Psychopharmacology Update

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Psychopharmacology Update
- Treatment of Depression
  - New thoughts on treatment of depression
  - Depression and comorbidities
  - Depression in children
- Treatment of Psychosis
  - New developments in treatment
  - Use of antipsychotics in children
- Treatment of ADD/ADHD
  - Monitoring for abuse of stimulants
- Treatment of Anxiety and Sleep Disorders
- Treatment of Bipolar Affective Disorder
- Treatment of Dementia

What’s New
- A push for new drugs
- WHY?
  - Mostly because of patient intolerance
  - Maybe due to lack of efficacy
  - Can we develop anything stronger?
  - A few niche markets have cropped up
  - THE MARKET

Antidepressants
- For years, the question dictating drug development has been: How can we reduce side effects of these drugs to enhance compliance?
  - Subtext: To write more prescriptions?
- Not: DO WE HAVE EVIDENCE THAT THEY ARE REALLY WORKING TO RELIEVE DEPRESSION?
  - This can lead one to look to the wrong kind of evidence to guide practice.

Depression
- The most common psychiatric disorder
- One in 5 individuals with major depression receives adequate treatment.
  - Much lower in African Americans and Mexican Americans
- At least half of the antidepressants prescribed in the US are for people who do NOT meet the criteria for depression.

Do Antidepressants Work?
- New studies seem to indicate...maybe?
- 13 to 14 million Americans suffer from clinical depression/year.
- At least 32 million will have an episode at some point in their life.
- 57% of those affected seek treatment and are helped by medication.
- These drugs seem to work the best in very severe depression.
Drugs for Depression

- Controversial—are we over-treating? Under-treating?
- Do these drugs even work?
- How much of efficacy is related to a placebo effect?

Do Antidepressants Work?

- New data indicate that antidepressants are no better than placebo in mild to moderate depression.
  - Psychotherapy is the best treatment here.
  - But... for most patients, help is sought from a primary care provider, or insurance may not cover therapy, or they may not have access to counseling.
  - Should they at least try an antidepressant?

A Little History About SSRIs

- Does Serotonin enhance mood?
- Evidence from a SINGLE study with an obsolete agent suggested that elevations of serotonin and NE in the synapse were associated with reversal of depression.
  - This study was small and done in the 1950s.

Based on this Evidence...

- The class of SSRIs was built.
  - Even though subsequent studies proved that high doses of drugs that raise serotonin in the synapses of depressed patients showed NO enhancement of mood
  - And a new drug that is as effective as Prozac against depression works by lowering serotonin levels in the synapse.

Classifications of Antidepressants

- SSRIs
  - Citalopram (Celexa)
  - Escitalopram (Lexapro)
  - Fluoxetine (Prozac)
  - Paroxetine (Paxil)
  - Sertraline (Zoloft)
- SNRIs
  - Desvenlafaxine (Pristiq)
  - Duloxetine (Cymbalta)
  - Venlafaxine (Effexor)

Classifications of Antidepressants

- MAOIs
  - Phenelzine (Nardil)
  - Selegiline (Eldepryl)
  - Tranylcypromine (Parnate)
- Atypical +SSRI
  - Olanzapine + Fluoxetine (Symbyax)
- Atypical Antipsychotics
  - Aripiprazole (Abilify)
  - Olanzapine (Zyprexa)
Classifications of Antidepressants

- **Tetracyclic Antidepressants**
  - Mirtazapine (Remeron)
- **Tricyclic Antidepressants**
  - Amitriptyline (Elavil)
  - Desipramine (Norpramin)
  - Imipramine (Tofranil)
  - Nortriptyline (Pamelor)
  - Protriptyline (Vivactil)
  - Trimipramine (Surmontil)

- **Bupropion (Wellbutrin)**
- **Nefazodone (Serzone)**
- **Trazodone**

Antidepressant Therapy by Subtype

- **Catatonic**: ECT
- **Melancholic**: TCAs, bupropion, mirtazapine, and trazodone
- **Atypical**: SSRIs, T3, modafinil, and atomoxetine
- **Seasonal**: Phototherapy, SSRIs
- **Hormonal**: SSRIs, estrogens, Omega-3 FAs
- **Bipolar**: Lithium, antipsychotics, anticonvulsants, pindolol, pramipexole, and buspirone

Antidepressant Therapy by Symptom

- **Insomnia**: Mirtazapine, bupropion
- **Hypersomnia**: Bupropion, modafinil, T3, methylphenidate
- **Decreased appetite**: Mirtazapine
- **Hyperphagia**: Atomoxetine

So How Do I Treat…?

