OBJECTIVES

- Discuss general principles regarding use of psychotropic medications
- Review how medications work in the body and considerations for use in children
- Overview of specific medications and indications for use in the pediatric population
Treatments for Emotional and Behavioral Problems

Educational
- Information

Behavioral
- Address functions
- External modifications

Biomedical
- Target underlying neurological functioning
Biomedical Treatments

Focus on the potential links between:

- Symptoms of the disorder (expressed in behavior)

  and

- Neurobiologic systems involved in the etiology and pathogenesis of the symptoms (e.g., specific neurotransmitter systems)

**Pharmacological or medication treatments**

- Most widely used biomedical treatment for behavioral and emotional problems in children
Biomedical Treatment: Medication

Typically considered when problem or symptoms of the disorder:

- Significantly interfere with an individual’s functioning
- Have not responded or shown suboptimal response to appropriate behavioral interventions, or
- Pose an acute safety risk
How Medications Work in the Body

- Most drugs alter central nervous system function by acting at the level of the individual nerve cell.
- The human brain contains approximately 20 billion neurons.
- Groups of neurons in the brain have specific functions:
  - some are involved with thinking, learning, and memory.
  - some are responsible for receiving sensory information.
  - some communicate with muscles, stimulating them into action.
How Medications Work in the Body

Each neuron has a cell body, an axon, and many dendrites

- The cell body controls all of the cell's activities
- The axon extends out from the cell body and transmits messages to other neurons
- Dendrites also branch out from the cell body. They receive messages from the axons of other nerve cells
How Medications Work in the Body

- Modulation of neuronal activity via neurotransmitters (i.e., communication between neurons) is a fundamental mechanism of brain function.
- The actions of neurotransmitters and their effect on target neurons are complex and still poorly understood.
How Medications Work in the Body

Considerations include:

- **Pharmacodynamics** – what the drug does to the body
- **Pharmacokinetics** – what the body does to the drug
How Medications Work in the Body

Considerations include:

- **Pharmacodynamics** – what the drug does to the body
  - Mechanisms of drug action
  - Neurotransmitter systems
- **Pharmacokinetics** – what the body does to the drug
Pharmacodynamics

Drug administration can facilitate or inhibit neurotransmitter systems in the brain in several ways:

• By altering the synthesis of the neurotransmitter
• By interfering with the storage of the neurotransmitter
• By altering the release of the neurotransmitter
• By interfering with the inactivation of the neurotransmitter (by enzymes or reuptake)
• By interacting with receptors
Pharmacodynamics

How Drugs Work on the Nervous System

- Synthesis
- Packaging
- Release
  - (+) (autoreceptors)
  - (+/-) (heteroreceptors)
- Release
  - (-) (autoreceptors)
- Reuptake
- Breakdown
- Actions at Receptor

Action Potential
Synthesis
Transmitter substance
Pharmacodynamics

Considerations include:

- **Pharmacodynamics** – what the drug does to the body
  - Mechanisms of drug action
  - Neurotransmitter systems
- **Pharmacokinetics** – what the body does to the drug
Neurotransmitter Systems

glutamatergic
GABAergic systems

cholinergic
serotonergic
noradrenergic
dopaminergic

widely distributed
densely packed in circumscribed areas of brain which project to their target areas - lead to more circumscribed effects
How Medications Work in the Body
Pharmacokinetics

Considerations include:

- Pharmacodynamics – what the drug does to the body
  - Mechanisms of drug action
  - Neurotransmitter systems
- Pharmacokinetics – what the body does to the drug
Pharmacokinetics

The time course and effects of medication on the body (what the medication does to the body) depend on:

- Absorption
- Distribution
- Biotransformation
- Half-life
- Steady-state concentration
- Excretion
Psychotropic Medication

any drug prescribed to stabilize or improve mood, mental status, or behavior

• includes medications typically classified as antidepressants, antianxiety, etc.

• includes other medications not typically classified as psychotropic when such medication is prescribed to improve or stabilize mood, mental status or behavior (e.g., an antiepileptic medication prescribed for affective disorders)

• includes herbal or nutritional substances when such substances are used to stabilize or improve mood, mental status, or behavior
Classification of Psychoactive Drugs

• various ways of doing this
  By the chemical grouping of the drug
    e.g., barbiturates
  By the action of the drug
    e.g., stimulants, dopamine blockers
  By the therapeutic use
    e.g., antidepressant, antipsychotic

• the most common classification scheme is by therapeutic use
Names of Drugs

Trade, Proprietary or Brand Name

- usually a “catchy”, unique name that will appeal to doctors and patients
  - such as Oblivon for a sleeping pill
- trade names written with an initial uppercase letter and often carry the superscript ® for registered trade name

Generic Name

- written with lowercase initial letter and the name is derived from the chemical structure of the drug
  - For example: Ritalin is the brand name for methylphenidate (generic)
Drug Effects

- when a drug is used therapeutically, the desired action is termed the **therapeutic effect**

- the effects of all drugs are dose-dependent
  - the amount of drug that is administered determines both qualitative and quantitative aspects of its effects
  - very low doses - no observable effects
  - high enough doses - toxic reactions
Side Effects

