Pediatric Psychopharmacology in Primary Care

Part 1: ADHD, Behavior, & Sleep

A

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Disclosure

I have no relevant financial relationships with the manufacturer(s) of any commercial product(s) and/or provider(s) of commercial services discussed in this CME activity.

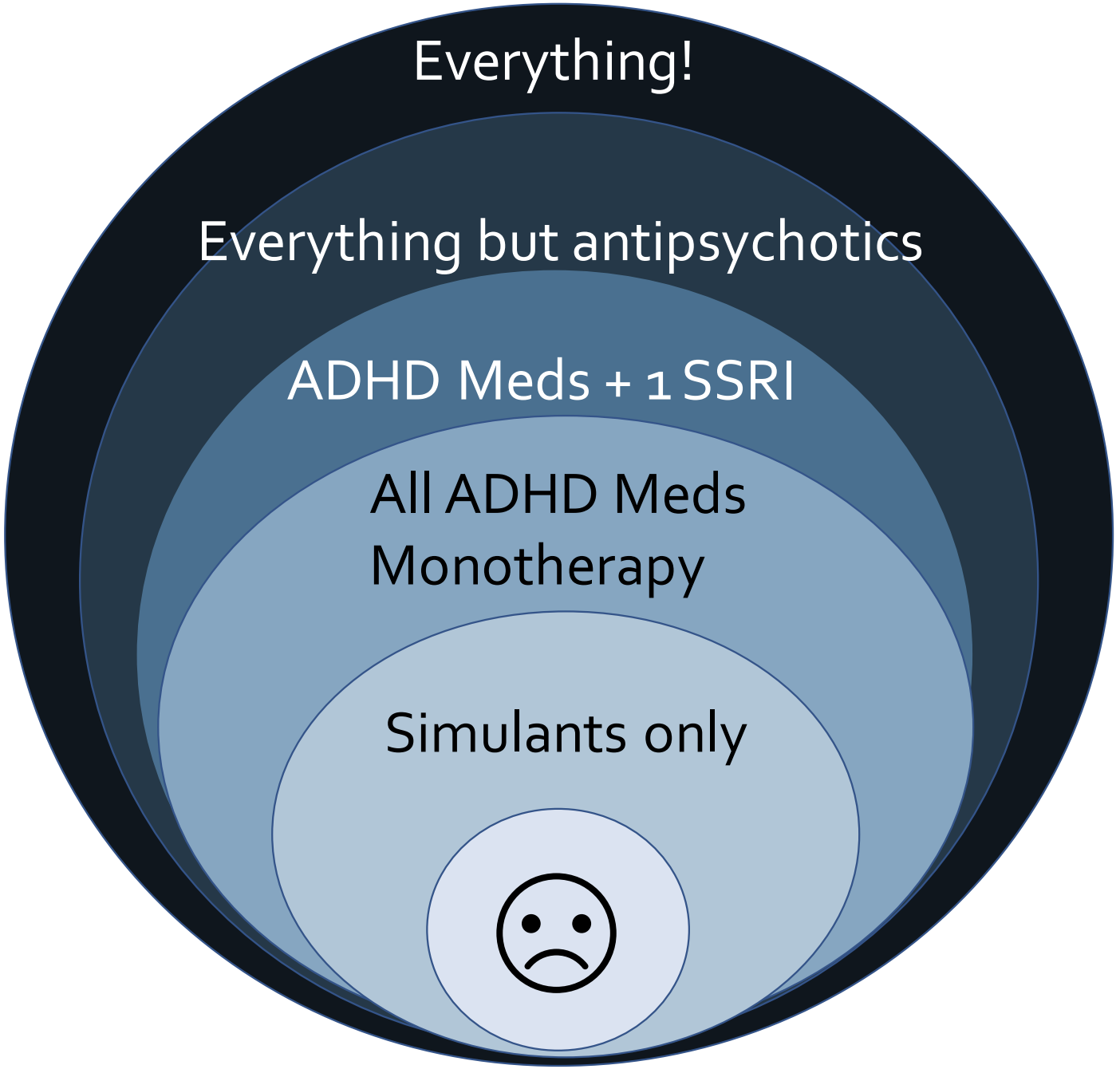
I **do** intend to discuss unapproved/investigative use of commercial products in my presentation.

