Pediatric ADHD in Primary Care

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Objectives:

- 1. Identify attention deficit hyperactivity disorder (ADHD)
- 2. Discuss treatment options
- 3. Recognize strategies to address side effects of common medications used to treat ADHD

Case 1:

- 6 year male old presents with his mother and grandmother, for a behavioral check up. A couple of months into the school year, they were informed by his school that he is inattentive, loud, fidgety, and constantly disrupting the class. It is a struggle to get him to transition from one activity to the next. He rushes through his work or fails to turn in. Peers do not want to play with him as he is too rough, gets into their personal space and cannot wait for his turn. Grandmother, who babysits him as he was kicked out of the afterschool program, says he is often on electronics, or running at a 100 miles an hour. Mother wonders if he is depressed, as he is getting singled out. He has also told her he does not like school, and it takes forever to get him out the door in the mornings.
- No formally diagnosed mental health conditions in the family. Parents are divorced. The patient's father, who works in construction, reportedly dropped out of high school. No known history of abuse. Medical history is unremarkable, except for asthma.

What is the likely diagnosis?

What is ADHD?

- Childhood onset neurodevelopmental disorder, characterized by a persistent, developmentally inappropriate pattern of inattention, distractibility, restless overactivity, impulsiveness, and other deficits of executive function (1).
- Impairment of the ability to "plan your work and work your plan" (2).

(Sources: 1. Clinical manual of Child and Adolescent Psychopharmacology, 3rd ed., 2017 2. Lewis's Child and Adolescent Psychiatry, 5th ed., 2018)

ADHD epidemiology

- Prevalence: ~ 7.2% of children worldwide (~2.5 – 4.4 % of adults)
- **Persistence**: ~75 % from childhood into adolescence, ~50% from childhood into adulthood
- ADHD symptom severity, comorbidity, parental MH problems **predict** persistence (MTA study)
- Gender: males > females (children - 4:1 for hyperactive ADHD, 2:1 for inattentive ADHD; adults - 1.6:1)
- Risk factors: genetic inheritance (heritability ~75%), very low birth weight (<1.5 kg = 2-3 x higher risk), maternal smoking during pregnancy, severe early deprivation
- Minor risk factors/associations: prenatal alcohol exposure, TBI in children, food additives, artificial colors, excess sugar, or reduced intake of essential fatty acids and minerals (iron, zinc)
- Adults with a childhood history of ADHD have higher than expected rates of antisocial and criminal behavior, injuries and accidents, employment and marital difficulties, health problems, teen pregnancies and children out of wedlock

(Sources: Wolraich et al. Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents, 2019; Practice Parameter for the Assessment and Treatment of Children and Adolescents With Attention-Deficit/Hyperactivity Disorder, 2007; McGough JJ. New Insights from the MTA: Who outgrows ADHD and What becomes of Those Who Don't.2016; Diagnostic and Statistical Manual of Mental Disorders, 5th ed., 2013; www.uptodate.com)

DSM 5 criteria

- Persistent pattern of inattention **and/or** hyperactive-impulsive symptoms.
- Symptoms and/or behaviors that have persisted **≥ 6 months in ≥ 2 settings** (e.g., school, home, church).
- Symptoms have negatively impacted academic, social, and/or occupational **functioning**.
- In patients aged < 17 years, **≥ 6** symptoms are necessary; in those aged ≥ 17 years, ≥ 5 symptoms are necessary.
- Several inattentive or hyperactive-impulsive symptoms were present **prior to age 12**
- Not exclusively during schizophrenia/another psychotic disorder, not explained by another mental disorder (including substance use)

(Source: Diagnostic and Statistical Manual of Mental Disorders, 5th ed., 2013)

Inattention symptoms:

- a. Fails to give close attention to details/ makes careless mistakes
- b. Difficulty sustaining attention in tasks or play activities
- c. Does not seem to listen when spoken to directly
- d. Does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace
- e. Difficulty organizing tasks and activities
- f. Avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort
- g. Loses things necessary for tasks or activities
- h. Easily distracted by extraneous stimuli
- i. Forgetful in daily activities