- any other action is a side effect
  - side effects may be adverse, beneficial, or innocuous
  - adverse drug reactions include
    - toxic effects due to overmedication
    - common side effects that appear at therapeutic dosages
    - idiosyncratic side effects (e.g., allergic reactions) that are not clearly related to dose
  - side effects vary from mild to life-threatening
  - side effects may develop insidiously over a long period of time or may occur in an idiosyncratic and unpredictable fashion
Side Effects

Behavioral Effects

Agitation and Restlessness
Sedation
Impaired memory
Hostility, Disinhibition, Aggression
Switch mania
Sleep disturbances
Withdrawal reactions
Suicidal ideation
Side Effects

**Cardiovascular Effects**
hypertensive reaction
orthostatic hypotension
cardiac conduction delays

**Endocrine and Metabolic Effects**
hyperprolactinemia
hypothyroidism
nephrogenic diabetes insipidus
hypercalcemia
weight gain
Side Effects

Hematologic Reactions
- aplastic anemia
- agranulocytosis
- leukocytosis
- eosinophilia
- benign leukopenia
- thrombocytopenia

Hepatic effects
- changes in liver functions
Side Effects

Reproductive and Adverse Sexual Effects
changes in libido
priapism
impotence
ejaculatory and orgasmic disturbances

Renal and Genitourinary System Effects
polyuria
incontinence and enuresis
urinary retention
renal failure
Side Effects

Immunologic and Gastrointestinal Effects

Xerostomia (dry mouth)
Dysphagia (may result in aspiration and asphyxiation)
Gastroesophageal reflux
Nausea, vomiting and GI discomfort
Constipation or abnormal distension
Diarrhea

Convulsive effects
Side Effects

Neuromuscular Effects

myoclonus
nocturnal myoclonus
action (inaction) tremor of upper extremities
acute extrapyramidal symptoms (including dystonia, neuroleptic-induced parkinsonism, bradykinesia, akinesia, tremor, and rigidity)
akathisia
tardive symptoms
neuroleptic malignant syndrome
Preferred Drug Lists

- In some states, Medicaid, like other insurance companies, has a list of medications that patients can obtain for free or at a reduced cost.

- These Preferred Drug Lists (PDL) serve to contain costs and seek to assure that prescribed medications are in line with typical prescribing practice.

- PDLs often use many generic medications that have a similar composition to the brand-name medications.
Generic A.D.H.D. Drug, Not Equivalent to the Brand, Is in Use Anyway

By KATIE THOMAS  JUNE 16, 2015

When Dr. Louis Kraus, a chief of child psychiatry at a hospital in Chicago, writes prescriptions for patients who have attention-deficit hyperactivity disorder, he often chooses Concerta, an extended-release form of the drug Ritalin that gives patients relief from their symptoms for as long as 12 hours.

He was unconcerned when, a few years ago, pharmacies began substituting lower-cost generic alternatives for brand-name Concerta — after all, generic drugs are widely seen as effective and account for the overwhelming majority of prescriptions
Drug Development

Each year, thousands of medications are tested for clinical use, but few are approved by the Food and Drug Administration (FDA) and make it to market.

- It takes an average of 8.5 years for a drug to gain approval
- Estimates of cost range from hundreds of millions to over a billion dollars per new drug
FDA Drug Approval

- The U.S. Food and Drug Administration (FDA) must approve all medications that are available for prescription.

- This means that the FDA has agreed with the results of studies demonstrating that a drug is an effective and safe treatment for a specific condition in a specific population.
“Off Label” Medication Usage

- A licensed physician is allowed to prescribe any medication if it is used for a good scientific reason.
- If a medication is prescribed for a condition or in a population for which it has not received FDA approval, this is called “off label” usage.
FDA Black Box Warnings

- Some psychotropics medications have FDA Black Box Warnings.

- Medicines with black box warnings are still FDA approved, but their use requires particular attention and caution regarding potentially dangerous or life threatening side effects.
## Drug Development in ADHD

<table>
<thead>
<tr>
<th>Year</th>
<th>Medication – FDA approval for ADHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1955</td>
<td>MPH</td>
</tr>
<tr>
<td>1960’s</td>
<td>Dextroamphetamine</td>
</tr>
<tr>
<td>1982</td>
<td>Ritalin SR</td>
</tr>
<tr>
<td>1996</td>
<td>Adderall</td>
</tr>
<tr>
<td>1998</td>
<td>Pemoline (Cylert) – approval withdrawn 2005</td>
</tr>
<tr>
<td>2000</td>
<td>OROS MPH (Concerta)</td>
</tr>
<tr>
<td>2001</td>
<td>Mixed Amphetamine Salts (Adderall XR), Diffucaps MPH (Metadate CD), d-MPH (Focalin)</td>
</tr>
<tr>
<td>2002</td>
<td>Atomoxetine (Strattera), SODAS MPH (Ritalin LA)</td>
</tr>
<tr>
<td>2005</td>
<td>d-MPH-XR SODAS (Focalin XR)</td>
</tr>
<tr>
<td>2006</td>
<td>Transdermal MPH (Daytrana)</td>
</tr>
<tr>
<td>2007</td>
<td>Lisdexamfetamine Dimesylate (Vyvanse)</td>
</tr>
<tr>
<td>2009</td>
<td>Guanfacine extended release (Intuniv)</td>
</tr>
<tr>
<td>2010</td>
<td>Clonidine extended release (Kapvay)</td>
</tr>
<tr>
<td>2012</td>
<td>extended-release oral suspension MPH (Quillivant XR)</td>
</tr>
</tbody>
</table>
Role of Medication