- Comorbidities associated with depression

Anxiety

- MAOIs should be considered, especially in the patient who does not respond to SSRIs.
  - Remember dietary and drug interactions
- Mirtazapine, trazodone, or buspirone
- Maybe a touch of Ativan
ADHD
- Sustained release bupropion may be a benefit
- Consider expense though…30 pills/$100

Sexual Dysfunction Secondary to SSRI Use
- Bupropion
- Buspirone
- Mirtazapine
- Cyproheptadine
- Yohimbine
- Nefazodone
- Or switch antidepressants…

Chronic Pain
- Duloxetine (Cymbalta)
- Venlafaxine (Effexor)
- Milnacipran (Savella)—recently approved to treat fibromyalgia; approved to treat depression outside the US

Obsessive-Compulsive Disorder
- High-dose SSRIs
- Antipsychotics
  - Risperidone
  - Haloperidol

New Indications for Antidepressants
- Fluoxetine for bipolar, PMDD
- Paroxetine for PMDD
- Olanzapine/fluoxetine (Symbyax) for bipolar, treatment-resistant depression

Other Treatments for Depression
- Second generation antipsychotics
  - Risperidone, aripiprazole, and quetiapine
- Lithium
  - May augment SSRIs and prevent relapse
- Stimulants
  - May be efficacious in the elderly (Methylphenidate + citalopram)
**Other Treatments…Maybe**

- Pindolol
  - For bipolar, yes. Unipolar—maybe early treatment (first 4 weeks)
- Omega-3 fatty acids
  - For bipolar, post-partum—maybe
- Pramipexole (Mirapex)
  - Dopamine agonist
- Non-Drug TX: Stimulation, exercise, and PSYCHOTHERAPY

**Considerations for Prescribing Antidepressants**

- Observe patient for worsening symptoms or suicidality
- Do not discontinue antidepressants abruptly
- Watch changing drug regimens—when drugs are added or subtracted
- The “efficacy” of antidepressants may be why patients require two, three or even four drugs before they find one that works for them.

**Something to Watch…**

- Infusions of Ketamine to treat depression in treatment-resistant patients
  - Caused dissociation for about 90 minutes, but relieved depression for 24 hours
  - Patients get 3 treatments/week

**Treatment of Depression in Children**

- Pharmacologic Strategies
  - In 2004, FDA called for Black Box warning on antidepressants for increased suicidal thoughts/tendencies especially in adolescent populations.
  - Many of the drugs used in this age group were not approved for use.
  - Mood improvement may take a month, but sense of hopelessness/suicidal thoughts may occur within days of treatment.

**Antidepressants for Pediatric Use**

- How many are approved?

**Antidepressants for Pediatric Use**

- Fluoxetine (Prozac) and Escitalopram (Lexapro)
- Prozac starting dose 10 mg/day, max dose 60 mg/day
- Lexapro dose is 10 mg/day
- Side effects (SE) include nausea, anorexia, headaches, insomnia, anxiety; is a major inhibitor of certain liver enzymes
- Follow-up!
**Antidepressants for Pediatric Use**
- But other drugs are used, right?
  - The use of sertraline, citalopram, and fluvoxamine is considered off-label. Paroxetine is not indicated in children because of increased suicidal thoughts; may be used for obsessive-compulsive disorder.
  - Start with lowest dose possible!
  - Gastrointestinal side effects, insomnia, and anxiety are especially worrisome.
  - TCAs and MAOIs: Use with caution; use is considered unlabeled.

