

Medication Update

Depression, Anxiety, Insomnia, Agitation, Bipolar Disorder, and ADD

General Principles:

- To consider meds there should be at least moderate impairment in function
- If considering meds also consider and encourage counseling/therapy referral
- This is a limited review and discusses some treatment options
- I tend to favor medications that have been around for awhile (meds advertised as the latest and greatest often turn out not to be)
- Check for substance abuse history and consider treating that first (or concurrently) if it appears primary or is a significant contributor to symptoms
- Ask about potential of pregnancy before initiating meds

Depression:

- Look for symptoms of: decreased mood, energy, and concentration, self denigrating thoughts, lack of enjoyment/pleasure, change in appetite/sleep habits (early morning awakening is a classic sign), hopelessness, suicidal ideation. Symptoms should persist for at least a couple of weeks before prescribing unless this is an early recurrence of the illness.
- **Always check for** a personal or family history of **bipolar disorder/mania** (periods/at least 4 plus days of elevated mood, decreased need for sleep, inflated self-esteem, increased spending/sexual activity/religious preoccupation to the point that it interferes with the ability to function) as that may effect your medication choice (consider mood stabilizer or psychiatric consult). If you give an antidepressant to someone with bipolar disorder (or a predisposition to bipolar disorder) without using a mood stabilizer there is a chance of precipitating a manic episode.
- Types of antidepressants we will discuss: SSRI's, SNRI's, Wellbutrin, Remeron. They all have the same efficacy. Picking an antidepressant is tricky. The two main reasons for picking an antidepressant are: has it worked for the student before or has a close blood relative responded to a specific medication. What side effects are you looking to emphasize or avoid?
- Starting and increasing the dose: Tend to start antidepressants at the lowest therapeutic dose or if worried about side effects, start at half the lowest therapeutic dose. For example the dosage range for Zoloft is 50-200mg/d. You could start at 50 or 25mg/d. If side effects are minimal/tolerable I will increase the dose every 2 weeks by 50mg (25mg if worried re side effects) until there is a response or the student has intolerable side effects. Theoretically it could take 6 weeks to realize the full benefit of a particular dose. However, if you started a

- student on 25mg and increased the dose by 25mg every 6 weeks it would take 10.5 months to get to a full dose of 200mg and perhaps a few more weeks to see if the full dose to work. That is a long time for the student to suffer, and what if the Zoloft doesn't work and you need to consider a 2nd medication trial!
- The two main reasons that antidepressants don't work is they are not tried in a high enough dose or for a long enough period of time (if side effects are tolerated and there is minimal response antidepressants should be pushed to their top dose and kept there for about 4wks – if there is then no response you can confidently eliminate that medication as helpful for that particular student)
 - **When to augment treatment with other medications:**
 - If you are at the maximum dose of an antidepressant for several weeks with no effect, there is no point in augmenting, just taper and discontinue the medication and try something new
 - If you are at the maximum dose for several weeks and there is a partial response that is the time for augmenting (can also consider augmenting when you are at a moderate dose with partial response but can't go higher due to side effects). Tend to add a low dose of an antidepressant from a different class that works with a different neurotransmitter. It doesn't make sense to augment an ssri with another ssri (in fact that would increase the risk of serotonergic syndrome). You could also consider augmentation with a mood stabilizer or an atypical antipsychotic.
 - **When to refer:**
 - Depends on the comfort/experience of the provider
 - Whenever uncomfortable or have a question should at least get a consult
 - Some providers will be comfortable prescribing one trial of an antidepressant
 - Many providers are comfortable with anxiety, insomnia, and depression but would refer for suspicion of bipolar disorder or psychotic symptoms.
 - **Off Terms and Study Abroad:** If students are stable with their illness and on their dose of medication then I am comfortable prescribing for them when they are away from school. I ask them to check in with me if they have any trouble and that they give me an update at least once a month. I am reluctant to initiate an antidepressant or mood stabilizer medication if a student will be leaving in the next week or two as there is not adequate time to see if medication will be helpful and there isn't the opportunity to provide adequate followup.
 - **Frequency of Appointments:** initially I tend to meet with students every 1-2 weeks until there is improvement in symptoms, then I space out meetings depending on symptoms and stability to between 1-3 months.
 - **Length of treatment:** rule of thumb: 12 months for 1st episode, 2 years for 2nd episode, longterm for 3rd episode
 - Antidepressants and **Suicidality:** FDA reports of possible increased suicidality with antidepressants. Likely due to depression and side effect of akathisia (an inner sense of restlessness/"ants in your pants" which has caused side effect of suicidality in other types of meds), important to discuss this possibility with students and document the informed consent. Risk thought to be greatest in the 1st couple of weeks after starting or increasing the dose of antidepressant. 0-100