Medication is:

• is a single component of a broad treatment plan
• is usually considered when behavior interventions have been unsuccessful or the behavior is presumed to be of organic origin
• use increases as the number and severity of the individual’s behavior problems increase
• are often used to treat specific diagnoses as well as specific target symptoms
Role of Medication

Generally used to treat psychiatric disorders or specific problem behaviors, including:

<table>
<thead>
<tr>
<th>ADHD</th>
<th>OCD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mood Disorders</td>
<td>Aggression/Irritability</td>
</tr>
<tr>
<td>Anxiety</td>
<td>Inattention</td>
</tr>
<tr>
<td>Sleep Problems</td>
<td>Hyperactivity</td>
</tr>
<tr>
<td>Psychiatric Disorders</td>
<td>Impulsivity</td>
</tr>
</tbody>
</table>
Role of Medication

In individuals with developmental disabilities, medications can be used to target specific challenging behaviors or psychiatric disorders, including:

- aggression
- rigid behaviors
- self-injury
- inattention
- hyperactivity
- sleep problems
- mood disorders
- anxiety
- repetitive behaviors (stereotypies, compulsive actions, obsessive thinking)
Principles of Medication Use

Standard medication management principles should be followed such as the Practice Parameters and/or Standard Practice Guidelines developed by the American Academy of Pediatrics or the American Academy of Child and Adolescent Psychiatry.

Evaluation of the drug response using repeated assessment measures and monitoring of side effects is necessary to determine the effects of the treatment.
Medication Management

3 STAGES

**Baseline:** collection of medical information and behavioral observations for later comparison with treatment.

**Titration:** experimental process of trying different doses or types of medication and evaluating therapeutic response and side effects.

**Maintenance:** periodic monitoring of the child’s functioning on the optimal dose selected during the titration stage. Adjustments in the dose or drug may be made in response to changes in functioning or side effects.
Pharmacotherapy

Commonly used classes of medications to treat psychiatric and behavior problems include:

- antipsychotics
- stimulants
- antidepressants
- antimanicants
- anxiolytics
- anticonvulsants
- selective norepinephrine reuptake inhibitors
Specific Medications

Stimulants
Stimulants - Indications

Attention Deficit Hyperactivity Disorder
ADHD with comorbid disorders (including mental retardation, Fragile X Syndrome, Tourette Syndrome)
hyperactivity in developmental disorders
narcolepsy
adjunctive treatment in refractory depression
Stimulant Medications

• Stimulant medications are the most studied, most commonly used first-line agents for ADHD treatment

• Stimulant medications improve:
  - core symptoms: inattention, impulsivity, hyperactivity
  - associated symptoms: cognition, on-task behavior, academic performance, social function, defiance, and aggression

• Good response in preschoolers, school-age children, adolescents and adults
Stimulant Medications

- two primary classes of stimulants
  - amphetamines
  - methylphenidate (MPH)
- response rate for any one particular stimulant is approx. 70%
- no predictors of response have been identified
- all stimulants are generally of comparable efficacy
- there is significant individual variability in response to a particular stimulant
Stimulant Medications

MPH-based and amphetamine-based stimulants have different effects at the neurotransmitter level

- **MPH** inhibits the activity of the dopamine transporter protein involved in the reuptake of dopamine from the synaptic cleft
- **Amphetamines** have a dual effect – blocks the reuptake of dopamine and norepinephrine
Methylphenidate Effect

Figure 4
DOPAMINE REUPTAKE INHIBITION
Schematic diagram of presynaptic and postsynaptic components of CNS neurons communicating via dopamine transmission. Shaded area is the extraneuronal space where methylphenidate is likely to exert its action by blocking reuptake of dopamine via the dopamine transporter.24

Pre-frontal cortex

Human brain

Dopamine-producing nerve cell (sending nerve cell)

Axon

Dopamine synaptiic vesicle

Dopamine

Dopamine transporter

Synapse

Methylphenidate works here to inhibit reuptake of dopamine back into sending nerve cell

Receiving nerve cell

Adderall Effect

Dopamine Neurotransmission Relative to ADHD
- Enhances signal
- Improves attention

Norepinephrine Neurotransmission Relative to ADHD
- Dampens noise
- Enhances executive operations
- Increases inhibition
Stimulant Medications

• If initial stimulant does not work at the highest feasible dose, then an alternate stimulant should be recommended

