

# An Introduction to Pediatric Psychopharmacology

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## Foreword

I am grateful to Dr. Sandra DeJong, a skilled child psychiatrist, for providing a concise introduction to pediatric psychopharmacology. The following article should be very helpful for pediatricians who routinely prescribe such medication or as useful background information for those who do not.

I asked Dr. DeJong to write this article because I do not prescribe psychotropic medication in my practice. When parents request that medications be considered for their child, or when I think such meds may be helpful, I am more comfortable referring them to physicians like Dr. DeJong, who have the training and experience to prescribe safely. Interested pediatricians should review not only her disclaimer but also her cautionary "general points." I urge them to keep those points in mind and to consider consulting regularly with a psychopharmacologist. I would also advise them to take advantage of other suggestions in this web site. They include taking a careful history, not only of the child but also the family, asking themselves, periodically, "Who is the real patient?" as well as considering the benefits of counseling approaches for the child and the family.

Dr. DeJong will review this site regularly and update it as new data becomes available.

- Dr. Howard King, MD

## Disclaimer

The information below is intended as general guidelines to the pediatrician. In no way is this information intended to guide specific practice with specific patients.

## Some General Points:

**DO NO HARM** - As with all medications, psychotropic medications work best when the diagnosis is correct. In certain cases, they can make thoughts, feelings and behaviors worse, or cause physical problems. When in doubt regarding a diagnosis or treatment, an evaluation by a qualified mental health professional is advised.

**MULTIMODAL TREATMENT** - Medications alone are rarely the optimal treatment for a psychiatric problem. Other treatment modalities such as individual psychotherapy, family therapy, individual tutoring, school accommodations, group therapy, community supports such as social clubs, etc., are often warranted.

**FDA APPROVAL** - Until recently, the FDA did not require that psychiatric medications under development be studied in children. As a result, many medications that are increasingly used in children and adolescents have not been FDA approved. However, in most cases, there is good clinical evidence supporting the use of these medications for specific disorders.

**START LOW, GO SLOW** &ndash; Psychotropic medications for children should be initiated at a careful dose, and dose increases should be cautious.

## ADHD Medications

### What's New?

- Stimulants still the first-line agent in those without tics, severe anxiety, glaucoma, mood instability
- Isolated single active isomers
- Long-acting preparations
- Transdermal methylphenidate &ndash; &ldquo;Methypatch&rdquo;; awaiting FDA approval
- Atomoxetine (Strattera) &ndash; nonstimulant ADHD medication; inhibits norepinephrine reuptake; approved by FDA in 12/02; may be preferable in context of stimulant side effects including tic exacerbation and insomnia; has been shown to be equal but not superior to methylphenidate in efficacy.

- Multimodal Treatment of ADHD Study (Arch Gen Psychiatry. 1999; 56:1073-1086) clearly supports use of medications and therapy for ADHD

## Medication Treatment for ADHD

### STIMULANTS

Dosing  
Side effects  
Other

Methylphenidates &ndash; Short acting

Methylphenidate(Ritalin)

Start 5mg qd-tid up to 60mg qdPeaks 1-3hLasts 2-4h

Appetite suppression, sleep disturbance, tic exacerbation, stomachache, HA, emotional lability, rebound effect  
Avoid late pm dosing

Dextro-methylphenidate (Focalin)

Start 2.5mg qd Peaks 1-4h Lasts 2-5h  
Same  
Same

Methylphenidates &ndash; Long-acting

Extended-release methylphenidate (Concerta)

Start 18mg qam up to 54mg qd Peaks 8h Lasts 12h  
Same, but generally less rebound, less emotional lability  
Capsule with osmotic release mechanism; capsule must remain intact

Sustained release methylphenidate (Ritalin SR, Metadate ER, Methylin ER)

Start 10mg qamPeaks 3hLasts 5-8h  
Same

Metadate CD

Start 10mg qamPeaks 5hLasts 8h

&ldquo;Diffucap&rdquo; bead release mechanism; can open and sprinkle beads.