scale (zero is the depths of depression and 100 is regular happy self), risk of suicide actually highest at 20-30 when student has more energy to take action – likely a factor in why there is also an increased suicide risk when people are discharged from the hospital. While rare we have had students report an increase in impulsivity or suicidality after starting an antidepressant medication.

- **“Prozac Poop Out”**: rarely a dose of an antidepressant that has worked for several months will stop working. This phenomenon has been called prozac poop out. Generally bumping up the dose of the antidepressant will work. Occasionally you will need to change meds. This could be due to the medication working less or a recurrence or worsening of the underlying depression.
- The antidepressant medications discussed here are **relatively safe in overdose** but can interact with alcohol (get drunk quicker and can interfere with the ability of the medication to work)
- Common Medical issues that can look like depression: low thyroid, anemia, mono, lyme disease
- **Walmart \$4 medication list** (\$4 for 30d supply and \$10 for 90d supply without use of insurance. Includes: **Celexa, Prozac, Lithium, Paxil, Trazodone, Prazosin**
- **SSRI's**: (in addition to Major Depression these meds are also used for: GAD, Dysthymia, OCD, Panic Disorder, Bulimia; tend to need higher doses when treating OCD and Bulimia)
 - Tend to be the 1st line of antidepressants, newer meds tend to claim quicker efficacy but I don't think there is much difference. The usual response is within 3-5wks but with all the meds about 20% of students appear to have a significant positive response within 2 wks.
 - Class includes: **Prozac/Fluoxetine** (20-80mg/d), **Zoloft/Sertraline** (50-200mg/d), **Celexa/Citalopram** (20-40mg/d) risk of prolonged QT interval at higher doses, **Lexapro/Escitalopram** (5-20mg/d), and Paxil/Paroxetine (20-60mg/d). I **tend NOT to use Paxil** due to sedation and potential for liver side effects.
 - For students who are very sensitive to side effects you can start with half the lowest dose (ie 10mg/d for prozac). I tend to bump up the dose every couple of weeks if there is little if any response.
 - **Serotonergic Syndrome** (too much serotonin in brain, often from taking 2 SSRI's at same time or switching from prozac/long half life directly to another SSRI): nausea, confusion, hyperthermia, tremor, increased HR/BP, seizures, coma, death. Ask if student already taking St. Johns Wort as it works with serotonin as well
 - **Withdrawal Syndrome** from SSRI's: rare with prozac (due to long half life), flu like symptoms: dizziness, lethargy, nausea, irritability
 - **Side Effects** include: Headaches, upset stomach, nausea, akathisia/anxiety, vivid dreams, night sweats, rare weight gain, increased energy or fatigue, sexual side effects (if asked, 40-60 percent of students will report some sexual side effects – primarily decreased responsiveness/delayed or absent orgasm, partial or incomplete erections, but also some decreased interest). Most side effects lessen in first few

weeks but sexual side effects tend to persist. Often difficult to distinguish between sexual dysfunction due to depression and side effect of medication

- What to do with **Sexual Side Effects**: decrease dose, change med, add wellbutrin (75-300mg), periactin/ciproheptadine 4-8mg po thirty minutes before sexual activity
- Odds and Ends: prozac is long-acting (roughly 7day half-life vs about 1 day for rest of group)
 - I think of **prozac** for students who are: obsessive or have OCD, very forgetful (not a big deal if you forget a dose), sensitive to rejections. Serotonin withdrawal syndrome not a concern with long half-life. It is a hassle if prozac doesn't work and you want to change to another antidepressant that works with serotonin as you have to wait to avoid serotonergic syndrome.
 - **Zoloft**: a tried and true medication
 - **Celexa** and **Lexapro** (Lexapro is just Celexa cut in half, the active, left side). Lexapro is available in generic and is about the same price as Celexa. Lexapro is advertised as having all of the benefits and none of the side effects. I have seen all of the side effects with Lexapro but if I have a student who is very concerned about side effects I will try it. I haven't had as much luck with Lexapro as I have with Prozac and Zoloft so they remain my top choices.
- **Depression and Pregnancy: Prozac and Zoloft** are the most studied and have been determined to be the **safest antidepressants to use in pregnancy**. Since depression is recurrent for many people it would be helpful for women to know if they have a positive response to Zoloft or Prozac in case they decide to have children in the future and need treatment. **MGH** has a very useful website regarding womens mental health which also covers research regarding pros and cons of using medication during pregnancy.