• Sub-optimal responders to a given stimulant may benefit from a trial with an alternate stimulant
Stimulants - Preparations

methylphenidate (Ritalin, Methylin, Metadate)
  - long acting preparations: Ritalin-SR, Ritalin LA, Methylin-ER, Metadate-ER, Metadate-CD, Concerta, Daytrana
    * Methylin comes in a chewable tablet form
    ** Daytrana delivers MPH via a transdermal patch
    *** Quillivant XR is long-acting MPH liquid preparation

dexmethylphenidate (Focalin)
  - long acting preparation: Focalin XR

dextroamphetamine (Dexedrine, Dextrostat)
  - long acting preparation: Dexedrine spansules

mixed amphetamine salts products (Adderall)
  - long acting preparation: Adderall XR

lisdexamfetamine dimesylate (Vyvanse)
  - prodrug of dextroamphetamine
Stimulants – Side Effects

- most side effects are transient and dose dependent
- common side effects include: insomnia, decreased appetite, mild increase in heart rate and BP, weight loss, headache, nausea
- rare side effects include: behavioral rebound, psychosis, anxiety or depression
Stimulants – Side Effects

- Concerns with stimulant use include:
  - Stimulant associated growth deficits
  - Increased risk for development or exacerbation of tics
  - Increased risk for substance abuse
  - Possible carcinogenesis (Feb, 2005)
  - Possible cardiovascular side effects
  - Increased risk of psychosis and other psychiatric effects
methylphenidate - Concerta

- Immediate release of MPH in overcoat of the tablet (22%) followed by progressive 8-hour release from drug subcompartments (78%)
- designed for a 12 hour duration
methylphenidate - Ritalin LA

- 2 phase release bead technology
- 50% immediate release / 50% delayed release
- 10, 20, 30, and 40 mg capsules can be sprinkled
- designed for 9-hour duration
methylphenidate - Metadate CD

- 2 phase bead technology
- 30% immediate release / 70% delayed release
- 10, 20, 30, 40, 50, and 60 mg capsules
- designed for 9 hour duration of action
• Methylphenidate Transdermal System (MTS)
• approved for ages 6-11 years
• comes in 4 sizes that deliver 10mg, 15mg, 20mg, and 30mg of MPH over 9 hours
methylphenidate - Daytrana

- Backing
- Drug/Adhesive Mix
- Release Liner

Evenly dispersed methylphenidate blend

Adhesive

Magnified view
methylphenidate - Daytrana
methylphenidate - Daytrana
dexmethylphenidate - Focalin

- dexmethylphenidate – d-isomer of MPH
- short acting, immediate release formulation with approx. 5 hr duration of action
- reportedly “smoother” response than MPH with fewer side effects (esp. insomnia)
dexmethylphenidate - Focalin XR

- 50% immediate release / 50% delayed release
- up to a 12-hour duration of efficacy
- 5, 10, 15, 20, 25, 30, 35 and 40 mg capsules can be sprinkled
Mixed amphetamine salts - Adderall XR

- Longer acting version of Adderall with 2-bead delivery system
- 50% immediate \ 50% delayed release
- duration of action may extend to 10-12 hours
- 5, 10, 15, 20, 25, 30 mg capsules can be sprinkled
Lisdexamfetamine is a novel prodrug in which an amino acid is bound to the amphetamine molecule.

This bond can only be broken through enzymatic processes in the gastrointestinal tract.

Available in 10, 20, 30, 40, 50, 60 and 70 mg capsules.
# Long-Acting Stimulant Preparations

<table>
<thead>
<tr>
<th>Formulation</th>
<th>AM/PM effect (%)</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Concerta</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18, 27, 36, 54 mg</td>
<td>30% IR 70% next 8 hr</td>
<td>12 hours</td>
</tr>
<tr>
<td><strong>Adderall XR</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5, 10, 15, 20, 25, 30 mg</td>
<td>50% / 50%</td>
<td>10 - 12 hours</td>
</tr>
<tr>
<td><strong>Metadata CD</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10, 20, 30, 40, 50, 60 mg</td>
<td>30% / 70%</td>
<td>8 - 9 hours</td>
</tr>
<tr>
<td><strong>Ritalin LA</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10, 20, 30, 40 mg</td>
<td>50% / 50%</td>
<td>9 hours</td>
</tr>
<tr>
<td><strong>Focalin XR</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5, 10, 15, 20, 25, 30, 35, 40 mg</td>
<td>50% / 50%</td>
<td>10 - 12 hours</td>
</tr>
<tr>
<td><strong>Daytrana (MPH)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10, 15, 20, 30</td>
<td>Continuous</td>
<td>Duration + 3 hrs</td>
</tr>
<tr>
<td><strong>Vyvanse</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10, 20, 30, 40, 50, 60, 70 mg</td>
<td>Prodrug</td>
<td>12 hours</td>
</tr>
</tbody>
</table>
## ADHD Medication Guide

### Methylphenidate Derivatives – Long Acting/Extended Release

<table>
<thead>
<tr>
<th>Brand</th>
<th>Strength</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concerta</td>
<td>18 mg</td>
<td>27 mg</td>
</tr>
<tr>
<td>Focalin XR</td>
<td>5 mg</td>
<td>10 mg</td>
</tr>
<tr>
<td>Ritalin LA</td>
<td>10 mg</td>
<td></td>
</tr>
<tr>
<td>Metadata</td>
<td>10 mg</td>
<td></td>
</tr>
<tr>
<td>Methylin ER</td>
<td>10 mg</td>
<td></td>
</tr>
<tr>
<td>Ritalin SR</td>
<td>10 mg</td>
<td></td>
</tr>
<tr>
<td>Daytrana</td>
<td>10 mg</td>
<td></td>
</tr>
</tbody>
</table>

