Some Tips for Helping Families Cope with Traumatic Events

- Self Care- Breath, be self aware, be/act calm
- Remind your children they are safe
- Share news as to what happened, let them hear it from you first, while reassuring their safety
- Manage the Media, limit exposure to news coverage
- Listen, reassure, answer questions honestly
- Schools are already planning on how to support kids and families
- Maintain routines- yup, back school, in person or distance
- Plan fun activities

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SOME RESOURCES – Coping with Traumatic Events

- NCTSN.org
- AACAP.org
  - Facts for Families
    - Terrorism and War: how to talk to children
- Child Mind Institute
  - Helping Children Cope After A Traumatic Even
- ACCESS MENTAL HEALTH CT

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Management of ADHD with Poor Response to Initial Treatment, Comorbid Anxiety, Depression or Disruptive Behavior.

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Disclosure

- Richard J. Miller, MD, FAACAP
  - Financial disclosure: contract with ACCESS Mental Health CT
  - No commercial conflicts of interest
  - Off-label use of medications may be discussed

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Learning Objectives

After attending this session, the participants will be able to:

- Describe some of the different causes of poor response to initial treatment for ADHD.
- Outline strategies for primary care providers to approach assessment and treatment for patients whose outcome is complicated by poor response to initial treatment or co morbid conditions.
- Guide families through decision-making process regarding treatment options

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"Prerequisites"

- This talk was developed for practitioners who are already comfortable with the initial evaluation and treatment of ADHD in the primary care settings.
- It is assumed the clinician is familiar with and has experience prescribing approved medication for ADHD including Stimulants (Methylphenidate and Amphetamine), Alpha Agonists (Clonidine and Guanfacine) and Atomoxetine.
- However, we will start with a very brief review of ADHD 101"
- We will not be discussing nonpharmacological interventions, which are the first initial treatment of choice.

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ADHD Criteria: DSM 5 same as DSM IV TR

Inattention

1. Careless/inattention to detail
2. Problem concentrating
3. Doesn't seem to listen
4. Doesn't finish tasks
5. Difficulty organizing
6. Avoids tasks requiring sustained effort
7. Loses important items
8. Easily distracted
9. Forgetful

Hyperactivity/Impulsivity

1. Squirms/fidgets
2. Can't stay seated
3. Runs/climbs excessively
4. Can't work/play quietly
5. "Driven by a motor"
6. Talks excessively
7. Blurts out answers
8. Can't wait turn
9. Intrudes/Interrupts

Inappropriate for developmental level; significant impairment; two or more settings; not otherwise explained

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DSM 5: PRESENTATIONS not “subtypes”

- Distinction found between inattention (IA) and Hyperactive/Impulsivity at time of assessment but does not hold true over time
- New specifiers: **PRESENTATIONS**
  - **Hyperactive-impulsive presentation** (6 or more hyperactive-impulsive symptoms but 5 or fewer inattentive symptoms)
  - **Inattentive presentation** (6 or more inattentive symptoms but 5 or fewer hyperactive-impulsive)
  - **Combined presentation** (6 or more of each set)
  - **Other specified and Unspecified**

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Evaluation of AD/HD

- **ADHD IS A CLINICAL DIAGNOSIS**
- Diagnosis requires:
  - Comprehensive history
  - Interview with parent and **child**
  - Physical examination
  - Information from school
  - Rating scales (Vanderbilt, Conners, Etc.
- Check for other problems that look like AD/HD or come with it*
- Goal: Understand THIS child; establish working relationships with parents, child and school

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Assessment Visit

- Interview of caregivers and CHILD (separately if possible)
- Obtain Pertinent Targeted History including
  - Onset and pattern of development of symptoms
  - How it presents in different settings
  - Sleep and Screen habits
  - What patient and family have tried before
  - Family history of ADHD, Anxiety, Bipolar disorder, psychosis, suicidal behavior, trauma or substance abuse
  - History of stressful events
  - Ask about anxiety, depression, substance abuse, suicidal self or other injurious ideation or behavior.
  - Medications, caffeine, herbal supplements, nicotine and substance use
- Review reports and rating scales

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Assessment Strategies for ADHD

- USE RATING SCALES
  - Vanderbilt Parent and Teacher ADHD Scales
  - Connor's Parent and Teacher ADHD Scales

    Note that Vanderbilt scales also include screens for co-morbid conditions such as anxiety, and behavioral disturbances as well as impairment indicators)
  - Obtain info from School
    - School rating scales
    - School based Assessment including psycho-educational testing
  - Obtain Other Collateral Information
    - Develop and Utilize "OBSERVER FORMS" to collect observations from different caretakers and collaterals (or use our forms)

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American Academy of Pediatrics Clinical Practice Guideline for ADHD in Children and Adolescents - update

- Revised in 2011 and again 10/2019
- Expanded age ranges: **4 - 18** from 6-12
- Discussion treatment approaches for different age groups

ADHD Clinical Practice Guideline: Implementing the Key Action Statements —An Algorithm and Explanation for Process of Care for the Evaluation, Diagnosis, Treatment and Monitoring of ADHD in Children and Adolescents https://pediatrics.aappublications.org/content/144/4/e20192528

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Office Based Non-Medical Interventions

- Provide education about ADHD (Child & Family)
- Office based therapy approaches
  - Supportive counseling
  - Family Counseling
    - empowering parents
    - behavioral approaches
    - the importance of providing structure in home

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Non-Pharmacological Interventions:

- Mental Health Centers/Outpatient Therapy
  - Behavioral Therapy
  - Parent Behavior Management Therapy
  - Neurofeedback
- Parent Support Groups
- School-system
  - Establish collaborative COMMUNICATION
  - School-based assessment
  - Accommodations and specialized services
  - Counseling-individual and group

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Medication Based Treatment

- Primary Care Providers
  - Psychopharmacology (Psychostimulants and Non-stimulants)
  - Treatment monitoring and case management
- **AMHCT** is here to help PCP and Family with Referrals
  - Assessment with recommendations
  - Assessment and treatment
- Referral Providers/Specialists
  - Psychiatry
  - Psychiatric Nurse Practitioners
  - Developmental-Behavioral Pediatrics (if available)\
  - Behavioral Neurologists

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Management of Poor Response or Adverse Effects of Medication

- It's helpful to know the tools in the toolbox.
- Although we are assuming you are familiar with ADHD medications and dosing. Let's take a moment to review the similarities and differences of the available medication options
- We will focus on principles and helpful concepts rather than dosing. "How to cook vs giving recipes"

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FDA Approved Medications for ADHD

- FDA Approved
  - Stimulants
    - Methylphenidate
    - Amphetamine
  - Non-Stimulants
    - Alpha Adrenergic Agonists
      - Clonidine
      - Guanfacine
      - (ER approved IR not approved)
  - Antidepressant Related
    - Atomoxetine

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Non-FDA Approved Medications

- Antidepressants
  - Bupropion
  - TCAs (imipramine, desipramine, nortriptyline)

- Narcolepsy Medications
  - Modafinil (Dopamine reuptake inhibitor)
  - Armodafinil
  - Solriamfetol??? (“Sunosi”) (dopamine and Norepi reuptake inhibitor)
    Recently approved for narcolepsy & daytime somnolence.
    No Data yet

Other:
- Amantadine

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Psychostimulant Medications

- All stimulants used in the USA are either Methylphenidate or Amphetamine derivatives.
- Methylphenidate and Amphetamines both inhibit norepinephrine and dopamine transporter functioning, which acts to **increase central dopamine and norepinephrine activity which improves attention and executive functioning***
- However, there are some differences for example Amphetamine also inhibits Monoamine Oxidase activity and has some pre-synaptic intracellular activity. As such it may have greater potency affecting benefit and adverse effects.

