MANAGING ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) IN CHILDREN WITH COMORBIDITIES

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- Mudassar Tariq, MD and Yen Phan, PharmD report no relationships with proprietary entities related to the content of this activity.
- Persons involved in planning of this activity have reported no relevant financial relationships with any commercial interest.

DISCLOSURE

- Some medications mentioned may not be FDA-approved for children for the indications identified
- Brand names, kept to a minimum, are used when necessary to differentiate products

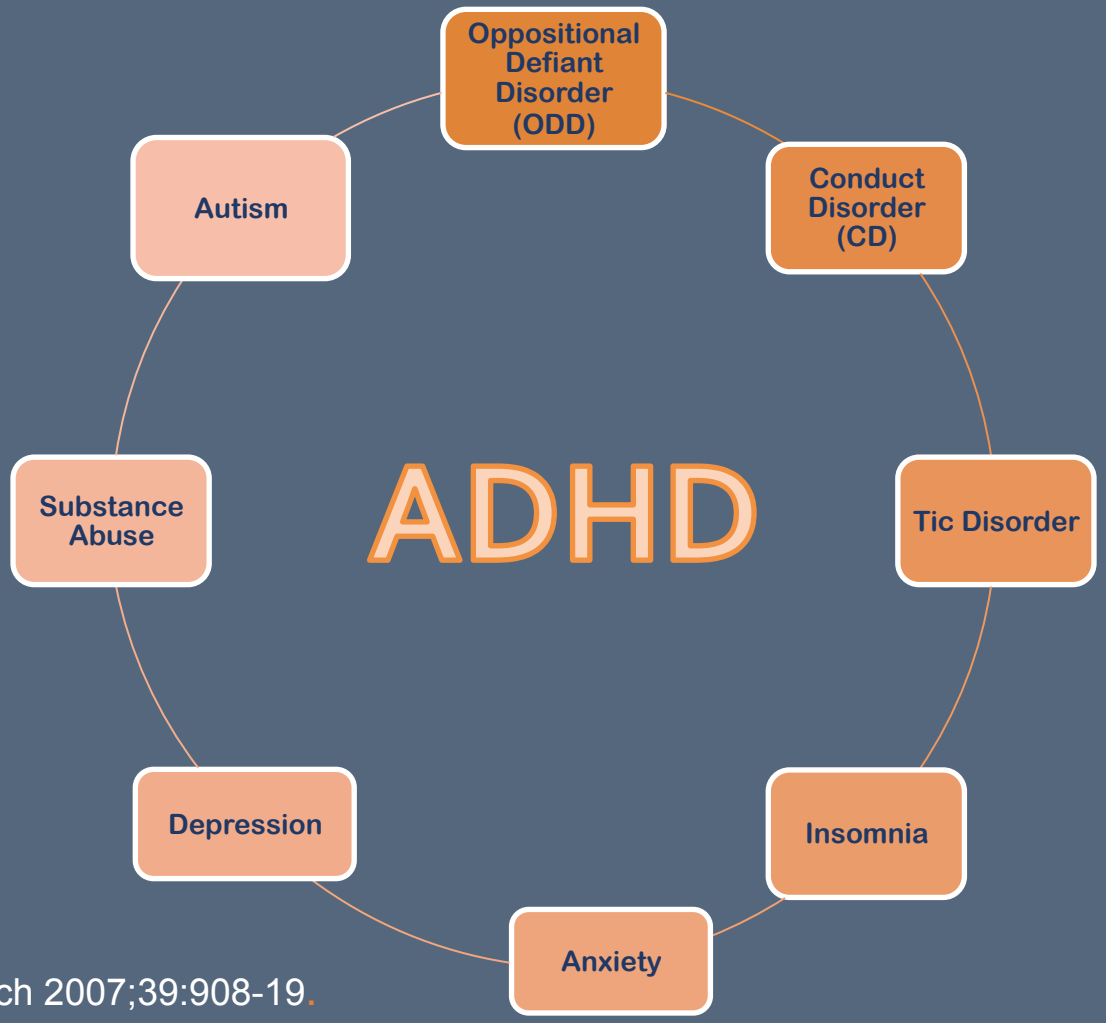
OBJECTIVES

- Evaluate current pharmacologic treatment options for attention-deficit hyperactivity disorder (ADHD)
- Discuss comorbid conditions associated with ADHD
- Describe pharmacological and psychosocial therapy treatment options for ADHD with comorbidities
- Identify situations where a psychiatric referral is appropriate