### Methylphenidate Derivatives – Short Acting/Immediate Release

<table>
<thead>
<tr>
<th>Brand</th>
<th>Strength</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>Focalin</td>
<td>2.5 mg</td>
<td>5 mg</td>
</tr>
<tr>
<td>Ritalin</td>
<td>5 mg</td>
<td>10 mg</td>
</tr>
<tr>
<td>Methylin</td>
<td>5 mg</td>
<td>10 mg</td>
</tr>
<tr>
<td>Methylin Chewable §</td>
<td>2.5 mg</td>
<td>5 mg</td>
</tr>
<tr>
<td>Methylin Solution §</td>
<td>5 mg/5 ml</td>
<td>10 mg/5 ml</td>
</tr>
</tbody>
</table>

- **Indicates a generic formulation is available; generic products are not shown.**

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*Disclaimer: The ADHD Medication Guide was created by Dr. Andrew Adirman of the North Shore-LIJ Health System. The North Shore-Long Island Jewish Health System is not affiliated with the owner of any of the brands referenced in this Guide. This Guide should not be used as an exclusive basis for decision-making. The user understands and accepts that if the health system were to accept the risk of harm to the user from use of this Guide, it would not be able to make the Guide available because the cost to cover the risk of harm to all users would be too great. Thus, use of this ADHD Medication Guide is strictly voluntary and at the user’s sole risk.

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http://www.adhdmedicationguide.com/
# ADHD Medication Guide

## Amphetamine Derivatives – Long Acting/Extended Release

<table>
<thead>
<tr>
<th>Brand</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vyvanse® ¥</td>
<td>20mg, 30mg, 40mg, 50mg, 60mg, 70mg</td>
</tr>
<tr>
<td>Adderall XR†</td>
<td>5mg, 10mg, 15mg, 20mg, 25mg, 30mg</td>
</tr>
<tr>
<td>Dextroamphetamine</td>
<td>5mg, 10mg, 15mg</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Brand</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adderall®</td>
<td>5mg, 7.5mg, 10mg, 12.5mg, 15mg, 20mg, 30mg</td>
</tr>
<tr>
<td>Dextroamphetamine</td>
<td>5mg, 10mg</td>
</tr>
<tr>
<td>ProCentra® (Bubblegum Flavor)</td>
<td>5mg/5ml</td>
</tr>
</tbody>
</table>

## Non-Stimulants

<table>
<thead>
<tr>
<th>Brand</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intuniv® +</td>
<td>1mg, 2mg, 3mg, 4mg</td>
</tr>
<tr>
<td>Kapvay™</td>
<td>0.1mg, 0.2mg, 0.3mg</td>
</tr>
<tr>
<td>Strattera®†</td>
<td>10mg, 18mg, 25mg, 40mg, 60mg, 80mg, 100mg</td>
</tr>
</tbody>
</table>

### Medication Administration Key

- † Must be swallowed whole
- ¥ Can be dissolved in liquid
- § Chewable
- ‡ Capsule can be opened and medication sprinkled on applesauce

### AGES FOR WHICH MEDICATIONS HAVE AN FDA INDICATION FOR TREATMENT OF ADHD.

<table>
<thead>
<tr>
<th>Brand</th>
<th>2-5 Year</th>
<th>6-12 Year</th>
<th>12-16 Year</th>
<th>17 Year</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vyvanse® ¥</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Adderall XR†</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
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<tr>
<td>Adderall®</td>
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<td>✔</td>
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</tr>
<tr>
<td>ProCentra®</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
</tbody>
</table>

*Disclaimer: The ADHD Medication Guide was created by Dr. Andrew Adesman of the North Shore-LIJ Health System. North Shore-LIJ Health System is not affiliated with the owner of any of the brands referenced in this Guide.

The ADHD Medication Guide is a visual aid for professionals caring for individuals with ADHD. The Guide includes only medications indicated for the treatment of ADHD by the FDA. In clinical practice, this guide may be used to assist patients in identifying medications previously tried, and may allow clinicians to identify ADHD medication options for the future. Medications have been arranged on the card for ease of display and comparison, but dosing equivalence cannot be assumed. Practitioners should refer to the FDA-approved product information to learn more about each medication. Although every effort has been made to depict each medication in its actual size and color, we cannot guarantee that there are not minor distortions in the final image. This guide is accurate as of September 20, 2011. For updates, visit www.ADHDMedicationGuide.com.