Learning Objectives

Learners will

1. Select safe and appropriate medication to treat pediatric ADHD
2. Integrate behavioral and medical intervention when managing pediatric sleep disruptions

What is your current pediatric psychopharm practice?



CASE 1: Cam
8-year-old 2nd grader

Kindergarten

- Inattentive, hyperactive: pulled from circle time to run in the gym

1st grade accommodations: pedal bike in class

2nd grade: some calls about impulsivity causing peer situations, academics OK

What would you do?

1. Request IEP testing
2. Complete parent and teacher attention scales
3. Complete broad-based screener
4. Start methylphenidate
5. Refer

What happened

1. Teacher said there is no need for IEP testing
2. Parent: 6/9 inattention, 8/9 hyper-impulsive
   No anxiety, depression, oppositionality
3. Teacher 2/9 inattention, 5/9 hyper-impulsive
   No anxiety, depression, oppositionality
4. Pediatric Symptom Checklist: score = 16
   28 or higher: indicates need for further assessment
   Only items related to activity level are highly rated
5. No referrals available anytime soon

Now what?

Risk vs. Benefit

Parents opt to wait

CASE 1: 9-year-old Cam

3rd grade: not going well

School counselor & lunch bunch group

IEP testing

- Intact cognitive and academic
- Teacher and parent forms ++ADHD
- Vulnerability for anxiety disorder

Behavior consistent with ADHD
Executive Function deficits

What would you do?

1. Start methylphenidate
2. Start mixed amphetamine salts
3. Start nonstimulant ADHD medication
4. Refer

What I did

Dex-methylphenidate 5 mg XR PO QAM

- No problem, not clear there's a difference

Dex-methylphenidate 10 mg XR PO QAM

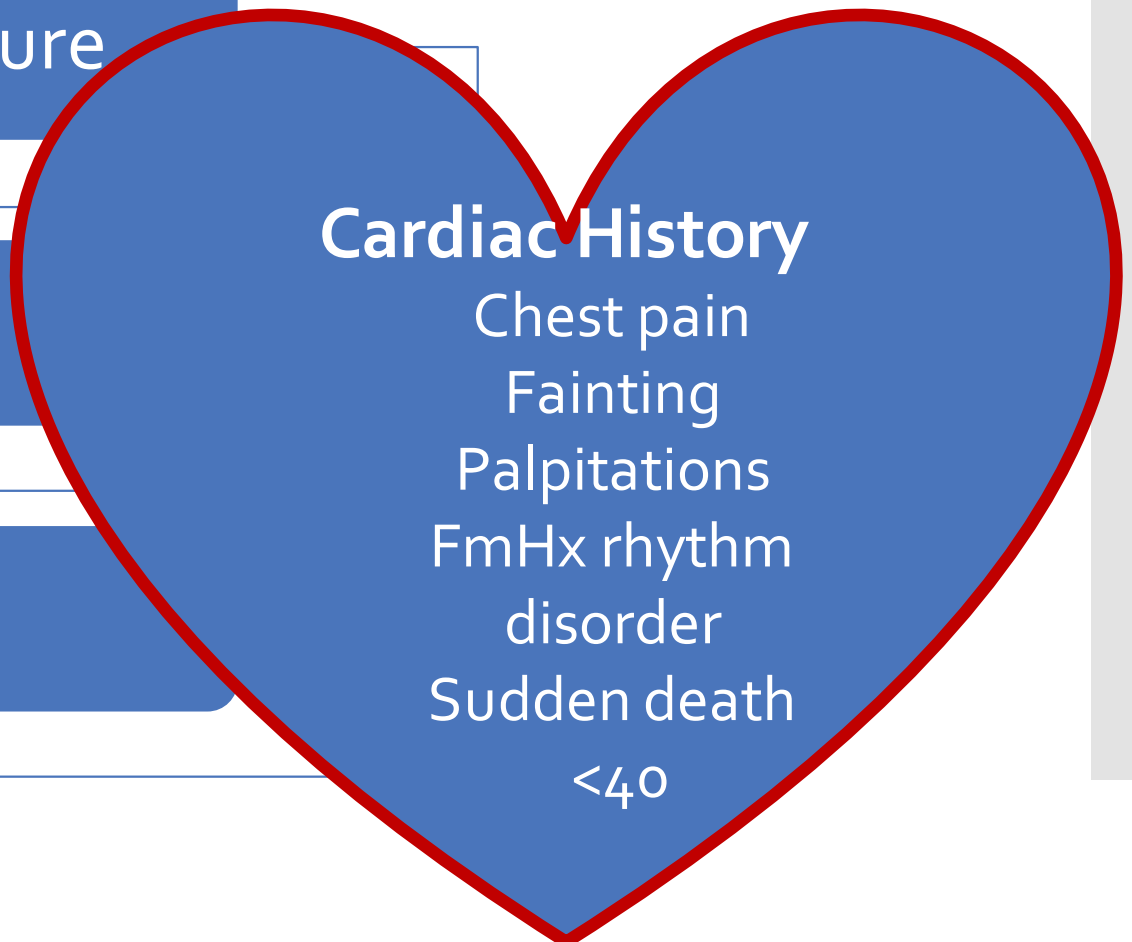
- Less impulsive, less shouting
- Much better