**How Long Should Therapy Last?**
- Within the first year of therapy, consider withdrawing the patient
  - If relapse is imminent….restart!

**New Depression Data**
- In 2010, patients with mild, moderate, or severe depression showed no significant improvement in depression symptoms due to antidepressants over patients receiving placebo.
  - Only patients with very severe symptoms showed benefit
  - This accounts for 13% of people with depression

**New Depression Data**
- The “chemical imbalance” theory has no direct evidence to support it. Elevating or lowering serotonin levels does not affect mood.
  - Why do patients get ‘better’ on higher doses or switched drugs? When matched with placebos, there was no significant difference. Patients expected to get better.
  - Is that the greater good?

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**Antipsychotics**
- First generation: Effective against the positive symptoms of schizophrenia; sometimes used to manage mania in BPAD, Tourette’s, NV, dementia, Huntington’s chorea
  - Cause a variety of side effects, most notably extrapyramidal
    - Acute dystonia (hours to five days)
    - Parkinsonism (five to 30 days)
    - Akathisia (five to 60 days)
    - Tardive dyskinesias (months to years)
    - Tardive dyskinesia (Months to years)
Antipsychotics

Here, the evidence was fairly good that the drugs we had relieved the signs and symptoms of psychosis.
- First-generation antipsychotics (FGA) were effective but...
- Side effects were limiting.
- The push was for newer drugs with broader coverage of symptoms and a better side effect profile.

Other SE Seen With the FGAs

- Prolactin release
- Weight gain
- Sedation
- Dry mouth, urinary retention, constipation, blurred vision, tachycardia
- Orthostatic hypotension

Positive and Negative Symptoms of Schizophrenia

- Positive: Hallucinations, delusions, disordered thinking and speech, combative, agitation, aggression, paranoia
- Negative: Social and emotional withdrawal, low affect, poor judgment and insight, decreased verbal interaction, poor self-care

First-Generation Antipsychotics

- Chlorpromazine (Thorazine)
- Thioridazine (Mellaril)
- Loxapine (Loxitane)
- Molindone (Moban)
- Perphenazine
- Trifluoperazine
- Thiothixene (Navane)
- Fluphenazine (Prolixin)
- Haloperidol (Haldol)
- Pimozide (Orap)

Antipsychotics

- FGAs range in potency
  - Low-potency—chlorpromazine (Thorazine)
  - Medium-potency—molindone (Moban)
  - High-potency—haloperidol (Haldol)
- High-potency agents actually cause fewer side effects overall, and are preferred for initial therapy.
- Some even approved for young children.

Drugs for Psychosis

- What’s new: Expanding antipsychotic drug use in young people
  - For schizophrenia, bipolar, autism
- Approved drugs are aripiprazole, olanzapine, quetiapine, risperidone for bipolar mania and schizophrenia.
- Aripiprazole and risperidone are approved for aggression associated with autism.
**Second Generation Antipsychotics**
- Clozapine (Clozaril, FazaClo)
- Olanzepine (Zyprexa)
- Risperidone (Risperdal)
- Paliperidone (Invega)
- Quetiapine (Seroquel)
- Ziprasodone (Geodon)
- Aripiprazole (Abilify)

**Antipsychotics**
- Clozapine is the most effective drug for schizophrenia but it can cause agranulocytosis.
- All SGAs cause SE including metabolic effects (weight gain, dyslipidemia, diabetes), and some can cause seizures and anticholinergic effects.
- Extrapyramidal symptoms (EPS) are far less, however…

**SE of Antipsychotics in Children**
- Greater incidence than seen in adults
- Sedation
- EPS (except for akathisia)
- Withdrawal dyskinesia
- Prolactin elevation
- Weight gain and metabolic abnormalities
  - Dyslipidemia

**How Much Weight Do Kids Gain?**
- After 10.8 weeks…
  - Olanzapine—18.7 lbs
  - Quetiapine—13.4 lbs
  - Risperidone—11.7 lbs
  - Aripiprazole—9.7 lbs
- Lipids, glucose, and insulin were variously affected as well depending on agent
- Must weigh benefit versus cardiometabolic risks

