally eliminated.

B. Diazepam

Used in acute withdrawal only.

C. Disulfiram

Hepatically metabolized, hepatotoxic.

D. Naltrexone

Hepatically metabolized, hepatotoxic.

Opioid Dependence

- Refer to chapter

Smoking Cessation

- 3 Broad classes
  - Nicotine Replacement
  - Bupropion
  - Varenicline

Nicotine Replacement

- Advantage: Multiple Formulations
- Patch: Can be combined with PRN forms
- PRN formulations:
  - Gum: park and chew
  - Inhaler: no eating within 15 minutes
  - Lozenge: dissolve in mouth
  - Nasal Spray: not for reactive airway disease
- Can use nicotine replacement therapy with stable heart disease

Bupropion

- SR formulation used
- Start 7 days prior to quitting
- Treat for minimum of 8 weeks, up to 6 months
- Same contraindications and cautions as for depression

Varenicline

- Start 1 week prior to quit date
- Patients can smoke up to 35 days afterward
- Use for a minimum of 12 weeks; can continue for additional 12 weeks.
- Neuropsychiatric symptoms
- Combining with NRT increases side effects
- Can combine with bupropion
- Caution with heart disease, CrCL <30 mL/min

Smoking Cessation

PF is a 54 yo man wants to quit smoking. His PMH includes asthma, CAD s/p 3 v CABG (5 years ago) and CrCl 28 mL/min.

Which medication is best?

A. Bupropion
B. Nicotine Nasal Spray
C. Nicotine Patch
D. Varenicline

New Case; 1-595 to 1-596

Smoking Cessation Case

A. Bupropion

Not contraindicated for either heart disease nor renal insufficiency.

B. Nicotine Nasal Spray

Not recommended for use with asthma.

C. Nicotine Patch

Reasonable alternative in a patient with stable heart disease

D. Varenicline

Use cautiously with heart disease and renal insufficiency

New Case; 1-595 to 1-596

Questions?