DISCLOSURES

• He receives royalties from Hogrefe Publishing Group as editor of the *Clinical Handbook of Psychotropic Drugs for Children and Adolescents: 4th Edition.*

• He will be discussing off-label indications in this presentation for the following medications: bupropion, benzodiazepines, buspirone, carbamazepine, divalproex sodium, lamotrigine, l-methylfolate, long-acting injectable antipsychotics, mirtazapine, oxcarbazepine, propranolol
LEARNING OBJECTIVES

• Educate pediatric patients and family members about the risks and benefits of antidepressants, anxiolytics, antipsychotics, mood stabilizers, and ADHD medications

• Identify appropriate monitoring parameters for youth taking antidepressants, anxiolytics, antipsychotics, mood stabilizers, and ADHD medications
• Antidepressants
• Anxiolytics
• Anticonvulsant Mood Stabilizers
• Lithium
• Antipsychotics
• Medications for Attention-deficit/hyperactivity Disorder (ADHD)
ANTIDEPRESSANTS

• Selective serotonin reuptake inhibitors (SSRIs)
• Serotonin and norepinephrine inhibitors (SNRIs)
• Mirtazapine (Remeron)
• Bupropion (Wellbutrin)
• Tricyclic antidepressants (TCAs)
• Monoamine oxidase inhibitors (MAO-Is)
# Antidepressants—FDA Approvals

<table>
<thead>
<tr>
<th>Medication</th>
<th>Class</th>
<th>Bipolar Depression</th>
<th>Generalized Anxiety Disorder</th>
<th>Major Depressive Disorder</th>
<th>Obsessive-Compulsive Disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clomipramine</td>
<td>TCA</td>
<td></td>
<td></td>
<td></td>
<td>Age ≥ 10 years</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>SNRI</td>
<td></td>
<td>Age ≥ 7 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Escitalopram</td>
<td>SSRI</td>
<td></td>
<td></td>
<td>Age ≥ 12 years</td>
<td></td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>SSRI</td>
<td></td>
<td></td>
<td>Age ≥ 8 years</td>
<td>Age ≥ 7 years</td>
</tr>
<tr>
<td>Fluoxetine/olanzapine combo tablet</td>
<td>SSRI/AP</td>
<td>Age ≥ 10 years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td>SSRI</td>
<td></td>
<td></td>
<td></td>
<td>Age ≥ 8 years</td>
</tr>
<tr>
<td>Sertraline</td>
<td>SSRI</td>
<td></td>
<td></td>
<td></td>
<td>Age ≥ 6 years</td>
</tr>
</tbody>
</table>

AP=antipsychotic; SSRI=selective serotonin reuptake inhibitor; SNRI=serotonin and norepinephrine reuptake inhibitor; TCA=tricyclic antidepressant

EFFICACY OF SSRIS, SNRIS, AND PLACEBO IN PEDIATRIC DISORDERS

- Benefit small and disease specific
- High placebo response
- Drug response in pediatrics different than adult populations

- Fluoxetine should be considered in those who do not have access or respond to psychotherapy

- Higher SI rate with venlafaxine

- Do to limitations with data reporting, authors are not confident with the accuracy of the above statements
(A) **Adolescents with SSRI-resistant MDD**

- **Switch to new SSRI**
  - (citalopram, fluoxetine, paroxetine*; 20–40 mg/day)
- + CBT
- No therapy

- **Switch to SNRI**
  - (venlafaxine; 150–225 mg/day)
- + CBT
- No therapy

(B) **TORDIA Take-home points:**

1. Higher response rates with CBT with either medication class switch
2. Similar response rates with a switch to a different SSRI vs. switching to venlafaxine
3. However, venlafaxine has a significantly greater side effect burden than SSRIs

COMBINATION OF FLUOXETINE WITH COGNITIVE BEHAVIORAL THERAPY

- Randomized, double-blind, placebo-controlled, multicenter clinical trial
- 153 patients aged 15-25 years with moderate-severe MDD
- Weekly CBT +/- fluoxetine 20 mg daily
- Results:
  - MADRS 12-week reduction -13.7 (CBT/placebo) vs. -15.1 (CBT/fluoxetine) p=.39
  - Suicide attempts: 5 (CBT/placebo) vs. 1 (CBT/fluoxetine) p=.21
  - Exploratory analysis suggests fluoxetine benefit in comorbid anxiety disorder/older age

