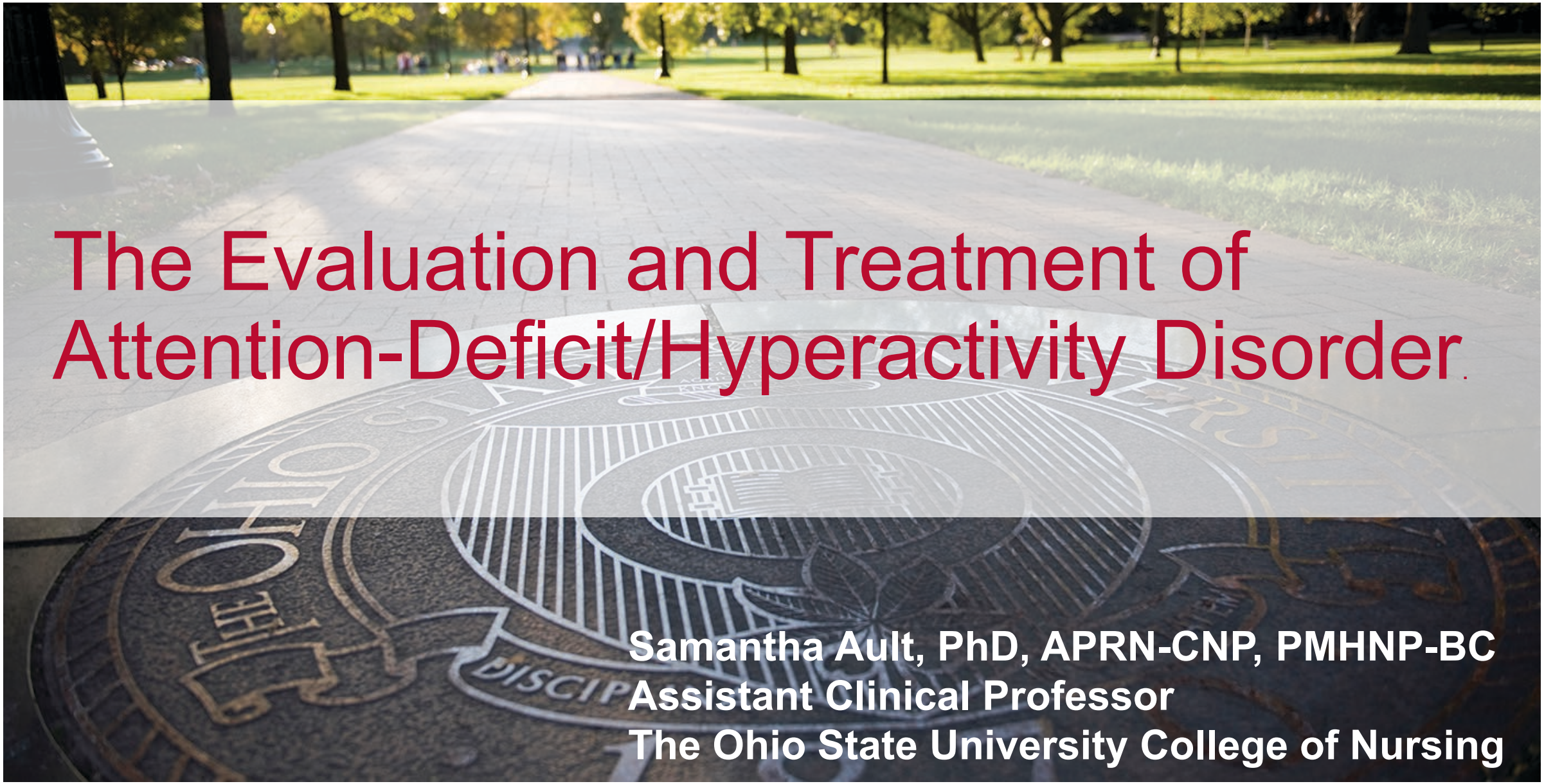

The Evaluation and Treatment of Attention-Deficit/Hyperactivity Disorder.

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Learning Objectives

1. Identify first and second line treatment for ADHD for pediatric and adult patients.
2. (RX)Understand diagnosing and treating adult ADHD.
3. (RX)Assess patient response to psychotropic treatment in adult and pediatric patients.
4. (RX)Identify uses for non-stimulant medication in the treatment of ADHD.
5. (RX) Able to score the Vanderbilt screening tool to assess for ADHD and ADHD treatment gains.
6. Increase their knowledge on the neurobiological factors contributing to ADHD.

Overview

- Etiology and prevalence of ADHD
- Reviewing EBP guidelines for ADHD
- Overview of psychopharmacological treatment of ADHD focusing on new agents
- Managing side effects from ADHD medications
- Treatment of ADHD with common comorbid mental health disorders
- Discuss the treatment of special populations for ADHD

Disclosures

- No COI to disclose
- Brand names of some medications will be used to differentiate new formulas
- Off-label use of medications will be discussed and identified

ADHD PREVALENCE

2-8% in preschool	4-12% in elementary school-aged children	6% in adolescents	4.5% in adults (~1/2 of children with ADHD go on to have ADHD as adults)
Preschool and school aged boys have higher rates of ADHD	Inattentive type is more prevalent in girls and older children	Twin studies have shown significant heritability for ADHD as high as 76%	Parents and siblings of children with ADHD have a 4-5 times higher probability of having ADHD than the general population