Methylphenidate Preparations

GENERIC	BRANDNAME	DOSES (DURATION)
Methylphenidate	Ritalin	5, 10, 20 mg (3-4 hr)
	Methylphenidate Chew	2.5, 5, 10 mg (3-5 h)
	Methylphenidate Solution	5 mg/5 ml, 10 mg/5 ml (3-5h)
	Metadate ER	10, 20 mg (6-8h)
	Metadate CD	10, 20, 30, 40, 50, 60 mg (8-12h)
	Contempla-XR-ODT	8.6, 17.3, 25.9 mg (up to 12h)
	Aptensio XR	10, 20, 30, 40, 50, 60 mg (up to 12h)
	Quillivant XR	5 mg/ml (up to 12h)
	Quillichew ER	20, 30, 40 mg (6-8 h)
	Jornay	20, 40, 60, 80, 100 mg (12h)
	Adhansia XR	25, 35, 45, 55, 70, 85 mg (16h)
Dex-methylphenidate + serdexmethylphenidate	Azstarys	26.1/5.2, 39.2/7.8, 52.3/10.4 mg (up to 13 h)
Methylphenidate SR	Ritalin SR	20 mg (6-8hr)
Methylphenidate OROS	Concerta	18, 27, 36, 54 mg (10-12h)
Dex-methylphenidate	Focalin	2.5, 5, 10 mg (5-6hr)
	Focalin XR	5,10, 15, 20 (10-12h)
Methylphenidate LA	Ritalin LA	10, 20, 30, 40 mg (8-12h)
	Daytrana	10, 15, 20, 30 mg (9-12h)

ADHD symptom and medication monitoring

- Heart rate
- Blood Pressure
- Weight
- Height



Liang et al. Int. J. Environ. Res. Public Health 2018, 15, 1789.