(Source: Diagnostic and Statistical Manual of Mental Disorders, 5th ed., 2013)

Hyperactivity-impulsivity symptoms:

- a. Fidgets with or taps hands or feet or squirms in seat.
- b. Leaves seat in situations when remaining seated is expected.
- c. Runs about or climbs in situations where it is inappropriate.
- d. Unable to play or engage in leisure activities quietly.
- e. Is often "on the go," acting as if "driven by a motor".
- f. Talks excessively.
- g. Blurts out an answer before a question has been completed.
- h. Difficulty waiting his or her turn.
- i. Interrupts or intrudes on others.

(Source: Diagnostic and Statistical Manual of Mental Disorders, 5th ed., 2013)

Specifiers

- **Combined type**: If inattention and hyperactivity-impulsivity criteria met for the past 6 months.
- **Predominantly inattentive type**: If inattention criteria is met but hyperactivity-impulsivity criteria is not met for the past 6 months.
- **Predominantly hyperactive/impulsive type**: If hyperactivity-impulsivity criteria is met but inattention criteria is not met over the past 6 months

Partial remission (fewer than full criteria in the last 6 months)

Mild, Moderate, Severe (depending on level of impairment)

(Source: Diagnostic and Statistical Manual of Mental Disorders, 5th ed., 2013)

Comorbidity

- 54%-84%: oppositional defiant disorder (ODD)
- ~25% with combined type: conduct disorder
- 15%-19%: nicotine and/or other substance abuse disorders
- 25%-35%: coexisting learning or language problem
- ~33%: anxiety disorders
- ~30%: mood disorder
- Other: DMDD, autism, tic disorders, OCD

(Sources: Practice Parameter for the Assessment and Treatment of Children and Adolescents With Attention-Deficit/Hyperactivity Disorder, 2007; Diagnostic and Statistical Manual of Mental Disorders, 5th ed., 2013)

Differential diagnoses (1):

- Oppositional defiant disorder (resist work/school tasks due to defiance, negativity, hostility)
- Intermittent explosive disorder (impulsive, aggressive, no problems with sustaining attention, rare in childhood)
- Specific learning disorder (no impairment outside of school work)
- Intellectual disability (not evident during non academic tasks)
- Autism (social disengagement, isolation, indifference to facial/tonal communication cues, cannot tolerate change)
- Anxiety disorders (inattention/restlessness is from worry/rumination)
- Depressive disorders (inattention during a depressive episode)
- Stereotypic movement disorder (fixed, repetitive, eg body rocking, hand flapping, self biting vs generalized, non-repetitive in ADHD)
- Tourette's disorder (premonitory urge, build up of stress, relief after tic)

(Sources: Diagnostic and Statistical Manual of Mental Disorders, 5th ed.,2013; www.uptodate.com)

Differential diagnoses (2):

- Bipolar disorder (episodic inattention, hyperactivity, impulsivity; elevated mood, grandiosity, other features such as hypersexuality; rare in preadolescence)
- Disruptive mood dysregulation disorder (pervasive irritability, intolerance of frustration; impulsivity, inattention not essential)
- Substance use disorders (need clear evidence of ADHD before substance misuse)
- Personality disorders (may share disorganization, social intrusiveness, emotional and cognitive dysregulation)
- Reactive attachment disorder (disinhibited subtype particularly; social disinhibition, lack of enduring relationships)
- Medication induced (eg, bronchodilators, isoniazid, neuroleptics leading to akathisia, thyroxine, steroids)
- Neurodevelopmental syndromes (eg, Fragile X, fetal alcohol), epilepsy, CNS infection, TBI

(Sources: Diagnostic and Statistical Manual of Mental Disorders, 5th ed., 2013; www.uptodate.com)

Assessment (1):