ADHD PRESENTATION

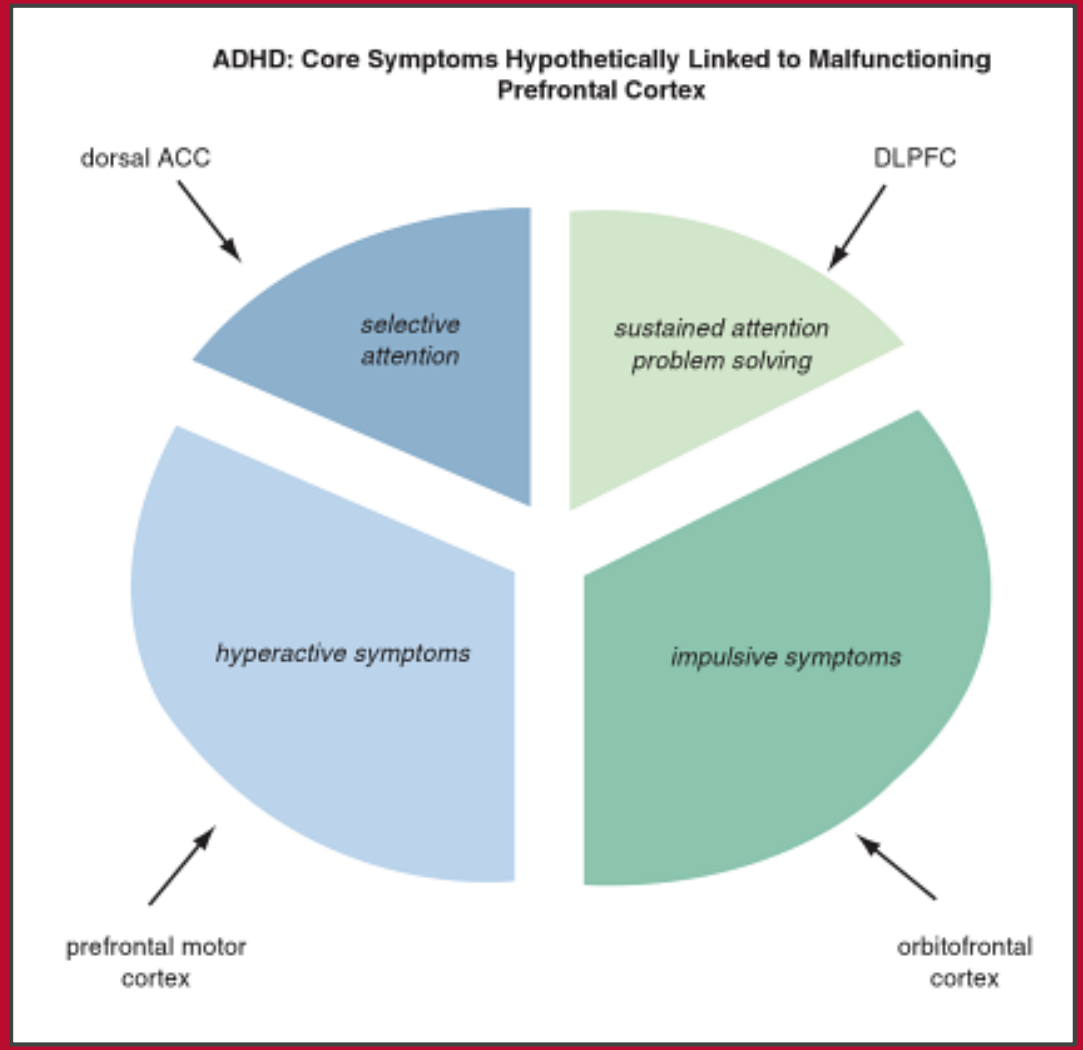
Younger children – more hyperactivity, impulsivity, and often aggression

Hyperactivity and impulsivity tends to decrease with age but can persist into adulthood in other ways such as risk-taking behaviors

The impulsivity, aggression, and risk-taking behaviors can often lead to ODD or conduct disorder diagnosis

Comorbidities – ODD and CD, depression, anxiety, bipolar disorder, Tourette syndrome, developmental learning disorders, substance use disorders, LOW SELF-ESTEEM, IMPAIRED FAMILY AND/OR PEER RELTATIONSHIPS, AGGRESSION

ADHD Etiology



It’s complex, and we are still working on this…

- Deficits in executive functioning – impairments in response inhibition, vigilance, working memory, and some measures of planning
- Some evidence that ADHD is genetic – heritability approx. 76%
- Associated with markers at multiple chromosomes
- Multiple genes found to have some association – the dopamine 4 and5 receptors, dopamine transporter, and enzyme dopamine β-hydroxylase, the serotonin transporter gene, the serotonin 1B receptor, and the synaptosomal-associated protein 25 gene
- Neuroimaging – reduced white and gray matter, decreased frontal and temporal lobe volume
- Dysfunction and disrupted connections with prefrontal cortex and other areas of the brain
- Perinatal stress, low birth weigh, TBI, maternal smoking during pregnancy, severe early deprivation (maltreatment)
  - **Ordinary variations in parenting practices do not contribute to the etiology of ADHD**
- Dopaminergic and noradrenergic neural mechanisms likely play a role in the pathophysiology of ADHD
  - Hypothesized hypodopaminergic state – benefit of stimulants which blocks DAT and increases synaptic dopamine

ADHD Treatment Guidelines

AACAP Practice Parameter 2007

AACAP's 13 Recommendations

1. Screening for ADHD for Every Patient's Mental Health Assessment
2. Evaluation – interviews with patients and parents, gather collateral information when indicated, collect information about patients school/work day, collect patient's medical/social/family histories
3. Unremarkable medical history → no labs or neuro testing needed
4. psychological and neuropsychological tests are not mandatory for diagnosing ADHD, but should be performed if hx suggests low general cognitive ability or low achievement in language or math relative to patient's intellectual ability
5. Evaluate for comorbid psychiatric disorders
6. Treatment - a comprehensive treatment plan.

AACAP's 13 Recommendations

7. Start initial psychopharmacological agent that is approved by the FDA for treatment of ADHD
8. If none of the FDA approved agents worked out, take careful review of the diagnosis and consider behavior therapy and/or use medications not approved by the FDA for treatment of ADHD
9. Monitor for side effects during treatment
10. If ADHD symptoms remit, then psychopharmacological treatment of ADHD alone is satisfactory
11. If there is a less than optimal response to medications, has a comorbid disorder, or experiences stressors in life – psychosocial treatment in conjunction with medication is often beneficial
12. Assess patient periodically for need of continued treatment
13. Monitor height and weight throughout treatment

ADHD Treatment Guidelines

- Be sure to evaluate and treat comorbid disorders
- Provide psychoeducation
- Link with community supports and additional school resources
- Psychosocial therapies – behavioral therapy alone *can* produce results.
- MTA – Multimodal Treatment Study of Children with ADHD
  - Evaluated long term safety and efficacy of leading treatments for ADHD – behavior therapy and medications and combination tx
  - Core ADHD sx improved equally in the combo group and the medication only group
  - Combo group had modestly better outcomes for the non-ADHD symptoms (oppositional and aggressive sx) and positive functioning

ADHD Treatment Guidelines

- Stimulants are the gold-standard treatment for ADHD and highly efficacious
- Free to choose any of the two stimulants types – methylphenidate (MPH) or amphetamine (AMPH)
  - Two are equally efficacious
  - Pros vs cons of immediate release vs controlled releases
  - What is on insurance formulary?
  - Parent/child preference
- Adult-sized adolescents may need doses of MPH in adult ranges to achieve response
- No global therapeutic window in ADHD patients
- Each patient has a unique dose-response curve
- Treat optimally!!
  - Select appropriate starting dose and titrate upward every 1-3 weeks until maximum dose is achieved, side effects prevent further titration, or symptoms of AHDD remit – whichever occurs first