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Easy, Only two medicines to choose from

- No such luck

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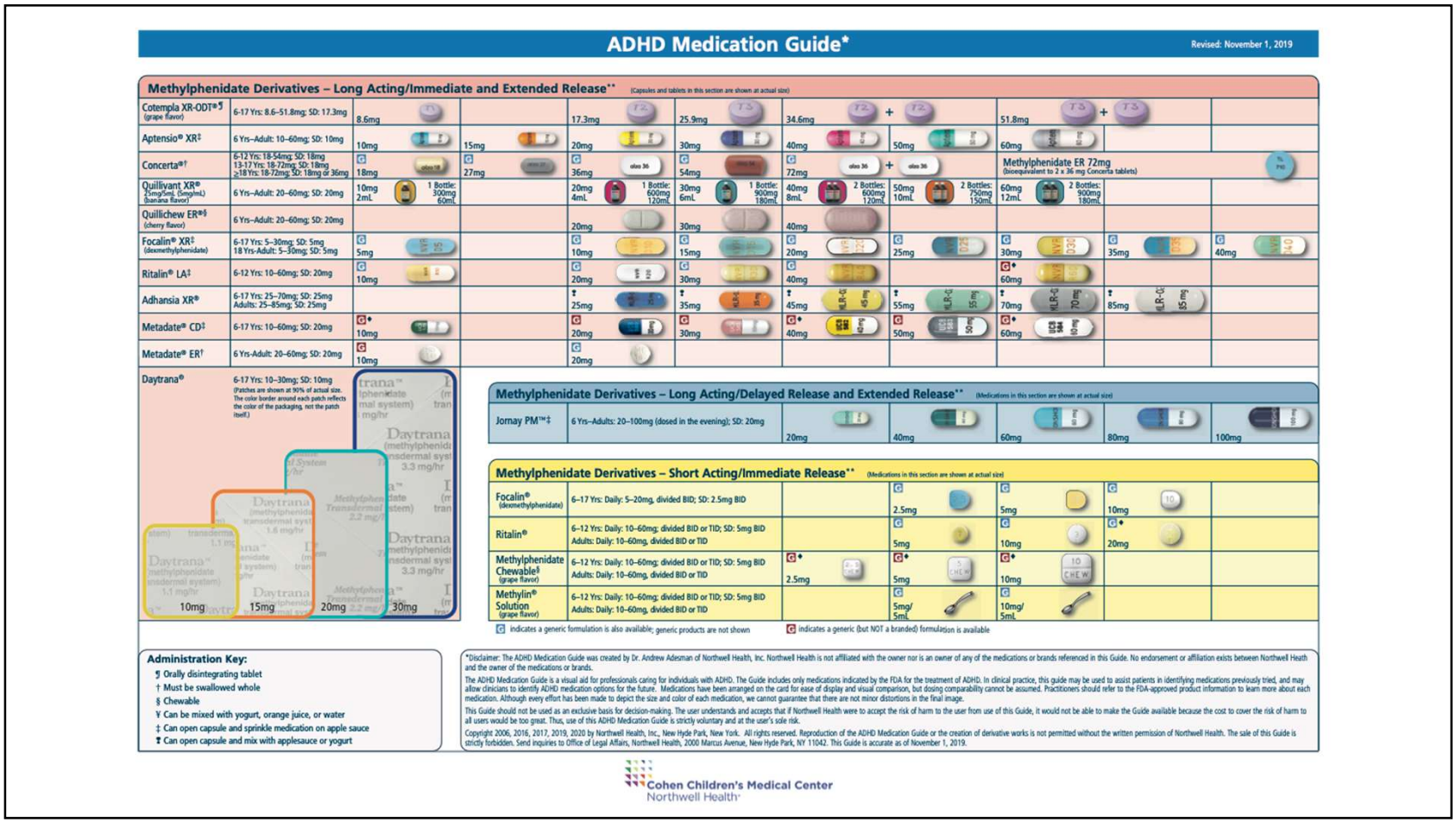

ADHD Medication Guide*

Revised: November 1, 2019

Methylphenidate Derivatives – Long Acting/Immediate and Extended Release**

(Capsules and tablets in this section are shown at actual size)

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	
Aptensio® XR‡	6 Yrs–Adult: 10–60mg; SD: 10mg	10mg	15mg	20mg	30mg	40mg	50mg	60mg	
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	27mg	G 36mg	G 54mg	G 72mg		Methylphenidate ER 72mg (bioequivalent to 2 x 36 mg Concerta tablets)	
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			
Focalin® XR‡ (dexmethylphenidate)	6-17 Yrs: 5–30mg; SD: 5mg 18 Yrs-Adult: 5–30mg; SD: 5mg	G 5mg		G 10mg	G 15mg	G 20mg	G 25mg	G 30mg	G 35mg — G 40mg
Ritalin® LA‡	6-12 Yrs: 10–60mg; SD: 20mg	G 10mg		G 20mg	G 30mg	G 40mg		G◆ 60mg	
Adhansia XR®	6-17 Yrs: 25–70mg; SD: 25mg Adults: 25–85mg; SD: 25mg			↑ 25mg	↑ 35mg	↑ 45mg	↑ 55mg	↑ 70mg	↑ 85mg
Metadate® CD‡	6-17 Yrs: 10–60mg; SD: 20mg	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®	6-17 Yrs: 10–30mg; SD: 10mg (Patches are shown at 90% of actual size. The color border around each patch reflects the color of the packaging, not the patch itself.)	10mg	15mg	20mg	30mg				

Methylphenidate Derivatives – Long Acting/Delayed Release and Extended Release**

(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 Derivatives – Short Acting/Immediate Release**

(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	

G indicates a generic formulation is also available; generic products are not shown

G◆ indicates a generic (but NOT a branded) formulation is available

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
ǂ Can open capsule and mix with applesauce or yogurt

*Disclaimer: The ADHD Medication Guide was created by Dr. Andrew Adesman of Northwell Health, Inc. Northwell Health is not affiliated with the owner nor is an owner of any of the medications or brands referenced in this Guide. No endorsement or affiliation exists between Northwell Heath and the owner of the medications or brands.

The ADHD Medication Guide is a visual aid for professionals caring for individuals with ADHD. The Guide includes only medications indicated by the FDA for the treatment of ADHD. In clinical practice, this guide may be used to assist patients in identifying medications previously tried, and may allow clinicians to identify ADHD medication options for the future. Medications have been arranged on the card for ease of display and visual comparison, but dosing comparability cannot be assumed. Practitioners should refer to the FDA-approved product information to learn more about each medication. Although every effort has been made to depict the size and color of each medication, we cannot guarantee that there are not minor distortions in the final image.

This Guide should not be used as an exclusive basis for decision-making. The user understands and accepts that if Northwell Health were to accept the risk of harm to the user from use of this Guide, it would not be able to make the Guide available because the cost to cover the risk of harm to all users would be too great. Thus, use of this ADHD Medication Guide is strictly voluntary and at the user's sole risk.