BACKGROUND

- ADHD is a chronic condition that causes significant impairment in academic performance, family and social relationships, and self-care
- Children with ADHD often have co-existing disorders that present challenges to treatment
- Consensus is needed to address these complexities and develop a standard of care

COMORBIDITIES



Pliszka S. J Am Acad Child Adolesc Pysch 2007;39:908-19.

Am Acad Ped 2011; 128(5): 1007-22.

CURRENT GUIDELINES

- Goal of therapy: improvement of function in 3 domains

- Management strategies

Psycho-education

Behavioral therapy

Pharmacotherapy

Am Acad Ped 2011; 128(5): 1007-22.

CURRENT GUIDELINES

Key recommendations from American Academy of Pediatrics

	Preschool age (4-5 years)	School age (6-11 years)	Adolescents (12-18 years)
Recommendation	Behavioral therapy initiated first line[A]. Medications may be considered if moderate to severe dysfunction exists, weigh risks vs. benefits[B].	Behavioral therapy[B] and/or medications[A] are recommended, preferably both.	Behavioral therapy[C] and/or medications[A] are recommended, preferably both.
	[A,B,C] Grading for quality of evidence		

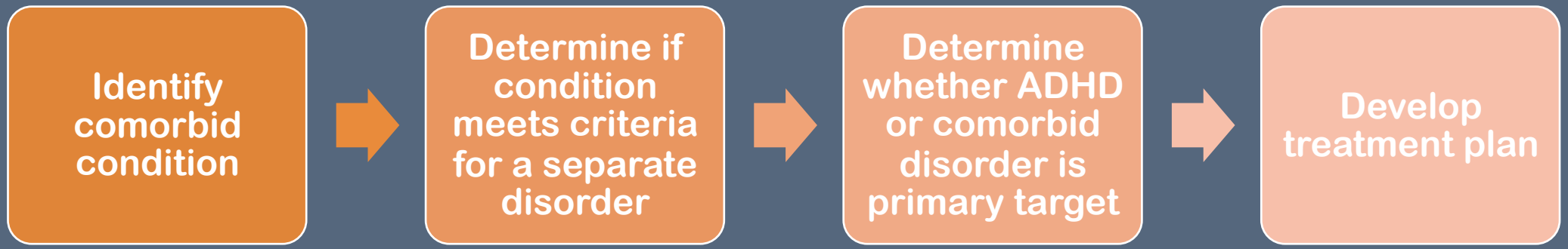
Am Acad Ped 2011; 128(5): 1007-22.

FDA-APPROVED ADHD MEDICATIONS

Stimulants	Non-stimulants	
Amphetamine, Methylphenidate	**Atomoxetine**	**Guanfacine ER, Clonidine ER**
• First-line treatment option • Trial one drug in each stimulant group before moving to non-stimulants	• Consider first if medication diversion is a concern	• Consider first if medication diversion is a concern • Approved as adjunctive therapy to stimulants
• Adverse effects: Loss of appetite, abdominal pain, headaches, sleep disturbance, decreased growth velocity, hallucinations (rare), sudden cardiac death (rare)	• Adverse effects: Somnolence, GI symptoms, decrease in appetite, suicidal thoughts, hepatitis (rare)	• Adverse effects: Somnolence, dry mouth, hypotension, bradycardia

Am Acad Ped 2011; 128(5): 1007-22. ; Lexi-Comp, Inc.