ADHD Screening – Vanderbilt

- Parent forms and teacher forms
- 43 questions for teacher, 55 for parents for initial scale forms
- Likert scale 0 (never) to 3 (very often) for mood and ADHD symptoms
- performance questions rated 1 (excellent) to 5 problematic
- Academic performance and classroom behavior questions included on teacher forms
- Easy scoring guide and area for teacher/parent to make comments
- Follow up forms are briefer and ask about side effects to medications (none, mild, moderate, severe) for several common and severe side effects to ADHD medications

NICHQ Vanderbilt Assessment Scale—PARENT Informant

Today's Date: _____ Child's Name: _____ Date of Birth: _____

Parent's Name: _____ 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 behaviors in the past 6 months.**

Is this evaluation based on a time when the child ☐ **was on medication** ☐ **was not on medication** ☐ **not sure?**

Symptoms	Never	Occasionally	Often	Very Often
1. Does not pay 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 when given directions and fails to finish activities (not due to refusal or failure to understand)	0	1	2	3
5. Has difficulty organizing tasks and activities	0	1	2	3
6. Avoids, dislikes, or does not want to start tasks that require ongoing mental effort	0	1	2	3
7. Loses things necessary for tasks or activities (toys, assignments, pencils, or books)	0	1	2	3
8. Is easily distracted by noises or other 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 when remaining seated is expected	0	1	2	3
12. Runs about or climbs too much when remaining seated is expected	0	1	2	3
13. Has difficulty playing or beginning quiet play activities	0	1	2	3
14. Is "on the go" or often acts as if "driven by a motor"	0	1	2	3
15. Talks too much	0	1	2	3
16. Blurts out answers before questions have been completed	0	1	2	3
17. Has difficulty waiting his or her turn	0	1	2	3
18. Interrupts or intrudes in on others' conversations and/or activities	0	1	2	3
19. Argues with adults	0	1	2	3
20. Loses temper	0	1	2	3
21. Actively defies or refuses to go along with adults' requests or rules	0	1	2	3
22. Deliberately annoys people	0	1	2	3
23. Blames others for his or her mistakes or misbehaviors	0	1	2	3
24. Is touchy or easily annoyed by others	0	1	2	3
25. Is angry or resentful	0	1	2	3
26. Is spiteful and wants to get even	0	1	2	3
27. Bullies, threatens, or intimidates others	0	1	2	3
28. Starts physical fights	0	1	2	3
29. Lies to get out of trouble or to avoid obligations (ie, "cons" others)	0	1	2	3
30. Is truant from school (skips school) without permission	0	1	2	3
31. Is physically cruel to people	0	1	2	3
32. Has stolen things that have value	0	1	2	3

D4 NICHQ Vanderbilt Assessment Scale—TEACHER Informant

Teacher's Name: _____ Class Time: _____ Class Name/Period: _____

Today's Date: _____ Child's Name: _____ Grade Level: _____

Directions: **Each rating should be considered in the context of what is appropriate for the age of the child you are rating and should reflect that child's behavior since the beginning of the school year. Please indicate the number of weeks or months you have been able to evaluate the behaviors: _____.**

Is this evaluation based on a time when the child ☐ **was on medication** ☐ **was not on medication** ☐ **not sure?**

Symptoms	Never	Occasionally	Often	Very Often
1. Fails to give attention to details or makes careless mistakes in schoolwork	0	1	2	3
2. Has difficulty sustaining attention to tasks or activities	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 (not due to oppositional behavior or failure to understand)	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	0	1	2	3
7. Loses things necessary for tasks or activities (school assignments, pencils, or books)	0	1	2	3
8. Is easily 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. Loses temper	0	1	2	3
20. Actively defies or refuses to comply with adult's requests or rules	0	1	2	3
21. Is angry or resentful	0	1	2	3
22. Is spiteful and vindictive	0	1	2	3
23. Bullies, threatens, or intimidates others	0	1	2	3
24. Initiates physical fights	0	1	2	3
25. Lies to obtain goods for favors or to avoid obligations (eg, "cons" others)	0	1	2	3
26. Is physically cruel to people	0	1	2	3
27. Has stolen items of nontrivial value	0	1	2	3
28. Deliberately destroys others' property	0	1	2	3
29. Is fearful, anxious, or worried	0	1	2	3
30. Is self-conscious or easily embarrassed	0	1	2	3
31. Is afraid to try new things for fear of making mistakes	0	1	2	3

ADHD Psychotropic Agents

Stimulants & Non-stimulants

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Stimulant Medications

- Indications: ADHD (hyperactive, inattentive, combined, impulsivity)
- Preparations: tablets, capsules, liquid, ODT, transdermal patch
- Metabolism:
  - Amphetamines are partially metabolized by the liver and partially excreted (unchanged)
  - Methylphenidates are fully metabolized by the liver and excreted in urine
- Rapidly absorbed
- Combined pharmacotherapy may be necessary due to comorbid psychiatric disorders in as many as 1/3 of children diagnosed with ADHD
  - Which do you treat first?
- Augmenting agents may be necessary
- No need for EKG prior to starting stimulant treatment UNLESS there is cardio risk factors (patient history and/or family history)

MOA - Stimulants

- **Indirect** agonists on the PFC noradrenergic and dopaminergic systems modulating glutamate signals
- They increase attention to “signals” and decrease attention to “noise”
- Work to enhance arousal in the PFC
- Increase extracellular dopamine levels in the brain including the reward and addiction pathways through interacting with dopamine transporter (DAT)
- MPH and AMPH boost norepinephrine and dopamine neurotransmission in the prefrontal cortex. Both increase dopamine release → enhances one’s response to environmental stimuli.
- MPH
  - Inhibits presynaptic dopamine transporters of central adrenergic neurons
  - Inhibits norepinephrine transporters to a lesser degree
  - Increases synaptic cleft concentration of dopamine → amplifying the dopaminergic neurotransmission
- AMP
  - Competitive inhibitor of dopamine
  - Acts directing on dopamine transporter and norepinephrine transporter binding sites as a pseudo-substrate.
  - Increase catecholamine release

Short-acting Stimulants

Short-acting methylphenidate	Preparation	Onset	Duration	Starting dose	Max dose range
Methylphenidate (Methylin/Ritalin)	Tablet (Ritalin) Liquid (Methylin)	~30 min	3-5 hours	2.5mg (3-5 YO) 2.5-5 mg (6 YO +)	4–5-year old: 2.5–30mg/day. 6 years +: 5–60mg/day. Given in divided dose qd-tid
Dexmethylphenidate (Focalin)	Tablet	~30 min	4-5 hours	2.5 mg BID (6 YO +)	2.5-20mg/day in divided doses