<http://www.womensmentalhealth.org/>

Wellbutrin (Bupropion/Zyban), increases brain dopamine levels, XL formulation is nice as it can be dosed just once/day (150-300mg qam)

Uses: depression, ADD, smoking cessation

- *side effects*: no sexual side effects (often added to SSRI's to treat sexual side effects), decreased appetite, wt loss, insomnia, anxiety, dry mouth, headache, tremor, avoid with pts who are actively purging as they may be at increased risk of seizures. Also avoid with h/o seizures or significant head trauma. Make sure you document that you have asked about active bulimia and h/o seizures.

- This can be a very popular medication as it is the most activating antidepressant, has no sexual side effects and can cause weight loss
- Not a great idea for people who are very anxious as it can make that symptom worse

SNRI's

Effexor (Venlafaxine), increases serotonin and norepinephrine, 75-300mg/d (given once a day with sustained release or twice a day with regular)

Uses: depression, eating disorders, generalized anxiety disorder (GAD)
side effects similar to SSRI's

Withdrawal Syndrome:

- **Effexor** has the **worst withdrawal syndrome** of any of the antidepressants. Students who stop the medication prematurely, forget it on vacation, or just taper it too quickly can have significant flu-like symptoms that last up to 2wks. Can also report "electric shocks" shooting through their head.

Cymbalta (Duloxetine), 30-120mg/d

Uses: depression, eating disorders, GAD

Side effects: similar to ssri's

Pristiq (Desvenlafaxine), 50-100mg/d

Similar uses and side effects to other snri's

Remeron (Mirtazapine), structurally unique, increases serotonin and norepinephrine levels, 15-45mg/d given at nite

Uses: depression (sometimes used in low dose -7.5-15mg/d as an adjunct to Wellbutrin. Side effects cancel each other out and get benefit of different neurotransmitter)

Side Effects: very few sexual side effects, main side effects are fatigue (paradoxically is more sedating at lower doses) and weight gain, dry mouth, dizziness, constipation

Antianxiety meds

Benzodiazepines:

- Can be habit forming, bind to GABA receptor/inhibitory neurons, same site as alcohol, potentially addictive, can have serious withdrawal if used in large doses daily for more than a month. Begin to worry if student needs increasing doses to get same effect. Potentially dangerous in overdose due to respiratory depression (especially if combined with alcohol)

- Side Effects: sedation (be careful with driving or heavy machinery), definite strong interaction with alcohol (**Don't Use With Alcohol**), can have a paradoxical disinhibition
- I tend to use mainly 2 benzodiazepines:
 - **Ativan/Lorazepam** for episodic short lasting anxiety
 - **Klonopin/Clonazepam** for constant anxiety
 - I tend to **avoid Xanax/Alprazolam**. It works very well but is highly addictive and very difficult to wean patients off of.

Klonopin (Clonazepam), a benzodiazepine, initial dose is generally 0.5mg once or twice a day (many students benefit from just a 0.25mg dose), relatively long acting, half life approx 30-40 hrs. Less addictive because of long half-life

Uses: social phobia, GAD, mania, OCD, dep with anx until antidep works. in gen used short term but can be used long term for GAD/OCD
side effects: fatigue, dizziness

Ativan (lorazepam), a short acting benzodiazepine. (can dose 0.5-1mg po qid prn, I tend to only prescribe it for a couple of times a day because if a student really needs coverage 4x/d then they would be better off with Klonopin). Fast acting. Half life approximately 12hrs. Very useful for panic, sleep, episodic, or predictable anxiety. It is the only benzo that is well absorbed IM. Very useful for urgent issues of: combativeness, severe agitation