EVALUATION & ASSESSMENT



Clinical pearl: Optimize ADHD treatment first, which may resolve coexisting symptoms of another disorder.

Am Acad Ped 2011; 128(5): SI1-121.

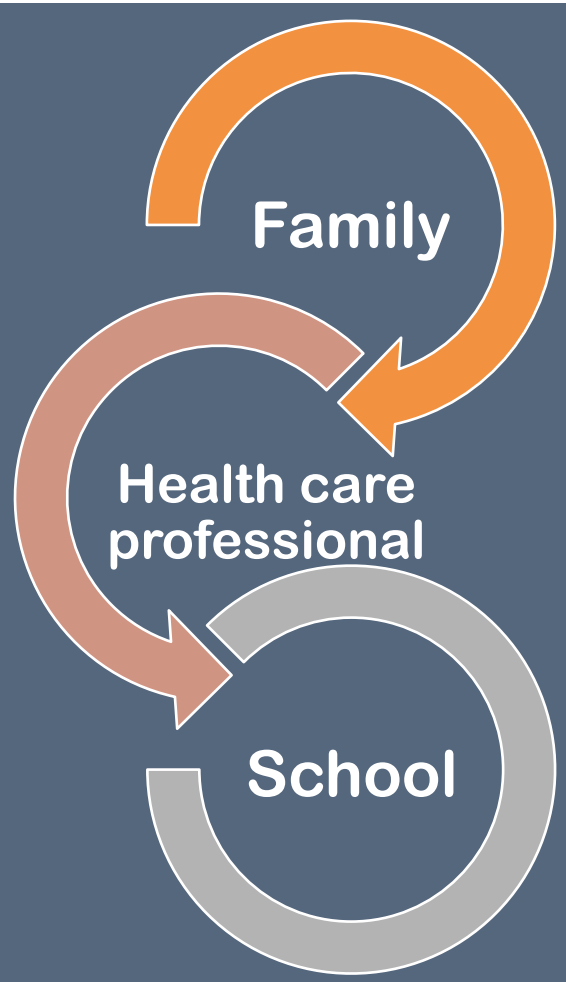
THE IMPORTANCE OF PSYCHOEDUCATION

- Cornerstone of therapy
- Thorough education on cause of disease, symptoms, treatment, monitoring parameters, prognosis
- Empower patient and family members to be active participants in their treatment
- Mix of written materials, pictures, videos

Am Acad Ped 2011; 128(5): SI1-121.

FAMILY & SCHOOL RELATIONSHIPS

- Successful management requires maintaining a strong relationship with patient families and schools
- Collaborate to identify target goals, discuss progress, and make assessments
- Establish team with coordination plan



Am Acad Ped 2011; 128(5): SI1-121.

BEHAVIORAL INTERVENTIONS

Parent training	• Training parents to develop skills and techniques to modify child's behavior
Classroom management	• Creating structure in the classroom to enhance social and academic learning
Peer interventions	• Social skills training to improve peer relationships

Am Acad Ped 2011; 128(5): SI1-121.

PARENT TRAINING

- Goal is to alter the motivation of the child to control inattention, hyperactivity, and impulsivity
- Train parents to develop skills and techniques
  - Effectively provide positive reinforcement
  - Decrease or eliminate child's inappropriate behavior (planned ignoring)
  - Learn how to give successful commands
  - Learn how to carry out punishments in a responsible way

Am Acad Ped 2011; 128(5): SI1-121.

CLASSROOM MANAGEMENT

- Goal is to shape child's behavior in the classroom
- Token economy
  - Reinforce positive behaviors
  - "Punish" inappropriate behaviors
  - Tokens cashed in for rewards or privileges
- Daily behavior report card communicated to parents who reinforce consequences at home
- 504 Rehabilitation Act for classroom adaptations

Image credit: http://www.thelearningcommunity.us/about-us/faqs.aspx

Am Acad Ped 2011; 128(5): SI1-121.