Future revisions of the ADHD Medication Guide can be viewed at www.ADHDMedicationGuide.com

Laminated copies of the ADHD Medication Guide can be obtained at: www.ADDWarehouse.com

For questions or comments, contact Dr. Andrew Adesman at ADHDMedGuide@NSH.edu
Specific Medications

Selective Norepinephrine Reuptake Inhibitor
atomoxetine - Strattera

- Indicated for treatment of ADHD
- Highly selective blockade of the norepinephrine transporter
- Non-controlled substance
- Recommended dose: 0.5 – 1.4 mg/kg/day
- Several studies showed that once daily dosing strategy similar to twice-daily dosing
- May take up to 2-4 weeks to see optimal benefit
atomoxetine - Strattera

Safety data

- diastolic BP and heart rate increase (not clinically significant)
- 20% with decreased appetite (weight decrease seen only in first 9-12 weeks of treatment)
- no significant lab or EKG changes
- no exacerbation of tics or anxiety
- insomnia not a significant side effect

*** need to watch for abnormal liver function
*** black box warning – may increase suicidal thoughts
atomoxetine - Strattera

Safety concerns

Dec, 2004
- FDA announced a labeling change for Strattera indicating a potential for severe liver damage

Sept, 2005
- FDA requires a black box warning that Strattera may increase suicidal thoughts

Feb, 2006
- The British Medicine and Healthcare Products Regulatory Agency released an initial report associating Strattera with seizures and QT interval prolongation based on a small number of reports
Specific Medications

Antidepressants
Antidepressants - Indications

- major depressive disorder
- enuresis
- ADHD
- anxiety disorders (e.g., school phobia, separation anxiety, panic disorder, and obsessive-compulsive disorder)
- sleep disorders (night terrors)
- some cases of self-injury in individuals with DD
Classes of Antidepressants

**Selective Serotonin Reuptake Inhibitors (SSRIs)**
- fluoxetine (Prozac)
- paroxetine (Paxil)
- citalopram (Celexa)
- fluvoxamine (Luvox)
- sertraline (Zoloft)
- escitalopram (Lexapro)

**Others**
- bupropion (Wellburtin)
- venlafaxine (Effexor)
- mirtazapine (Remeron)
- trazodone (Desyrel)
- nefazodone (Serzone)

**Tricyclics**
- amitriptyline (Elavil)
- imipramine (Tofranil)
- desipramine (Norpramin)
- nortriptyline (Pamelor)

**Monoamine Oxidase Inhibitors (MAOIs)**
- phenelzine (Nardil)
- tranylcypromine (Parnate)
## FDA-Approved Pediatric Age Ranges and Indications for Antidepressant Medications

### Table: FDA-Approved Pediatric Age Ranges and Indications

<table>
<thead>
<tr>
<th>Antidepressant</th>
<th>Age Range (Years)</th>
<th>6</th>
<th>7</th>
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</table>

- **Yellow**: childhood enuresis
- **Red**: MDD
- **Blue**: OCD

*Fluoxetine is FDA approved for the treatment of MDD in pediatric patients up to 18 years old.*


August, 2013
Antidepressants

SSRIs:
- Selectively blocks the reuptake of serotonin
- Side Effects: irritability, headaches, insomnia, nervousness, drowsiness or fatigue, anorexia, nausea, or diarrhea (safer side effect profile)

** concerns regarding antidepressants and increased risk for suicidal ideation in children/adolescents

FDA recommended visit frequency:
weekly x 4 weeks; every 2 weeks for next month; and at the end of 12th week of taking the drug
Antidepressants

bupropion (Wellbutrin):
- chemically unrelated to the tricyclic or other known antidepressants; weak inhibitor of norepinephrine and dopamine reuptake
- Side Effects**: irritability, anxiety, insomnia, reduced seizure threshold (with high doses)

venlafaxine (Effexor):
- strongly inhibits serotonin and norepinephrine reuptake
- Side Effects**: nausea, dry mouth, sweating, dizziness, nervousness, constipation, anorexia

*** black box warning – may increase suicidal thoughts
Antidepressants

Tricyclic Antidepressants:
- mechanism of action is the blocking of the reuptake of norepinephrine and serotonin in presynaptic neurons
- Side Effects**: dry mouth, constipation, sedation, weight gain, BP changes, tremor, change in cardiac conduction (causal link between DMI and sudden death)

Monoamine Oxidase Inhibitors:
- inhibit the intracellular metabolism of dopamine, norepinephrine and serotonin
- Side Effects**: changes in blood pressure, weight gain, need to follow dietary restrictions

*** black box warning – may increase suicidal thoughts
Specific Medications

Antipsychotics
Antipsychotics - Indications

Behavior disorders with severe agitation, aggression, and self-injury
Adjunctive treatment in depression and anxiety
Dyskinetic movement disorders (e.g., Tourette Syndrome)
Irritability in autism
Psychotic disorders
Schizophrenia (exacerbations and maintenance)
Mania (in conjunction with a mood stabilizer)
  – Bipolar disorder
Antipsychotics

Traditional antipsychotics

Low potency: chlorpromazine (Thorazine) thioridazine (Mellaril)

Intermediate potency: loxapine (Loxitane)

High potency: haloperidol (Haldol) thiothixene (Navane)
Antipsychotics

New or Atypical Antipsychotics

clozapine (Clozaril)
quetiapine (Seroquel)
olanzapine (Zyprexa)
risperidone (Risperdal)
aripiprazole (Abilify)
ziprasidone (Geodon)
paliperidone (Invega)
asenapine (Saphris)
lurasidone (Latuda)
iloperidone (Fanapt)
Antipsychotics