- In **any** mental health assessment, *screen* for ADHD (inattention, impulsivity, and hyperactivity) and ask for impairment.
- Assess for the symptoms using DSM criteria (patient, parent); seek information from school/daycare; gather info on duration, severity, onset, impairment
- At least one ADHD rating scale (eg, Vanderbilt ADHD Diagnostic Parent and Teacher Scales)
- Assess for comorbidity (eg, ODD and CD, depression, mania, anxiety disorders, tic disorders, learning disability, substance abuse, psychosis)
- Histories: Family, Medical, Perinatal, Social, Trauma, Past psychiatric

(Sources: Wolraich et al. Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents. 2019; Practice Parameter for the Assessment and Treatment of Children and Adolescents With Attention-Deficit/Hyperactivity Disorder, 2007; www.uptodate.com)

Assessment (2):

- If medical history unremarkable, laboratory or neurological testing **not** indicated [hyperthyroidism (hyperactivity, agitation), lead exposure (prenatal or during development), sleep apnea, RLS, hearing/vision impairment]
- Psychological and neuropsychological tests (**NOT** mandatory but recommended if suspicion of *low cognitive ability or learning deficit*)
- ROS: sleep disturbances/sleep patterns, dietary history, child and family cardiac history and cardiac review of systems
- Physical exam (height, weight, blood pressure, heart rate, dysmorphic features, neurologic and cardiac examination, vision and hearing, coordination, verbal or motor tics)

(Sources: Practice Parameter for the Assessment and Treatment of Children and Adolescents With Attention-Deficit/Hyperactivity Disorder, 2007; www.uptodate.com)

Case 2:

- A 7 year old female, recently diagnosed with ADHD, inattentive type, presents with her parents requesting medication. She did poorly during the last school year, hence, they want to start treatment in the summer, so that she starts off the next school year well. She has no cardiac illness, history of cardiac symptoms, or FH of sudden death. There is a FH of ADHD in the father and a couple of his siblings, but none were treated. They are wary of stimulants, and have heard "bad" things about Ritalin in particular, but are willing to consider all options.

What would be an initial medication?

Initiating a treatment plan:

- Parental and child **psychoeducation** (discussion of treatment options, risks/benefits, prognosis of ADHD)
- Coordination with **school**; might need school based accommodations
- Treatment of **coexisting** conditions
- **Superiority** of medication vs behavioral therapy/psychosocial services (except in pre-school age – parent training in behavior training (PTBM)
- Greater **effect size** of stimulants vs nonstimulants (1 to 0.7)
- Approximately **three-quarters** or more (90%) of children and adolescents will respond well to one or more of the medications used for ADHD
- **Chronic** illness approach
- **Behavior therapy** may be recommended as **an initial treatment** if the patient's ADHD symptoms are mild with minimal impairment, the diagnosis of ADHD is uncertain, parents reject medication treatment, or there is marked disagreement about the diagnosis between parents or between parents and teachers.
- In **preschoolers**, parent training in behavior management (PTBM) is advised first, with medication reserved for those who still have significant behavior problems.
- In **elementary/middle aged kids (6-11)**, FDA approved med + PTBM and/or behavioral classroom intervention
- In **adolescents (12-17),** FDA approved med; if robust response to med, with normative academic, family, and social functioning, psychopharmacological treatment alone is satisfactory

(Sources: Wolraich et al. Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents. 2019; Practice Parameter for the Assessment and Treatment of Children and Adolescents With Attention-Deficit/Hyperactivity Disorder. 2007; AACAP ADHD resource center – Parents'Medication Guide; Charach et al., "Interventions for preschool children at high risk for ADHD: a comparative effectiveness review." Pediatrics. 2013; www.uptodate.com)

Principles of behavioral parent training

- (1) information about ADHD,
- (2) learn to attend more carefully to their child's misbehavior and to when their child complies,
- (3) establish a home token economy,
- (4) use time out effectively,
- (5) manage noncompliant behaviors in public settings,
- (6) use a daily school report card, and
- (7) anticipate future misconduct.

