Common Side Effects of Psychiatric Medications
Why This is a Big Deal

• Common
• Of patients taking an SSRI:
  52% had three or more adverse effects
  55% had 1 or more “a lot” or “extremely” bothersome
• Nonadherence: The biggest problem in psychopharmacology!

“Medications don’t work in people who don’t take them”

C. Everett Koop
Former Surgeon-General
How common is it?

- 802 pts on single AD: **24%**
- Men 34.2%, Women 32.5%. May be more severe in women

Relative Incidence

• Largely absent: Bupropion, Mirtazapine

• Lower: Vilazodone

• High: SSRIs, Duloxetine, Vortioxetine (Lower)

• Higher: Paroxetine, Venlafaxine
Non-pharmacological Strategies

Wait-and-Watch?
• 10% partial improvement, 10% full improvement
• Consider if mild, orgasmic, < 4 to 6 months

Drug Holidays?
• Effective for sertraline & paroxetine in 50%, not for fluoxetine

Montejo AI et al. (2001). PMID 11229449.
Vilazodone & Sexual Dysfunction

- Two phase III RCTs that used specific questionnaires (ASEX, CSFQ). Moderate SD at Baseline
- On questionnaires, vilazodone=placebo (overall/subscales)
- > 1 sexual dysfunction symptom spontaneously reported as occurring during the study: vilazodone 8%, placebo 0.9
- Commonest - decreased libido: vilazodone 3.7 %, placebo 0.2 %

Add Bupropion?

- Only three small RCTs done in the US: all three negative
- Two larger RCTs published by a single author in Iran: positive
- Would be MUCH better if you could SWITCH to it rather than to add it
- Consider if patient is still depressed, problem is mainly with desire

This diamond-shaped blue pill is:

A. Sildenafil
B. The greatest invention since sliced bread
C. Both A and B
Add Sildenafil?

- RCTs
- CGI-SF 55% of sildenafil vs 4% were either “much improved” or “Very much improved”
- Arousal, erectile function, ejaculation, orgasm, and overall satisfaction improved
- Sildenafil not as effective for women

Add Testosterone Gel?

- For patients with low or low normal morning testosterone level. Starting with 5 gm of 1%
- More efficacious than placebo gel in men* and women**
- In most cases, check level. If low/ low normal, refer to specialist for treatment

*Amiaz et al. (2011) J Sex Marital Ther. PMID: 21707327.
Antidepressant-Induced Excessive Sweating (ADIES)
PDR (> 2 X placebo)

- ≥ 20% Bupropion 22%
- ≥ 10% Venlafaxine 14%, Citalopram 11%, Paroxetine 11%
- ≥ 5% Levomilnacipran 9%, Fluoxetine 8%, Sertraline 8%, Duloxetine 6%, Escitalopram 5%,
- < 5% Atomoxetine 4%, Lisdexamfetamine 3%, Modafinil 1%, Buspirone 1%
Clinical Presentation

• Prominent in the upper body, face, scalp, neck, and chest
• Tends to occur in bursts that may also be superimposed on a baseline increase in sweating
• Nearly half - tended to sweat more than others even before the antidepressant

Management

• **Wait-and-watch?** In many, ADIES persists for as long as the antidepressant is taken

• **Antiperspirants?** But sweating mostly on scalp, face, and upper chest

• **Dose reduction?** If feasible, can be tried

• **Change antidepressant?** If feasible, from bupropion or an SNRI to an SSRI (other than paroxetine). Or even try a different SSRI
Antidotes

• Terazosin: 1 mg HS, can increase at weekly intervals to 4 to 6 mg at bedtime*
• Can cause: Dizziness/lightheadedness; hypotension, especially orthostatic; dry mouth
• Glycopyrrolate (Robinul®):** does not cross the blood-brain barrier to a significant extent

Orthostatic Hypotension
Psychotropic Medications

• Blocking of alpha-1 receptors
• Antidepressants – especially SNRIs, trazodone, irreversible MAOIs, TCAs (least – nortriptyline)
• Antipsychotics – especially risperidone, quetiapine
• Benzodiazepines – often not appreciated
Assessment

1. Dizziness vs. Faintness
2. Have person rapidly stand up in your presence
   See if the subjective complaint is reproduced on change in posture
   (Be ready to catch the patient)
   Also, get an idea about how significant it is
3. Measure orthostatic BP and pulse
   After lying (or sitting) down for a few minutes
   After standing for two minutes
   Drop in SBP of $\geq 20$ mmHg
   Usually with increase in pulse
   Drop between 10 to 20 mmHg?
Management

1. **Look for it in the high-risk patient:**
   Older
   Baseline BP low (e.g., 100/60 mmHg)
   Dehydration
   On antihypertensive medication or diuretic
   Significant cardiovascular or cerebrovascular disease
2. Choice of psychiatric and non-psychiatric medications in the predisposed patient

3. Minimize peak levels of the medication: Sustained-release OR in multiple split doses

4. Patient education:
   - Actively prevent dehydration
   - Get up slowly to give body time to adjust
   - Don’t try to be “brave”
Advanced Strategies

1. T.E.D. stockings
   Knee high or Thigh high
2. Add salt to the diet
3. Fludrocortisone
Nausea
### Nausea: PDR (> 2 X placebo)