Short-acting amphetamines	Preparation	Onset	Duration	Starting dose	Max dose range
Dextroamphetamine-Amphetamine (Adderall)	Tablet	~30 min	4-6 hours	2.5mg (3-5 YO) 5mg (6 YO +)	3–5-year old: 2.5–30mg/day. 6 years +: 5–40mg/day. Given in divided dose qd-tid
Dextroamphetamine IR (Zenzedi, ProCentra)	Tablet (Zenzedi) Liquid (ProCentra)	~30 min	4-6 hours	2.5mg (3-5 YO) 5mg (6 YO +)	3–5-year old: 2.5–40mg/day. 6 years +: 5–40mg/day (>40mg rarely needed). Given in divided dose qd-tid
Amphetamine (Evekeo, Evekeo ODT):	Tablet ODT	~30 min	4-6 hours	2.5mg (3-5 YO) 5mg (6 YO +)	3–5-year old: 2.5–40mg/day. 6 years +: 5–40mg/day. Given in divided dose qd-tid

Intermediate-acting Stimulants

Intermediate-acting amphetamine	Preparation	Onset	Duration	Starting dose	Max dose range/day
Dextroamphetamine (Dexedrine):	ER Capsule	~60 min	6-8 hours	6-11 YO: 5mg 12 YO+: 10mg	5mg-60mg/day (QD or BID)

Intermediate-acting methylphenidate	Preparation	Onset	Duration	Starting dose	Max dose range/day
Metadate CD	ER Capsule	~90 min	6-8 hours	6 YO+: 20mg	20mg-60mg (or 2mg/kg/day up to 60mg/day) (QD or BID)
Ritalin LA	ER Capsule	~30-60 min	6-8 hours	6 YO: 20mg	20mg-60mg (or 2mg/kg/day up to 60mg/day) (QD or BID)

Long-acting Stimulants

Long-acting amphetamines	Preparation	Onset	Duration	Starting dose	Max dose range/day
Dextroamphetamine-Amphetamine ER (Adderall XR)	ER capsule	1-1.5 hours	10-12 hours	6 YO +: 10mg	6-12 YO: 10mg-30mg 12 YO+: 10mg-40mg 18 YO+: 10mg-60mg
Lidsdexamfetamine (Vyvanse)	ER capsule & chewable tablet	~1-2 hours	10-13 hours	6 YO +: 30mg (can start lower)	6 YO+: 10mg-70mg
Adzenys XR-ODT	ODT tablet	~1 hour	12 hours	6 YO +: 6.3mg	6-12 YO: 3.1mg-18.8mg 13-17 YO: 3.1mg-12.5mg
Mydayis	ER capsule	~1 hour	16 hours	13 YO+: 12.5mg	13 YO+: 12.5mg-25mg
Dyanavel XR	ER liquid	1 hour	13 hours	6 YO+: 2.5mg-5mg	6 YO+: 2.5mg-20mg

Long-acting methylphenidate	Preparation	Onset	Duration	Starting dose	Max dose range/day
Methylphenidate ER (Concerta)	ER tablet	1-2 hours	8-12 hours	6 YO+: 18mg	6-12 YO: 18mg – 54mg 13 YO+: 18mg – 72mg
Methylphenidate ER transdermal patch (Daytrana)	Transdermal patch (wear for 9 hours, remove for 15 hours)	2 hours	12-17 hours	6 YO+: 10mg	6 YO+: 10mg – 30mg
Quillivant XR	Liquid	45-60 min	12 hours	6 YO+: 20mg	6 YO+: 20mg - 60mg
Cotempla XR-ODT	ODT tablet	1 hour	12 hours	6-17 YO: 17.3mg	6-17 YO: 8.6mg – 51.8mg
Quillichew ER	Chewable tablet	45-60 min	8 hours	6 YO+: 20mg	6 YO+: 20mg - 60mg
Dexmethylphenidate ER (Focalin XR)	ER capsule	1-1.5 hours	8-12 hours	6 YO+: 5mg	6 YO+: 5mg - 30mg

IR + ER Formulas

- Adhansia XR
  - methylphenidate ER
  - 20% IR, 80% ER
  - Starting dose 25mg
  - Max dose 85mg
  - 25mg, 25mg, 45mg, 55mg, 70mg, 85mg
  - Capsule
  - Can sprinkle into applesauce/yogurt
  - 6 years +
  - Duration 12-16 hours
- Aptensio XR
  - methylphenidate ER
  - 40% IR, 60% ER
  - Starting dose 10mg
  - Max dose 60mg
  - 10mg, 15mg, 30mg, 40mg, 50mg, 60mg
  - Capsule
  - Can sprinkle into applesauce
  - 6 years +
  - Duration up to 12 hours

NEW AGENTS - Mornings rough + need all day coverage?

- **Azstarys**
  - Serdexmethlyphenidate/dexmethlyphenidate
  - IR & ER capsule in one
  - 3 doses – 26.1mg/5.2mg, 39.2mg/7.8mg, 52.3mg/10.4mg
  - Recommended to start at 39.2mg/7.8mg – can increase to highest dose after 7 days
  - 6 years +
  - Capsule
  - Can sprinkle into 2 oz of water or 2 tablespoons of applesauce/food
  - Duration 8-13+ hours
  - Serdexmethlyphenidate is a prodrug of dexmethylphenidate that is converted to dexmethylphenidate in the GI tract (like Vyanse)

- **Jornay PM**
  - Methylphenidate
  - Give approx. 12 hours before you want it to kick in
  - Comes in 20mg increments
  - Start at 20mg, increase by 20mg/day q 7 days.
  - Max dose 100mg/day
  - Most patients find their optimal dosing around 60-80mg
  - 6 years +
  - Capsule - can be opened and sprinkled into applesauce
  - Should last throughout the day, approx. 14-16 hours after delayed onset
  - Majority of drug is absorbed in the colon - lower appetite suppression reported

Stimulants

Contraindications

- Medication hypersensitivity
- Use of MAOI's concurrently or within the last 14 days
- Glaucoma

Drug Interactions

- Antihypertensive drugs: monitor blood pressure and adjust dosage of antihypertensive drug as needed
- Lithium may inhibit the stimulatory effects of amphetamines
- When used with TCAs, the actions of both may be enhanced

Precautions

- Hx of psychotic symptoms
- Hx of bipolar disorder with unstable mood symptoms
- Uncontrolled seizures
- Hypertension or strong family hx as well as childhood obesity and HTN
- Family hx of stroke
- Cardiac structural defects
- Family hx of exercise intolerance or extreme SOB with exercise
- Cardiomyopathy
- Serious arrhythmias
- Hx of syncope, palpitations
- Hx of sudden cardiac death below age of 35 YO of a family member

