Psychoeducational Interventions*

- Cognitive-Behavioral Treatment
  - Impulse control
  - Anger management
- Classroom strategies and modifications
  - FBAs (Functional Behavior Assessments)
  - 504 / IEP specifics
- Parent Education and Empowerment
  - www.parentshelpingparents.com
  - www.schwablearning.org
  - www.schoolpsychiatry.org

ADHD Treatments (Medication options)*

- Teaching Points
  - Warnings about ADHD drugs should NOT dissuade providers from using these drugs
  - Psychostimulants remain the drugs of choice for ADHD
  - It is important to "fine tune" medications by ascertaining effects over the day

Warnings about ADHD drugs*

- 12/04 Strattera: black box warning about possible hepatitis following 2 reports of hepatitis
- 2/05 Adderall:FDA Alert- should not be used in individuals with underlying cardiac abnormalities following 12 sudden unexpected deaths over time Adderall in USA; only XR available in Canada and pulled from market
- 6/05 Ped Adv Com of FDA-Will delay labeling change to all MPH products of side effects of psychiatric (visual hallucination, psychosis, aggression) and cardiovascular until amphetamines and atomoxetine also evaluated in early 2006
- 6/05 Lilly observed increase in aggression and hostility "not statistically significant", but will add information to Strattera label voluntarily

Warnings about ADHD drugs*

- 10/05 Canada re-allowed Adderall XR back on market
- 11/05 FDA requires Black Box warning on Strattera for increased risk of suicidality 4/1000
- 2-3/06 FDA advisory committee recommends black box warnings for CV risk on psychostimulants
  - Committee votes only a parent guide and NOT a black box warning
- 3/06 European review highlights increased risk of seizures and QTc prolongation with Strattera

Special Issues: Pharmacotherapy in Youth*

- Clinician must have good working alliance with both the patient AND the parents (a dual alliance)
- Children and (especially) teens may be reluctant consumers
- Children should be told that they may not recognize changes in themselves before the first medication trial
- Importance of school placement and teacher-doctor alliance
- Each school may have different requirements for medicating children
- From MTA study (discussed later), parents recognize side effects and teachers recognize efficacy

ADHD Treatments*

- MTA study: *Arch Gen Psychiatry* Vol 56, 1073-1086, Dec 1999
  - 579 children with ADHD-CT; 7-9.9 yrs; 6 sites; 14 month parallel-design
  - 4 different treatment groups:
    - Medication mgmnt (titration plus 30" monthly visits)
    - Intensive behav treatment (parent, school, child components)
    - Optimal combination of both
    - "Usual" community care

ADHD Treatments*

- MTA study: **conclusions**
  - All 4 groups showed sizable reduction in symptoms over time
  - *ADHD symptoms*: Combo. and med-only groups had significantly greater improvement than those given intensive behav tx or "usual" community care (UCC)
  - ADHD with co-morbid anxiety disorder: behavioral treatment was similar to medication tx, and both were superior to UCC

MTA study: cont'd.*

- *Combined behavioral intervention and stimulant medication--(multimodal treatment), yielded no statistically significantly greater benefits than medication management "alone" for the core symptoms of ADHD*

- Note that the "medication management" in this study occurred for 30 minutes, 1x per month
  - *"usual community care" average for visit frequency was 1-2x per year*

ADHD Treatments*

- MTA study: cont'd.
  - *Non-ADHD symptoms*: (social skills, parent-child relations, oppositional-aggressive behavior, internalizing symptoms, academic achievement)
    - The 3 MTA-delivered treatments were very similar, with the combined treatment arm being consistently superior to UCC.
- Highly anxious children with ADHD may represent a subgroup of children with unique treatment needs
- 13 % placebo response in MTA study
  - May have been related to alliance with MD and research team

ADHD Treatments*

- MTA study: 2 year follow-up (*PEDIATRICS* ,113 (4); April 2004, pp. 762-769)
  - Consistent use of stimulant medication was associated with maintenance of effectiveness but continued "mild growth suppression" (1 cm per year over 2 years).
  - Further follow-up will help to address question of growth (ultimate ht. suppression vs. longer time to finish growing)
  - Medication holidays may be prudent clinical practice (summertime, holidays)