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 30%</td>
<td>Divalproex ER 48%, Venlafaxine 31%</td>
</tr>
<tr>
<td>&gt; 20%</td>
<td>Paroxetine 26%, Vortioxetine 26%, Sertraline 25%, Vilazodone 23%, Bupropion 22%, Fluoxetine 22%, Atomoxetine 21%, Citalopram 21%</td>
</tr>
<tr>
<td>&gt; 10%</td>
<td>Escitalopram 15%, Modafinil 11%, Risperidone 11%</td>
</tr>
<tr>
<td>&gt; 5%</td>
<td>Lamotrigine 7%, Mixed amphetamine salts 7%, Lisdexamfetamine 6%</td>
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</tbody>
</table>
Nausea

- Particularly unacceptable, evolutionary?
- Most frequent cause of discontinuation in antidepressant clinical trials
- Consider pancreatitis or drug-induced hepatitis
Basic Strategies

- Take medication after food
- Titrate antidepressant up over one week. Shown to cut incidence of nausea by half
- Sustained-release/ split dose/ with separate meals
- High fat, e.g., spoonful of peanut butter
- Ginger root 550 mg Two pills three times a day
- Treat GERD/ gastritis with PPIs

Next Steps

- Ondansetron orally disintegrating tablet OR granisetron transdermal patch
- Add mirtazapine 15 to 30 mg/day. Blocks 5HT-3 receptors, just like the setrons
- Metoclopramide 10 mg every 8 hours if needed
Dry Mouth
Dry Mouth

• Wide variety of psychiatric medications
• Anticholinergic effects, adrenergic effects, serotonergic effects
• May cause dental caries, oral ulcers
Dry Mouth: Management

- Increased oral hygiene
- Eating foods that stimulate production of saliva, like carrots, apples, and celery
- Using sugarless chewing gum or candy
- Sucking on dry ice
- Drinking excessive fluids is not helpful, but while eating can be helpful in swallowing food and may improve taste of food
Dry Mouth: Management

- Cool mist humidifier, day and night, and especially in the winter
- Biotene (gel, oral rinse, gum, toothpaste, etc)
Dry Mouth: Management

- Other saliva substitutes/oral moisturizers like cellulose gum, glycerin (e.g., Oasis moisturizing mouth spray), Salivart®, Oralube®, Xero-lube®, etc.
- Xylitol-containing chewing gum
Tremor
Tremor: PDR (> 2 X placebo)

- > 20%  Lithium, Divalproex 25%, Bupropion 21%
- > 5%    SSRIs 8%, Olanzapine 6%, Aripiprazole 6%
- < 5%    Lamotrigine 4%, Vilazodone 2%, Quetiapine 2%, Buspirone 1%
Tremor: Management

- Reduce caffeine, but caution with lithium
- Sustained-release preparations
- Take medication at bedtime (peak during sleep)
- Anticholinergics (e.g., benztropine 2-6 mg/day) or amantadine
- Propranolol, usually 60-120 mg/day. Long acting?
Akathisia
Incidence

- Ziprasidone 16%
- Aripiprazole 13%
- Lurasidone 9%
- Risperidone 8%
- Olanzapine 6%
- Quetiapine 4%
Management

• Wait-and-watch is not recommended for most cases
• Increase in dose of the antipsychotic in the first few days is a risk factor, so titrate up slowly
• Usually dose dependent, so decrease dose if possible

Management

- Change from antipsychotic with greater akathisia (e.g., aripiprazole)
- Propranolol 20 mg twice daily on day 1, then 40 mg twice daily
- NOT cardioselective beta-blockers like metoprolol

Management

- Clonazepam
- NOT anticholinergics
- Review of six studies: 5-HT2A antagonists, including mirtazapine

Rathbone and Soares-Weiser (2006.)
Laoutidis and Luckhaus (2014.)
Weight Gain
Weight Gain & Psychiatric Meds

• Most psychiatric medications!
• Tip: don’t just look at MEAN change in weight; also look at proportion of patients in each group who gained or lost ≥ 7% of baseline body weight
• Tip: MUST compare to placebo
• Mechanisms: H1 or 5HT2C blockade
• Choice of medication is the KEY!
• Especially high weight gain: mirtazapine, olanzapine, clozapine
• Newly approved second-generation antipsychotics (asenapine, iloperidone, lurasidone and paliperidone): low weight gain potential*

*De Hert et al. (2012). CNS Drugs. PMID: 22900950.
Metformin?

- Metformin for atypical antipsychotic-induced wt gain?
- 7 RCTs (398 patients)
- Metformin > Placebo
- Those with >10% increase, metformin reduced weight by 7.5%

Topiramate?

- 8 RCTs in pts with wt gain on atypical antipsychotics
- Topiramate efficacious, mean decrease -2.83 kg

Side Effects of Psychiatric Medications

Rajnish Mago, MD
Take Home Points

• Side effects - common, distressing, and a leading cause of non-adherence
• For each side effect -- menu of options (non-pharmacological and pharmacological)
• Most importantly, choose medications with a lower risk of the side effect(s) that it is particularly important to avoid
• With vigorous efforts, we may reduce suffering, keep more patients on the medications, and improve overall outcomes