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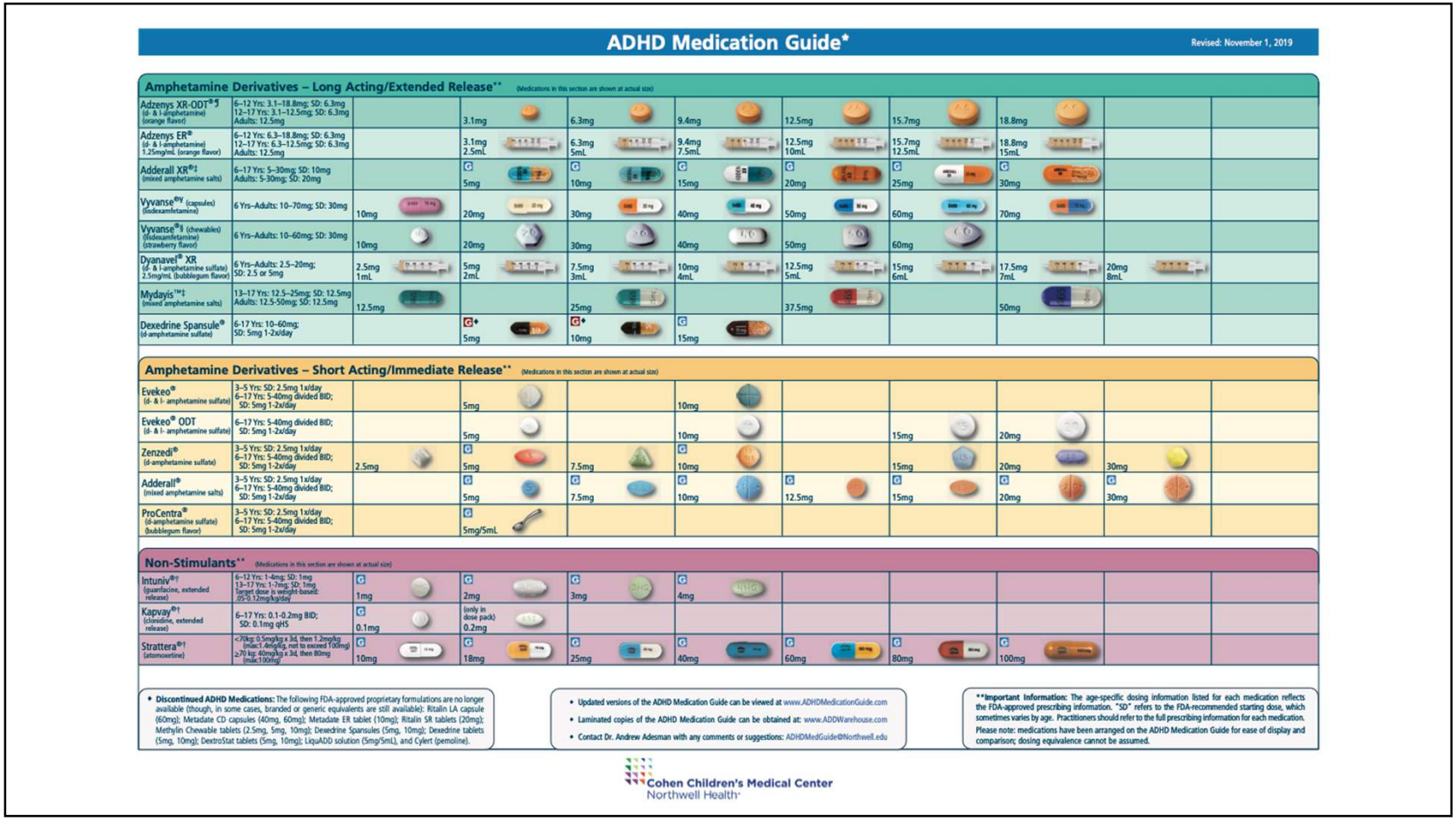

ADHD Medication Guide*

Revised: November 1, 2019

Amphetamine Derivatives – Long Acting/Extended Release**

(Medications in this section are shown at actual size)

Adzenys XR-ODT®¶ (d- & l-amphetamine) (orange flavor)	6–12 Yrs: 3.1–18.8mg; SD: 6.3mg 12–17 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 12–17 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		G 5mg	G 10mg	G 15mg	G 20mg	G 25mg	G 30mg		
Vyvanse®Ψ (capsules) (lisdexamfetamine)	6 Yrs–Adults: 10–70mg; SD: 30mg	10mg	20mg	30mg	40mg	50mg	60mg	70mg		
Vyvanse®§ (chewables) (lisdexamfetamine) (strawberry flavor)	6 Yrs–Adults: 10–60mg; SD: 30mg	10mg	20mg	30mg	40mg	50mg	60mg			
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		
Dexedrine Spansule® (d-amphetamine sulfate)	6-17 Yrs: 10–60mg; SD: 5mg 1-2x/day		G✦ 5mg	G✦ 10mg	G 15mg					

Amphetamine Derivatives – Short Acting/Immediate Release**

(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 6–17 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 Target dose is weight-based: .05-0.12mg/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 3d, then 1.2mg/kg (max1.4mg/kg, not to exceed 100mg ≥70 kg: 40mg/kg x 3d, then 80mg (max:100mg)	G 10mg	G 18mg	G 25mg	G 40mg	G 60mg	G 80mg	G 100mg		

- **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); Dexedrine Spansules (5mg, 10mg); Dexedrine tablets (5mg, 10mg); DextroStat tablets (5mg, 10mg); LiquADD solution (5mg/5mL), and Cylert (pemoline).

- Updated versions of the ADHD Medication Guide can be viewed at www.ADHDMedicationGuide.com
- Laminated copies of the ADHD Medication Guide can be obtained at: www.ADDWarehouse.com
- 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 comparison; dosing equivalence cannot be assumed.

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Why so many? What's the difference

Stimulants have some idiosyncratic Pharmacokinetic and Pharmacodynamic properties

- IR is very short acting (2-4 hour)
- Stimulants have somewhat different effects when blood level is increasing vs decreasing
- Maximum benefit occurs while the blood level is slowly increasing
- Adverse effects can be different at onset, peak and offset.
- Therefore, dosage curve is very important and varies with medication and preparation
- Ex. insomnia can be caused by rebound or extended duration

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"It's All About the Curve"

The Ideal Dosage Curve

- Rapid Onset, followed by slow increase and gradual offset
- Sufficient duration of action of benefit (might be shorter for elementary school student but longer for high schooler)
- Ideally once a day administration
- Minimum adverse effects
- Dosage response curve varies with different preparations and individual's (pharmacokinetics and pharmacodynamic differences)