**Percentage of Obese Children**

**How to Choose an Antipsychotic**
- Like anything else! Look at:
  - Does it work?
  - Can your patient afford it?
  - Will your patient tolerate it?
- SGAs prescribed 10X more than FGAs
How to Choose an Antipsychotic

• But looking at the evidence…
  ◦ SGAs are no more effective than many FGAs (except for Clozapine)
  ◦ SGAs do cause fewer EPS but cause dangerous metabolic effects
  ◦ FGAs are much cheaper than SGAs
    • Haldol $50/year
    • Risperidone $2000/year
    • Clozapine $4000/year

Consider patient history:
  ◦ If positive for diabetes, heart disease or dyslipidemia, consider an FGA
    • Aripiprazole and Ziprasidone also have lower incidence of metabolic effects
  ◦ If treatment resistant, consider Clozapine
  ◦ Consider cost
  ◦ Consider compliance and depot formulations

Antipsychotics—Other News

• Long-acting olanzapine
  ◦ Given as an IM injection
  ◦ Works for 2-4 weeks
  ◦ Problems with use: sedation/delirium syndrome after injection, weight gain
  ◦ Benefits with use: increased compliance, steady drug levels

Other New(er) Antipsychotics

• Paliperidone (Invega Sustenna): Injected once monthly for the treatment of acute and chronic schizophrenia in adults
  • Risperidone (Risperdal Consta): Overlap with risperidone, then give by IM injection every two weeks

New Antipsychotics

• Iloperidone (Fanapt): Atypical for the treatment of acute schizophrenia. Antagonist at D2, D3, 5HT2A and some NE sites.
  ◦ Causes hypotension, priapism and other SE related to blockage of the NE site.
• Asenapine (Saphris): Atypical for treatment of acute schizophrenia and manic episodes associated with bipolar disorder. Blocks D2 and 5HT2A receptors.

Antipsychotics—Other News

• Inhaled loxapine (Loxitane)
  ◦ Used for agitation in patients with schizophrenia or bipolar disorder
  ◦ Fast-acting—effects were seen within 10 minutes and lasted as long as 24 hours.
  ◦ Patients could take another dose within 2 h if needed
  ◦ Less traumatic than an injection!
Antipsychotic Data
- Old drugs have EPS as side effects that patients do not tolerate well.
- But the metabolic SE of new drugs—especially in children—may be more dangerous.
  - Insulin, metformin, and lifestyle changes must be encouraged to deal with these.

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What are Prescription Stimulants?
- A class of drugs that enhance brain activity.
- Prescription stimulants were used historically to treat asthma, obesity, neurological disorders, and a variety of other ailments, before their potential for abuse and addiction became apparent.

ADHD and Stimulants
- Most common neuropsychiatric syndrome in children
  - > 2 million children affected in US
  - Incidence in boys is 2-3 x that in girls
  - Usually symptoms appear between ages 3-7
  - Symptoms may persist into adolescence and adulthood
- Ritalin in most-prescribed drug

What are the Effects of Stimulants?
- Stimulants increase the amount of norepinephrine and dopamine in the brain, which increases breathing, blood glucose, blood pressure, heart rate, and constricts blood vessels. Effects can feel like increased alertness, attention, and energy along with a sense of euphoria.

Usually Prescribed For...
- Narcolepsy
- Attention-deficit hyperactivity disorder (ADHD) – hyperactivity, impulsivity, inability to concentrate
- Depression that does not respond to other treatment
Effects in the Body

- Stimulants enhance brain activity, causing an increase in alertness, attention, and energy.
- As a result, the drugs are prescribed for use first thing in the morning. In abuse, stimulants may be used to offset sleepiness late in the day.

In Normal Use....

- The normal user of stimulants should take these drugs once a day.
- Drug holidays are encouraged.
  - Weekends
  - School holidays
  - Spring break, Christmas, and summer vacation
- Regular assessment should be done to determine if continued use is necessary.