## Amphetamines &dash; Short acting

### Amphetamine mixed salts (Adderall)

Start 2.5mg qd-bid; upper limit 60mg/day Peaks 1-3h Lasts 5h

Same

Intermediate half-life; less rebound

### Dextroamphetamine (Dexedrine)

Start 2.5mg qd-bid up to 40mg qd Peaks 1-3h Lasts

5h

Same

## STIMULANTS (continued)

Dosing

Side effects

Other

## Amphetamines &dash; Long-acting

### Adderall XR

Start 10mg qam Peaks 1-4h Lasts 9h

Same

Can open and sprinkle beads.

### Dexedrine spansules

Start 5mg qam Peaks 1-4h Lasts 6-9h

Same

### Pemoline (Cylert)

Start 18.75 mg qd up to 112.5 mg qd

Hepatotoxicity; monitor LFTs. Others like methylphenidate.

Long-acting. Long half life.

## NOREPINEPHRINE REUPTAKE INHIBITOR

Strattera

Start 10-25 mg (weight dependent) up to 80 mg qd  
CYP2D6 inhibitor; GI side effects, appetite suppression  
24/7 coverage; no insomnia

ANTI-DEPRESSANTS

Imipramine (Tofranil)

Start 10-20mg bid up to 150 mg/day, increasing q2w  
Sleepiness, anticholinergic side effects, lower seizure threshold, EKG changes, blood pressure changes  
Taper if stopping. Don't use if hx of conduction problems. Consider baseline EKG

Nortriptyline (Pamelor)

Start 10-25mg, target dose 10-150mg/day in div doses  
Same  
Not helpful with comorbid depression

Juvenile-Onset Depression

Symptoms of Depression: "SIGECAPS"

DEPRESSED MOOD +

- SLEEP disturbance
- Loss of INTEREST/pleasure
- GUILT/worthlessness
- Decreased ENERGY
- Decreased CONCENTRATION
- Change in APPETITE

- PSYCHOMOTOR retardation or agitation
- SUICIDALITY

#### Features often unique to adolescents

- Increased sleep
- Irritability; negativistic or mixed mood state
- Increased food intake and weight gain
- Social withdrawal
- Decline in academic performance
- Masking by comorbid disorders (e.g. substance abuse, conduct disorder)

#### How to distinguish from juvenile-onset bipolar disorder

- JBPD is not like stereotype of adult "manic-depression," but phenomenology is controversial and under active study
- ?More chronic, continuous with long episodes
- ?Frequently mixed depressed/irritable/manic
- Mania characterized by hyperactivity, agitation, developmentally-dependent grandiosity (not euphoria)
- A complicated disorder that requires child psychiatry

#### How to approach depression in the pediatric office

- Identify depression and any comorbidities
- Ask about family history of mood disorders and suicide
- Assess stressors, family's dysfunction, other supports including school
- Provide psychoeducation and support, including re safety issues (e.g. lock up Tylenol, store gun with local police)
- Consider possible medical causes, e.g. anemia, hypothyroidism, lead, substance abuse, infectious mononucleosis
- Consider psychotherapy referral, SSRI and/or atypical antidepressant

trial

#### Examples of questions to ask the patient

- Do you feel bad (sad, grumpy, mad) inside most days?
- Are you acting differently because of how bad you're feeling?
- Do you feel so bad that life doesn't seem worth living?
- Have you actually thought of ways you might hurt yourself, or even kill yourself?