2 weeks later parent calls:

It takes 2 hours to fall asleep

Children and Adolescents	Rate
Typical Children	1-6%
Psychiatric and neurodevelopmental disorders	50-75%
ADHD	50-60%
Autism	44-83%
Down Syndrome	76%

Sleep Disturbances

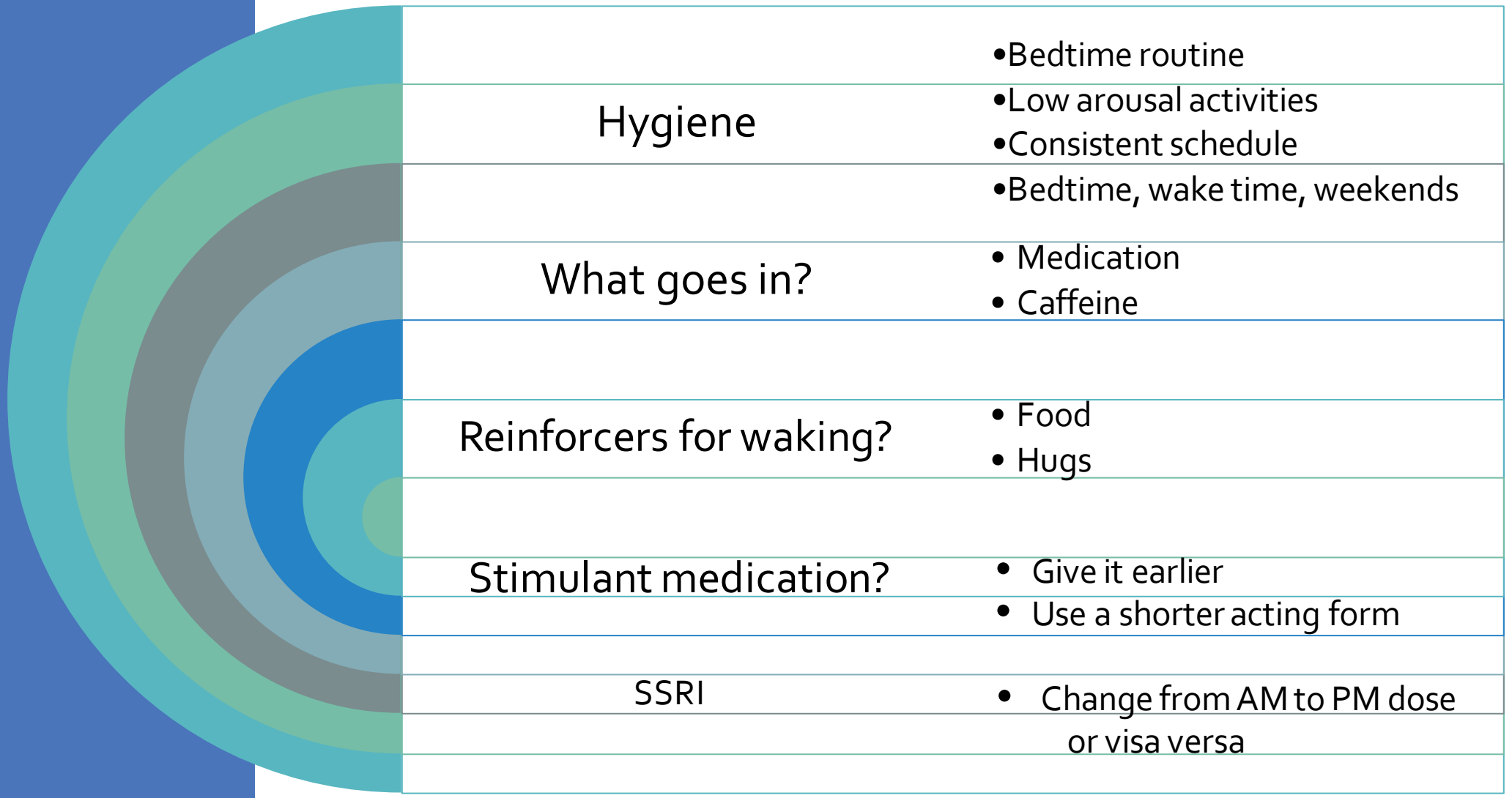
Bassell, et al. Sleep problems in Children with Down Syndrome. *Am J Med Genet A*.2015 August; 167(8):1830-1835.