FIGURE 3 Relative Risk of Antidepressant-Related Adverse Events (AEs), Suicidality, and Discontinuation Secondary to AEs

- SNRIs vs. placebo
- SSRI vs. placebo
- SSRI vs. SNRI

Adverse Events:
- suicidality
- sedation
- nausea
- insomnia
- headache
- diarrhea
- discontinuation
- activation
- abdominal pain

Risk (95% Credible Interval)
# BUPROPION

- **Brand names:** Wellbutrin; Zyban; Aplenzin; Fortivo XL

<table>
<thead>
<tr>
<th>Author</th>
<th>Disease state</th>
<th>Methods</th>
<th>Outcomes</th>
<th>Safety</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muramoto 2007</td>
<td>Nicotine Use Disorder</td>
<td>Prospective, randomized, double-blind, dose ranging trial; All received brief counseling</td>
<td><strong>6 week abstinence:</strong> placebo 5.6%; 150 mg BUP 10.7%; 300 mg BUP 14.5%</td>
<td>Headache &amp; Cough higher in placebo group (p&lt;.05) Dropouts: anxiety, SI, depression, palpitations, sleep disturbance</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>24-week abstinence:</strong> placebo 10.3%; 150 mg BUP 3.1%; 300 mg BUP 13.9%</td>
<td></td>
</tr>
<tr>
<td>Monuteaux 2007</td>
<td>Nicotine Use Disorder &amp; ADHD</td>
<td>Prospective, randomized, double-blind, dose ranging trial; No counseling</td>
<td><strong>Positive cotinine screen at any time point</strong> 28% placebo; 46% BUP (p=.14)</td>
<td>No difference between groups (p&lt;.05) No dropouts due to ADRs</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Post Hoc:</strong> Stimulant treated patients 73% reduction in smoking initiation (p=.03)</td>
<td></td>
</tr>
<tr>
<td>Author</td>
<td>Disease state</td>
<td>Methods</td>
<td>Outcomes</td>
<td>Safety</td>
</tr>
<tr>
<td>------------</td>
<td>---------------</td>
<td>-------------------------------------------------------------------------</td>
<td>--------------------------------</td>
<td>----------------------------------------------------------------------</td>
</tr>
</tbody>
</table>
| Daviss 2001 | MDD or dysthymia & ADHD | Open-label trial (n=24)  
Timeline: 8+ weeks  
Dosing: up to 3 mg/kg twice daily | CGI-Depression Scale: 87% responders  
CGI-ADHD Scale: 62% responders | No significant change in vital signs or weight  
ADRs higher than placebo lead-in phase: rash 13%; irritability 8%; tremor 4%; tic 4% |
| Glod 2004  | MDD           | Open-label trial (n=11)  
Timeline: 8-weeks  
Dosing: 362 mg (mean); 300-400 mg (range) | SIGH-SAD 8-week responders: 63%  
Dropouts: GI upset (n=1), SI/psychosis (n=1), worsening depression (n=1) | >50%; insomnia & weight loss  
40-50%; dry mouth  
10-20%; headache  
5-10%; agitation & lightheaded |
| Kweon 2019 | MDD           | Retrospective review (n=127)  
Timeline: 12-weeks  
Dosing: 180 mg (mean); 75-300 mg (range) | CGI-Depression Scale: 12-week responders: 46%  
Dropouts: 37% total; 15% from ADR; 12% not effective; others lost to follow-up | 5-10%; irritability, dizziness, insomnia, appetite decrease, anxiety, headache  
2-4%; fatigue, psychosis, nausea, tremor, tic, nervousness  
0.5-2%; SI, seizure, hypersomnia, rash, constipation |

BUPROPION OVERDOSE RISK

• Objective: Compare effects of SSRIs vs. Bupropion overdoses

• Methods: Search of National Poison Data System from 2013 to 2017 coded “suspected suicide”