OPPOSITIONAL DEFIANT DISORDER & CONDUCT DISORDER

ODD (45-65%)

- Losing temper
- Defiant around adults

CD (8-25%)

- Running away
- Skipping school
- Lying
- Stealing

- ODD is most common coexisting disorder among very young children or adolescents with ADHD
- Children with CD display more aggressive behavior towards others, often violating rules and social norms
- Early intervention is key in preventing development of more serious mental health issues

Steiner M. J Am Acad Child Adolesc Pysch 1997; 36(10): 122-39S.

OPPOSITIONAL DEFIANT DISORDER & CONDUCT DISORDER

TREATMENT

Psychotherapy

- Individual therapy
- Behavioral management (parent training)
- Multi-systemic therapy

Medications

Alpha$_2$ agonists	Antipsychotics
Guanfacine immediate release (IR) • Children ≥ 6 years old: Initiate at 0.5 mg/day. (ADHD dosing) • Titrate every 3-4 days up to 4 mg/day. **Clonidine (IR)** • Children ≥ 5 years old: Initiate at 0.05 mg/day. (ADHD dosing) • Titrate weekly up to 0.4 mg/day in 2 or 3 divided doses.	**Risperidone** • Children ≥ 4 years old: Initiate at 0.01 mg/kg/day. • Titrate weekly up to 0.06 mg/kg/day in 1 or 2 divided doses. • Max dose: 2 mg/day

Steiner M. J Am Acad Child Adolesc Pysch 1997; 36(10): 122-39S. ; Lexi-Comp,Inc.

MEDICATION SAFETY

	Alpha$_2$ agonists	Antipsychotics
Adverse Effects	• Bradycardia, hypotension (dose dependent) • Xerostomia • Sedation, headache • Skin rash	• Weight gain • Dyslipidemia, hyperglycemia • Extrapyramidal symptoms • Hyperprolactinemia • Somnolence
Monitoring Parameters	• Blood pressure, heart rate	• Growth (weight, height, BMI, waist circumference) • Abnormal involuntary movement • Blood pressure, heart rate • Blood glucose, A1C, lipid panel
Other	• Use with caution in severe cardiovascular disease • Slowly taper when discontinuing therapy to avoid rebound hypertension	• Vigilance in monitoring is necessary due to lack of long-term safety data in pediatrics

CASE #1

CASE #1 (JC)

- John C. is a 10 year old Caucasian male who comes to clinic for a follow-up evaluation ADHD medication management.
  - He was diagnosed with ADHD at age 7 and has been stable on Methylphenidate ER 36 mg daily. His mother reported that John has been oppositional and not following directions. He took a pack of gum to school yesterday and when his teacher asked him to hand over the gum, he refused and was sent to the principal's office. He became disrespectful and refused to comply with instructions. He has been irritable and has been getting angry easily. He has poor frustration tolerance and deliberately annoys others.

1.) What diagnosis should be made?

Oppositional defiant disorder

2.) What treatment should be initiated?

Start behavioral therapy

CASE #1 (JC)

- He was referred for individual therapy for 3 months. His mother has received parent training and has been using a reward system to promote positive behaviors. She has been praising him for good behaviors. However, his behavior remains unchanged. He continues to get upset easily and his teachers still report oppositional behaviors at school. His mother asks if there is a medication that can help.

- Which medications, if any, should be initiated?

Guanfacine 0.5 mg/day or Clonidine 0.05 mg/day

SUBSTANCE ABUSE (15-19%)

- Adolescents should be routinely screened for signs of abuse (CRAFFT*)
- To be considered a disorder, substance use must cause dysfunction in one or more domains:
  - Psychiatric/behavioral, family, school, recreational, medical
- If ADHD is newly diagnosed in a substance abuse patient, refer for therapy and counseling before starting medications (due to risk for drug abuse).