Focus on **manipulation of antecedents of behavior** and **reinforcement techniques** – key components of parent training for children with ADHD, associated with better outcome ; higher doses of psychoeducation – negative parental outcome

(Sources: Practice Parameter for the Assessment and Treatment of Children and Adolescents With Attention-Deficit/Hyperactivity Disorder, 2007; Dekkers et al. Meta-analysis: Which Components of Parent Training Work for Children With ADHD? JAACAP. April, 2022)

Behavioral interventions:

- Maintaining a daily schedule
- Keeping environmental distractions to a minimum
- Providing specific and logical places for the child to keep their schoolwork, toys, and clothes
- Setting small, reachable goals
- Rewarding positive behavior (eg, with a "token economy")
- Identifying unintentional reinforcement of negative behaviors
- Using charts and checklists to help the child stay "on task"
- Limiting choices
- Finding activities in which the child can be successful (eg, hobbies, sports)
- Using calm discipline (eg, time out, distraction, removing the child from the situation)

(Source: www.uptodate.com)

Medications

A. Stimulants (FDA approved)

1. Methylphenidate compounds (eg, Ritalin, Focalin, Concerta)
2. Amphetamine compounds (eg, Adderall, Dexedrine, Vyvanse)

B. Non-stimulants (FDA approved)

1. NE reuptake inhibitors (atomoxetine, viloxazine)
2. Alpha agonists (guanfacine, clonidine)

C. Combination therapy (Alpha agonists + stimulants) (FDA approved)

D. Antidepressants (buproprion, tricyclic antidepressants – imipramine, nortriptyline) (not FDA approved)

Attention-Deficit/Hyperactivity Disorder (ADHD): Parents' Medication Guide (AACAP ADHD Resource Center, 2020)

Methylphenidate (MPH) for ADHD					
Medication	**Starting Dose**	**How Supplied**	**Dosage Form**	**Duration of Medication Effects**	**Given how many times a day?**
Adhansia XR	25 mg	25, 35, 45, 55, 70, 85 mg	capsules	Up to 16 hours	Once
Aptensio XR	10 mg	10, 15, 20, 30, 40, 50, 60 mg	capsules	12 hours	Once
Azstarys XR	26.1/5.2 mg	26.1/5.2, 39.2/7.8, 52.3/10.4 mg	capsules	12 hours	Once
Concerta	18 mg	18, 27, 36, 54 mg	capsules	12 hours	Once
Contempla XR	8.6 mg	8.6, 17.3, 25.9 mg	disintegrating tablets	12 hours	Once
Daytrana	10 mg	10, 15, 20, 30 mg	patch	6–16 hours	Once
Focalin	2.5 mg	2.5, 5, 10 mg	tablets	4–5 hours	Two to three times
Focalin XR	5 mg	5, 10, 15, 20 mg	capsules	10–12 hours	Once
Jornay PM	20 mg	20, 40, 60, 80, 100 mg	delayed-release capsules	12 hours	Once
Metadate CD	20 mg	10, 20, 30, 40, 50, 60 mg	capsules	8 hours	Once
Quillivant	<10 mg	25 mg	suspension	12 hours	Once
Quillichew	<10 mg	20, 30, 40 mg	chewable tablets	8 hours	Once
Ritalin IR	5 mg	5, 10, 20 mg	tablets	3–4 hours	Two to four times

Attention-Deficit/Hyperactivity Disorder (ADHD): Parents' Medication Guide (AACAP ADHD Resource Center, 2020)

Amphetamine (AMPH) for ADHD					
Medication	**Starting Dose**	**How Supplied**	**Dosage Form**	**Duration of Medication Effects**	**Given how many times a day?**
Adderall	2.5–5 mg	5–30 mg	tablets	6 hours	Once to twice
Adderall XR	2.5–5 mg	5, 10, 15, 20, 25, 30 mg	capsules	12 hours	Once
Adzenys XR	6.3–12.5 mg	3.1, 6.3, 9.4, 12.5, 15.7, 18.8 mg	disintegrating tablets	12 hours	Once
Dexedrine Spansule	5 mg	5, 10, 15 mg	spansules	6 hours	Once to twice
Dexedrine Tablets	2.5–5 mg	5, 10, 15, 20 mg	capsules	3–5 hours	Two to three
Dyanavel XR	2.5–5 mg	2.5 mg	suspension	13 hours	Once
Evekeo	2.5–5 mg	5, 10 mg	tablets	3–5 hours	Two to three
Mydayis	12.5 mg	25, 50 mg	capsules	Up to 16 hours	Once
Vyvanse	30 mg	20, 30, 40, 50, 60, 70 mg	capsules	12–14 hours	Once