Cortese S, et al. Sleep and alertness in children with attention-deficit/hyperactivity disorder: a systematic review of the literature. Sleep. 2006 Apr 1;29(4):504-11.

Chhangani, et al. Pharmacology of Sleep Disorders in Children and Adolescents. Pediatr Clin N Am 58 (2011) 273–291.

What would you do?

Sleep


Hygiene
•Bedtime routine
•Low arousal activities
•Consistent schedule
•Bedtime, wake time, weekends
What goes in?
• Medication
• Caffeine
Reinforcers for waking?
• Food
• Hugs
Stimulant medication?
• Give it earlier
• Use a shorter acting form
SSRI
• Change from AM to PM dose or visa versa

Primary Care Sleep Management

Developmental

- Age-appropriate
- Limit testing

Sleep Associations

- Fall asleep in parental bed
- Fall asleep in caregiver arms

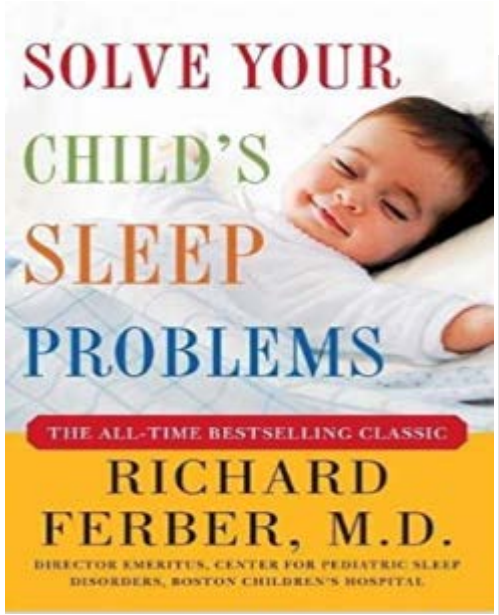
Sleep Schedule

- Weekdays, weekends
- Daylight Savings

Internal State

- Anxiety, Trauma
- Depression

Obstructive Sleep Apnea



Sleep Log

Name: DOB: / / Doctor: Unit #:

Date started: / / Comments:

List Medications:

Day	6p	7	8	9	10	11	Midnight	1	2	3	4	5	6	7	8	9	10	11	Noon	1	2	3	4	5	Comments

Day	6p	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	Comments
Ex.																									

Key: ↑=out of bed ↓=in bed Filled in=asleep

Practice Change!

https://www.freeprintablemedicalforms.com/preview/Sleep_Diary_Adult

Primary Care Behavior Management

Typical Development

- Age-appropriate
- Limit testing

Developmental Difference

- Language delay
- ADHD, Autism
- Intellectual Disability

Environmental

- Bullying, Trauma
- Life Changes, Losses

Internal State

- Anxiety
- Depression
- Sleep deprivation

Parent Management Training

- Addresses patterns of family interaction that sustain disruptive behavior
- Identify ABCs: Antecedent-Behavior-Consequence
  - acknowledge/accept child's emotional experiences
  - model labeling & coping with strong emotions
  - parental consistency
- Focus on increasing
  - positive parent-child interactions
  - emotional communication skills

Systematic Review 2017 (12 studies):

ADHD & Sleep Meds

Clonidine, melatonin and L-theanine: improvements in sleep-onset latency & total sleep duration

Zolpidem, eszopiclone and guanfacine failed to show any improvement when compared with placebo

Clonidine, melatonin, L-theanine, eszopiclone & guanfacine: well tolerated, mild - moderate adverse events

Zolpidem associated w/ neuropsychiatric adverse effects

eszopiclone= Lunesta®
zolpidem=Ambien®
l-theanine= amino acid in green tea

Anand et al. Paediatr Drugs. 2017 Jun;19(3):235-250.

