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ADHD 300: Beyond the basics

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Disclosures

I have no financial or professional disclosures

There will be discussion of non-FDA approved drugs

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Learning Objectives

- At the end of the session, the learner will be able to:
  1. Integrate knowledge of the diagnosis and management of ADHD in children with comorbid disorders into their primary care patient management plans.
  2. Improve their management of youth with ADHD who do not have sufficient relief from first line medication.
  3. Understand the diagnostic criteria for anxiety, with and without tics, explosive anger disorder, and autism.
  4. Incorporate medication-based approaches to decreasing patient's core symptoms in primary care management plans.

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ADHD Basics

Presentations:
Hyperactive/impulsive
Inattentive
Combined

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Diagnostic Requirements

- Must cause significant impairment in more than one domain
  - This must be established!
- Treatment is symptomatic and does not change pathology
  - Much like other chronic issues (Wolraich, Chan, et al., 2019)
- Symptoms naturally occur in children and youth
  - Must be developmentally inappropriate!
- Is managed very differently before age 6 and after
- Must present by age 12

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Diagnostic Requirements

Must rule out other conditions which share symptoms

- Prenatal/perinatal exposures/injuries
- Family history
- Learning disorders
- Intellectual disorders
- Depression
- Anxiety
- Environmental factors
- Trauma
- Other mental illness

Wolraich, Chan, et al., 2019; Wolraich, Hagan, et al., 2019)

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ADHD Risk Factors

Family history	Trauma	Lead exposure	Premature birth/low birth weight
Prenatal and intrapartum complications	Maternal substance use- esp alcohol and tobacco	Maternal pregnancy illness	Maternal depression and/or psychosocial stress
Parenting stress	Race- African American children < white children	Socioeconomics- Medicaid recipients < diagnosis and appropriate treatment	Prefrontal cortex and subcortical brain changes

(Cummings et al., 2017)

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Case 1

- Jacob is an active 10 year-old recently diagnosed with ADHD. He was started on methylphenidate 18mg OROS daily one month ago. He has mild anorexia during the day, no difficulty with insomnia. Mom reports his impulsivity is worse and he is now getting into trouble at school for "meltdowns" where he has yelled, fought, and damaged classroom property. She states he even started coming into her room at night because he is worried there is a "bad man" in the house. When questioned, mom says she gives him his medication every day before 8 am. She stopped the medicine 2 days ago and she has already noticed his anger decreased.

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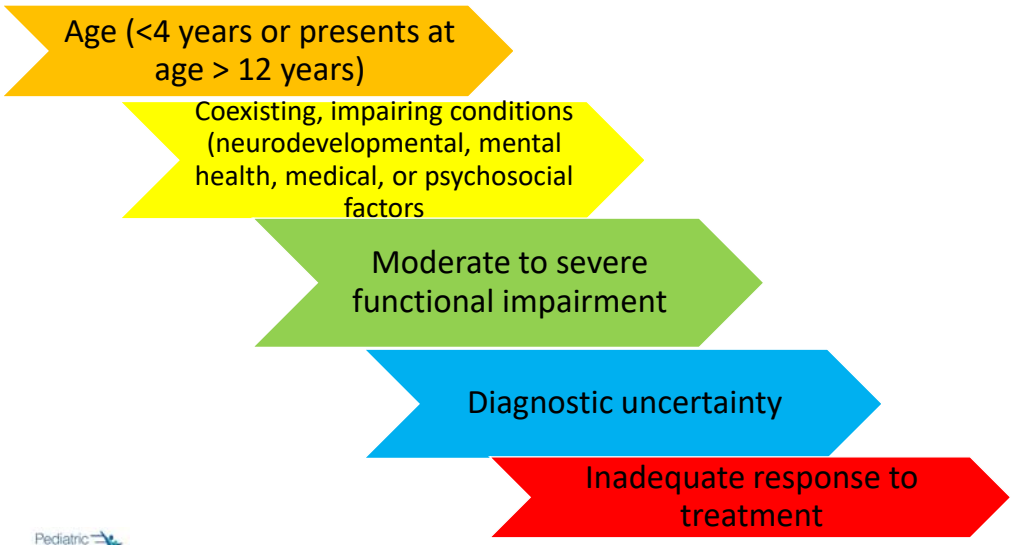
Complex ADHD