CHADD's National Resource Center on ADHD

ADHD MEDICATIONS APPROVED BY THE US FDA

NON-STIMULANTS

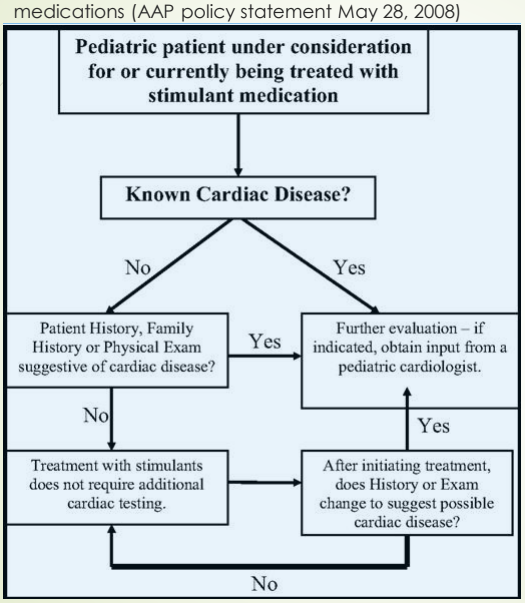
3

Class	Brand Name	Generic Name	Duration	Available Dosage Strengths
Norepinephrine reuptake inhibitor	Strattera®	atomoxetine hydrochloride (capsule)	24 hours	10mg 18mg 25mg 40mg 60mg 80mg 100mg
	Qelbree™	viloxazine extended-release (capsule)	24 hours	100mg 150mg 200mg
Alpha agonist	Kapvay®	clonidine hydrochloride - extended-release (tablet)	12–24 hours	0.1mg 0.2mg
	Intuniv®	guanfacine hydrochloride - extended-release (tablet)	12–24 hours	1mg 2mg 3mg 4mg

US Food & Drug Administration. Medication Guides

This chart is supported by Cooperative Agreement Number NU38DD000002 from the Centers for Disease Control and Prevention (CDC). The contents are solely the responsibility of the authors and do not necessarily represent the official views of CDC.

Cardiac evaluation of children and adolescents receiving or being considered for stimulant medications (AAP policy statement May 28, 2008)



Cardiac risk

- Stimulant therapy does **not** increase the risk of sudden cardiac death in patients without underlying cardiac disease
- There is also **no evidence for serious adverse cardiovascular complications** in children with **known** cardiovascular diseases including congenital heart disease, treated with stimulants
- If the patient does have cardiac disease, or if the history and PE is suggestive of cardiac disease, suggest **consultation** with ped cardiologist; even so, it is extremely unlikely that stimulant medications would be contraindicated totally.

(Source: Stuart Berger. "Attention deficit hyperactivity disorder medications in children with heart disease." Current Opinion in Pediatrics. Volume 28 Number 5 October 2016).