Stimulant Side Effects

- Decreased appetite, Weight loss
- Increased anxiety
- Increased agitation
- Increased aggression
- Insomnia
- Headaches
- Irritable moods
- Rebound effects or “drop off irritability”
- Mild elevations in B/P and HR
- Subdued – “seems sad”
- Tremors
- Seizures (rare if no family hx or current seizure disorder)
- Onset of psychotic symptoms
- Priapism
- Peripheral vasculopathy (Reynaud’s phenomenon)
- Long term suppression of growth – relatively minimal

Management of Side Effects

- Decreased appetite, Weight loss
  - Anticipate and educate about this side effect
    - AMPH>MPH>non-stimulant
  - Monitor appetite, weight, and height at least every 6 months
  - Ask about appetite at baseline – prior to initiation of stimulant!
  - Encourage high calorie meals, snacks
  - Reduce dose/switch
  - Medication “holidays”
  - Refer to growth specialist if needed
  - Pediasure or equivalent
  - cyproheptadine (Periactin)
- Tics
  - Observe tic intensity over 3 months without medication change (if you can)
  - Reduce dose
  - Use other medication
  - Combo therapy – alpha agonist, dopamine receptor blockers (DRBAs)
  - Do they have underlying Tourette’s disorder?
  - Are they one a DRBA for a mood disorder and having TD/EPS?
  - Need referral to neurology?

Management of Side Effects

- Rebound hyperactivity
  - Consider low dose IR med in late afternoon (booster dose)
  - Consider switching to stimulant with different release mechanism
  - ER BID?
  - Consider adjunctive alpha agonist
  - Consider non-stimulant
- Crying/Mood Lability/Apathy/Irritability
  - Differentiate from pre-treatment moods
  - Is it rebound effect (when med is wearing off)?
  - Decrease dose
  - Consider switch to alternative stimulant class or non stimulant

Non-stimulants for ADHD: Strattera

- Atomoxetine (Strattera)
  - SNRI
  - Blocks NE reuptake and acts as an **indirect** agonist on the PFC adrenergic receptors to enhance attention via glutamatergic activity
  - Capsule
  - GI side effects
  - Sedation – go slower with titration
  - Rapidly absorbed after administration
  - Excreted in urine and feces, metabolized through CYP450 2D6 enzyme system
  - In general, stimulant are more efficacious for ADHD tx. Some potential benefit in ASD population and with patients with comorbid ADHD/anxiety (not robust).
  - Do not use with TCA's or Wellbutrin

Dosing:

70 kg or Less: -Initial Dose: 0.5 mg/kg/day orally. -Maintenance dose: Increase dose to 1.2 mg/kg/day after a minimum of 3 days at the initial dose. -Maximum dose: 1.4 mg/kg/day or 100 mg/day, whichever is less.

Over 70 kg: -Initial Dose: 40 mg/day orally. -Maintenance dose: Increase dose to 80 mg/day after a minimum of 3 days at the initial dose. -Maximum dose: After 2 to 4 additional weeks, the dose may be increased up to 100 mg/day in patients who have not achieved an optimal response.

Strattera: Side Effects

- Sedation/fatigue- (more common in children)
- GI upset, including N/V
- Decreased appetite
- Weight loss
- Increased HR & BP (usually not clinically significant)
- Insomnia
- Dizziness
- Anxiety
- Agitation
- Aggression
- Irritable Mood
- Headache

Strattera: Contraindications and Precautions

- Known hypersensitivity (contraindication)
- Concomitantly with MAOI or within 2 weeks (contraindication)
- Narrow angle glaucoma due to increased risk of mydriasis (contraindication)
- Current or hx of pheochromocytoma (contraindication)
- Hx of several cardiovascular disorder
- Hx of poor appetite and weight gain
- Hx of chronic GI symptoms
- Strong family hx of bipolar disorder- hypomania/mania
- Prior hx of SI or attempt
- Hx of liver damage

NEW AGENT Non-stimulants for ADHD: Qelbree

Viloxazine (Qelbree)

- Indicated for 6-17 YO
- SNRI
- Triple reuptake inhibitor (NET, DAT, SERT)
- ER capsule: 100mg, 150mg, 200mg
- Excreted in urine and feces, metabolized through CYP450: 2D6 enzyme system and UGT: 1A9, 2B15 substrate
- Can open capsule but do not crush/chew contents

Dosing

- 6-11 YO: Start 100mg PO qd, can increase by 100mg/day per week, max: 400mg
- 12-17 YO: Start 200mg PO qd, can increase to 400mg after 1 week, max: 400mg
- Severe Renal Impairment: Initial dosage is 100 mg once daily. Titrate in weekly increments of 50 mg to 100 mg to a maximum recommended dosage of 200 mg once daily

Common Side Effects: Qelbree

- Somnolence (can take at bedtime)
- Decreased appetite
- Fatigue
- Nausea, vomiting
- Insomnia
- Irritability

Qelbree:

Contraindications

- Concomitant administration of sensitive CYP1A2 substrates or CYP1A2 substrates with a narrow therapeutic range
- Known hypersensitivity Concomitantly with MAOI or within 2 weeks

Precautions

- Hx of several cardiovascular disorder
- Hx of poor appetite and weight gain
- Strong family hx of bipolar disorder- hypomania/mania
- Prior hx of SI or attempt
- Hx of liver damage or eGFR<30
- Advise patients to use caution when driving or operating hazardous machinery due to potential somnolence
- HTN, tachycardia

Non-stimulants for ADHD: Alpha-Adrenergic Receptor Agonist

- Clonidine
  - Catapres – IR preparation
  - Kapvay – ER preparation
- Guanfacine
  - Tenex – IR preparation
  - Intuniv – ER preparation

Safety and efficacy has not been established under the age of 6 years.