ADHD Treatments* (medication options)

- Established Treatments
  - Psychostimulants (1st line)
  - Atomoxetine (1st line)
  - Bupropion (2nd line)
  - TCAs (2nd- 3rd line)
- Probable Efficacy
  - Modafinil
  - Alpha-2 agonists

ADHD Treatments* (medication options)

- Possible efficacy
  - Omega-3, -6 Fatty Acids (Fish Oil, Flax Seed Oil)
  - Venlafaxine
  - Beta-blockers
- Effective, but impractical: MAOIs
- *Likely ineffective*
  - SSRIs
  - Caffeine
  - St. John's Wort

Stimulants*

- "stimulate" certain areas of the brain to focus better
  - FDA classifies a substance as "psychostimulant" if nucleus accumbens is activated
- in use for "behavioral disorders" in children since 1930's
- many studies to document safety and efficacy
- 70-85% response rate
  - do not use this to confirm diagnosis!

Stimulants*

- benefits: improved focus, concentration, attention span; reduced hyperactivity, impulsivity, and fidgeting
- side effects: irritability, stomachache, headache, dysphoria, zoned-out effect, appetite suppression, sleep problems, height velocity slow-down (<10%)
- Amphetamine formulations may produce more sleep/ appetite problems, especially at higher doses

Stimulants*

- Special consideration
  - Motor tics
  - Depression
  - Anxiety d/o (children w/ co-morbid anxiety may improve on MPH, according to MTA study)
  - Seizure d/o
  - Children under 6 years old may be safely treated, starting with methylphenidate, once all psychosocial treatments have been implemented
    - PATS (Pre-school ADHD Treatment Study) is one of many to document safety and efficacy
      - Young children may be more sensitive to side effects
      - Consider weight-based dosing for children under 25 kg: 1mg/kg/day (MPH); 0.5 mg/kg/day (AMPH)

Methylphenidate Formulations

Brand	Type	Dosage forms (mg)	Est. duration (hrs)	Max daily dose [mg] *Range 0.3-1.0mg/kg/day*
Generic	IR	5,10,20	2.5 - 4	[60]
Ritalin	IR	5,10,20	2.5 - 4	[60]
	SR	20	6 - ?	
	LA***	20	8-10	
Methylin	IR*	5,10,20	2.5 - 4	[60]
	ER	5,10,20	6 -8	
Focalin	IR	2.5,5,10	3-5	[20-30]
	XR***	5, 10, 15, 20	8-10	
Metadate	ER	10,20	6-8	[60]
	CD***	20	8 -12	
Concerta	ER	18, 27,36,54	10 - 12	[72]
Daytrana	patch	10, 15, 20, 30	9-12	[30]

[ ] Some patients may tolerate higher doses.
* Available in chewable tablets and liquid
*** May be sprinkled on food
Chart adapted from Glen R. Elliott, PhD, MD

Amphetamine Formulations

Brand	Type	Dosage forms (mg)	Est. duration (hrs)	Max daily dose (mg) *Range 0.15-0.5 mg/kg/day*
Generic	IR	5,10,20	3-6	40 *
Dexedrine	IR	5,10	4-5	40 *
	Spansules**	5, 10, 15	5-9	
Adderall	IR	5, 7.5, 10, 12.5, 15, 20, 30	4-6	40*
	XR**	5-30 mg , (in 5-mg increme nts)	8-10	
Vyvanse	Lisdex-amfetamine	2.5,5,10	8-10	70
		5, 10, 15, 20		

*Some patients will tolerate higher doses. **may be sprinkled on food
Chart adapted from Glen R. Elliott, PhD, MD

Adderall XR*
-delivers mixed salts using immediate and time-released beads:
50% immediate
50% delayed

Concerta
-delivers MPH using immediate release coating and delayed release osmotic mechanism:
22% immediate
78% delayed

Metadate CD
-biphasic delivery of MPH using immediate and delayed release beads in capsule:
30% immediate
70% delayed

Ritalin LA
-biphasic delivery of MPH using immediate and delayed release beads in capsule:
50% immediate
50% delayed

Focalin XR
-biphasic delivery of *dextro* MPH using immediate and delayed release beads in capsule
50% immediate
50% delayed