Rate of sudden death is low

- Rate of sudden death in the general pediatric population estimated at 1.3-8.5/100,000 patient-years
- Estimated rate of sudden death in treated children with ADHD for the exposure period January 1, 1992 to December 31, 2004 : **0.2**/100,000 patient-years for MPH, **0.3**/100,000 patient-years for amphetamine, and **0.5**/100,000 patient-years for atomoxetine (the differences between the agents are not clinically meaningful)
- Rate of sudden death of children taking ADHD medications do not appear to exceed the base rate of sudden death in the general population

(Sources: Practice Parameter for the Assessment and Treatment of Children and Adolescents With Attention-Deficit/Hyperactivity Disorder, 2007; Wolraich et al. Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents. 2019)

Choosing a medication

- Pretreatment **baseline** for common side effects associated with pharmacotherapy for ADHD (eg, appetite, sleep pattern, headaches, abdominal pain).
- Adolescent patients should be assessed for **substance use** or abuse. Those with signs and symptoms of substance abuse should undergo evaluation and treatment for addiction before treatment for ADHD (if possible)
- Taking stimulant medication as children **neither increases nor decreases** their risk of becoming addicted later (UCLA, 2013); prior data suggested treatment lowered risk of addiction
- Discuss treatment **options** available
- If **no** contraindication, may start with stimulant from **any** class
- "Start low and go slow"
- *Atomoxetine* can be considered initial med if - active substance use, comorbid anxiety or tics (0.5 mg/kg body wt for at least 3 days, then 1.2 mg/kg body wt)
- Long/short acting and formulation depends on family preference, patient characteristics

(Sources: Practice Parameter for the Assessment and Treatment of Children and Adolescents With Attention-Deficit/Hyperactivity Disorder, 2007; Humphreys et al. Stimulant Medication and Substance Use Outcomes -A Meta-analysis. *JAMA Psychiatry*. 2013; Rutter's Child and Adolescent Psychiatry, 6th ed., 2015; www.uptodate.com)

Preschoolers (age 3-5)

- AAP considers **methylphenidate** first line **if** pharmacological treatment deemed necessary (AAP 2011)
- *Short-acting* stimulants often used as initial treatment in **small children (<16 kg)**
- **Methylphenidate** used in Preschool ADHD Treatment Study (PATS)
- Starting dose methylphenidate 2.5 mg bid (or equivalent)
- **FDA approved** options are Dexedrine and Adderall
- Higher rate of emotional **adverse events** in this age group, including crabbiness, irritability, and proneness to crying
- Some tolerate amphetamines better
- Titrate more conservatively; lower mean doses may be effective
- AACAP Preschool Psychopharmacology Working Group recommends a **discontinuation trial after 6 months** to reassess underlying psychopathology

(Sources: Wolraich et al. Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents. 2019; Practice Parameter for the Assessment and Treatment of Children and Adolescents With Attention-Deficit/Hyperactivity Disorder, 2007; Rutter's Child and Adolescent Psychiatry, 6th ed., 2015; www.uptodate.com)

Interventions with limited evidence

- **Micronutrient** supplementation (vitamins, minerals, AA, antioxidants); a couple of studies show promise (gain in height; 1 study showed improvement in inattention, emotional dysregulation and aggression)
- Omega-3/Omega-6 Fatty Acids; multiple studies; mild-modest improvement; potential dose response effect of eicosapentaenoic acid (EPA)
- **External trigeminal nerve stimulation (eTNS);** FDA approved (2019) for children ages 7-12, who are not taking medication; 8 hrs during the night; 1 study, no long term data
- Interventions with little to no benefit – mindfulness (might help as part of comprehensive program), physical exercise (at least 60 min/day), Vitamin D supplementation (with methylphenidate; small improvement), cognitive training, diet modification, EEG biofeedback, supportive counseling, cannabidiol oil (anecdotal)
- Video game based interventions - **Endeavor Rx** (granted marketing authorization 2020); age 8-12 (inattentive, or combined type); 25 minutes, 5 days a week, for at least 4 consecutive weeks

(Sources: Stevenson, Jim. Editorial: Accumulating Evidence for the Benefit of Micronutrients for Children With ADHD. May 2022; Blotch MH, Qawasmi A, JAACAP, 2011; https://www.fda.gov/news-events/press-announcements/fda-permits-marketing-first-medical-device-treatment-adhd; www.uptodate.com; Gan et al. The Effect of Vitamin D Supplementation on Attention-Deficit/Hyperactivity Disorder: A Systematic Review and Meta-Analysis of Randomized Controlled Trials.2019; https://www.endeavorrx.com/about-endeavorrx/).