#### Treatment of Depression

- Multimodal approach
- Manage psychosocial stressors
- Include parents
- Address school issues
- Psychoeducation of child and family

#### Classes of Antidepressants

- Selective Serotonin Reuptake Inhibitors
- Atypical antidepressants (bupropion, venlafaxine, nefazodone, mirtazapine)
- Tricyclic antidepressants
- Monoamine Oxidase Inhibitors (MAOIs) (phenelzine, tranylcypromine, selegiline)

#### Antidepressants and the Pediatrician: Suggestions

- Consider becoming familiar with ONE SSRI and ONE atypical antidepressant
- Prioritize your treatment: Start with a safety evaluation; arrange for a next visit for further evaluation and assessment of treatment needs, including medication

- Discuss with your practice group what billing codes you may use for further visits

#### Issues with SSRIs

- Delayed efficacy (3-6 weeks)
- Annoying but not life-threatening side effects
- Generally safe in overdose
- Fluoxetine approved for use in juveniles; controlled data support the use of fluoxetine, sertraline and citalopram in children; paroxetine is also supported by one controlled study but see FDA warning below.
- Most common side effects
  - 1) Sexual dysfunction
  - 2) Nausea
  - 3) Sleep disturbance
- Beware of activation, precipitating a mania.  
A child who is activated on an antidepressant, or who has an underlying bipolar disorder and has been precipitated into a manic phase by the antidepressant, may be agitated, hyperactive, unable to sleep. Treatment is to stop the medication.
- Discuss sexual dysfunction, change in appetite.
- TADS (Treatment of Adolescent Depression Study), a multisite study comparing fluoxetine, cognitive behavioral therapy and combination treatment, is underway.

#### SSRI Side-Effects (Kutcher, 1997): Relatively common

- Sexual dysfunction
- Dizziness
- Sweating
- Diarrhea
- GI distress
- Sexual disturbances
- Headaches
- Fatigue
- Restlessness

- Initial insomnia
- Weight gain

#### SSRI Side-Effects (Kutcher, 1997): Relatively uncommon

- Delayed micturition
- Blurred vision
- Hypomanic symptoms
- Tachycardia
- Seizures
- Skin rashes
- Hypersomnia
- Sexual dysfunction
- Dry mouth
- Tremor
- Constipation
- Bleeding/bruising

#### A clinical approach to side effects

- Side-effects are very idiosyncratic in children; if a child develops a symptom on the SSRI, it may well be the SSRI.
- Determine with the child and family how impairing the side effect(s) is (are) and make a risk-benefit analysis re continuing the medication.

#### SSRI Discontinuation Syndrome

Most documented with paroxetine (Paxil) and fluvoxamine (Luvox), probably because they have shorter half-lives and no active metabolite

- Dizziness, paresthesias, asthenia, nausea, visual disturbance and headache
- Taper all SSRIs except possibly fluoxetine (Prozac) because of its long half-life

## SSRIs: Dosing

- Start at  $\frac{1}{4}$  to  $\frac{1}{2}$  of adult starting dose
- For young children, if well tolerated go up to half of adult starting dose after 1-2 weeks and wait 3-4 weeks.
- For adolescents, if well tolerated go up to adult starting dose after 1-2 weeks and wait 3-4 weeks.
- If some evidence of response, consider more time OR slow dose increase.
- If no evidence of response, consider slow dose increase, augmentation with lithium, or switching to another SSRI; if prohibitive side effects, switch to another SSRI.

## SSRIs: Drug-Drug Interactions

The SSRIs are known to inhibit metabolism of various cytochrome P450 isoenzymes. The effect is to raise the level of any co-administered medication which may be metabolized by the same isoenzyme.

For example, sertraline (Zoloft), citalopram (Celexa), fluoxetine (Prozac) and fluvoxamine (Luvox) are all metabolized by the P450 IIIA4 isoenzymes. So is erythromycin. Thus, coadministration of, say, sertraline and erythromycin may actually increase erythromycin levels, thus increasing the risk of side effects from erythromycin.