Image credits: https://www.pexels.com; www.publicdomainpictures.net

Adolescents with ADHD are at greater risk for smoking, alcohol use, and engaging in risky behaviors.

*CRAFFT= Screening tool for substance abuse in adolescents

Bukstein O. J Am Acad Child Adolesc Pysch 2005: 44:609-21.

CRAFFT SCREENING TOOL

- **C**- Have you ever been in a **CAR** driven by someone (including yourself) who was under the influence of alcohol or drugs?
- **R**- Do you ever use alcohol or drugs to **RELAX**, feel better about yourself, or fit in?
- **A**- Do you ever use **ALCOHOL** or drugs alone by yourself?
- **F**- Do you every **FORGET** things you did while using alcohol or drugs?
- **F**- Do your family or **FRIENDS** ever tell you to cut down on alcohol or drug use?
- **T**- Have you gotten into **TROUBLE** while using alcohol or drugs?

Am Acad Ped Committee Substance Abuse 2011; 135(4): e1105

ANXIETY (10-30%)

- Anxiety can be a complication or a comorbid disorder
- Initiate psychosocial interventions as first-line
  - Cognitive behavioral therapy (CBT)
  - Parent training
- Second line- Selective Serotonin Reuptake Inhibitors (SSRI's)

Fluoxetine	Sertraline
• Children ≥ 7 years old • Initiate at 10 mg once daily • Titrate after 4-6 weeks by 10 mg increments • Max dose 60 mg/day	• Children ≥ 6 years old • Initiate at 25 mg once daily • Titrate upwards by 25 – 50 mg increments every 4-6 weeks • Max dose 200 mg/day

BLACK BOX WARNING
Monitor for worsening depression, agitation, or suicidality in patients age 25 and under.

Connolly S. J Am Acad Child Adoles Pysch 2007; 46:2, 267-83.

DEPRESSION (10-18%)

- Depression is usually diagnosed at a later age than ADHD
- Initiate psychosocial interventions first
  - Cognitive behavioral therapy
  - Individual therapy
- Second line- SSRI's

Fluoxetine	Sertraline	Escitalopram
• Children ≥ 8 years old • Initiate at 10 mg once daily • Titrate every 4-6 weeks up to 20 mg/day	• Children ≥ 6 years old • Initiate at 12.5 mg once daily • Titrate every 4-6 weeks to 100 mg/day • Max dose 200 mg/day	• Children ≥ 12 years old • Initiate at 10 mg once daily • Titrate up to 20 mg every 4-6 weeks

BLACK BOX WARNING
Monitor for worsening depression, agitation, or suicidality in patients age 25 and under.

**Other SSRI's may be used off-label*

Birmaher B. J Am Acad Child Adoles Pysch 2007; 46:11, 1503-25.

MEDICATION SAFETY

	SSRI's
Adverse effects	• GI symptoms, sleep changes (insomnia/somnolence, nightmares) • Diaphoresis • Headaches • Akathisia • Changes in appetite • Sexual dysfunction • Serotonin syndrome • Behavioral activation • Increased risk of bleeding
Monitoring parameters	• Monitor for worsening depression, agitation, or suicidality in patients age 25 and under (Black Box Warning)
Other	Gradually taper when discontinuing therapy to reduce incidence of withdrawal

CASE #2

CASE #2 (JA)

- Jessica A. is a 13 year-old Hispanic female who was diagnosed with ADHD at age 9. She has been taking Lisdexamfetamine 20 mg daily for 4 years.
  - She reports that medication has been helping but her grades are dropping. She reports feeling anxious often, especially in social situations. She admits to changing her plans last minute because of her nerves. She is unable to identify a cause of her anxiety but states that she's afraid that sometimes she's unable to speak because words don't come out right, which causes a lot of embarrassment.