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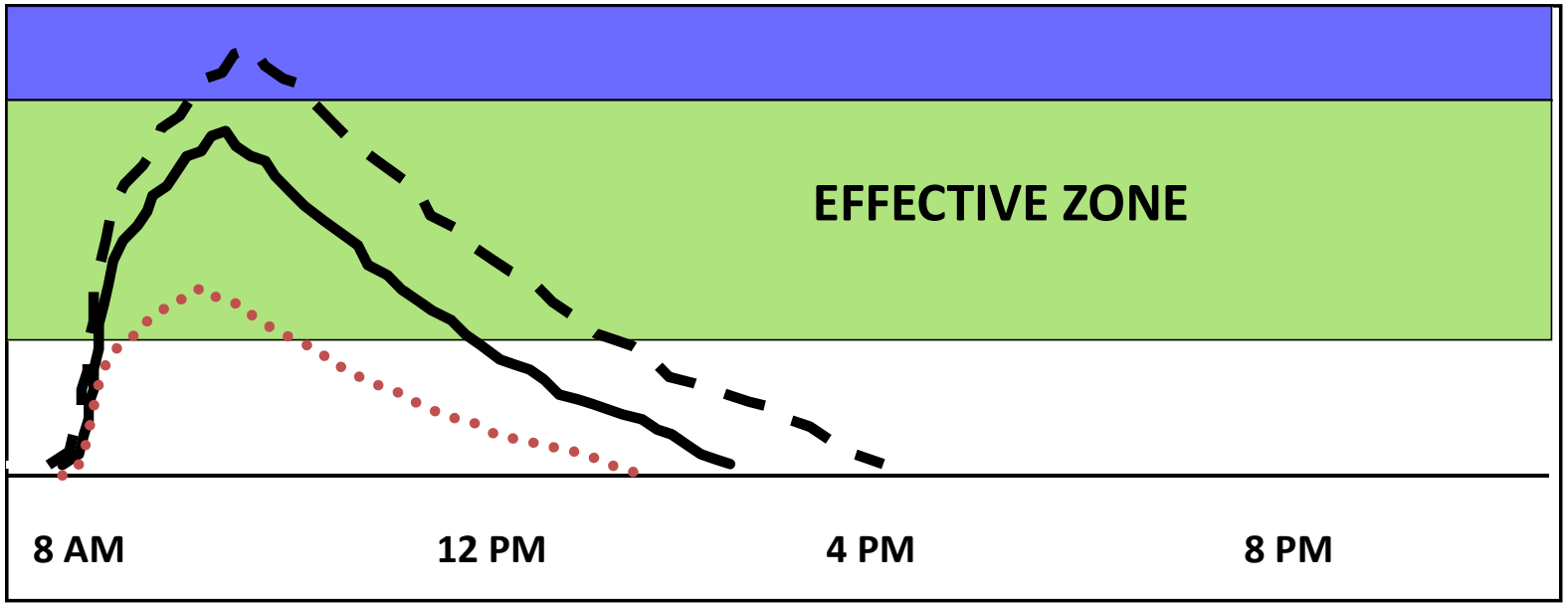
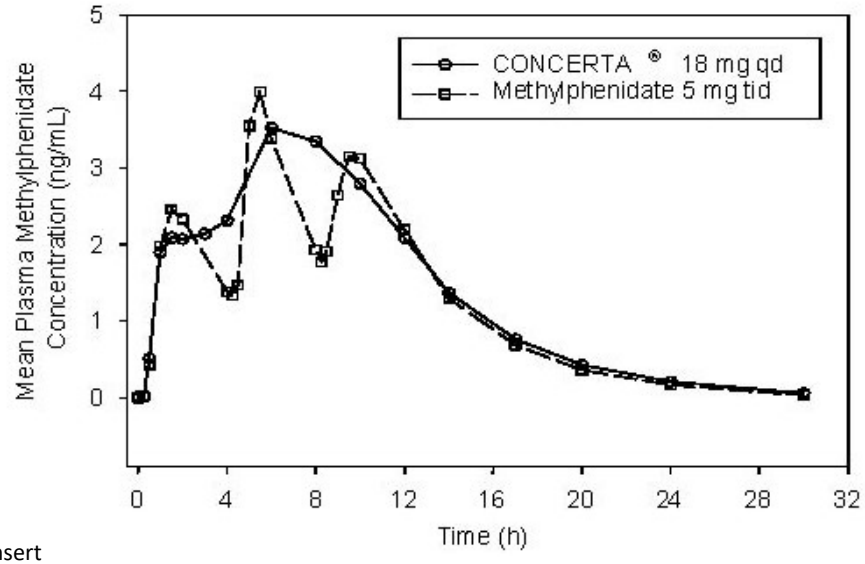
DOSE CURVE -Immediate Release stimulant

Individual Response



Dosage Curve – Extended Release

- "Concerta" vs immediate release MPH



From Package Insert

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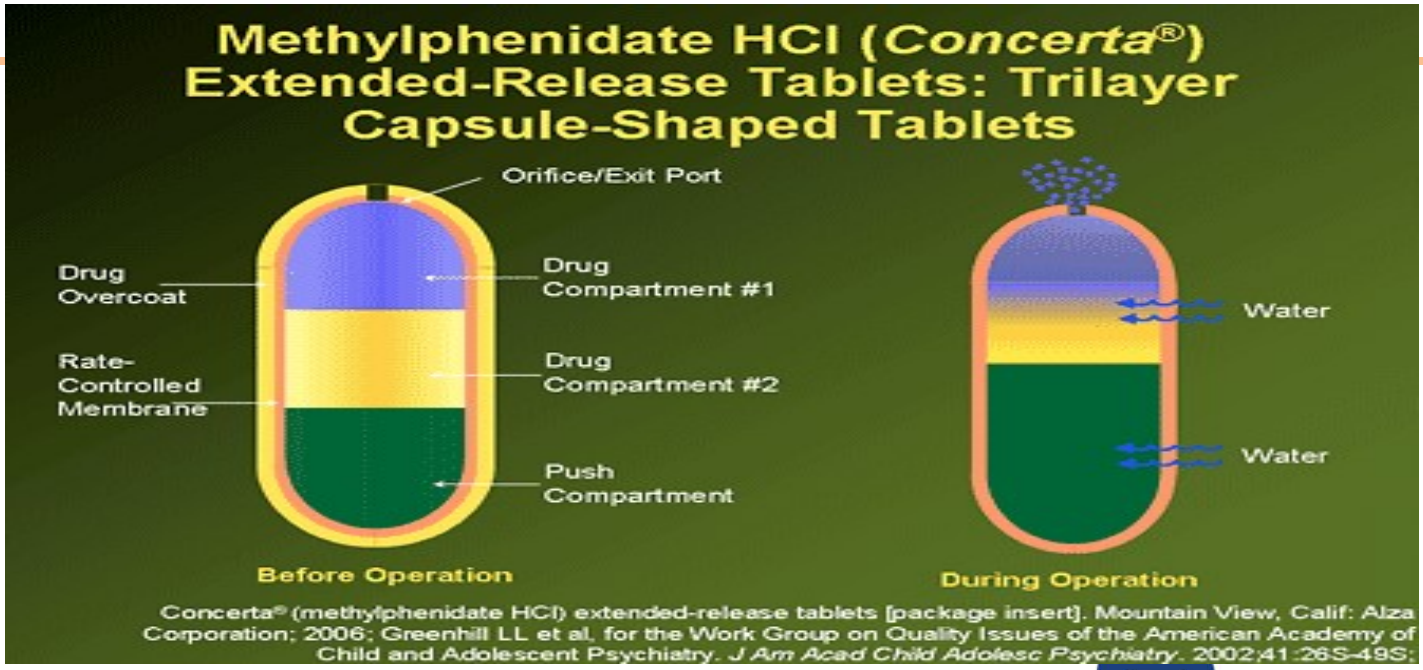
OROS Methylphenidate aka Concerta®



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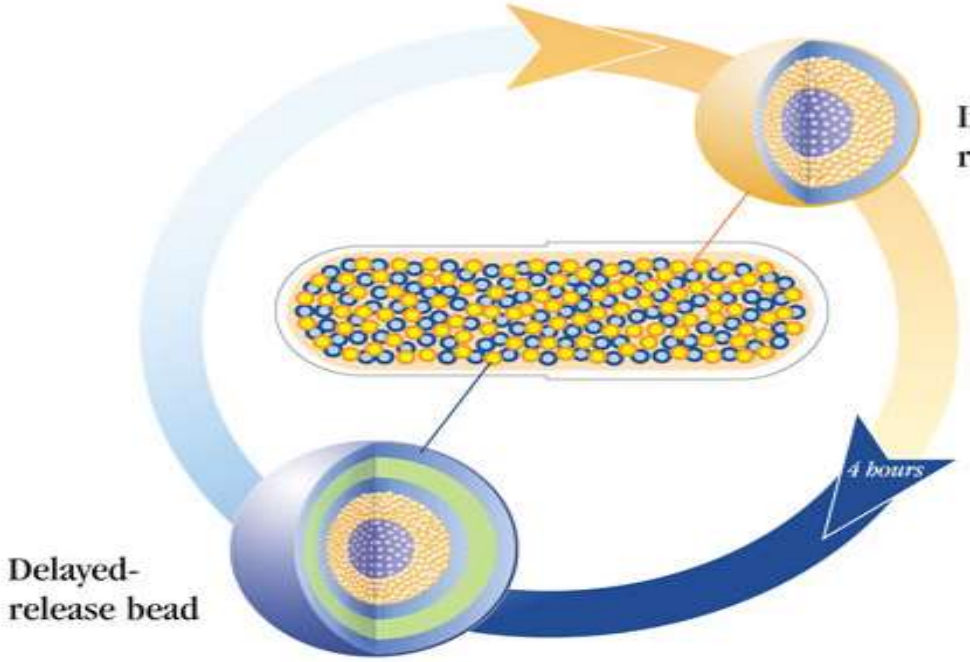
Bead Technology e.g. Adderall XR ®



Why so many? What's the Difference?