- Indications: ADHD (hyperactivity/impulsivity), **sleep disturbance (clonidine)**, aggression, Tourette's disorder/tics
- Preparations: tablets, ER tablets, transdermal patch (clonidine)
- Central action on post-synaptic alpha 2A receptors in pre-frontal cortex. Inhibits the endogenous release of NE in the brain.
- Act as **direct** agonists on the PFC adrenergic receptors to enhance attention
- May augment other treatment modalities for ADHD

Non-stimulants for ADHD: Alpha-Adrenergic Receptor Agonist

- Metabolized by the liver and excreted by kidneys
- Do not take guanfacine ER (Intuniv) with high- fat meals
- Avoid substituting clonidine preparations for one another on a mg per mg basis-different pharmacokinetic profiles

Dosing: guanfacine & clonidine

- Dosing ranges for Quanfacine IR is 1-2 mg/d in divided doses and ER- 1-4mg/d (not to exceed 4mg/d).
  - With young children I will start with 0.5mg qam then BID
  - Some providers prefer Intuniv AM dosing, others prefer hs dosing
- Clonidine IR (Catapres): 0.1-0.4mg/day in divided doses (not to exceed 0.4mg/d).
- Clonidine (Kapvay (extended release), start with 0.1mg at hs and can increase dosing up to 0.4mg/d in divided dosing with most at hs. Some take it in AM.

Side Effects: clonidine & guanfacine

- Sedation (especially for clonidine IR)
- Hypotension
- Potential to worsen or induce depressive symptoms (occurs in 3% of children)
- Dizziness, dry mouth, sedation, fatigue, constipation, weakness/asthenia, GI pain
- Rebound hypertension/withdrawal syndrome (agitation, nervousness, headache) can occur with abrupt cessation - gradual taper recommended especially on extended releases
- Can induce or exacerbate depression, irritability, dysphoria
- Can cause increased appetite and weight gain, headaches and rash.
- Stuffy nose (clonidine ER)
- Increased body temperature (clonidine ER)

Guanfacine (Tenex/Intuniv)

- Has longer duration of action than clonidine
- Rebound hyperactivity is minimal
- Less sedation
- Intuniv does not always last as long as it is intended, may find more benefit with Tenex BID dosing.

Guanfacine & Clonidine: Contraindications and Precautions

- Know hypersensitivity
- Significant CV disease
- Current depressive target symptoms
- Past hx of depression
- Family hx of mood disorder
- Prior hx of SI or attempt

Caution with concomitant use with: CNS depressants, calcium channel blockers Digitalis, Beta Blockers

Other Non-Stimulant Medications

- Bupropion (Wellbutrin)
- Elavil/TCA's
- Haloperidol (Haldol)*
- SGA's* (aripiprazole in particular for impulsivity)
- Fluoxetine (Prozac)*
- Clomipramine*
- MAOIs*
- Venlafaxine (Effexor)*
- Modafinil*
- Amantadine*
- Omega-3 Fatty Acids*

* = limited clinical data or have problematic side effects or are rarely used

Other or Alternative Treatments for ADHD

- Omega-3 Fatty Acids
  - Overall a lack of efficacy found for the use of omega-3 fatty acids in treating ADHD, but generally well-tolerated and no known serious reactions in the studies
- Vitamin D
  - Meta-analysis shows that youth with ADHD had lower serum concentrations of 25-hydroxyvitamin D than children without ADHD
- Amantadine
  - Anecdotal reports that low-doses of amantadine have been used to treat ADHD

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Methylphenidate Formulations – Long Acting** (Capsules and tablets in this section are shown at actual size)

Adhansia XR®†	6-17 Yrs: 25–70mg; SD: 25mg Adults: 25–85mg; SD: 25mg					25mg		35mg		45mg		55mg		70mg		85mg			
Concerta®†	6-12 Yrs: 18-54mg; SD: 18mg 13-17 Yrs: 18-72mg; SD: 18mg >18 Yrs: 18-72mg; SD: 18mg or 36mg	G	18mg	G	27mg	G	36mg	G	54mg	G	72mg	+		Methylphenidate ER 72mg (bioequivalent to 2 x 36 mg Concerta tablets)					
Aptensio® XR‡	6 Yrs–Adult: 10–60mg; SD: 10mg (biphasic – 40/60)		10mg		15mg		20mg		30mg		40mg		50mg		60mg				
Cotempla XR-ODT®§ (grape flavor)	6-17 Yrs: 8.6–51.8mg; SD: 17.3mg		8.6mg				17.3mg		25.9mg		34.6mg	+			51.8mg	+			
Focalin® XR‡ (dexmethylphenidate)	6-17 Yrs: 5–30mg; SD: 5mg 18 Yrs-Adult: 5–30mg; SD: 5mg (biphasic – 50/50)	G	5mg			G	10mg	G	15mg	G	20mg	G	25mg	G	30mg	G	35mg	G	40mg
Quillivant XR® 25mg/5mL (5mg/mL) (banana flavor)†	6 Yrs–Adult: 20–60mg; SD: 20mg		10mg 2mL		1 Bottle: 300mg 60mL		20mg 4mL		1 Bottle: 600mg 120mL 30mg 6mL		1 Bottle: 900mg 180mL 40mg 8mL		2 Bottles: 600mg 120mL 50mg 10mL		2 Bottles: 750mg 150mL 60mg 12mL		2 Bottles: 900mg 180mL		
Quillichew ER®§ (cherry flavor)	6 Yrs–Adult: 20–60mg; SD: 20mg						20mg		30mg		40mg								
Ritalin® LA‡	6-12 Yrs: 10–60mg; SD: 20mg (biphasic – 50/50)	G	10mg			G	20mg	G	30mg	G	40mg			G†	60mg				
Metadate® CD‡	6-17 Yrs: 10–60mg; SD: 20mg (biphasic – 30/70)	G†	10mg			G	20mg	G	30mg	G†	40mg	G	50mg	G†	60mg				
Metadate® ER†	6 Yrs-Adult: 20–60mg; SD: 20mg	G	10mg			G	20mg												
Daytrana® (patch)	6-17 Yrs: 10–30mg; SD: 10mg (The color border around each patch reflects the packaging color, not the patch itself.)	G	10mg 1.4"x1.4"	G	15mg 1.5"x1.9"	G	20mg 1.5"x2.6"	G	30mg 1.5"x3.9"										

Methylphenidate Pro-Drug Formulations - Long Acting** (Medications in this section are shown at actual size)

Azstarys®‡ (dexmethylphenidate + serdexmethylphenidate)	6-12 Yrs: 26.1/5.2 – 52.3/10.4; SD: 39.2/7.8 mg; 13 Yrs – Adult: 39.2/7.8 – 52.3/10.4; SD: 39.2/7.8mg	26.1mg SDX / 5.2mg d-MPH	39.2mg SDX/ 7.8mg d-MPH	52.3mg SDX/ 10.4mg d-MPH		

Methylphenidate Formulations – Long Acting/Delayed Onset** (Medications in this section are shown at actual size)

Jornay PM®‡	6 Yrs–Adults: 20–100mg (dosed in the evening); SD: 20mg	20mg	40mg	60mg	80mg	100mg	

Methylphenidate Formulations – Short Acting** (Medications in this section are shown at actual size)