Sleep Aids: (always think of sleep hygiene tips: caffeine, nicotine, diet, exercise, regular bedtime and wake up time, chance to unwind/relax, write "to do" list for next day)

- **Ambien:** a non-benzodiazepine, benzodiazepine. "Walks like a Duck". Supposedly not habit forming but I have definitely seen students develop tolerance to its effects. Usual dose is 5-10mg at bedtime. Side Effects can include: drowsiness, hangover, visual hallucinations, not remembering things that happen after medication taken (ie phone calls). Don't use with alcohol. Best used short term, ideally 2wks or less. Recommend that students turn off phone and computer when take ambien and get in bed to minimize chance of doing things they don't remember.
- **Lunesta** (1-3mg po qhs), and **Sonata** (5-20mg po qhs) are very similar to Ambien
- **Trazodone/Desyrel:** a very sedating antidepressant that works with serotonin. So sedating it is almost never used to treat depression because you can't get to antidepressant dosages. For insomnia the dose is 25-150mg po qhs. It is not habit forming. Side Effects include feeling drowsy/hungover in the morning,

priapism (painful erection can happen very rarely, if erection occurs for more than 3hrs student should get medical attention and stop using trazodone). A good choice for chronic insomnia or someone with substance abuse problem

- **Ativan:** see above
- **Seroquel/Quetiapine:** atypical antipsychotic which is sedating. Usual dose for insomnia is 12.5-100mg. This is an off label use for this medication. Can be considered for students who: have significant anxiety/agitation and perhaps a mild thought disorder along with their trouble falling asleep; have a substance abuse problem and don't respond to trazodone and you want to avoid a medication that could be habit forming; have nightmares or PTSD. Side Effects include: sedation, wt gain, poor glucose control, can result in increase in lipids, rare tardive dyskinesia and neuroleptic malignant syndrome. Can increase risk for heart disease or diabetes. Ideally used on short term basis (2-3 wks). Also useful for students with episodic intense anxiety/emotional dysregulation who you don't want to use a benzo with (can use 25-50mg bid prn)
- **Prazosin/Minipress:** can be useful for students with PTSD, nightmares and sleep disruption. 1-4mg. It is an antihypertensive that blocks post synaptic alpha-adrenergic receptors which results in vasodilation and decreased blood pressure. Side Effects can include drowsiness, dizziness, and low blood pressure.

Treating Agitation:

- **Mild/Moderate Agitation:** consider Ativan 0.5-1mg every 4-6hrs as needed
- **Moderate/Severe Agitation:** consider Seroquel 12.5 -100mg every hour until calm (maximum dose: 800mg/d). Zyprexa/Olanzapine 2.5-5mg every hour until calm. Side effects similar to Seroquel (listed above). Maximum dose of Zyprexa 20mg/d
- **Very Severe Agitation: 4 point restraints, won't take oral medication:** consider Haldol 5mg IM and Ativan 1mg IM, can repeat x 1 if still very agitated in 1hr. If has history of needing more medication for severe agitation can start with 10mg of IM Haldol and 2mg of IM Ativan. Important to have student under constant observation if receiving IM meds and in restraints. Possible side effects with Haldol/Haloperidol include: sedation, akathisia/restlessness, neuroleptic malignant syndrome (increase temperature, rigidity, decreased responsiveness – send to ICU), parkinsonian side effects, dystonic reactions.

Bipolar Disorder: (see symptoms above under depression section)

- **Lamictal/Lamotrigine:** quite popular as it is fairly well tolerated and easy to use. Dosage range for bipolar disorder is 100-200mg/d. Side effects can include: fatigue, GI sx's, foginess, suicidal thoughts, and Stevens Johnson Syndrome (a very rare autoimmune reaction that effects the bodies mucosal membranes and

can cause sloughing and bleeding and can potentially be fatal). Because of the risk of Stevens Johnson Syndrome, Lamictal is started at a low dose, 25mg, and is increased by 25mg every week until reach a dose of 100mg/d. Can continue to increase the dose by 25mg per week up to 200mg/d if no response at lower doses. If a student has an rash in their mouth (that is not a cold sore) it makes sense to stop the medication and get a medical evaluation.