Efficacy of both traditional and atypical antipsychotics attributed to their effect on dopamine (DA) neural transmission

- **Traditional antipsychotics**: DA receptor antagonists
- **Atypical antipsychotics**: relatively weaker DA binding and high affinity for several serotonin receptors
# Atypical Antipsychotics and Mechanism of Action

<table>
<thead>
<tr>
<th>Drug</th>
<th>Pharmacodynamics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risperidone</td>
<td>• Antagonist with high affinity binding to 5-HT2 and D2 receptors</td>
</tr>
<tr>
<td></td>
<td>• Antagonist at H1, and α 1–2 receptors</td>
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<tr>
<td>Aripiprazole</td>
<td>• Partial agonist at D2 and 5-HT1A receptors, antagonist at 5-HT2A receptors</td>
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<tr>
<td></td>
<td>• High affinity for D2, D3, 5-HT1A, and 5-HT2A receptors; moderate affinity for</td>
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<tr>
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<td>D4, 5-HT2C, 5-HT7, - α - adrenergic and H1 receptors</td>
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<tr>
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<td>• Moderate affinity for the serotonin reuptake site and no appreciable affinity</td>
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<tr>
<td></td>
<td>for cholinergic muscarinic receptors</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>• Selective monaminergic antagonist with high affinity binding to 5-HT2A/2C,</td>
</tr>
<tr>
<td></td>
<td>5-HT6, D1–4, histamine H1, and α1-adrenergic receptors</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>• Antagonist with high affinity binding to 5-HT2 and D2 receptors</td>
</tr>
</tbody>
</table>
# Atypical Antipsychotics and Mechanism of Action

<table>
<thead>
<tr>
<th></th>
<th>Pharmacodynamics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Quetiapine</strong></td>
<td>• Antagonist at D1-2, 5HT 1A–2A, norepinephrine transporter (NET), H1, M1, and α1b-2, receptors</td>
</tr>
<tr>
<td><strong>Paliperidone</strong></td>
<td>• Antagonist at D2 receptors and 5- HT2A receptors</td>
</tr>
<tr>
<td></td>
<td>• Also antagonist at α1–2 and H1 receptors</td>
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<tr>
<td><strong>Asenapine</strong></td>
<td>• High affinity for serotonin 5-HT1A, 5-HT1B, 5-HT2A, 5-HT2B, 5-HT2C, 5- HT5-7 receptors, dopamine D1–4 receptors, α1and α2-adrenergic receptors, and histamine H1 receptors</td>
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<tr>
<td></td>
<td>• Moderate affinity for H2 receptors</td>
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<tr>
<td><strong>Iloperidone</strong></td>
<td>• High affinity to serotonin 5-HT2A and dopamine D2 and D3 receptors</td>
</tr>
<tr>
<td></td>
<td>• Moderate affinity for dopamine D4, serotonin 5-HT6 and 5- HT7, and norepinephrine NEα1 receptors</td>
</tr>
</tbody>
</table>
FDA-Approved Pediatric Age Ranges and Indications for Atypical Antipsychotics

<table>
<thead>
<tr>
<th>Drug</th>
<th>Age Range (Years)</th>
<th>Schizophrenia</th>
<th>Bipolar I Disorder: Manic or Mixed</th>
<th>Irritability with Autistic Disorder</th>
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<tbody>
<tr>
<td>aripiprazole[3]</td>
<td>5</td>
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<td>risperidone[7]</td>
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</tbody>
</table>

* Risperidone should not be used by patients older than age 16 who have been diagnosed with irritability with autistic disorder.


August, 2013
Atypical Antipsychotics - Side Effects

Most common side effects include:
Sedation, constipation, disrupted sleep, increased appetite and weight gain, prolactin elevation, extrapyramidal symptoms

Many of these common side effects are transient and decrease after 2 to 4 weeks

Potentially more serious side effects include insulin resistance, tardive dyskinesia, malignant hyperthermia

*** black box warning – may increase suicidal thoughts
# Antipsychotics - Side Effects

<table>
<thead>
<tr>
<th></th>
<th>Extrapyramidal</th>
<th>Sedation</th>
<th>Weight Gain</th>
<th>Anticholinergic</th>
<th>Risk for Diabetes</th>
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</thead>
<tbody>
<tr>
<td>Abilify</td>
<td>+/-</td>
<td>+</td>
<td>+/-</td>
<td>+/-</td>
<td>-</td>
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<tr>
<td>Risperidal</td>
<td>+</td>
<td>++</td>
<td>++</td>
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<tr>
<td>Zyprexa</td>
<td>+/-</td>
<td>++</td>
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<td>Seroquel</td>
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<td>Geodon</td>
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</table>

*** black box warning – may increase suicidal thoughts
Because of the lack of evidence, we are unable choose a Best Buy atypical antipsychotic for children with schizophrenia, bipolar disorder, pervasive developmental disorders, or disruptive behavior disorders. Instead, our medical advisors recommend that parents carefully consider the potential risks and benefits. Children with those disorders should receive comprehensive treatment, which includes cognitive behavioral therapy, parent management training, and specialized educational programs, along with any potential drug therapy.
Specific Medications