Effects of Short-Term Use

- Elevated blood pressure
- Increased heart rate
- Increased respiration
- Suppressed appetite
- Sleep deprivation
- A “wearing off” effect as short-term drugs stop working. This can be lessened with caffeine (Mountain Dew, coffee, energy drink).

Effects of Long-Term Use

- Potential for physical dependence and addiction
- Stimulants have many “desirable” gains…increased alertness, attention, weight loss.
- Euphoric feelings are most intense when the user snorts or injects the drug.
- Increased risk for cardiovascular effects, seizures, paranoia, hostility, agitation

A Brief History...

- Attention deficit hyperactivity disorder (ADHD) was once called “minimal brain dysfunction” before the DSM renamed it.
  - ADD vs. ADHD
- Ritalin was a drug looking for a disorder.
- Guess which nation consumes 85% of the world’s Ritalin?

Who Takes the Most Ritalin?
Ritalin Use Through the Ages

Federal Classification and Penalties

- Many stimulants are Schedule II
  - Schedule II drugs must have a written prescription to be refilled
  - One-month supply only
  - Class A felony for illicit trading in these drugs
- Strattera is an exception—it is a non-controlled substance.

Ritalin as a Drug of Abuse

- Ritalin prescriptions have increased 1000% over the past decade.
- Ritalin is the most stolen controlled substance in the US.
- Permanent lung damage can result from injected Ritalin.
- Loss of nasal cartilage and nose bleeds are seen with snorted Ritalin.

Ritalin in the Schoolyard

- Sold for about $10 per pill
- Usually crushed and snorted to give a high like cocaine
- Sometimes called “kiddie cocaine”
- Kids can “cheek” the medicine if given at home to snort it or sell it later.
- When coming down from the drug, agitation, depression, mood swings may be seen.

Snorting Ritalin

Stimulants

- Dextroamphetamine (Dexedrine, Dextro Stat)
- Methylphenidate (Ritalin, Metadate, Methylin and Concerta, Daytrana)
- Dexamphetamine (Focalin)
- Amphetamine mixture (Adderall)
- Lisdexamfetamine (Vyvanse)
- Note: Atomoxetine (Strattera) is a non-stimulant; its abuse potential is lower because results take about a week to be seen.
Drugs and Duration

- Ritalin, methylin: Three to five hours
- Ritalin SR, metadate ER, methylphenidate ER: Six to eight hours
- Concerta, metadate CD, Ritalin LA: Up to 14 hours
- Focalin: Four to five hours
- Focalin XR: Up to 12 hours
- Dexedrine, DextroStat: Four to six hours
- Dexedrine Spansules: Six to 10 hours
- Adderall: Four to six hours
- Adderall XR: 10 to 12 hours
- Vyvanse: 10 to 12 hours
- Strattera: 24 hours

Potential Side Effects

- Dangerously high body temperature or an irregular heartbeat after taking high doses
- Cardiovascular failure or lethal seizures
- For some stimulants, hostility or feelings of paranoia after taking high doses repeatedly over a short period of time.

Drug Interactions With Stimulants

- Over the counter (OTC) decongestant medications (Sudafed, Phenylephrine)—high BP, irregular HR
- Antidepressants, unless supervised by a physician (Nardil, Prozac, Paxil)—psychosis, high HR
- Some asthma medications (Proventil)—high HR
- Any drug that raises blood pressure is a dangerous combination (energy drinks??).
- Any drug that affects mood should be assessed (alcohol!).

Ritalin

- Methylphenidate: JIF, MPH, Skippy, the smart drug, vitamin R, kiddie cocaine
- Injected, swallowed, or snorted
- May cause an increase or decrease in blood pressure, psychotic episodes, digestive problems, weight loss, loss of appetite.

Judicious Prescribing of Stimulants

- Goal is to increase attention span, decrease impulsivity, hyperactivity, distractibility. Most children do well for two to three years on stimulants, then the drugs have little benefit.
- This may be enough time for child to learn strategies for dealing with impulse/hyperactivity issues.
- Cognitive therapy plus stimulants appears to be the most helpful.
- Assess!