• Results:
  • 30,026 cases identified
  • Sertraline and fluoxetine ~60% cases; Bupropion 11% cases
    • Bupropion increased risk of death 0.23% vs 0% (p<.001)
    • Bupropion increased serious ADRs 58% vs 19% (p<.001)
      • Seizure 27%, hallucination 29%, cardiopulmonary resuscitation 0.51%, intubation 4.9%, need for vasopressors 1.1%, need for benzodiazepines 34%

• An open-label, multicenter pilot study for adolescent MDD

• Population: 23 subjects; mean age 16 ± 1.9 years; baseline HAM-D-17 score ≥18

• Intervention: Mirtazepine 30-45 mg nightly (mean 32.9 mg)

• Assessment: HAM-D-17 at 3-14 days prior to baseline, baseline, days 8, 15, 22, 29, 43, 57, and 85

• Adverse effects: tiredness (17%); increased appetite (8.7%); dizziness (8.7%); increased dreaming, nervousness, edema (4.3%)

• Rainka 2019
  • Retrospective review of heterogeneous sample of 190 patients aged 7-20
  • No standardized benefits assessment performed or appropriate comparator
  • LMF receiving patients had higher ADR reporting (22 vs 14%) (p=.015)

• Dartois 2019
  • Case series of 10 adolescents with treatment resistant depression
  • Concurrent medication changes occurred in 9 patients
  • Range of treatment 16-73 weeks
  • 8 patients had moderate to significant improvement
SUICIDAL IDEATION

• 2004 FDA Boxed Warning
• Based on 24 short-term trials for nine antidepressants (>4400 patients)
• 4% (drug) vs. 2% (placebo) suicidal ideation
• Recommendations to family
  • Daily observation and frequent prescriber visits
  • Avoid significance of overdose by reducing quantity of tablets

## SUICIDAL IDEATION

<table>
<thead>
<tr>
<th>Age Range</th>
<th>Drug-Placebo Difference in Number of Cases of Suicidality per 1000 Patients Treated</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Increases Compared to Placebo</td>
</tr>
<tr>
<td>&lt;18</td>
<td>14 additional cases</td>
</tr>
<tr>
<td>18-24</td>
<td>5 additional cases</td>
</tr>
<tr>
<td>25-64</td>
<td>Decreases Compared to Placebo</td>
</tr>
<tr>
<td>≥65</td>
<td>1 fewer case</td>
</tr>
<tr>
<td></td>
<td>6 fewer cases</td>
</tr>
</tbody>
</table>

OUTLINE

• Antidepressants
• Anxiolytics
• Anticonvulsant Mood Stabilizers
• Lithium
• Antipsychotics
• Medications for Attention-deficit/hyperactivity Disorder (ADHD)
<table>
<thead>
<tr>
<th>Medication</th>
<th>FDA Approvals</th>
<th>Dosing</th>
<th>Safety</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzodiazepines</td>
<td></td>
<td>Not specified</td>
<td>Generally not established in youth anxiety</td>
</tr>
<tr>
<td>• Alprazolam (Xanax)</td>
<td></td>
<td>Seizure disorder</td>
<td>Adults: CNS depressant; sedation; fall risk; abuse potential; SI warning</td>
</tr>
<tr>
<td>• Diazepam (Valium)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Clonazepam (Klonapin)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Lorazepam (Ativan)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Buspirone (Buspar)</td>
<td></td>
<td>2.5-5 mg twice daily; max of 60 mg/day</td>
<td>Drowsiness; HA; dizziness; “activation” reported</td>
</tr>
<tr>
<td>Hydroxyzine (Vistaril/Atarax)</td>
<td>Pruritus</td>
<td>10-50 mg single dose</td>
<td>Drowsiness; dry mouth; constipation; increased appetite; QTc prolongation</td>
</tr>
<tr>
<td>Propranolol (Inderal)</td>
<td></td>
<td>10-20 mg thrice daily</td>
<td>Vital signs; abrupt stopping</td>
</tr>
<tr>
<td>Gabapentin (Neurontin) &amp; Pregabalin (Lyrica)</td>
<td>Partial seizure</td>
<td>Wide range</td>
<td>SI warning; CNS depressant; abuse potential; coordination; blurred vision</td>
</tr>
</tbody>
</table>