- NEW guidelines from SDBP
- Barbaresi WJ, Campbell L, et al. Society for Developmental and Behavioral Pediatrics Clinical Practice Guideline for the Assessment and Treatment of Children and Adolescents with Complex Attention-Deficit/Hyperactivity Disorder. J Dev Behav Pediatr 2020; 41:S1–S23.
- Barbaresi WJ, Campbell L, et al. The Society for Developmental and Behavioral Pediatrics Clinical Practice Guideline for the Assessment and Treatment of Children and Adolescents with Complex Attention-Deficit/Hyperactivity Disorder: Process of Care Algorithms. J Dev Behav Pediatr. 2020b; 41:S1-17.

What is complex ADHD?



(Barbaresi, Campbell, et al., 2020)

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Back to Jacob

- We did a SCARED, PHQ9 and re-did his Vanderbilt scale.
  - Vanderbilt positive for H/I and In symptoms, PHQ9- 8, SCARED positive for anxiety disorder, separation anxiety, and social anxiety disorder
- Confirmed his prenatal history was negative for maternal illness, maternal substance use and confirmed he had no perinatal difficulties.
- Development is normal
- Academic achievement has been good until this academic year when mom noticed his core symptoms.

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Generalized anxiety

- Characterized by marked worry and anxiety that the individual finds hard to control
  - Irritability
  - Fatigue
  - Sleep problems
  - Difficulty sleeping
  - Impaired concentration
  - Somatization
  - Need for reassurance
  - Self-consciousness

- More common in children with behavioral inhibition, those with negative experiences that condition for phobias, CA/N, ASD, SAD, parental psychiatric disorders,& environmental stress

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Signs and symptoms

- Verbalized sense of unease
- May have sympathetic response (panic disorder is most extreme cause)
- Frequently afraid that harm will occur to self or parents/loved ones
- *Developmentally inappropriate* fear

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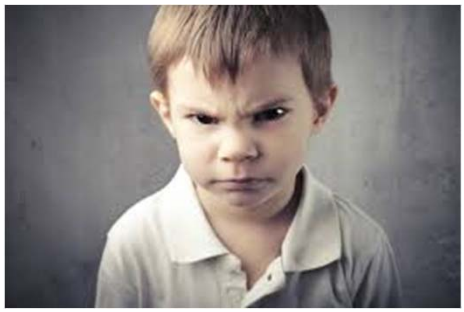
Signs and symptoms

- Commonly present with somatic complaints- esp H/A and SA
- Many end up with OCD behaviors
- Crying, irritability and anger may be misunderstood as oppositionality or defiance



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Generalized anxiety

- DSM 5: inappropriate or intrusive worry that results in significant impairment/distress. Worry is assoc w/feelings of restlessness, fatigability, impaired concentration, irritability, sleep disturbance and/or muscle tension is difficult to control
  - Adults need 3 to meet criteria, kids need 1
  - Sx at least 6 mos, occurring on most days
- Kids often worry about school, athletic performance, being on time, and fear of bad things happening

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Management

- Don't worry about normal fears
- Don't use fears for discipline or behavioral control
- Research supports behavioral modification, CBT and mindfulness-based therapy
- Individual/family therapy
- Desensitization (controversial in kids)
- Classroom modification- modified time for assignments, alternate testing sites. Use an IEP

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Med Management

- A meta-analysis of 9 RCTs (sertraline, fluoxetine, fluvoxamine, venlafaxine, paroxetine, duloxetine, atomoxetine) found both SSRI and SNRI improved symptoms at 2 weeks, but at week 2 there were class differences that showed that SSRIs work better and were significantly different for the next 10 weeks.
  - ½ of treatment response for both groups happens by week 4
  - SSRI treatment response is no differ over time for high vs. low SSRI doses but higher doses resulted in improved symptoms at 2 weeks

Strawn, Mills, Sauley & Welge. (2018). The impact of antidepressant dose and class on treatment response in pediatric anxiety disorders: A meta-analysis. *JAACAP 57*(4): 235-242.