- First be familiar with the differences
  - Primary ingredient (MPH vs AMP)
    - Racemic vs Mono isomer (ex MPH vs d-MPH or Dex vs MAS)
  - Immediate release vs Extended
    - Type of Extended release (OROS, beads, multi-layer tablet etc.)
- Administration form
    - (Capsule, Tablet, Chewable, ODT, Concentrate, Patch)
- Generic vs Brand

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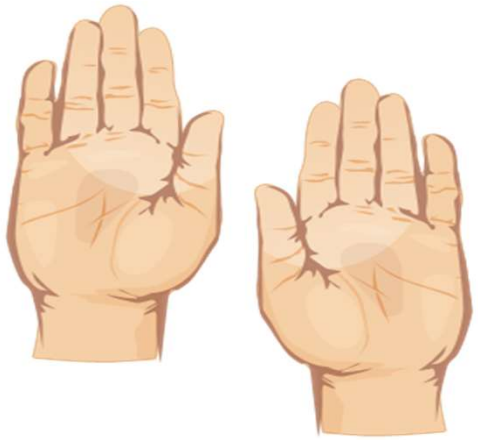
Dexmethylphenidate: Focalin® and Focalin XR ®

- Methylphenidate is racemic mixture with both dextro (right twisted) and levo (left twist) molecules
- Only right-handed is active
- Both can contribute to side effects
- Focalin® uses ½ the dose of MPH
- May have clinically lower intensity of SE
  - Slightly longer acting
  - Slightly different “quality”



Brams M 2012

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KEY Stimulant References to have on hand.

- **NORTHWELL HEALTH MEDICATION GUIDE**
  - http://www.adhdmedicationguide.com

- **New Formulations of Stimulants: An Update for Clinicians**

  R.Steingard et Al. J of Child and Adolescent Psychopharmacology V29,Number 5, 2019 pp324-339

  Has very practical tables of grouped by ingredient and duration of action listing ingredients, dosing and mechanism.

  As well as equivalencies.

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Non Stimulants: Alpha Agonists

- Alpha Adrenergic Agonists:
  - Clonidine, Clonidine ER (“Kapvay”), clonidine patch.
  - Guanfacine, Guanfacine ER (“Intuniv”)

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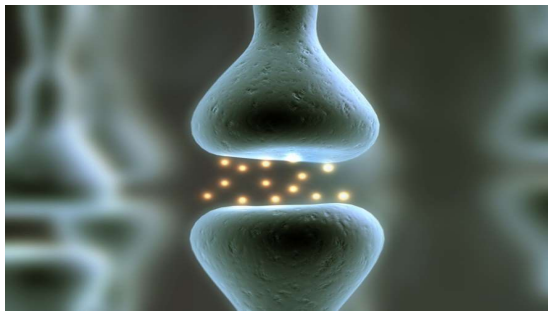
Adrenaline/Noradrenaline system



- Locus Coeruleus
- Amplifies **ALERT** signal
- Alpha 2 receptors
  - auto-receptors post synaptic
  - Measure and adjust amt in synapse
  - Alpha 2 agonists trick nerve into thinking too much in synapse
  - Message takes a few days to get to cell body
  - Down-regulates

Kollins SH 2011

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Alpha Agonists - Indications

- Alpha Adrenoreceptor agonist, post-synaptic
  - Prefrontal cortex
  - Increases delay-related firing PFC neurons
- Severe hyperactivity / impulsivity
- Aggression / ODD / Over-reactivity
- Tics
- ADHD with motor tics
- ADHD with atypical features (irritability)
- Sleep onset problems

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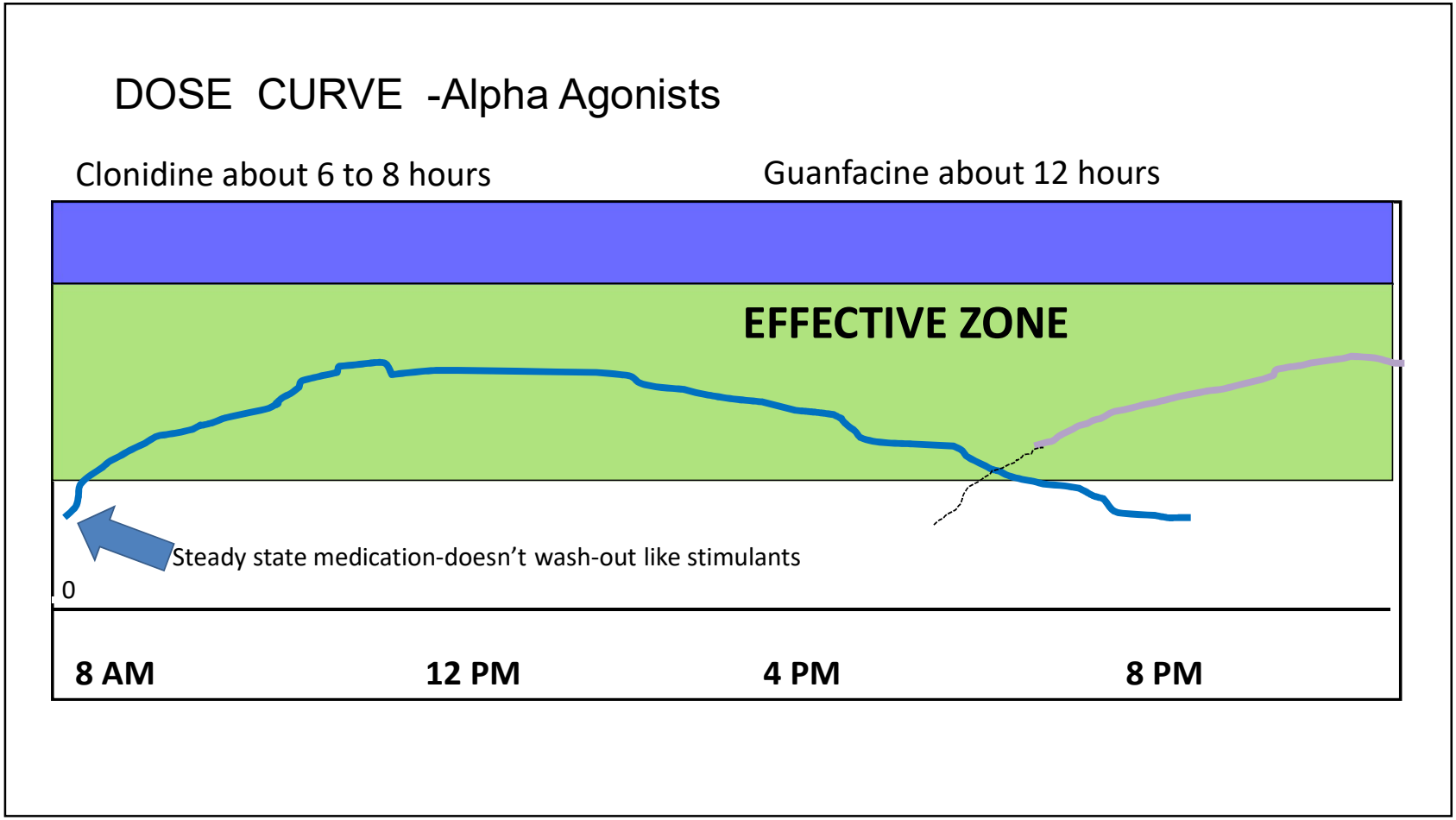
DOSE CURVE -Alpha Agonists
Clonidine about 6 to 8 hours
Guanfacine about 12 hours
EFFECTIVE ZONE
Steady state medication-doesn't wash-out like stimulants
0
8 AM
12 PM
4 PM
8 PM