1. What diagnosis should be made?

   Anxiety

2. What treatment should be initiated?

   CBT

3. How should her ADHD be addressed?

   Obtain a new set of Vanderbilt screening tests to assess if Lisdexamfetamine dose is appropriate

CASE #2 (JA)

- Jessica started CBT and completed a course of psychotherapy. Repeat Vanderbilt assessments indicate moderate ADHD symptoms.
- What adjustments are needed to her ADHD therapy?

  Increase dose to 30mg

- Jessica reported improved attention with new dose. Her anxiety symptoms are still present and she has started experiencing panic attacks. Last week, she felt extremely nervous during lunch time and had to leave the cafeteria.
- What are your next steps?

  Add an SSRI, continue ADHD therapy

VANDERBILT ASSESSMENT TOOL

Vanderbilt Assessment Scale—Parent Informant # 6175

Name of child:_____ Gender:_____ Age:___ Grade:_____Date: _____

Completed by: _____ Parent's Phone Number: _____

Directions: Each rating should be considered in the context of what is appropriate for the age of your child. When completing this form please think about your child's behavior in the past 6 months.

Is this evaluation based on a time the child __ was on medication __ was not on medication __ not sure?

	Symptoms	Never	Occasionally	Often	Very Often
1.	Does not pay close attention to details or makes careless mistakes with, for example, homework	0	1	2	3
2.	Has difficulty keeping attention to what needs to be done	0	1	2	3
3.	Does not seem to listen when spoken to directly	0	1	2	3
4.	Does not follow through on instructions and fails to finish schoolwork, chores, or duties	0	1	2	3
5.	Has difficulty organizing tasks and activities	0	1	2	3
6.	Avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (e.g., schoolwork or homework)	0	1	2	3
7.	Loses things necessary for tasks or activities (e.g., toys, school assignments, pencils, books, or tools)	0	1	2	3
8.	Is distracted by extraneous stimuli	0	1	2	3
9.	Is forgetful in daily activities	0	1	2	3
10.	Fidgets with hands or feet or squirms in seat	0	1	2	3
11.	Leaves seat in classroom or in other situations in which remaining seated is expected	0	1	2	3
12.	Runs about or climbs excessively in situations in which remaining seated is expected	0	1	2	3
13.	Has difficulty playing or engaging in leisure activities quietly	0	1	2	3
14.	Is "on the go" or often acts as if "driven by a motor"	0	1	2	3
15.	Talks excessively	0	1	2	3
16.	Blurts out answers before questions have been completed	0	1	2	3
17.	Has difficulty waiting in line	0	1	2	3
18.	Interrupts or intrudes on others (eg, butts into conversations/games)	0	1	2	3
19.	Argues with adults	0	1	2	3
20.	Loses temper	0	1	2	3

NICHQ Vanderbilt Assessment Scales
www.nichq.org

TIC DISORDER (8-34%)

- Classified as simple or complex tics
  - Motor and/or vocal tics
- Tics preceded by a *premonitory urge* that is relieved after tics are expressed
- The course can wax and wane over time
- Average age for diagnosis of tics and ADHD is 7 years
- Controversy exists regarding whether tics are caused by stimulants
  - Some evidence that methylphenidate is less likely to cause tics

Murphy T. J Am Acad Child Adoles Pysch 2013; 52(12): 1341-59.

TIC DISORDER
TREATMENT

- Treatment of the disorder depends on severity and functional impairment on daily activities
  - Only initiate medications if quality of life is affected

Psychosocial interventions

- Habit Reversal Training
  - Awareness training and competing response

Medications

Alpha$_2$ agonists *First line*	Antipsychotics *Second line*
Clonidine IR	**Haloperidol**
• Children ≥ 7 years: Initiate at 0.025 or 0.05 mg/day • Titrate gradually up to 0.4 mg/day in 3 or 4 divided doses	• Children ≥ 3 years: Initiate at 0.25- 0.5 mg/day in 2 to 3 divided doses • Titrate gradually up to 4 mg/day
Guanfacine IR	**Risperidone**
• Children ≥ 6 years: Initiate at 0.5 mg/day • Titrate gradually up to 4 mg/day in 2 or 3 divided doses	• Children ≥ 7 years: Initiate at 0.25-0.5 mg/day • Titrate gradually to 6 mg/day in 2 divided doses

Murphy T. J Am Acad Child Adoles Pysch 2013; 52(12): 1341-59. ; Lexi-Comp,Inc.