Melatonin

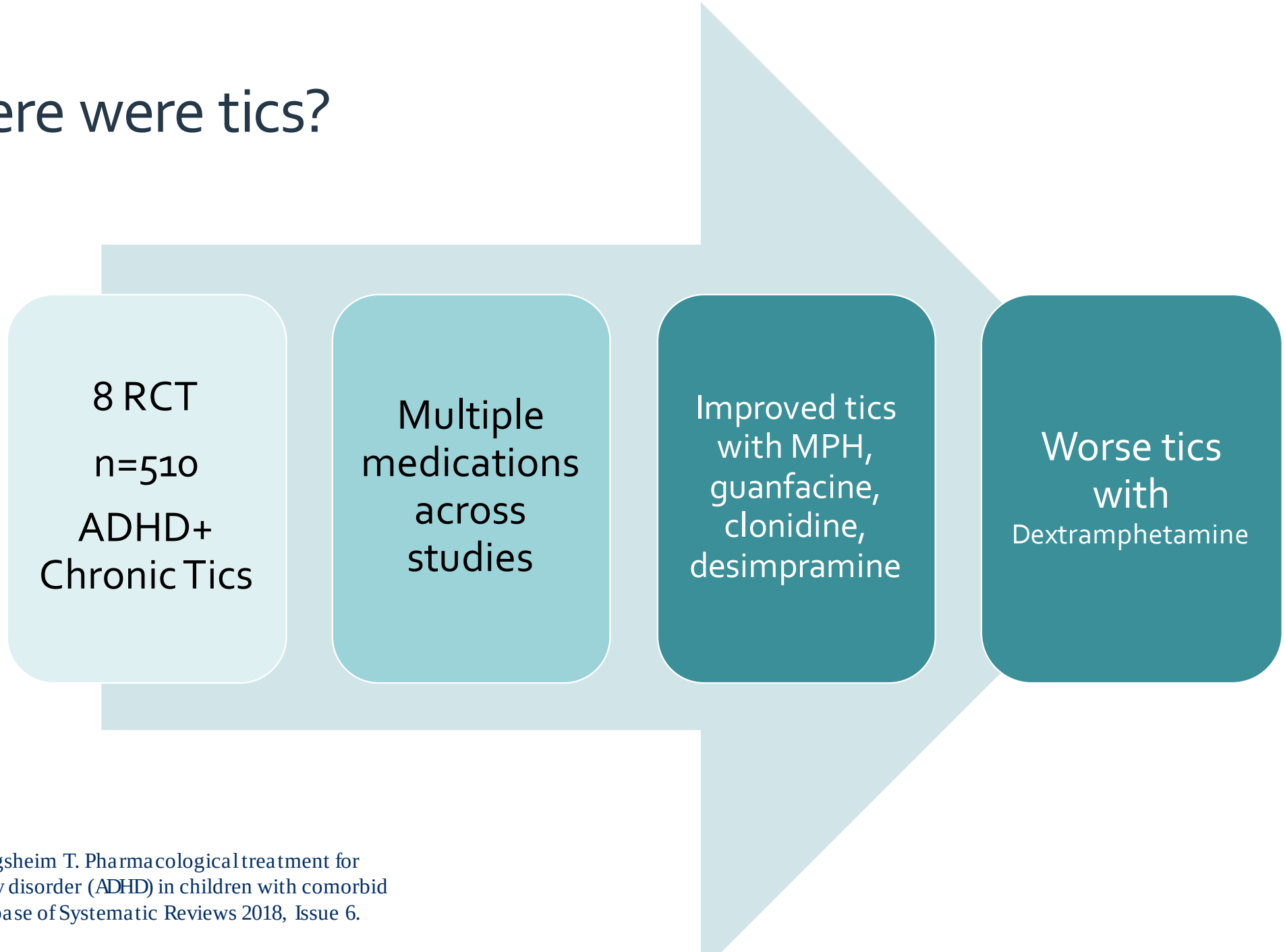
Dosing

- 0.5-12 mg/ dose
- Onset 30-60 minutes

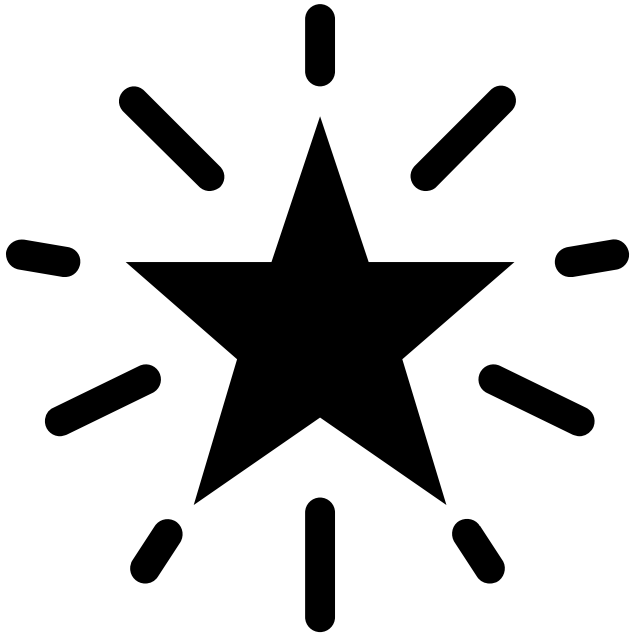
Management

- Generally well-tolerated, occasional daytime somnolence
- Unknown long-term effects
- Lower seizure threshold, rare gynecomastia, hepatitis
- Avoid in those with immune disorders, on immunosupressants, corticosteroids

What if there were tics?



Osland ST, Steeves TDL, Pringsheim T. Pharmacological treatment for attention deficit hyperactivity disorder (ADHD) in children with comorbid tic disorders. Cochrane Database of Systematic Reviews 2018, Issue 6.



Cam

Doing well on 10 mg Focalin XR and 3 mg melatonin

Case 2: Tyler

6 yr old 1st grader with ADHD & Dyslexia
ADHD interferes with learning and friendships
Parents request starting medication.

Mother is prescribed mixed amphetamine salts for ADHD. She did not like methylphenidate.

What would you do?

1. Methylphenidate immediate release
2. Mixed amphetamine salts immediate release
3. Long-acting methylphenidate
4. Long-acting mixed amphetamine salts
5. Guanfacine