Focalin® (dexmethylphenidate)	6–17 Yrs: Daily: 5–20mg, divided BID; SD: 2.5mg BID		G 2.5mg	G 5mg	G 10mg	
Ritalin®	6–12 Yrs: Daily: 10–60mg; divided BID or TID; SD: 5mg BID Adults: Daily: 10–60mg, divided BID or TID		G 5mg	G 10mg	G† 20mg	
Methylphenidate Chewable§ (grape flavor)	6–12 Yrs: Daily: 10–60mg; divided BID or TID; SD: 5mg BID Adults: Daily: 10–60mg, divided BID or TID	G† 2.5mg	G† 5mg	G† 10mg		
Methylin® Solution (grape flavor)	6–12 Yrs: Daily: 10–60mg; divided BID or TID; SD: 5mg BID Adults: Daily: 10–60mg, divided BID or TID		G 5mg/5mL	G 10mg/5mL		

Administration Key:

§ Orally disintegrating tablet
† Must be swallowed whole
§ Chewable
¥ Can be mixed with yogurt, orange juice, or water
‡ Can open capsule and sprinkle medication on apple sauce
? Can open capsule and sprinkle medication into water or onto apple sauce
‡ Can open capsule and mix with apple sauce or yogurt

G Indicates a generic formulation is also available; generic products are not shown
G Indicates a generic (but NOT a branded) formulation is available

- Updated versions of the ADHD Medication Guide can be viewed at: www.ADHDMedicationGuide.com
- Laminated copies of the ADHD Medication Guide can be ordered on-line from the ADD Warehouse
- Contact Dr. Andrew Adesman with any comments or suggestions: ADHDMedGuide@Northwell.edu

**Important Information: The age-specific dosing information listed for each medication reflects the FDA-approved prescribing information. "SD" refers to the FDA-recommended starting dose, which sometimes varies by age. Practitioners should refer to the full prescribing information for each medication. Please note: medications have been arranged on the ADHD Medication Guide for ease of display and visual comparison; dosing comparability cannot be assumed.

♦Discontinued ADHD Medications: The following FDA-approved proprietary formulations are no longer available (though, in some cases, branded or generic equivalents are still available): Ritalin LA capsule (60mg); Metadate CD capsules (40mg, 60mg); Metadate ER tablet (10mg); Ritalin SR tablets (20mg); Methylin Chewable tablets (2.5mg, 5mg, 10mg); Daxadrine Spansules (5mg, 10mg); Daxadrine tablets (5mg, 10mg); DextroStat tablets (5mg, 10mg); LiquADD solution (5mg/5mL), and Cylert (pemoline).

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Amphetamine Formulations – Long Acting**

Medications in this section are shown at actual size

Dyanavel® XR (d- & l-amphetamine sulfate)	6 Yrs–Adults: 2.5–20mg; SD: 2.5 or 5mg	2.5mg	5mg	7.5mg	10mg	12.5mg	15mg	17.5mg	20mg
Dyanavel® XR (d- & l-amphetamine sulfate) 2.5mg/mL (bubblegum flavor)	6 Yrs–Adults: 2.5–20mg; SD: 2.5 or 5mg	2.5mg 1mL	5mg 2mL	7.5mg 3mL	10mg 4mL	12.5mg 5mL	15mg 6mL	17.5mg 7mL	20mg 8mL
Mydayis®‡ (mixed amphetamine salts)	13–17 Yrs: 12.5–25mg; SD: 12.5mg Adults: 12.5-50mg; SD: 12.5mg	12.5mg		25mg		37.5mg		50mg	
Adzenys XR-ODT®§ (d- & l-amphetamine) (orange flavor)	6–12 Yrs: 3.1–18.8mg; SD: 6.3mg 13–17 Yrs: 3.1–12.5mg; SD: 6.3mg Adults: 12.5mg		3.1mg	6.3mg	9.4mg	12.5mg	15.7mg	18.8mg	
Adzenys ER® (d- & l-amphetamine) 1.25mg/mL (orange flavor)	6–12 Yrs: 6.3–18.8mg; SD: 6.3mg 13–17 Yrs: 6.3–12.5mg; SD: 6.3mg Adults: 12.5mg		3.1mg 2.5mL	6.3mg 5mL	9.4mg 7.5mL	12.5mg 10mL	15.7mg 12.5mL	18.8mg 15mL	
Adderall XR®‡ (mixed amphetamine salts)	6–17 Yrs: 5–30mg; SD: 10mg Adults: 5–30mg; SD: 20mg (biphasic – 50/50)		G 5mg	G 10mg	G 15mg	G 20mg	G 25mg	G 30mg	
Dexedrine Spansule® (d-amphetamine sulfate)	6-17 Yrs: 10–60mg; SD: 5mg 1-2x/day		G♦ 5mg	G♦ 10mg	G 15mg				

Amphetamine Pro-Drug Formulations – Long Acting**

Medications in this section are shown at actual size

Vyvanse®¶ (capsules) (lisdexamfetamine)	6 Yrs–Adults: 10–70mg; SD: 30mg	10mg	20mg	30mg	40mg	50mg	60mg	70mg	
Vyvanse®§ (chewables) (lisdexamfetamine) (strawberry flavor)	6 Yrs–Adults: 10–70mg; SD: 30mg	10mg	20mg	30mg	40mg	50mg	60mg		

Amphetamine Formulations – Short Acting**

Medications in this section are shown at actual size

Evekeo® (d- & l- amphetamine sulfate)	3–5 Yrs: SD: 2.5mg 1x/day 6–17 Yrs: 5–40mg divided BID; SD: 5mg 1-2x/day		5mg		10mg				
Evekeo® ODT (d- & l- amphetamine sulfate)	6–17 Yrs: 5–40mg divided BID; SD: 5mg 1-2x/day		5mg		10mg		15mg	20mg	
Zenzedi® (d-amphetamine sulfate)	3–5 Yrs: SD: 2.5mg 1x/day 6–16 Yrs: 5–40mg divided BID; SD: 5mg 1-2x/day	2.5mg	G 5mg	7.5mg	G 10mg		15mg	20mg	30mg
Adderall® (mixed amphetamine salts)	3–5 Yrs: SD: 2.5mg 1x/day 6–17 Yrs: 5–40mg divided BID; SD: 5mg 1-2x/day		G 5mg	G 7.5mg	G 10mg	G 12.5mg	G 15mg	G 20mg	G 30mg
ProCentra® (d-amphetamine sulfate) (bubblegum flavor)	3–5 Yrs: SD: 2.5mg 1x/day 6–17 Yrs: 5–40mg divided BID; SD: 5mg 1-2x/day		G 5mg/5mL						