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Management

FDA Approved			
Name	Age	Indication	Dose
Duloxetine	7+	GAD	30-60 mg daily Start 30- may ↑ to 60 after week 2
Escitalopram	12+	OCD	10 mg daily Start 5 ↑ to 10 after a week
Fluoxetine	8+	OCD	20- 60mg daily Start 10- may ↑ by 10 q14d
Sertraline	6+	OCD	6-12yo: 25-200mg daily 13-17yo: 50-200mg daily Start lowest dose and ↑ by 25-50mg/week

https://www.cms.gov/Medicare-Medicaid-Coordination/Fraud-Prevention/Medicaid-Integrity-Education/Pharmacy-Education-Materials/Downloads/ad-pediatric-factsheet11-14.pdf

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Management

- Other medications
  - Busipirone- not FDA approved and poor data in children and teens
  - Buproprione- not FDA approved and poor data in children and teens
  - Venlafaxine ER- not FDA approved, RCTs show effectiveness in GAD, social anxiety
  - Clomipramine- not FDA approved, RCT data shows effectiveness in OCD
  - Atomoxetine- not FDA approved for anxiety but RCTs show effectiveness in treating co-occurring ADHD and anxiety.

Wehry et al. (2015). Assessment and treatment of anxiety disorders in children and adolescents. *Curr Psychiatry Rep* 17: 52

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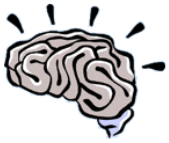
Serotonin Syndrome

- Can be fatal
- HTN, diaphoresis, agitation, dizziness & weakness
- Can happen if SSRI and St Johns Wort
- Stops when D/C drugs

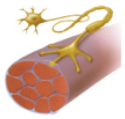
Serotonin syndrome

Rapid onset
Combination of 2+ serotonin agonists



Mental status changes
Agitation
Pressured speech

Autonomic instability
Tachycardia
Diarrhea
Shivering
Diaphoresis
Mydriasis



Neuromuscular abnormalities
Clonus
Hyperreflexia (lower > upper)
Tremor
Seizure

Rx
Benzodiazepines
Hydration/Cooling
Cyproheptadine

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Discontinuation Syndrome

- Caused by SSRI and SNRI
- Duloxetine and longer half-life SSRI (fluoxetine)
- Happens when medications stopped without tapering
  - Often described as “the flu”
  - We have serotonin receptors in the GI tract
- Symptoms- dizziness, N/V, fatigue, irritability, H/A, insomnia, diarrhea, chills, paresthesias, vivid dreams, and rarely psychosis, suicidality and a feeling of being removed from oneself

Image- https://www.verywellmind.com/ssri-discontinuation-syndrome-378682

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Complex ADHD

- Nonpharmacologic interventions must include psychoeducation about all conditions
- Use of evidence-based behavioral and educational treatments
  - Behavioral-parent training
  - Behavioral classroom management
  - Behavioral peer interventions
  - Organizational skills training
- Don't forget CBT and other psychological approaches to anxiety
  - COPE training!
- What about sleep hygiene?

(Barbaresi, Campbell, et al., 2020)

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Case 2

- Jordan is a 13 year-old with a history of facial tics and verbal tics which result in significant anxiety. He was also diagnosed with ADHD as an elementary school student, but his family decided to use non-pharmacologic interventions at that time. Since being in middle school, his struggles with academics and staying on track have worsened and his mom now come to your office for "ADHD medication". On exam, you notice simple facial tics and an occasional vocal tic.

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Tics

Tourette Syndrome is a DSM 5 diagnosable condition

- Must begin by age 18
- Must be present for at least 1 year
- Must have at least two motor tics and one vocal tic throughout the course of the disease.
  - Don't need to present concurrently, but should have been present at some point throughout the illness course.