- **Lithium:** an oldy and a goody. A bit more of a hassle due to range of side effects and need for monitoring with blood draws. Dosage range tends to be between 900-1800mg/d. Therapeutic blood levels tend to be between 0.6-1.0 mEq/L, though there may be some benefits at lower levels. Important to check blood level (12 hrs after last dose). Side effects can include GI symptoms, fatigue, tremor, thirst, and fluid retention. Can effect kidneys, thyroid, cardiac (arrhythmias), skin sensitivity. Lithium is excreted by the kidneys so it is important to stay well hydrated. If get dehydrated should stop meds as there is a risk of toxic blood levels if not eliminating drug. Important to check cbc, lytes, tsh, bun, creat before starting medication and then 3-4x/yr once on stable dose. Once start medication, titrate dose to therapeutic level, once at therapeutic level can monitor with other labs. Student may need a higher dose of lithium when they are manic than when they are at their normal mood.

ADD Meds

Most ADD medications are prescribed by primary care providers.

Decisions for your Health Service to make:

- Do you diagnose ADD?
- Do you initiated ADD medication treatment?
- Do you continue prescribing ADD medication for students who have a solid diagnosis and are on a stable dose of medication?
- Do you not manage ADD medications?

Diagnosis of ADD: inattentive, hyperactive, or combined:

- Dx can be made clinically
 - Look for evidence of impairment in function both in and out of academic setting dating to an early age
 - Rule out anxiety, depression, substance abuse, etc
 - It is possible if student is very bright, primarily inattentive, and lived in a an organized, structured setting that diagnosis would not be made until arriving at College
 - Great to get history from family
- If diagnostic picture is complicated (40% of students with ADD have a co-occurring disorder). Good to rule out Mood, Anxiety, and Substance Use disorders.
 - You can treat the clear co-occurring disorder and see if attention improves
 - Consider neuropsych testing
 - Referral to counseling office

Treatment of ADD:

- Treatment options include medications, psychotherapy, ADD coaching
- If you feel like students symptoms rise to the level of a disability you can fill out disability paper work and advocate for accommodations through your Accessibilities/Disabilities Office
- In general primary care providers will be providing medication management for student who have been diagnosed with ADD and are stable on their current medication regimen
- Types of Meds
- Stimulants
 - Methylphenitrate Group (general dosage range of 10-60mg/d)
 - Ritalin (reg, SR, LA), Methylin (Reg, ER), Concerta, Metadate (reg, CD), Focalin (reg, XR), daytrana (patch)
 - Dosing: would start at lowest dose (ie Concerta 18mg/d, if no or limited response after 2-3 days, would double dose and return to clinic in 2 wks for followup)

Amphetamine based

- Adderall (reg, XR dosage 5-30mg/d)
- Vyvanse (30-70mg/d) – a prodrug, less abusable
- Dexedrine (5-20mg/d) – more abusable
- Provigil/Modafinil 100-400mg/d – less potent, an idea if has intolerable se to above meds, some insurance will only cover for narcolepsy, it is expensive, some insurances require preauthorization from prescriber.

Main side effects with stimulants: cardiac (can offer EKG, encourage EKG if personal or family h/o cardiac dz), anxiety, insomnia, decreased appetite,

Interacts with other stimulants (caffeine) , etoh, drugs
Stimulants can improve or detract from social functioning

Have Policy with Prescribing Stimulants to refill 1 lost prescription with no ?'s but if lose 2nd prescription, need to wait until normal refill time or change to non- stimulant

- Non stimulant medication
 - Strattera/atomoxetine 40-100mg/d, a norepinephrine uptake inhibitor, takes 3-5wks to work, not abusable, fatigue is main side effect students complain about. Some risk of liver side effects.
 - Wellbutrin/Bupropion (150-300mg/d), blks reuptake of dopamine
No abuse potential – similar se to stimulants but generally less, don't want to use with student who have h/o seizures, or active bulimia. Good choice if h/o substance abuse or co-occurring depression
 - Alpha 2 Adrenergic Agonists (tend to be more effective with symptoms of hyperactivity, but can be helpful with inattentive symptoms as well)

- Intuniv/Guafacine (1-4mg/d), no abuse potential, main se are fatigue
 - Long half life, good for students with substance abuse hx and hyperactive sx
 - Monitor for risk of low blood pressure
- Clonidine (0.1-0.4mg/d)