ANTICONVULSANT “MOOD STABILIZING” DRUGS

• Carbamazepine (Tegretol)
• Divalproex sodium/valproic acid (Depakote, Depakene)
• Lamotrigine (Lamictal)
• Oxcarbazepine (Trileptal)
<table>
<thead>
<tr>
<th>Medication</th>
<th>FDA Approval</th>
<th>CANMAT Pediatric Bipolar Disorder Guideline Support</th>
</tr>
</thead>
<tbody>
<tr>
<td>Divalproex sodium (Depakote)</td>
<td>Absence, simple, and complex partial seizure</td>
<td>Mania: Third-line option BP Depression: Maintenance: First-line option</td>
</tr>
<tr>
<td>Lamotrigine (Lamictal)</td>
<td>Refractory epilepsy</td>
<td>BP Depression: Second-line option Maintenance: Augmentation, First-line option</td>
</tr>
<tr>
<td>Carbamazepine (Tegretol)</td>
<td>Complex partial seizure</td>
<td>No Recommendations for use</td>
</tr>
<tr>
<td>Oxcarbazepine (Trileptal)</td>
<td>Partial seizures</td>
<td><strong>NOT Recommended</strong>: BP mania or depression</td>
</tr>
<tr>
<td>Medication</td>
<td>Boxed Warnings</td>
<td>General Monitoring</td>
</tr>
<tr>
<td>------------------------------</td>
<td>---------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Divalproex sodium (Depakote)</td>
<td>Teratogenicity; hepatotoxicity; pancreatitis</td>
<td>SI, rash, VPA levels, ammonia, CBC/CMP, nausea, sedation, tremor, cognitive blunting, wt gain, menstrual disturbance, vision change, hair loss</td>
</tr>
<tr>
<td>Lamotrigine (Lamictal)</td>
<td>Life-threatening rash; benign rash</td>
<td>SI, rash, CBC/CMP, cognitive blunting, headache, tremor, ataxia, agitation, insomnia, dizziness</td>
</tr>
<tr>
<td>Carbamazepine (Tegretol)</td>
<td>Dermatologic reaction &amp; HLA-B*1502 allele; Aplastic anemia &amp; agranulocytosis</td>
<td>SI, rash, CBM levels, CBC/CMP, anticholinergic effects, tremor, ataxia, agitation, insomnia, hair loss, menstrual disturbance</td>
</tr>
<tr>
<td>Oxcarbazepine (Trileptal)</td>
<td>None</td>
<td>SI, rash, CBC/CMP, hyponatremia, sedation, headache, ataxia, blurred vision, dizziness, peripheral edema</td>
</tr>
</tbody>
</table>

ANTICONVULSANT DRUG-DRUG INTERACTIONS

- Carbamazepine (Tegretol)
  - Significant INDUCTION effects
- Oxcarbazepine (Trileptal)
  - Possible INDUCTION effects (dose related)
- Divalproex sodium/valproic acid (Depakote, Depakene)
  - Possible INHIBITION effects
- Lamotrigine (Lamictal)
  - Subject to induction or inhibition; dose titration altered due to this
<table>
<thead>
<tr>
<th>Induction effect size</th>
<th>Potent</th>
<th>Mild</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individual differences</td>
<td>Present in all individuals(^a)</td>
<td>Variable</td>
</tr>
<tr>
<td>Dose effects</td>
<td>None within therapeutic doses(^b)</td>
<td>Probably yes(^c)</td>
</tr>
<tr>
<td>Can be obscured by inhibition</td>
<td>No(^d)  (except phenytoin’s inhibition of CYP2C)</td>
<td>Yes</td>
</tr>
</tbody>
</table>