Clonidine (Catapres®)

- Alpha noradrenergic agonist
- Indications: ADHD, aggression, irritability, tics
- Dosing: 0.05 to 2.0 mg ~ 1 hour before bedtime
- If used for sleep onset may wear off ~ 4 AM
- Titrate up slowly and administer daily for monotherapy
- May need TID or even QID dosing if monotherapy
- 3 - 6 weeks to determine benefit for ADHD
- Less helpful with inattention than stimulants
- Side effects: sedation, headaches, depression, hypotension, rebound hypertension [wean off gradually]
- Adjunctive medication with stimulant
- Catapres® patch (change every FIVE days)

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*

Clonidine Extended Release – Kapvay ®

- FDA approved (2010 monotherapy; 2013 adjunctive)
- 0.1 mg, 0.2 mg tablets (must take whole)
- Twice daily dosing
- Lower peak concentration than IR, less sedating
- Indications: not first line; ADHD; tics; irritable/oppositional profile; side effects with stimulants; need for adjunctive therapy due to stimulant-related anorexia;
- Side effects: sedation, hypotension, psychiatric

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Guanfacine (Tenex®)

- Alpha 2a noradrenergic agonist (more selective)
- Dosing: 0.5 to 2.0 mg up to TID
- Longer half-life usually BID
- Administer DAILY
- Better effect on attention than clonidine
- Less sedation than clonidine
- Improvement ADHD Sx including some attention effects
- SE: insomnia, agitation, headaches

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Guanfacine Extended Release (Intuniv®)

- Intuniv (long-acting guanfacine) November 2009
- Alpha 2a adrenergic agonist
- Tablet: 1, 2, 3 and 4 mg; q day dosing with 1 week between dosage changes
- Main side effects: possible sedation, rebound hypertension if stopped abruptly
- Smooth sustained release
- Data suggest effective but not be as effective as stimulants
- Approved as adjunctive medication

Kollins SH 2012

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Atomoxetine (Strattera ®)

- Approved by FDA in November 2002
- Not controlled substance; low abuse potential
- Highly selective norepinephrine reuptake inhibitor
- Rapidly absorbed; not affected by food
- Peak plasma concentrations 1-2 hrs. p dose
- Hepatic cytochrome P450 2D6 pathway (~5% slow)
- Prolonged duration reported, effects next AM or give at dinner if mornings are particularly difficult
- Side effects: stomach upset, fatigue, agitation
- Black box: suicidal ideation, mania, liver enzyme (RARE)

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Atomoxetine- Who am I using it for?

- Response ~60 % (not stimulant naïve)
- Children who failed at least 1 stimulant
- **ADHD with tics**
- **ADHD with anxiety**
- **ADHD with ASD**
- ADHD with substance abuse
- ADHD with Dyslexia (+/-)
- Consider it for:
  - Children with problems evening/ early AM
  - Children who need continuous med

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Causes of Poor Response to Initial Treatment

- Medication related issues
  - Poor compliance
  - Adverse effects
  - Non-response
- Diagnosis or target symptom related issues
  - Misdiagnosis
  - Comorbid conditions

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Adverse Effects of Stimulant Medication

Common issues

- Appetite
- Sleep
- "Rebound" (wear off)

Less Common

- Stomachaches
- Headaches
- Emotionality
- Social withdrawal

Rare

- Tics
- Anticholinergic effects
- Cardiovascular
- Growth delay
- Picking

Really Rare

- Neuropsychiatric
- ?Lower seizure threshold

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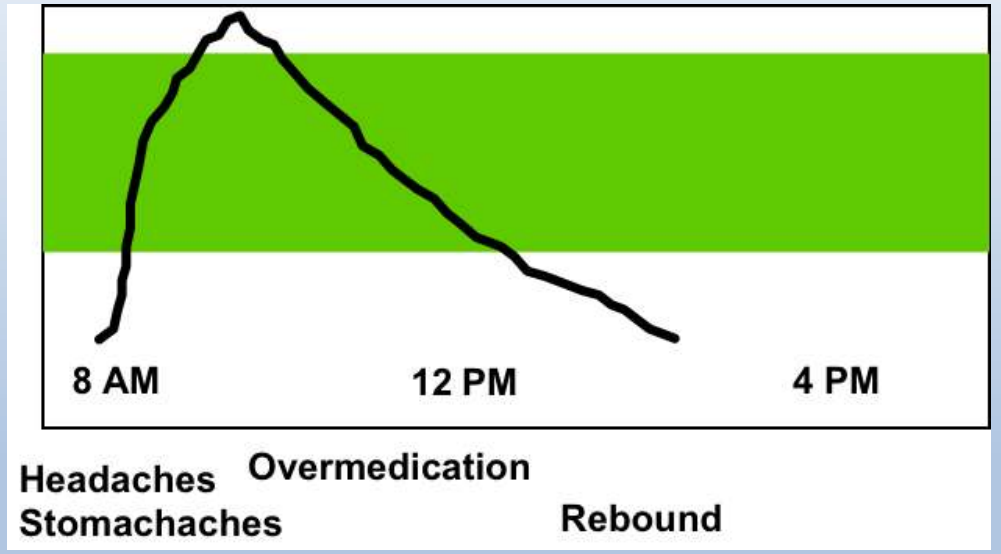
Example of timing related adverse effects



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Assessment of Adverse effects

- **Note the timing of the adverse reaction** (and benefits)
  - Adverse effects that occur during onset, peak and "offset" can often be addressed by changing dosing, schedule or preparation
  - Adverse effects that occur without regard to timing may require changes in medication type, look for other contributing factors or reassessment of diagnosis (diet, sleep, screen time, Allergies)
- **Review compliance, weekends, households**
- **Check for other medications**, caffeine, nicotine, decongestants, nutritional supplements. (Recreational substances as well)
- **While adjusting dosage and response Pt must take on weekends so family can observe peak effects at home or if only occurring at school**.

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Generics

- No real difference with IR formulations
- With Extended Release, how the tablet is made can vary with manufacturer and make significant difference.
  - Example: CONCERTA
    - What makes Concerta different is that is uses an OROS slow release system.
    - Newer Generics slipped though FDA approval with Non OROS slow release
    - After complaints, FDA rescinded Mallinckrodt and Kremers Urban Non OROS MPH ER as being Concerta Generic equivalents.
    - Write for Concerta and allow substitution do not write for MPH ER
  - Always check for change in generic when medication “stops working”

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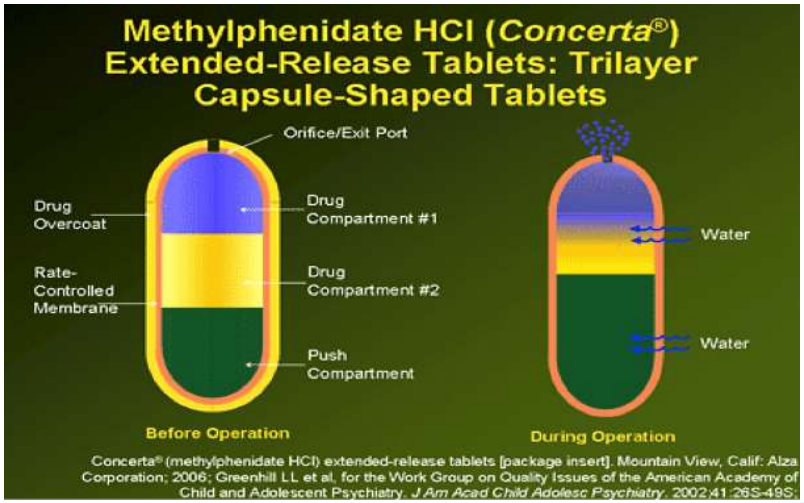
CONCERTA