AUTISM

- Diagnostic overlap presents challenges with differential diagnosis
- Treatment focuses on structured interventions in behavior, education, and communication
- Pharmacotherapy targets specific symptoms or conditions
  - Hyperactivity, irritability/aggression, anxiety, depression, stereotypies
- Treatment for hyperactivity:

Stimulants	Alpha$_2$ agonists
Methylphenidate • Titration dose varies with dosage forms. Max dose 100 mg	**Clonidine** • Children ≥ 6 years old: Initiate at 0.05 mg/day. Titrate every 3-7 days up to 0.4 mg/day
Amphetamine • Titration dose varies with dosage forms. Max dose 60 mg	**Guanfacine** • Children ≥ 6 years old: Initiate at 0.5 mg/day. Titrate every 3-4 days up to 4 mg/day

Volkmar F. J Am Acad Child Adolesc Pysch 2014; 52(2); 237-57.

INSOMNIA

- Stimulant-induced insomnia is common in children with ADHD
  - Adjust stimulant dose schedule to wear off by bedtime
- Treatment options
  - Sleep hygiene
  - Melatonin 3 mg at bedtime
  - Clonidine 0.1 - 0.3 mg at bedtime
  - Antihistamines
    - Hydroxyzine 0.6 mg/kg/dose (max dose: 100 mg)
    - Diphenhydramine 1 mg/kg/dose (max dose: 50 mg)
  - Trazodone 25 - 50 mg at bedtime (max dose: 200 mg)

Image credit: https://pixabay.com/en/baby-girl-sleep-child-toddler-1151351/

Am Acad Ped 2011; 128(5): 1007-22. ; Lexi-Comp, Inc.

BIPOLAR DISORDER (16-23%)

- Challenges exist in properly diagnosing bipolar vs. ADHD due to overlapping symptom criteria
- If bipolar is the primary condition, will result in impaired impulse control and judgement
- If coexisting bipolar disorder, refer to a psychiatrist for treatment

ADHD symptoms	BIPOLAR / MANIA symptoms
Inattention	Distractibility
Often talks excessively	More talkative than usual (erratic outbursts)
Acts as if driven by a motor	Increased goal-directed activity
Difficulty falling asleep	Decreased need for sleep (increased energy)
Chronic symptoms	Episodic patterns

McClellan J. J Am Acad Child Adolesc Pysch 2007; 46(1): 107-25.

WHEN TO REFER?

- During any step of therapy, consider referring to a child psychiatrist or other mental health specialist if:
  - Uncertain about diagnosis or continuing treatment
  - Two or more trials of different stimulants are ineffective
  - Antipsychotics are ineffective for aggressive behavior
  - Patient attempts suicide or displays self-injurious behavior
  - Patient experiences paradoxical reactions to medications
  - History of psychiatric hospitalization

Am Acad Ped 2011; 128(5): 1007-22.

CASE #1 CONTINUED…

CASE #1 (JC)

John C. is back for a follow-up with his mother, who is in tears explaining that he has now developed severe aggression. John has been caught stealing, has tried to set their pet cat on fire, and bullies other children at school. She is very distraught and is begging for help to control her son's aggressive behaviors.

What are your next steps?

Refer to psychiatrist

TAKE HOME POINTS

- When evaluating for ADHD, always assess for coexisting conditions
- Always treat pre-existing ADHD first
- Behavioral and psychosocial interventions are generally first line before considering medications
- Refer to a specialist at any time if you feel uncomfortable

THANK YOU!

Questions?