**Chronology**

<table>
<thead>
<tr>
<th></th>
<th>Potent</th>
<th>Mild</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>Weeks</td>
<td>Weeks</td>
</tr>
<tr>
<td>Maximum</td>
<td>Weeks</td>
<td>Weeks to months(^e)</td>
</tr>
<tr>
<td>De-induction</td>
<td>Weeks</td>
<td>Weeks to months(^f)</td>
</tr>
</tbody>
</table>
FIG. 1. Oxcarbazepine and quetiapine dose changes with associated quetiapine concentration to drug (C/D) ratios.
• Antidepressants
• Anxiolytics
• Anticonvulsant Mood Stabilizers
• Lithium
• Antipsychotics
• Medications for Attention-deficit/hyperactivity Disorder (ADHD)
• FDA approved ages ≥12 years

• CANMAT 2018 Guideline support
  • First-line BP mania option
  • First-line BP maintenance option
  • Second-line BP depression option

• Goal Lithium 12-hour concentration: 0.6-1.2 mEq/L

• Goal Dosing: ~20-30 mg/kg/day (divided doses)

LITHIUM MONITORING

• 12-hour lithium concentrations at concentration-steady-state

• Adverse events
  • Nausea/vomiting (>50%), diarrhea/abdominal pain (>20%), headache (65%), dizziness (>30%), increased urination (~30%) thirst, somnolence, appetite change (>15%), rash, congestion, blurred vision, back pain (~10%)

• Other monitoring
  • Kidney function
    • Drug-drug interactions
  • Thyroid function
  • Pregnancy

LITHIUM VS. OTHER MOOD-STABILIZING MEDICATION IN BIPOLAR DISORDER

• Naturalistic, longitudinal study of 340 youth
  • 10 year median follow-up
  • Evaluated 6-month blocks of time where patients took certain mood stabilizers

• Results
  • Lower suicide attempts (2% vs. 4%; p=.03)
  • Lower psychiatric status rating depression scores (p=.004)
  • Lower aggression scores (p=.0004)
  • No difference in hospitalizations, mania/hypomania, substance use disorders

“Typical/Conventional” or First-generation antipsychotics (FGAs)
- Haloperidol (Haldol) approved for pediatric tic disorder and Tourette’s syndrome

“Atypical” or Second-generation antipsychotics (SGAs)

“Atypical” or Third-generation antipsychotics (TGAs)
- Examples: aripiprazole (Abilify), brexpiprazole (Rexulti), cariprazine (Vraylar)
<table>
<thead>
<tr>
<th>Medication</th>
<th>Acute Schizophrenia</th>
<th>Bipolar 1 Manic Episode</th>
<th>Bipolar 1 Mixed Episode</th>
<th>Bipolar 1 Depressive Episode</th>
<th>Irritability Associated with Autism</th>
<th>Tourette's Disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole (Abilify)</td>
<td>Age ≥ 13</td>
<td>Age ≥ 10</td>
<td>Age ≥ 10</td>
<td>Age 6-17</td>
<td></td>
<td>Age 6-18</td>
</tr>
<tr>
<td>Asenapine (Saphris)</td>
<td>Age ≥ 10</td>
<td>Age ≥ 10</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lurasidone (Latuda)</td>
<td>Age ≥ 13</td>
<td></td>
<td>Age ≥ 10</td>
<td></td>
<td>Age 6-17</td>
<td></td>
</tr>
<tr>
<td>Olanzapine (Zyprexa)</td>
<td>Age ≥ 13</td>
<td>Age ≥ 13</td>
<td>Age ≥ 13</td>
<td>Age ≥ 10 with fluoxetine combo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paliperidone (Invega)</td>
<td>Age ≥ 12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quetiapine (Seroquel)</td>
<td>Age ≥ 13</td>
<td>Age ≥ 10</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risperidone (Risperdal)</td>
<td>Age ≥ 13</td>
<td>Age ≥ 10</td>
<td>Age ≥ 10</td>
<td>Age 5-16</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

AUGMENTATION FOR MDD

- No drugs are FDA-approved for this indication in youth
  - Antipsychotics
  - Lithium
  - Buspirone
  - Lamotrigine
  - Thyroid hormone
  - Stimulants
  - Bupropion
  - L-methylfolate
- There are no randomized, placebo-controlled studies evaluating this