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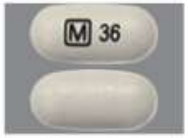
Concerta Generics OROS ≠ Non OROS MPH ER

Top Row: **Concerta Brand** (J&J/Alza)
Bottom: **Watson/Activis** OROS generic
Coat of IR MPH; osmotic pump (OROS)



Mallinkcroft MPH ER
Coat of IR MPH; Core diffusion-controlling membrane

Kremers Urban MPH ER
Coat of IR MPH; Core extended release beads (like Focalin XR)

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Treatment of Common Adverse Effects - Appetite

- Obtain baseline information on appetite and eating pattern
- About 30-50% have some decrease in appetite for lunch;
- Often Transient; decreases in 2 weeks
- Monitor height and weight
- PLAN for it and involve the child
- Can be managed
- Strategic eating: Breakfast, Planned Snacks(pre prepared), Divide and conquer dinner (half meal with family & save half for when medication wears off or before bed)
- Increase caloric density
- Switch stimulants; consider Atomoxetine, Alpha agonist
- Combine lower dose of stimulant with Alpha agonist or Atomoxetine
- Periactin (last resort)

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Adverse Effects - Sleep

- Ask about sleep behaviors at all visits
- **Obtain baseline sleep history** including environment, evening routines in household, bedtime routines, screen/media use, caffeine & supplements. Ask how pattern varies day to day and changed over time.
- Ask about what has been tried already.
- Is it trouble going to bed, trouble falling asleep once in bed or waking at night
- Increased sleep dysfunction in ADHD (5x)
- Stimulants can also delay sleep onset or sleep onset issues may be due to rebound or even the return of ADHD symptoms when meds have worn off; Some children fall sleep better with some medication still active in their systems.
- Is there an anxiety disorder or depression?

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Treatment of Sleep

- Educate child and family about sleep
- Being able go to sleep is a learned behavior. A skill that must be practiced and takes time to achieve. If they have to be exhausted to fall asleep, they do not have the skill to self sooth and down regulate arousal.
- “Sleep hygiene”- establish calm, consistent bedtime routines; Sleep environment. They may need direct assistance in establishing routines and skills.
- Removal of electronics; screen light tricks brain
- www.commonsensemedia.org
- IOS and Android parental controls and 3r party apps
- iCBT

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Treatment of sleep issues - Medication

- As an adjunct, if necessary, to other interventions.
- First check if due to med related issues , rebound, too high a dose or med wearing off. Can see different in sleep pattern on or off stimulant meds. (if rebound small hs dose might be considered!)
- Massage, herbal teas, bedtime (low sugar) snack, warm milk, turkey (tryptophan)
- Melatonin 1 to 6 mg 45-60 minutes before sleep. Dosage is not weight dependent and less is often better
  - Decreases sleep latency but doesn't increase duration
  - Dietary supplement; not regulated; use same brand
  - Can be used chronically; well tolerated;
  - Use slow release if there is middle insomnia
- Clonidine
  - 0.05 mg (1/2 of 0.1 mg tab) 30 minutes prior to sleep
  - Additional side effects include sleep architecture changes such as vivid dreams and reduced REM
  - Can sometimes exacerbate middle insomnia (if you wake up as or after it is wearing off)

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Other Common Adverse Effects

- Stomachaches and headaches
  - Commonly occur during onset/absorption, 45 to 90 minutes
  - Address by giving with meals, changing slow release prep or dosage.
- Queasiness; persistent; regular
- Rebound
  - Increased irritability (easily bothered), dysphoria or increased activity level that occurs during “offset” as medication wears off and may last ½ to 2 hours.
- Emotionality, dysphoric or flattened mood. Check pattern,
  - If during peak, onset or offset adjust dosage curve.
  - If occurs throughout day, adjust total dosage or change medication.

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Causes of Poor Response to Treatment

- **Poor Compliance**
- Non-response due to poor absorption?
  - Occasionally happens, try different preparation. Daytrana patch bypasses the GI tract and first pass hepatic metabolism.
  - Consider initiating treatment with IR medication then switch to ER
- **Mis-diagnosis**
  - Inattention and impulsivity are the "fevers of behavioral health." Lots of things can interfere with Attention besides ADHD
- "**Missed-diagnosis**": Comorbid conditions are very common and can interfere with response to ADHD treatment unless identified and addressed.

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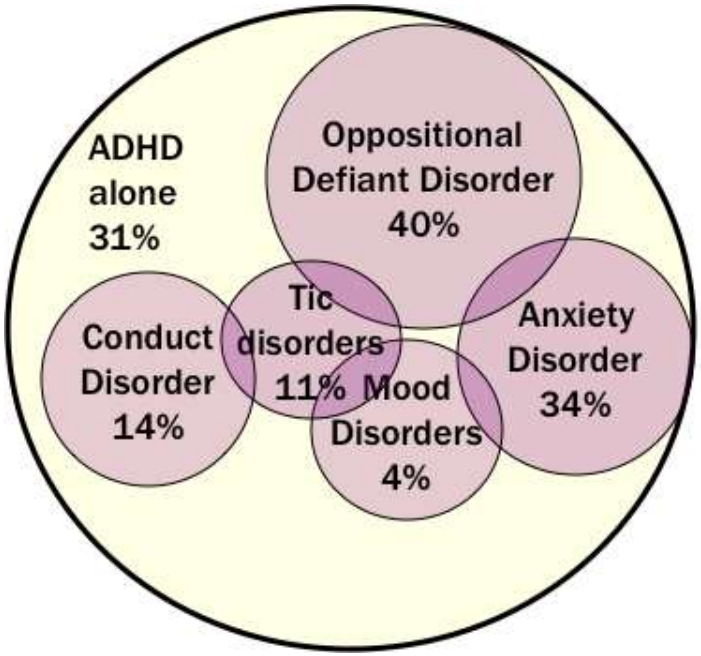
Common Comorbid Conditions



MTA study
N=579

Miller, K 2015

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Comorbid Conditions

- Anxiety
- Depression (more likely to be inattentive ADHD)
- Bipolar disorder (especially if first showing up in mid teens)
- DMDD
- Disruptive Behavior Disorders (ODD, Conduct Disorder)
- Tourette's/Tic Disorders
- Nicotine or other substance abuse
- These common co-morbid conditions also can cause inattention or Impulsivity on their own without co-morbid ADHD

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Misdiagnosis (Differential Diagnosis)

- PTSD (arousal dysregulation and behavioral triggers may mimic ADHD but ADHD is also frequently co-morbid)
- Inadequate sleep (insomnia, media use, etc.)
- Environmental /school/ family stressors
- Learning disabilities, especially language disorder
- FAS
- ASD (lack of shared goals/ focus) but there is also high comorbidity
- Medical Conditions (Thyroid disorders, anemia, seizure disorders, pinworm etc.)
- Caffeine, nicotine and herbal stimulants and energy drinks
- Substance abuse (especially if turning up mid teens)

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What next?