6. Extended release guanfacine
7. Other

Case 2 Tyler:
6 yr old 1st grader

ADHD & Dyslexia

6y 8mo: **MAS XR** 10mg: don't recall, didn't work, maybe unhappy

6y 9mo: **OROS MPH** 18mg ER **then** 27mg : weight loss despite calorie supplementation

Generic	Brandname	Doses (durations)
Dextroamphetamine	Dexadrine	5 mg (4-6hrs)
Dextroamphetamine SR	Dexadrine Spansule	5,10,15 mg (6-8 hrs)
Mixed Amphetamine Salts	Adderall	5,10,20,30 (4-6 hrs)
	Adderall XR	5,10,15,20,25,30 mg (8-12h)
	Mydayis	12.5, 25, 37.5, 50 mg (up to 16h)
d- and l-amphetamine sulfates	Adzenys ER	1.25 mg/ml
	Adzenys XR	3.1, 6.3, 9.4, 12.5, 15.7, 18.8 mg (up to 12h)
	Dynavel XR	2.5 mg/ml (up to 13 hr)
	Evekeo	5, 10 mg (4-6h)
d-amphetamine sulfate	Zenzedi	2.5, 5, 7.5, 10,15,20,30 mg (4-6 mg)
	Procentra	5 mg/5 ml (4-6 h)
Lisdexamfetamine dimesylate	Vyvanse Vyvanse Chewable	10,20,30,40,50,60,70 (up to 10h) 10,20,30,40,50,60

Amphetamine Preparations

http://www.adhdmedicationguide.com/pdf/adhd_med_guide_[1217]_022019_1526.pdf.
Krull K. Up To Date, AD/HD in Children and Adolescents: Treatment with Medication. Updated 2/19.