LONG-ACTING INJECTION
ANTIPSYCHOTICS IN YOUTH

• No drugs are FDA-approved for this indication in youth
• Some data suggests reduced relapse and hospitalization in adults
• Several SGA drugs approved in adults
  • Aripiprazole (Aristada, Abilify Maintain)
  • Olanzapine (Zyprexa Relprevv)
  • Risperidone (Risperdal Consta, Perseris)
  • Paliperidone (Invega Sustenna/Trinza)
RELEVANT WARNINGS & PRECAUTIONS

- Suicide thoughts
- Cognitive impairment
- Leukopenia, neutropenia, agranulocytosis
- Metabolic changes
- Neuroleptic malignant syndrome
- Orthostatic hypotension
- Pathological gambling or compulsions (aripiprazole and brexipiprazole)
- Seizure
- Tardive dyskinesia

ADVERSE EVENTS AND MONITORING

- Common
  - Sedation, dizziness, constipation, dry mouth, nausea, headache
- Metabolic
  - Increased appetite, weight gain, cholesterol increase, blood sugar increase, increased prolactin*
- Movement disorder
  - Dystonic reaction, akathisia (restlessness), drug-induced parkinsonism, tardive dyskinesia

Stahl et al. CNS Spectrums. 2017. 22(2):203-219
METABOLIC ADVERSE EVENTS

• Six month, naturalistic study in drug-naïve
  • 279 patients aged 4-17 years
  • Diagnosed with schizophrenia, mood disorder, disruptive behavior disorder
  • Weight gain
    • Olanzapine (11kg), risperidone (7.1 kg), quetiapine (6.3 kg)
  • Effect on lipid and glucose
    • Increased with olanzapine and risperidone, not quetiapine

• Three month, comparative trial in schizophrenia
  • 113 patients aged 15.7±1.4 years
  • Weight gain: quetiapine (4.88 kg), aripiprazole (1.97 kg)
  • Lipid and glucose values increased with quetiapine only

## Metabolic Monitoring

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>Monthly</th>
<th>Quarterly</th>
<th>Yearly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight</td>
<td>X</td>
<td>First 3</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Blood pressure</td>
<td>X</td>
<td></td>
<td>First 3, 6 months</td>
<td>X</td>
</tr>
<tr>
<td>Glucose</td>
<td>X</td>
<td></td>
<td>First 3, 6 months</td>
<td>X</td>
</tr>
<tr>
<td>Lipids</td>
<td>X</td>
<td></td>
<td>First 3, 6 months</td>
<td>X</td>
</tr>
</tbody>
</table>

*Children under age of 10 assessed more frequently

• Recommendations
  • Abnormal Involuntary Movement Scale (AIMS) at 3 months then annually

Lohr et al. CNS Spectrums 2015;20:4-14.
<table>
<thead>
<tr>
<th>Medication</th>
<th>Absorption</th>
<th>Metabolism</th>
<th>Common Pharmacokinetic Interactions</th>
</tr>
</thead>
</table>
| Aripiprazole     |                             | CYP3A4; CYP2D6      | **Inducers:** carbamazepine, oxcarbazepine, phenytoin  
**Inhibitors:** bupropion, fluoxetine, paroxetine                                                  |
| Asenapine        | Do not eat or drink within 10 minutes | CYP1A2              | **Inducers:** smoking tobacco, charred food  
**Inhibitors:** fluvoxamine                                                                   |
| Lurasidone       | Take with >350 calories      | CYP3A4              | **Inducers:** carbamazepine, oxcarbazepine, phenytoin  
**Inhibitors:**                                                                                       |
| Quetiapine       |                             | CYP3A4              | **Inducers:** carbamazepine, oxcarbazepine, phenytoin  
**Inhibitors:**                                                                                       |
| Paliperidone     | Extended-release formula only | UGT; CYP3A4 (minor) | **Inducers:** carbamazepine, phenytoin, rifampin  
**Inhibitors:** valproate                                                                              |
| Risperidone      |                             | CYP2D6              | **Inducers:**  
**Inhibitors:** bupropion, fluoxetine, paroxetine                                                        |
| Olanzapine       |                             | CYP1A2              | **Inducers:** smoking tobacco, charred food  
**Inhibitors:** fluvoxamine                                                                   |