## Serotonin Syndrome

- Usually occurs with the addition of a serotonergic agent to other meds
- Characterized by mental status changes, agitation, myoclonus, hyperreflexia, diaphoresis, shivering, tremor, diarrhea, incoordination, fever
- Need to rule out sepsis, neuroleptic malignant syndrome

NOTE: AS OF JUNE 2003, PAROXETINE IS UNDER REVIEW BY THE FDA DUE TO A REPORTED INCREASED RISK OF SUICIDALITY IN CHILDREN/ADOLESCENTS BEING TREATED WITH PAROXETINE FOR MAJOR DEPRESSIVE DISORDER. IT IS RECOMMENDED THAT NO TRIALS OF PAROXETINE BE INITIATED UNTIL THE FDA PROVIDES FURTHER GUIDANCE.

PATIENTS CURRENTLY ON PAROXETINE SHOULD CONSULT THEIR DOCTOR ABOUT WHETHER THEY NEED TO TAPER OFF THE MEDICATION. NO PATIENT SHOULD STOP THE MEDICATION ABRUPTLY BECAUSE OF THE DISCONTINUATION SYNDROME.

### Tricyclic Antidepressants

Evidence suggests these are not significantly better than placebo in treating child/adolescent depression

Atypical antidepressants (second-line treatment for depression in children/adolescents)

- Venlafaxine (Effexor) (not effective in one placebo-controlled study of juveniles with depression)
- Nefazodone (Serzone) (not effective in one placebo-controlled study of juveniles with depression)
- Mirtazapine (Remeron)
- Bupropion (Wellbutrin)

Atypical antidepressants: Venlafaxine (Effexor)

- Can cause diastolic hypertension, discontinuation syndrome
- May cause anxiety, nausea, insomnia, sedation, dizziness, constipation, stomachaches, headaches
- Usually clinically inconsequential medication interactions

Atypical antidepressants: Nefazodone (Serzone)

- Serotonin and NE reuptake inhibition
- Indicated for depression; ? Also useful for anxiety
- New blackbox warning re liver failure; monitor liver function tests at baseline, with dose increases, and at regular intervals on stable dose
- May cause nausea, sedation (slow titration), agitation, dry mouth, constipation, confusion

- Few sexual side effects
- ? Less activating
- A metabolic inhibitor with med-med interactions like the SSRIs

#### Atypical antidepressants: Mirtazapine (Remeron)

- One controlled study does not support its use in children/adolescents
- Alpha-2 presynaptic autoreceptor inhibition (like yohimbine)
- Also stimulates serotonin and NE release
- Blocks post-synaptic serotonin receptors, so may cause sedation, weight gain, nausea

#### Atypical antidepressants: Bupropion (Wellbutrin)

- Affects both dopamine and NE systems
- Effective anti-ADHD agent
- Effective for depression in adults
- Anti-smoking (Zyban)
- No sexual dysfunction, ?less manicogenic
- Not to be used with seizures, bulimia
- May cause appetite suppression, sleep disturbance, tic exacerbation, irritability (esp at too-high dose)
- Caution in combining with other drugs that can lower seizure threshold

#### Monoamine Oxidase Inhibitors

- Examples: Phenelzine (Nardil), Tranylcypromine (Parnate)
- Complicated to use (dietary restrictions and med interactions)
- BEWARE OF COMBINING WITH: Sympathomimetics, (e.g. Pseudoephedrine) (hypertensive crisis); Demerol, dextromethorphan, serotonergic agents (serotonin syndrome); TCAs (get symptoms like serotonin syndrome)

- Do not recommend use by pediatricians

## Anxiety Disorders

- Generalized anxiety disorder
- Social phobia, selective mutism
- Panic disorder
- Obsessive-compulsive disorder
- Post-traumatic and acute stress disorders
- Separation anxiety
- Specific phobia
- Adjustment disorder with anxiety

## Anxiety Disorders: General

- Most common psychiatric condition in children and primary cause of inattention
- If child meets criteria for one anxiety disorder, frequently meets others
- Controversial diagnostically because of this and comorbidity with other psychiatric disorders, lack of biological markers
- Good evidence for cognitive-behavioral treatment; one controlled study supports use of fluoxetine in juveniles; one open study supports use of fluvoxamine
- Highly familial
- Relationship to temperament (Chess and Thomas, Kagan's "inhibited child" work)
- Course tends to be chronic, (remission/relapse)
- Medical conditions such as hyperthyroidism, hypoglycemia, pheochromocytoma, and substance-induced anxiety, need to be ruled out