Guanfacine in ADHD

- Guanfacine (Intuniv) was recently approved for use in ADHD.
- Extended release alpha-adrenergic agonist that works in the CNS on the alpha-2 receptor.
  - Approved for children six and up
  - Start with 1 mg daily
  - Do not use with other antihypertensives, monitor heart rate and BP. May cause sedation, dizziness, somnolence, and bradycardia.
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**Benzodiazepines Used for Anxiety**
- Alprazolam (Xanax, Niravam)
- Chlordiazepoxide (Librium)
- Clonazepam (Klonopin)
- Clorazepate (Tranxene)
- Diazepam (Valium)
- Lorazepam (Ativan)
- Oxazepam (Serax)

**Benzodiazepines**
- Have a high therapeutic index
- May cause dependence
  - Withdrawal may include anxiety, sweating, insomnia, tremors, panic, dizziness, paranoia, delirium, seizures.
  - Discontinue gradually over several weeks or months

**Benzodiazepines and Panic Disorder**
- Considered second-line (to SSRIs) for panic because of the risk of dependence and because of recurrence of symptoms when discontinued.
- May be combined with an SSRI in initial therapy to give immediate relief, then taper.
- Alprazolam, clonazepam, and lorazepam most often used.

**Considerations of BZD Use**
- Watch other CNS depressants; OD with alcohol may be fatal because of respiratory depression
- Dependence may occur
- Anticholinergic effects
- Many BZDs have active metabolites which prolong effects of drug.

**Drugs for Anxiety and Insomnia**
- This group contained barbiturates, benzodiazepines, and non-benzodiazepines.
  - Barbiturates are too dangerous to use routinely for sleep disorders or to manage anxiety.
- Benzodiazepines may be used for both anxiety and insomnia, though not necessarily interchangeably.
Other BZD Considerations

- Some BZDs cause amnesia with use—this is sometimes desirable clinically.
  - Midazolam (Versed) is an example. It may be used during procedures where patient cooperation is needed.

Other BZD Considerations

- GHB and “Roofies” are modeled after this effect of BZDs and hence have the nickname of “date rape” drugs.
- The antidote for a BZD (or Roofie) overdose is Flumazenil (Romazicon), which reverses the sedative effect of these drugs.

Drugs for Sleep

- Benzodiazepines and non-BZDs
- Benzodiazepines are considered first-line for short-term treatment of insomnia
  - Decrease time-to-sleep, increase duration of sleep, decrease wakings during sleep
  - Best for occasional use due to rebound insomnia when discontinued

Benzodiazepines for Insomnia

- Triazolam (Halcion)
  - Onset 15 to 30 min, short duration
- Flurazepam
  - Onset 30 to 60 min, long duration
- Quazepam (Doral)
  - Onset 20 to 45 min, long duration
- Estazolam
  - Onset 15 to 60, intermediate duration
- Temazepam (Restoril)
  - Onset 45 to 60, intermediate duration

BZD-Like Drugs for Insomnia

- These drugs should be considered first-line drugs for insomnia.
- May be used in pregnancy
- Use should be intermittent
- All are controlled substances except Ramelteon.

BZD-Like Drugs for Insomnia

- Eszopiclone (Lunesta)
  - Onset 30 min, intermediate duration
- Zolpidem (Ambien, Ambien CR)
  - Onset 30 min, short/intermediate duration
- Zaleplon (Sonata)
  - Onset 15-30 min, ultrashort duration
- Ramelteon (Rozerem)—Melatonin agonist
  - Onset 30 min, short duration
Prescribing Drugs for Sleep

- These drugs should be used intermittently, and therapy should be short-term (two to three weeks).
- Check patient’s sleep hygiene
- Dosage escalation may indicate tolerance
  - Avoid this; rather, interrupt therapy so tolerance does not develop
- OTC drugs such as diphenhydramine (Sominex) and doxylamine (Unisom) may be used
  - Tolerance develops within one to two weeks.
- Alternatives such as melatonin and valerian may have some benefit