Commonly begin between 4 and 8 years old

Patients often report they can initially tell when a tic is coming on and express relief/comfort when they do them.

- Go from conscious to semi-conscious movement

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Tics and ADHD

- Commonly comorbid
- Fears of stimulants precipitating tics
- Cochrane Review entitled "Pharmacologic treatment for attention deficit hyperactivity disorder (ADHD) in children with comorbid tic disorders (2018)
  - Treatment with MPH, clonidine, MPH + clonidine, guanfacine and desipramine improve tic symptoms
  - Of stimulants, only high dose dextroamphetamine appeared to worsen tics (1 study)
  - Alpha agonists do not worsen tics

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Tic Management

- Psychotherapy called Comprehensive Behavioral Intervention for Tics (CBIT)has best evidence
  - Teaches them to recognize when the tic is coming on to make movements conscious again.
  - Identifying situations which trigger tics.
  - May involve relaxation techniques.
  - Identifies a replacement activity (e.g. deep breathing, grounding) to do instead of the tic.
- CPG from American Academy of Neurology (Pringsheim et al. 2019; *92*: 896-906)
  - If have tics w/functionally impairing ADHD ➡ ADHD treatment
  - Use CBIT
  - Alpha-adrenergics like clonidine and guanfacine may help
  - Antipsychotics should only be used when benefits outweigh risks
  - Can try Botulism toxin injections for adolescents with simple motor tics
  - Topiramate is a good alternative

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Tics and ADHD

- Stimulants are preferred
- According to Barbaresi et al., 2020 the following must be done:
  - Rule out non-tic behaviors like fidgeting, compulsions and stereotypies
  - Children with chronic or severe tics may require lower stimulant doses with an alpha-andrenergic agonist.
  - Don't forget about the close connection between tics and anxiety
  - Treat the most bothersome condition first

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Case 3

- Kaela is an 8yo female with a history of being placed on stimulants last year for treatment of ADHD. Her symptoms include hyperactivity, impulsivity and inattention. She was put on lisdexamphetamine 10mg chewable with minimal response. Mom says it helps her attention a bit, but she still angers easily, is behind in her reading (1 year) and math (2 years). Mom says she is a "bright child" who learned to read early. Developmental history is positive for “being slow” to talk and she required speech and OT during preschool years.
- Has been yelling, hitting, and punching desks in the classroom.
- Mom is very worried that she isn't making friends

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Autism

- DSM 5: one single diagnosis
  - Asperger Syndrome and PDD NOS are no longer listed
  - Core deficits in social commmunication/interaction and restrictive/repetitive behavior patterns
    - Difficulty undertsanding others' intent, unusual social communication, abnormal eye contact, hypo or hyper reactivity to stimuli, rigidity, difficulty processing visual and auditory communication.
    - Perseverative behaviors (may be compulsions), stereotypies (echolalia, hand flapping) often when struggling to understand others
  - If no intellectual disorder, may not be diagnosed until social difficulties are evident in school setting.
- Get care for developmental delay as soon as possible and not waiting for official diagnostic evaluation.
  - Older children can be referred to school for language and cognitive eval
  - Refer to get formal diagnostic evaluation

(Hyman SL, et al., 2020)

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Common Comorbidities

- Sleep disorders*
- Feeding problems- esp. food refulsal
- GI disorders- esp. constipation, diarrhea, reflux
- Obesity
- Anxiety*
- Wandering
- Seizures
- Aggression
- ***Attention Deficit Hyperactivity Disorder***

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Autism and ADHD

- High comorbidity (about 50%)
- Signs of inattention might be due to language issues
- Flight may happen if overwhelmed (looks like impulsivity and oppositionality)
- Must consider anxiety as a contributing factor
- The same medicines used for ADHD symptoms in those without ASD are appropriate for use in kids with ASD
  - Consider atomoxetine if comorbid anxiety is a worry