Antimanics
Antimanics

lithium carbonate (Lithobid, Eskalith)

indications:

• manic episodes of bipolar disorder
• lithium is the only mood stabilizer FDA-approved for children (>12) and adolescents
• unipolar depression/adjunct treatment in major depressive disorder
• behavior disorders with extreme agitation or aggression
Lithium - Side Effects

- weight gain
- sedation, confusion, headache
- electrolyte imbalances
- gastrointestinal distress
- renal dysfunction (polydipsia, polyuria)

*Need to monitor drug levels, thyroid function, EKG and electrolytes every 1-3 months once stabilized*
Specific Medications

Anxioltyics
Anxiolytics - Indications

- anxiety disorders
- seizure control
- night terrors and sleepwalking
- acute management of severe agitation
- adjunct treatment in mania and refractory psychosis
- Tourette Syndrome
Classes of Anxiolytics

Benzodiazepines
- alprazolam (Xanax)
- diazepam (Valium)
- lorazepam (Ativan)

Antihistamines
- diphenhydramine (Benadryl)
- hydroxyzine (Atarax)

Atypical anxiolytics
- buspirone (BuSpar)
Anxiolytics - Side Effects

- headache
- sedation and decreased cognitive performance
- behavior disinhibition
- gastrointestinal distress
- physical and psychological dependence (long-acting benzodiazepines)
- rebound or withdrawal reactions (short-acting benzodiazepines)
- blood abnormalities
- anticholinergic effects
Specific Medications

Antiepileptics
Antiepileptics - Indications

- seizure control
- bipolar disorder – mood stability
  - most evidence for Depakote and Lamictal
- adjunct treatment in major depressive disorder
- severe behavior problems
Antiepileptics

Examples include:
- carbamazepine (Tegretol)
- ethosuximide (Zarontin)
- sodium valproate (Depakote)
- oxcarbazepine (Trileptal)
- topiramate (Topamax)
- gabapentin (Neurontin)
- lamotrigine (Lamictal)
Antiepileptics - Side Effects

- sedation, fatigue
- behavioral disinhibition, overexcitement
- blood abnormalities
- anticholinergic effects

- Topamax – memory loss, difficulty concentrating
- Depakote – liver failure, panceratitis
- Lamictal – Stevens-Johnson Syndrome
- Tegretol – blood dyscrasias

**increased risk for suicidal ideation in children/adolescents**
Specific Medications

Alpha-2 Adrenergic Agonists
Alpha-2 Adrenergic Agonists

These centrally acting antihypertensive agents have more recently been reported as alternative or adjunctive treatments for:

- ADHD
- Tourette Syndrome
- behavior disorders with severe agitation, self-injury, or aggression
- adjunctive treatment of schizophrenia and mania
clonidine (Capatres)

• most common side effect is sedation
• other side effects include: hypotension, other cardiovascular effects, headache and dizziness, stomach ache, nausea, vomiting
• no clinically meaningful EKG changes have been noted
• daily doses of 0.4-0.5 mg/kg/day, maximum benefits may not be evident for several weeks
• comes in tablet and skin patch preparations
clonidine - Kapvay

- FDA approved in September, 2010 as a monotherapeutic agent in the treatment of ADHD in children and adolescents aged 6 to 17
- subsequently approved as an adjunctive therapy to stimulant medication in the same age group
- oral, non-stimulant, twice-daily therapy
- supplied in 0.1 mg tablets
guanfacine - Tenex

- much more binding specificity than clonidine
- usual daily dose 0.5 to 4.0 mg divided BID
- most common side effects are: lethargy, insomnia, irritability, and dry mouth (recent study with no clinically or statistically sig. Impact on BP or pulse)
guanfacine - Intuniv

- Intuniv™ became available in pharmacies in November, 2009
- FDA approved for the treatment of ADHD in children and adolescents aged 6 to 17
- extended-release tablet that is dosed once daily
- supplied in 1 mg, 2 mg, 3 mg and 4 mg strength extended-release tablets
Specific Medications

Beta-blockers
beta-blockers - Propranolol

• psychiatric indications:
  - performance anxiety disorder
  - disruptive behavior disorders, especially those manifesting explosive and violent behavior
  - self-injury and aggression in MR
  - aggression and panic in autism

• side effects include decreased heart rate and BP, fatigue, insomnia, mild symptoms of depression, shortness of breath (esp. in asthma), and GI distress
Drug Combinations

- although it is not uncommon in clinical practice, there are few reports in the literature concerning the simultaneous use of more than one medication
- usually considered in treatment-resistant patients
  patients with comorbid diagnoses
- use of two different medications may permit lower doses of each and decrease the potential for side effects
- further research is needed evaluating the overall safety and efficacy of various drug combinations
Summary

• Medication is widely recognized as a key treatment for serious psychopathology and behavior problems in children and adolescents

• Medication should be one component of a broad treatment plan

Treatment of children and adolescents with emotional and behavioral disorders is a TEAM SPORT