(note: only the *d*-version of MPH is active, thus only 1/2 the usual MPH dose is used)

Match the formulation with the needs of the patient and family*

- Have to know when youth "needs" the psychostimulant (e.g., early in AM for school only, or including homework, peer activities, week-ends)
- Parent and teen sometimes have definite preferences for one or another, and so do HMOs
- Train parents to observe efficacy and side effects through the day and into the evening

How to initiate dosing*

- Generally not by weight, unless patients are less than 25 kg (0.3- 1mg/kg/d for MPH)
  - (0.15 - 0.5 mg/kg/d for AMPH)
- Titrate to efficacy or intolerable side effects: start at 5 mg MPH or 2.5 mg AMP
  - Increase by 5 mg MPH, or 2.5 mg AMP every 3-5 days to first target dose, decided upon by doctor and family
  - Get weekly reports and adjust upward, checking for side effects and efficacy

The Art of Fine tuning*

- Must have accurate info about child/teen's performance "over the day"; use scales and listen to teachers: titrate as needed

- Can combine short and long-acting preparations
  - if dysphoric at days end, add MPH to Concerta at the end of the school day (no later than 3:30PM); Dex to Dex-spansules at the start of the day because of delayed effect of spansules

The Art of Fine-tuning –II*

- If only partial efficacy with stimulants, can "mix and match" with other anti-ADHD drugs (e.g., clonidine / guanfacine, bupropion, atomoxetine TCAs)
- Inform family, and be vigilant about checking for additive sympathomimetic side effects

Common errors in dosing psychostimulants*

- Failure to increase dosing slowly to maximum if no side effects (MTA study showed lower dosing in community sample

- Beginning with a dose that is too high
  - "Start low and go especially slow" with patients who are developmentally delayed
- Not assessing the duration of action; (may need to "bunch up " dosing with IR formulations)
- Failure to use another psychostimulant if the first or second trial fails
- Failure to use input from school

Serious side effects of psychostimulants*

- Sudden cardiac death
  - Anecdotal, but not irrelevant
  - Cases thus far have been primarily in patients with pre-existing cardiac conduction defects
  - Ask about history of sudden tachycardia, fainting, and family history of sudden cardiac death prior to initiating
- 30+ cases of psychosis or formal hallucinations: discontinue the medication
- Growth Suppression (MTA 2004) effects are likely to be made up in late teens or by drug holidays; especially at risk, those with nausea and vomiting
  - Plot heights every 3 months to ensure proper growth velocity

Tics and ADHD* (adapted from review by Plizska, 2006)

- Mild or moderate tics occur in a significant number of patients with or without ADHD pharmacotherapy
  - 5-18% of schoolchildren will experience a simple or complex tic in their lifetime
- Tics during ADHD treatment may improve even while psychostimulants are used; discontinue only if serious
- **Lipkin et al**, in a review of 122 children treated with stimulant medication found 9% developed transient tics and <1% developed chronic tics

Lowe et al. *JAMA* 1982;247:1729.
Sverd et al. *JAACAP* 1989;28:574.
Erenberg et al. *Neurology* 1985;35:1346.
Lipkin et al. *Arch Pediatr Adolesc Med* 1994;148:859.

Tics and ADHD* (adapted from review by Plizska, 2006)

- Many children with tics and ADHD can tolerate stimulants without an increase in tics
  - **Law & Schachar (1999):** 12-month study, 91 children
    - MPH treatment did not produce significantly more tics than placebo in children with or without mild-to-moderate preexisting tic disorder
  - **Gadow et al (1999):** 24-month study, 34 children with ADHD and tic disorder or Tourette's syndrome
    - stimulant treatment was effective in controlling ADHD symptoms without adversely affecting tics

Induction or Exacerbation of Tics*

(adapted from review by Plizska, 2006)

- Tics are usually transient
  - Rarely do patients develop a chronic tic disorder
- When tics do occur or are worsened
  - Decrease dose
  - Switch to another stimulant
  - Add adjunctive drug to treat tics
    - Clonidine / guanfacine
  - Try nonstimulant medication
    - Atomoxetine
    - Modafinil