(Hyman SL, et al., 2020)

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A Word About Disruptive Behavior Disorders

- Involve significant behavioral outbursts that may include aggression, self-injury, or inappropriate tantrums
  - Aggression towards others may be include bullying, verbal threats, phsyical attacks
  - Self-injury often head banging, slapping face, kicking or hitting hard objects
- Uncooperative and/or hostile
- Often in response to authority figure, stress or sense of being overwhelmed
  - Doesn't follow rules
- Willful destruction of property is common
- Behaviors may start to flee a stressful situation and then become unconscious during subsequent episodes
- 8- 68% of kids with ASD also have DBD (Hill et al., 2014)

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ADHD and DBD

- Psychosocial approaches that work with ADHD also work with DBD
  - Often need help in multiple settings (home, school, etc.)
- Make sure there are no other issues that contribute to the behaviors (SUD, expressive language problem, hearing deficit, etc.)
- Medications should be considered after therapeutic support and education fail
  - Stimulants are fist line (Barbaresi et al., 2020)
  - Close monitoring for side effects- teens need to be monitored for drug diversion/misuse
- Focus is on safety!

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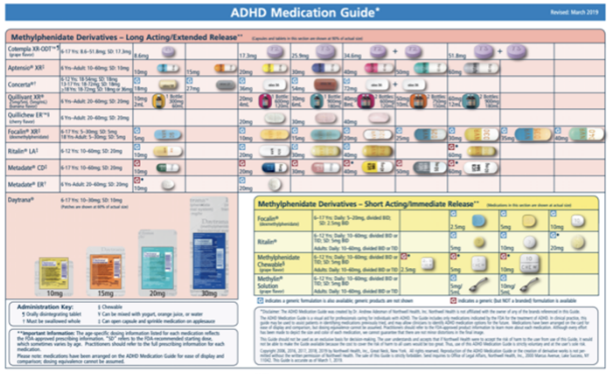
Let's talk ADHD Medications

Medications- www.adhdmedicationguide.com

- FDA Approved



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Medication Therapies

- Stimulants- best evidence and response
- NIMH Multi-Modal Treatment of ADHD study- 80% response, general response in trials 70-90%
- Specifically methylphenidate (ex Concerta, Ritalin, Quillivant) and amphetamine/dextroamphetamine (ex Adderall)
  - Significant side effects include anorexia and insomnia
- Can increase/cause tics (15-30% experience- often transient)
- Alpha 2 adrenergic agonists and non-stimulant (atomoxetine)

NIMH Multimodal website https://www.nimh.nih.gov/funding/clinical-research/practical/mta/multimodal-treatment-of-attention-deficit-hyperactivity-disorder-mta-study.shtml

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ADHD Medications

- MPH promotes dopamine release and blocks dopamine reuptake
- AMP block dopamine reuptake and may elevate selective release of synthesized dopamine
- Both also affect norepinephrine
- “Not sufficient evidence for pharmacogentic testing” per AAP guidelines

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Stimulant Side Effects

- Expected include mild anorexia, mild insomnia (<1hr/night)
- Common include H/A and GI upset
- Decreased growth (1-2 cm from predicted height- mostly first 3 years- catch-up growth happens)
- Dose adjustment or discontinuation needed for agitation, significant H/A or GI distress, psychosis, hallucinations, increased irritability, marked somnolence, worsening anxiety/depression

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Monitoring

- Baseline BP, pulse, height and weight to rule out contraindications and for growth monitoring
- Annual VS assessment
- Assess weight and objective measurement of loss of appetite at each visit.
- Screen for insomnia, headaches, social withdrawal, and tics
  - Look for behavioral problems on medications (anger, irritability, "meltdowns")