Titration/maintenance

- Titrate upward every 1 to 3 weeks, until max dose is reached, symptoms remit, or side effects prevent further titration
- Ask to contact office during titrations
- Get feedback on **school performance**
- Office visit in a month; monitor for treatment response, vitals (ht, wt, BP, HR) and side effects
- Use **lowest effective individual dose**
- Try a **stimulant from a different class** if the first one does not work
- Maintenance follow up 2-4 times/year
- Assess periodically to determine continued need for treatment or if symptoms have remitted; treat as long as symptoms remain present and cause impairment
- Due to persistence of symptoms, and maladaptive behaviors in teens, likely to need continued treatment through adolescence

(Sources: Practice Parameter for the Assessment and Treatment of Children and Adolescents With Attention-Deficit/Hyperactivity Disorder, 2007; Essentials of Child and Adolescent Psychiatry, 2006; www.uptodate.com)

Case 3:

- 13 year old male treated with Adderall for ADHD, presents for a follow up after a year. ADHD symptoms are well treated, but he has a low appetite. He barely eats any meal except his dinner. They note that he has outgrown a lot of the hyperactivity he used to exhibit, but off the medication, he still struggles with symptoms of inattention and executive function. His growth chart shows some plateauing and it has crossed 2 major percentiles.

What are treatment options you can consider?

Stimulant US boxed warning

- All stimulants – high potential for abuse and dependence
- Amphetamines - misuse of amphetamines may cause sudden death, serious cardiovascular adverse events

(Source: Clinical manual of Child and Adolescent Psychopharmacology, 3rd ed., 2017)

Stimulant and risk of growth suppression

Long-Term Suppression of Growth

Careful follow-up of weight and height in children ages 7 to 10 years who were randomized to either methylphenidate or non-medication treatment groups over 14 months, as well as in naturalistic subgroups of newly methylphenidate-treated and non-medication treated children over 36 months (to the ages of 10 to 13 years), suggests that consistently medicated children (i.e., treatment for 7 days per week throughout the year) have a temporary slowing in growth rate (on average, a total of about 2 cm less growth in height and 2.7 kg less growth in weight over 3 years), without evidence of growth rebound during this period of development. Published data are inadequate to determine whether chronic use of amphetamines may cause a similar suppression of growth, however, it is anticipated that they likely have this effect as well.

(Source: https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/010187s077lbl.pdf)

Growth suppression

- Schwart et al. 2014 – longitudinal study of 163,820 children ages 3-18, from Jan 2011 to Feb 2012, found **age** at 1st stimulant use and **longer** duration of stimulant use were associated with slower BMI growth earlier in childhood, and *more rapid rebound* to higher BMIs compared with controls in late adolescence
- Harstad et al. 2014 – prospective adult follow up of 5718 patients found **no** associations with stimulant and growth over a 2 year period of treatment
- Faraone et al.,2005a, Spencer, 2003 - stimulant-induced growth delays are greater in the first year of treatment but **attenuate** after that
- Spencer et al. 1996 – differential growth could be associated with the disorder itself and not only stimulant

(Source: Clinical manual of Child and Adolescent Psychopharmacology, 3rd ed.,2017)

Management of stimulant side effects

- **Loss of appetite, weight loss:**

- Appetite may improve with use

- Give med at or after meal, add calorie-enhanced snacks (eg, instant breakfast, frozen yogurt), offer food child likes for noon meal, feed promptly upon return from school

- Monitor growth charts (at least 1-2 times a year)

- Compare with parental height history

- If there is a change in height *or* weight that crosses **two** percentile lines (5th, 10th, 25th, 50th, 75th, 90th, and 95th are major percentiles)

→ Consider drug holiday, or switching to another ADHD medication.