- **REASSESS** if there is a poor or unexpected response to initial treatment not clearly related to an adverse response to medication.
- **Review history**. **Focus on pattern of symptoms** long term and day to day. when they started and how they evolved. Check for family history of comorbid or look alike conditions.
- **Interview with parent and child**
- Physical examination
- Information from school and other collaterals
- Rating scales Vanderbilt have screens for common comorbidities. PSC 17 or 35 are broader screens
- Check more closely for other problems that look like ADHD or come with it
- Goal: Understand **THIS** child; establish working relationships with parents, child and school

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ANXIETY and PTSD

- Anxiety has 10% -20% prevalence in children and up to 30% prevalence in teens and is Co- Morbid with ADHD in 1/3.
- Anxiety can present with impaired concentration & restlessness.
- ADHD medications can sometimes increase anxiety and occasionally cause anxiety like symptoms on their own.
- Careful history (family history, presence and pattern of anxiety symptoms) screening tools (SCARED, Vanderbilt, PSC 17 will usually help clarify.
- If co-morbid, stimulants can also occasionally improve anxiety, a careful trial can be helpful. If not treat Anxiety first with therapy and medication than reevaluate. Alpha agonists alone or in combination with stimulants can decrease anxiety related side effects and hyper-arousal, but do not directly treat anxiety.
- Atomoxetine may address ADHD with less chance of exacerbating anxiety.
- Referral and collaboration with mental health clinician is imperative

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Post Traumatic Stress Disorder

- Hyper-arousal, high reactivity and impulsivity are common in PTSD.
- ADHD is also frequently co-morbid as well.
- Kids with PTSD are often very sensitive to the adrenergic side effects of stimulants.
- Alpha agonists are often very helpful alone or in combination with Stimulants as they down regulate arousal and block some of the adverse effects of the stimulants and act as an adjunct.

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Tourette's and Tic Disorders

- Impulsivity and hyperarousal are common in Tic disorders
- Motor tics are common in childhood
- Tics wax and wane.
- Genetic factors important
- 50-60 % Tourette's have ADHD, (25 % OCD)
- Onset of ADHD Sx precedes onset of tics by 2 - 4 years
- ADHD Sx often more disabling than tics
- Treatment
  - Stimulants can either worsen or reduce tics. Start low, go slow.
  - Alpha agonists are first line for Tourette's and 2nd line for ADHD
  - Atomoxetine has a reduced incidence of worsening tics

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ODD and ADHD

- Ongoing pattern of excessive anger-guided disobedience, hostile and defiant behavior toward authority
- 40% incidence of Co-morbidity with ADHD
- ADHD increases risk of developing oppositional behavior
- Once pattern begins, behavioral treatment is crucial for both parents and child
- Even if there is a good response to stimulants it creates an increased opportunity to respond to behavioral and other therapeutic interventions.
- Alpha agonists can sometimes be helpful alone or as adjunct to stimulants.
- Carefully screen for co morbid conditions such as anxiety, depression, DMDD or Trauma/PTSD

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Depression

- 5-10% incidence in Children and Adolescents
- Mood disorders can be co morbid with ADHD
- Impaired concentration, loss of interest and decreased effort can sometimes appear like Inattentive ADHD.
- Screen with PHQ9
- When Co-occurring both need treatment.
- Wellbutrin can sometimes be used to treat ADHD as well as Depression

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Bipolar Disorder

- **Episodic** mood disorder with periods of depression, mania that are distinct from baseline and lasting a week or more
- While episodes of depression are usually present, the presence of at least one distinct episodes of Mania must occur. It is not persistent reactivity irritability or mood instability
- Impulsivity, impaired attention vary with mood episodes.
- When ADHD does co-occur you can either stabilize moods first then address attention if it persists. However it is safe to cautiously treat attention with stimulant medication. Even without mood stabilizers.
- This is a highly complex and severe disorder that usually requires multi-modal therapeutic interventions including complicated pharmacological treatment with SGAs and other mood stabilizers.

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Other Comorbid Mood and Disruptive Disorders

- DMDD (Disruptive Mood Dysregulation Disorder)
  - A pattern severe and recurrent temper outbursts that are grossly out of proportion in intensity or duration to the situation.
  - With persistently irritable or angry mood, most of the day and nearly every day
  - Behavioral and family treatment is primary. Optimal medication management is not yet clear but cautious trials of simulants +/- alpha agonists and or SSRI (especially if dysphoria is prominent). SGAs as well.
  - Look to co-morbid symptoms for treatment strategies
- Intermittent Explosive Disorder
  - Discrete episodes of severe behavioral outbursts with return to normal mood in between episodes
  - Alpha agonists
  - Substance abuse: Assess and treat first. Do not treat attentional side effects of substance abuse. Use with caution consider Atomoxetine, Concerta or Vyvanse with close monitoring.

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Severe Aggressive Outbursts

- TOSCA* (Treatment Of Severe Childhood Aggression)

Looked at the treatment of with ADHD and severe co-morbid aggression (due to various causes)

- Looked at treatment with parent training, Stimulants (MPH) and SGA (Risperidone)
- Bottom line was parent training + MPH + Risperidone had a significant improvement with added SGA for “hot” or reactive aggression outbursts but not “cold” or proactive aggression (where aggression is in anticipation of a reward).

*Aman Et LA JAACAP 2014;53

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Treatment: Family-Based

- Psych education about ADHD and comorbidity (Child & Family)
- Therapy approaches
  - Supportive counseling
  - Parent Behavioral Management Training or similar behavioral training
  - Family therapy – empowering parent, structure in home
- Accessing treatment
  - Insurance
  - ACCESS Mental Health CT

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Treatment: Community-Based

- Mental Health Centers/Outpatient Therapy
  - Behavioral Therapy
  - Group, Family and Intensive Therapy programs
  - Neurofeedback
- Parent Support Groups
- School-system
  - Establish collaborative COMMUNICATION
  - School-based assessment
  - Accommodations and specialized services
  - Counseling-individual and group

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Treatment: Medical Provider-Based

- Primary Care Providers
  - Psychopharmacology (Psychostimulants and Non-stimulants)
  - Treatment monitoring and case management
- Referral Providers
  - Psychiatry
  - Psychiatric Nurse Practitioners
  - Developmental-Behavioral Pediatrics (if available)
- Referral services
  - Assessment with recommendations
  - Assessment and treatment

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Practice Change to Consider

- Be aware and think about co-morbid conditions
- Be familiar with the differences between ADHD medications and how to switch between them or combine.
- "Practice Readiness" (AAP Mental Health Task Force)
  - Parent and School Packets
  - Behavioral Health Screening tools
    - Broad based screens to check for co morbid conditions followed by more specific screening tools where indicated.
- Identify resources in your community
  - Prepare handouts ready to give out.
- ACCESS Mental Health CT

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Other resources.

- AACAP Facts for Family
- AACAP Resource Centers
- AAP Mental Health Toolkit
- www.healthychildren.org (AAP website for families)
- www.schoolpsychiatry.org
- www.parentsmedguide.org
- **ACCESS MENTAL HEALTH CT 866-631-9835**

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Resources:

- **NORTHWELL HEALTH MEDICATION GUIDE**
  - http://www.adhdmedicationguide.com
- **New Formulations of Stimulants: An Update for Clinicians**
  R.Steingard et Al. J of Child and Adolescent Psychopharmacology V29,Number 5, 2019 pp324-339
- **ADHD Clinical Practice Guideline: Implementing the Key Action Statements** —An Algorithm and Explanation for Process of Care for the Evaluation, Diagnosis, Treatment and Monitoring of ADHD in Children and Adolescents
  - https://pediatrics.aappublications.org/content/144/4/e20192528
- **Dr Millers ADHD Medication Table**
  - Wheeler ACCESS MH 855-631-9835
  - JCordova@wheelerclinic.org,

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