• Antidepressants
• Anxiolytics
• Anticonvulsant Mood Stabilizers
• Lithium
• Antipsychotics
• Medications for Attention-deficit/hyperactivity Disorder (ADHD)
## ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) PHARMACOTHERAPY

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<td>1&lt;sup&gt;st&lt;/sup&gt; MPH or AMP alone</td>
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<td>Age 4-5: behavioral</td>
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<td>Age 6-18: MPH or AMP</td>
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<td>2&lt;sup&gt;nd&lt;/sup&gt; Atomoxetine</td>
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<td>3&lt;sup&gt;rd&lt;/sup&gt; Bupropion or TCA</td>
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AMP=Amphetamine; ER=extended release; IR=immediate release; MPH=Methylphenidate

PHARMACOLOGICAL TREATMENT IN CHILDREN AND ADOLESCENTS

- Bupropion
- Lisdexamfetamine
- Methylphenidate

PSYCHOSTIMULANTS

• “Immediately effective”
• C-II formulations
• ADRs
  • Insomnia, agitation, jitteriness
  • GI upset, weight loss, loss of appetite
  • Dry mouth, blurred vision possible
  • Growth suppression, early weight LOSS, possible weight GAIN later in life
  • Less common: Inc. blood pressure, irritability, tics, hallucination, “zombie-like” state

• Precautions
  • Tachycardia and HTN
  • Psychosis or mood disorder
  • Lower seizure threshold; growth suppression; visual disturbance; tic exacerbation; vasculopathy

• Warnings
  • Priapism (MPH); patch formulations-local reactions, loss of skin color; OROS MPH- GI obstruction

• Contraindications
  • Cardiovascular disease, glaucoma, hyperthyroidism, MAOI use, drug abuse

• Boxed Warnings
  • Abuse potential and sudden cardiac death
ATOMOXETINE

• Second line therapy in ADHD
  • Effect size 0.62 vs. IR stimulants (0.91) and ER stimulants (0.95)
  • Boxed warning for SI: 0.4% risk; no suicides

• Mechanism
  • Norepinephrine reuptake inhibitor; delayed onset

• Benefits compared to stimulants
  • Lower abuse potential, comorbid anxiety, lower tic disorder/psychosis risk

• Adverse events
  • Nausea/vomiting, sedation, anorexia, dizziness, elevated BP, liver injury

ALPHA-2 AGONISTS

• Guanfacine (Tenex, Intuniv) and Clonidine (catapress, Kapvay)

• Stimulation of alpha-2 in prefrontal cortex improves “signal-to-noise” ratio

• Reduces hyperactivity and impulsiveness

• Monitoring: sedation, dizziness, bradycardia, dry mouth, paradoxical reactions (uncommon)

FDA warnings for suicidal ideation are listed for all medication classes EXCEPT:

A. Anticonvulsants
B. Antidepressants
C. Atypical Antipsychotics
D. Lithium
Which of the following hold FDA-approvals for Major Depressive Disorder in youth? (Select all that apply)

A. Bupropion (Wellbutrin)
B. Citalopram (Celexa)
C. Escitalopram (Lexapro)
D. Fluoxetine (Prozac)
E. Mirtazepine (Remeron)
F. Adjunctive Quetiapine (Seroquel)
A 15-year-old female started lurasidone (Latuda) for bipolar depression. She had appropriate laboratory monitoring performed at drug initiation. Which assessments should be performed at a three-month follow-up visit? (Select all that apply)

A. Body weight  
B. Blood pressure  
C. Lipid profile  
D. Glucose (fasting) or HgbA1c  
E. Abnormal Involuntary Movement Scale (AIMs)
CONCLUSIONS

• Psychotherapy is especially important for pediatric MDD

• Close observation should be performed in youth prescribed antidepressants

• Not all “mood stabilizers” have the same level of evidence in pediatric bipolar disorder and drug-drug interactions should not be ignored

• Careful risk:benefit analysis is needed with antipsychotic drugs

• Psychostimulants remain first-line therapy in ADHD, but alternatives exist
PSYCHOPHARMACOTHERAPY IN YOUTH

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