(Sources: Wilens & Hammerness. Straight Talk about Psychiatric Medications for Kids, Guilford Press, 2016; Practice Parameter for the Assessment and Treatment of Children and Adolescents With Attention-Deficit/Hyperactivity Disorder, 2007; www.uptodate.com)

Management of stimulant side effects

- **Insomnia:**
- Encourage good **sleep hygiene**
- Administer stimulants **earlier** in day
- Change to **shorter acting** forms
- Discontinue afternoon or evening dosing
- Switch to atomoxetine
- *Medication options for insomnia:*

melatonin, clonidine, trazodone, mirtazapine, trazodone, anti-histamine

(Sources: Wilens & Hammerness. Straight Talk about Psychiatric Medications for Kids, Guilford Press, 2016; Rutter's Child and Adolescent Psychiatry, 6th ed; www.uptodate.com)

Management of stimulant side effects

Rebound phenomenon:

- Change to extended release or patch form; or increase dose
- Overlap stimulant dosing by about 30 min
- Add short acting stimulant 30 min before rebound
- Use additional treatment (eg, low dose clonidine/guanfacine or atomoxetine)

Mood lability:

- If at time of peak concentration, reduce dose or switch to longer acting
- If at wear off, see above
- Assess for comorbid mood or anxiety disorder

Psychosis:

- 0.10% in methylphenidate group, 0.21 % in amphetamine group
- Verify dose is taken appropriately
- Discontinue, and refer

(Sources: Wilens & Hammerness. Straight Talk about Psychiatric Medications for Kids, Guilford Press, 2016; Moran LV et al., "Psychosis with methylphenidate or amphetamine in patients with ADHD." 2019; www.uptodate.com)

Management of stimulant side effects

Dizziness:

- Monitor BP and HR
- Encourage fluids, midday snack, slow rise from sitting posture
- Switch to longer acting stimulant if associated only with peak effect

Cardiac symptoms (palpitations, tachycardia, syncopal episode, chest pain, shortness of breath):

- Consider stopping medication pending investigations, consider cardiology consult
- Note: Stimulants, on average, increase HR (1–2 beats per minute) and BP (1–4 mm Hg for systolic and diastolic BP) – clinically insignificant

Diversion or misuse:

- View PDMP data, consider non-stimulant or longer acting stimulant, controlled medication agreement, random drug screen

Priapism (stimulants and NE reuptake inhibitors)**:**

- educate, urological emergency, discontinue

(Sources: Wilens & Hammerness. Straight Talk about Psychiatric Medications for Kids, Guilford Press, 2016; Wolraich et al. Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents. 2019; www.uptodate.com)

Management of stimulant side effects

- **Tics:**

- Frequently comorbid, similar age of onset, waxing/waning, could be coincidental than causal

- 22 studies involving 2,385 children - meta-analysis of controlled trials does **not** support an association between new onset or worsening of tics and psychostimulant use

- May consider dose reduction, or a brief trial off, or a switch (atomoxetine, alpha agonists)

- Often tics diminish even while on stimulant, or might present when stimulant is removed

(Source: Cohen et al. Meta-Analysis: Risk of Tics Associated With Psychostimulant Use in Randomized, Placebo-Controlled Trials. *JAACAP*. 2015; www.uptodate.com)

Non-stimulants

Atomoxetine:

US Boxed warning: suicidal ideation (for both atomoxetine and viloxazine)

(0.037% atomoxetine vs 0.0% placebo; 1 suicide attempt/1,357 cases, no suicides)

Rarely hepatitis (LFTs not routinely recommended)

Stomachaches – after food

Initial sedation – improves over time; can administer initial 2 week dosing at bedtime, then move to am

Wear off – BID dosing, increase dose

Low efficacy – combination therapy (stimulant, alpha agonist)

Alpha agonists:

Sedation – improves with time, lower dose, change formulation, switch to other alpha agonist, add stimulant

Rebound headaches – hydration, better with time

Wear off – multi doses for IR, change formulation to XR

Depression/moodiness – change formulation, switch to other alpha agonist, look for comorbidity

(Source: Wilens & Hammerness. Straight Talk about Psychiatric Medications for Kids, Guilford Press, 2016).

Thank you!