Non-Stimulants**

Medications in this section are shown at actual size

Intuniv®† (guanfacine, extended release)	6–12 Yrs: 1-4mg; SD: 1mg 13–17 Yrs: 1-7mg; SD: 1mg Weight-based dosing: SD: 0.05-0.08 mg/kg/day, may increase to 0.12 mg/kg/day	G 1mg	G 2mg	G 3mg	G 4mg				
Kapvay®† (clonidine, extended release)	6–17 Yrs: 0.1-0.2mg BID; SD: 0.1mg qHS	G 0.1mg	(only in dose pack) 0.2mg						
Strattera®† (atomoxetine)	<70kg: 0.5mg/kg x 3days, then 1.2mg/kg (max 1.4mg/kg, not to exceed 100mg) >70 kg: 40mg x 3days, then 80mg (max 100mg)	G 10mg	G 18mg	G 25mg	G 40mg	G 60mg	G 80mg	G 100mg	
Qelbree®‡ (viloxazine)	6–11 Yrs: 100-400mg; SD: 100mg 12–17 Yrs: 200-400mg; SD: 200mg Adults: 200-600mg; SD: 200mg	100mg SPN 100	200mg SPN 200	300mg SPN 150 + SPN 150		400mg SPN 200 + SPN 200			

Cohen Children's Medical Center
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Treatment with Comorbid Psychiatric Disorders

ADHD & Anxiety

- Stimulants can increase symptoms of anxiety, tension, agitation
- When these symptoms are prominent, want to treat underlying mood disorder (first or concurrently depending on severity of each). If it's unclear, you may decide to try a non-stimulant.
- HOWEVER..
  - ADHD and anxiety symptoms overlap, and uncontrolled ADHD can produce anxiety
    - Always feeling unprepared and attentive would make me anxious too!
    - This could also lead to depression, poor self-esteem, etc.

ADHD + Sleep Disturbance

- Very common - approx. 70% of children with ADHD have sleep issues
- Relationship is complex and likely multifactorial
  - Coexisting primary sleep disorders
  - Comorbid psychiatric conditions
  - Concomitant psychotropic medications
  - “intrinsic” ADHD-related difficulty with settling down for bed
  - Possible circadian rhythm disruption
- Bedtime resistance
- Prolonged sleep onset latency (SOL) (most common)
- Nighttime awakenings
- Difficulties with early mornings
- Sleep-disordered breathing
- Daytime sleepiness
- 2.7x higher incidence of nocturnal enuresis for children with ADHD
- Taking stimulant too late in the day?

ADHD + Outbursts

- Meets criteria for mania → stabilize mood first → add ADHD medications

- DMDD+ ADHD or ADHD + ODD w/ outbursts → start and **optimize** stimulant + parent training
  - ADHD & outbursts improve → yay!
  - ADHD improves, outbursts persists → add mood treatment
  - ADHD and outbursts worsen → assess time of the day!
    - Rebound irritability when medication is worn off? → increase dose or booster dose.
    - If worse all day long → discontinue stimulant
  - ADHD and outbursts worsen → try non-stimulant, try mood medications
  - If unsure, have parents discontinue stimulant for a few days and keep track of outbursts characteristics.

SPECIAL POPULATIONS

ADULTS WITH ADHD

- ADHD impairing symptoms must be dated back to childhood (several sx present prior to the age of 12 – do TBI's complicate this?)
  - Does not have to be diagnosed in childhood
- Need 5 symptoms of ADHD instead of 6, still impairing and in 2+ settings
- 60-90% of pediatric patients with ADHD will continue to have ADHD symptoms as adults
  - Hyperactivity symptoms decreasing and capacity for coping skills increase
- Risk of not treating adult ADHD: greater difficulties professionally, job turnover, financial strain, difficulty maintaining healthy interpersonal relationships
- Most of this population remains untreated
- Adults have wider fluctuation in response to stimulants compared to children – but stimulants can still be extremely efficacious for adult ADHD
- Just as with children, there is no common therapeutic dosing range for stimulants. Each person is unique in their response.
- Stimulants can increase HR and systolic BP
- Screening available for adults – Adult ADHD Self-Reports Scale (ASRS)

FEMALES WITH ADHD

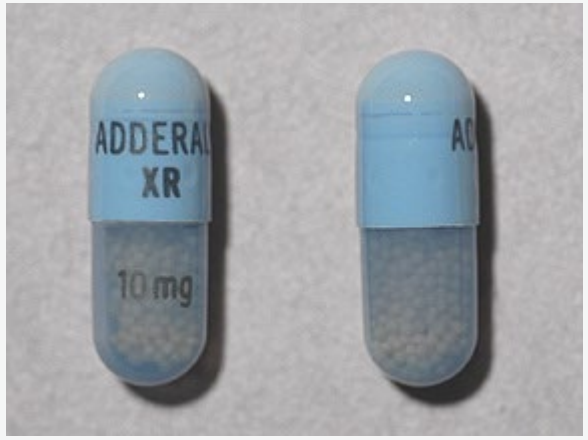
- Historically, cases of ADHD in females were overlooked due to high IQ of girls and they often only presented with signs of “anxiety” and “depression.”
- Girls more likely to be referred for emotional symptoms compared to neurodevelopmental disorders are more common among boys
- Girls are typically older when they are evaluated for AHDD and have more visits prior to being diagnosed compared to boys
- Social functioning impairment has been shown to be more significant in females compared to males
- Males slightly more impaired than females for educational functioning
- Similar impairment in “stress tackling” and no difference in working memory impairment between males and females

Stimulant Medication & Substance Abuse

- Risk vs. Benefit, overall should not be prescribed to someone with active substance use disorder or if there is diversion concern
- May actually prevent them from using illicit drugs:
  - The treatment of ADHD usually improves impulsivity and therefore reduces the risk of impulsively taking an illicit substance when offered to them
  - Patients whose ADHD is adequately treated are less likely to self-medicate their ADHD symptoms with substances that may slow down their thoughts and hyperactivity (e.g. alcohol and cannabis)
  - A patient with untreated ADHD may develop depression, anxiety, and/or ODD and this puts them at greater risk for developing a SUD or self-medicating
- No correlation between stimulant use during childhood and SUD in young adulthood, the risk of adulthood SUD actually may be reduced with appropriate stimulant treatment during youth

Stimulant Abuse Potential

- New longer duration preparation cause less potential for abuse
- Prodrugs (serdexmethylphenidate, Vyvanse) – not active until in the GI tract
- If taken once daily, there is no dosing outside the home and less abuse potential
- Concerta is paste-like and hard to inhale or inject



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