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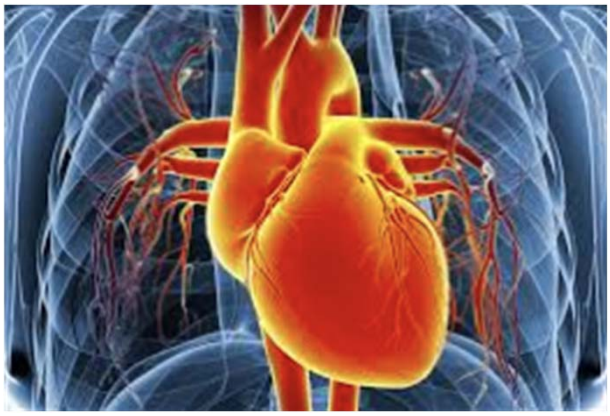
Concern with Mixed Amphetamine Salts



- Some concern about causing cardiovascular instability- Adderall XR controversy with SUD
- Led to black box warning
- New guidelines "Although concerns have been raised about sudden cardiac death among children and adolescents using stimulant medications, it is an extremely rare occurrence" and did not result in actual deaths. (Wolraich, et al, 2019, p.14)

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Cardiac Pre-Evaluation

Screen all children for:

Cardiac symptoms	Family history of sudden death, CV sx, Wolff-Parkinson-White, hypertrophic cardiomyopathy, and long QT syndrome.

Symptoms or concerning history merit referral to pediatric cardiology before using medications.

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Stimulants

If you don't get response with one drug (e.g. Adderall) try another (i.e. Ritalin)

Generally sleep and appetite problems are greatest with amphetamine and dextroamphetamine

Remember 40% respond to one drug, 40% respond to both

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Atomoxetine (Strattera)

- Contraindications.
  - Drug allergy to components.
  - Narrow-angle glaucoma.
  - Uses MAOI.
  - Use with caution for people with hypertension or cardiovascular disease.
- Takes 2-8 weeks for full response- so doesn't work right away
- Titrate up dose to minimize SE
- Common S/E- somnolence and GI distress
- Black box warning with suicidal ideation
- Rare- hepatitis

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Alpha-2 Adrenergic Agonists

- Guanfacine and clonidine
- May take 1 to 2 weeks to see effect
- Also effective at helping with concentration, first line if tics
- Indicated for aggression, anger, significant insomnia
- ***Need baseline ECG***
- Common SE- drowsiness, headache, constipation, dizziness, dry mouth, abdominal pain
- Contraindications- CV disease, hepatic or renal impairment

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Alpha Adrenergics

- Only age 6 years and older!
- Use care when discontinuing, don't stop suddenly, can result in rebound hypertension

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Other issues to consider

Drug diversion

Drug "holidays"

Non-response doesn’t mean med didn’t work

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References

- Barbaresi WJ, Campbell L, et al. Society for Developmental and Behavioral Pediatrics Clinical Practice Guideline for the Assessment and Treatment of Children and Adolescents with Complex Attention-Deficit/Hyperactivity Disorder. J Dev Behav Pediatr 2020; 41:S1–S23.
- Barbaresi WJ, Campbell L, et al. The Society for Developmental and Behavioral Pediatrics Clinical Practice Guideline for the Assessment and Treatment of Children and Adolescents with Complex Attention-Deficit/Hyperactivity Disorder: Process of Care Algorithms. J Dev Behav Pediatr. 2020b; 41:S1-17.
- Hill AP, Zuckerman KE, Hagen AD, et al. Aggressive behavior problems in children with autism spectrum disorders: prevalence and correlates in a large clinical sample. Res Autism Spectr Disord. 2014;8(9):1121–1133
- Hyman SL, Levy SE, Myers SM, et al. Executive Summary: Identfication, Evaluation and Management of Children With Austism Sepctrum Disorder. Pediatrics, 2020; 145: 5-64.
- Wolraich ML, Chan E, Froehlich T, et al. ADHD Diagnosis and Treatment Guidelines: A Historical Perspective. Pediatrics. 2019;144(4): e20191682
- Wolraich ML, Hagan JF, Allan C, et al. AAP SUBCOMMITTEE ON CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVE DISORDER. Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents. Pediatrics. 2019;144(4):e20192528

Pediatric Nurse Practitioners

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