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Treatment of BPAD

- Mood stabilizers
  - Lithium, valproic acid, carbamazepine
- Antipsychotics
  - Olanzapine, risperidone
- Antidepressants
  - SSRIs, venlafaxine, Wellbutrin
  (always combined with mood stabilizer)

Treatment of BPAD—Drug Selection

- Acute manic episodes: Valproic acid or lithium
  - A BZD may be added to relieve symptoms of insomnia, anxiety, agitation
- Acute depressive episodes: Bupropion or venlafaxine or SSRI + mood stabilizer
- Long-term prevention: Lithium, valproic acid, or a combination of the two

Lithium is a Difficult Drug to Use

- It has interactions with NSAIDs, diuretics, with sodium
- It has a narrow therapeutic index.
  - Below 1.5 mEq/L: NVD, fine tremor
  - 1.5 to 2.0 mEq/L: Coarse tremor, confusion, ECG changes, lack of coordination
  - 2.0 to 2.5 mEq/L: Serious ECG changes, coma, hypotension
  - Above 2.5 mEq/L: Convulsions, death

Other Drugs for BPAD

- Valproic acid (Depakene, Depacon, Depakote, Stavzor) works faster than lithium and is safer.
  - Watch for thrombocytopenia, pancreatitis, liver failure
- Antipsychotics now approved for BPAD include olanzapine, quetiapine, risperidone, aripiprazole, and ziprasidone.
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What Causes Dementia?
- Dementia is due to a decrease in Ach in certain parts of the brain.
- This affects speech, cognition, activities of daily living, and memory.
- Increasing Ach in the brain or decreasing rate of degeneration of Ach-rich neurons are treatment strategies.

Cholinesterase Inhibitors
- These drugs work to increase Ach in the brain by decreasing its rate of breakdown.
- Modest improvements in behavior, cognition, and function are seen.
- These drugs are recommended for all Alzheimer’s patients with mild to moderate disease.

- Cholinesterase Inhibitors
  - Used in patients with mild to moderate symptoms
  - Only 25% to 30% respond
  - These drugs are NOT curative.
  - Cholinergic side effects include gastrointestinal (GI) distress, headache, dizziness, and bronchoconstriction.
  - Doses start low, then increase to tolerance.
  - Donepezil, galantamine, and rivastigmine

- Donepezil (Aricept): Causes GI side effects and bradycardia
- Rivastigmine (Exelon): Causes significant GI SE including weight loss; patch may be better.
- Galantamine (Razadyne): GI SE and bronchoconstriction may be seen.

Memantine (Namenda)
- NMDA receptor antagonist
- This drug modulates the effect of glutamate at NMDA receptors, reducing the destructive effect of this neurotransmitter in the brain.
- This drug is reserved for moderate to severe AD.
Memantine (Namenda)

- Taken PO, this drug is well-tolerated.
- Dizziness, headache, confusion are main SE.
- Dosage starts at 5 mg/day for one week, then builds to 20 mg (10 mg bid) for maintenance.

Other Strategies to Prevent the Progression of AD

- Vitamin E and Selegiline: conclusive studies show little benefit of these
- NSAIDs: taking NSAIDs for 2 years or more decreased risk of developing AD by 80%—however, benefit was NOT seen after symptoms developed.
- Estrogen: does not reduce the risk of AD in older women
- Ginkgo Biloba: may show some promise improving cognitive performance and behavior

Dementia: Summary

- No drug treats the disease—they only slow its progression.
- Drugs are most effective when started early.
- Cholinergic SE are the most common.
  - Drugs with anticholinergic SE may reduce these.
- Memantine is a newer class of drugs for Alzheimer’s which may offer a neuroprotective effect.
- Adjunctive psychiatric drugs may be helpful in managing neuropsychiatric symptoms in these patients.
  - Risperidone (Risperdal) and olanzapine (Zyprexa)

As We Use These Drugs

- Consider the benefit to your patient
- Consider the RISK to your patient
- Consider the alternatives
  - Sometimes that means revisiting older therapeutic choices as well as non-drug choices
- Examine the evidence—does it really “fit” the practice?