## Obsessive Compulsive Disorder - PANDAS

- Pediatric
- Autoimmune
- Neuropsychiatric

- Disorders
- Associated with
- Strep

When to check for Strep (throat culture, ASO titer, anti-Dnase-B titer)

Any patient with tics, chorea, Obsessive Compulsive Disorder, choreiform movements who has:

- Abrupt onset of symptoms
- Abrupt exacerbation of symptoms
- Loss of a medication response
- History of good behavior with sudden dramatic behavioral difficulties (Leonard, 1999)

Treatment of Anxiety Disorders

Consider first: Cognitive Behavioral Therapy, family work, stress reduction, etc.

Consider meds if important functional impairment (e.g. not able to go on playdates, not going to school).

How to handle anxiety in the pediatric office

- Identify anxiety and functional impairment
- Identify comorbidities
- Take family history
- Rule out possible medical causes including substance abuse
- Provide psychoeducation, advice re relaxation techniques (exercise, pleasure activities, etc.)

- Ask patient to keep a journal of the A, B, Cs of his or her anxiety symptoms (antecedent, behavior, consequence, including any efforts to contain)

#### Medications for Anxiety

- SSRIs
- Tricyclics
- Buspirone
- Benzodiazepenes
- Beta-blockers
- Combination of the above

#### SSRIs for Childhood Anxiety Disorders

Increasing usage, although little data, for:

- Panic disorder
- Social phobia
- Generalized anxiety disorder
- Separation anxiety disorder

#### Buspirone (Buspar)

- 5HT-1A receptor agonist
- Clinical effects not uniform
- No pharmacokinetic studies in children
- May be helpful for GAD, ?with ADHD, in med-sensitive populations (e.g. brain-injured, PDD)
- Start 2.5-5 mg TID, up to 30-60 mg/d
- Delayed onset of anxiolytic action
- Advantages: mild side effects, no addictive potential
- ? Can cause hypertension

## Benzodiazepines

### Short half-life:

- Alprazolam (Xanax)
- Lorazepam (Ativan)

### Longer half-life:

- Clonazepam (Klonopin)
- Diazepam (Valium)

### Concerns about benzodiazepines

- Sedation, cognitive impairment
- Disinhibition
- Dependence/tolerance
- Potentiate effects of other medications
- Withdrawal side effects (need to taper)

### When to consider using benzodiazepines

- Short-term treatment of disabling symptoms, e.g. for school avoidance until an SSRI starts to "kick in";
- Recurrent panic disorder, as a prn or "security blanket"; (NOTE: clonazepam and alprazolam most effective for panic in adults)
- RARELY for short-term sleep difficulties

### Example of using a benzodiazepine

Problem: 9 yo with school avoidance secondary to social phobia and separation anxiety; develops panic symptoms when approaching school in parents' car

Solution: 0.25-0.5 mg of clonazepam (Klonopin) given 30-45 minutes before arrival at school to offset panic symptoms and allow desensitization therapy to occur; may need to adjust timing of dosing given wide range of time to onset

#### Sleep medications for children/adolescents

- Diphenhydramine (Benadryl) 25-50 mg
- Trazodone (Desyrel) 25-50 mg (Key potential side effect is priapism in males)
- Zolpidem (Ambien) 5-10 mg
- Clonidine (Catapres) 0.05-0.10
- Mirtazapine (Remeron) 7.5 mg

Always begin by emphasizing sleep hygiene.

#### Mesothelioma Cancer

The Lawyers of SimmonsCooper Law Firm Understand and Care about Mesothelioma Cancer. If you or a loved one has been diagnosed with Mesothelioma cancer, then your entire life has completely changed.