What would you do?

1. Try another stimulant
2. Try a nonstimulant
3. Repeat attention scales with details of school
    - What services?
    - When are his problems?
4. Broad band screener
    - Anxiety?
    - Depression?
5. Review testing
6. Refer

Case 2 Tyler:
8 yr old 2nd grader

ADHD & Dyslexia

6y 8mo: **MAS XR** 10mg: don't recall, didn't work, maybe unhappy

6y 9mo: **OROS MPH** 18mg ER **then** 27mg : weight loss despite calorie supplementation

6y 11mo: **lis-dexamphetamine** 10mg : didn't give it

7y 1 mo: **Guanfacine** 1mg x 4 months: less creative, sleepy, calmer

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GENERIC	BRANDNAME	DOSING (DURATIONS)
Atomoxetine	Strattera	0.5 mg/kg/day - 1.6 mg/kg/day (24h)
Clonidine	Catapres	.025 mg - 0.1 mg BID-QID (3-7h)
Clonidine XR	Kapvay	0.1 mg - 0.4 mg QD (12-16h)
Clonidine Patch	Catapres-TTS	0.1 mg, 0.2 mg, 0.3 mg (after 2-3d, lasts 7d)
Guanfacine	Tenex	0.25 mg -1 mg BID-TID (3-4 h)
Guanfacine ER	Intuniv	1 mg- 7 mg QD (6-8 h)
Viloxazine	Qelbree	100 mg – 400 mg qd (24h)

Non-stimulant ADHD treatments

Case 2 Tyler:
8 yr old 3rd grader

ADHD 8

6y 8mo: **MAS XR** 1[illegible] **OROS MPH** 18mg ER (1 tab in AM): don't rec[illegible]ork, maybe unhappy

6y 9[illegible] weight loss despite calorie [illegible]

[illegible]amine 10mg: never took it

[illegible]uanfacine 1mg: less creative, sleepy, calmer

7y 6mo: **MPH** 5mg BID: more focused, fresh at wear-off, trouble falling asleep

8y: **MPH 10mg ER + Clonidine** 0.05mg QHS (not helpful)

REFER

Atomoxetine

18 mg po qhs x 4 nights then

18 mg po qam x 3 days then

36 mg po qam (weight = ~30kg)

Not calling out, more focused

Great gains in math, some face clenching tics

Increased to 40 mg

Atomoxetine: SNRI

Elimated through p450 2D6 enzymatic pathway

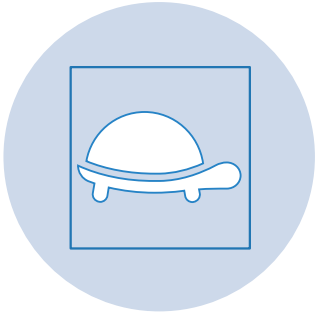
- Metabolism varies

Interaction

- Paroxetine (Paxil)
- Fluoxetine (Prozac)
- Dextromethorphan

Side effects:

- Abdominal pain, nausea, vomiting, fatigue, mood swings, dry mouth



Start low, go slow

Monitor side effects, target symptoms

Document every medication change and why it was made

Integrate behavior management for the best sucess

Take Home Points

Thank you!

ADHD symptom and medication monitoring

- ADHD-RS-IV
- SNAP IV
- Vanderbilt
- Conners'

Caring for Children with ADHD: A Resource Toolkit for Clinicians

https://shop.aap.org/Caring-for-Children-with-ADHD-A-Resource-Toolkit-for-Clinicians/

https://depts.washington.edu/dbpeds/Screening%20Tools/ScreeningTools.html

Atomoxetine has to be swallowed whole

Capsules

- Aptensio XR
- Dexadrine Spansule
- Focalin XR
- Lisdexamphetamine
- Metadate CD
- Mixed Amphetamine Salts
- Ritalin LA

Chewable

- Methyphenidate Chew
- Quillivant Chew
- Vyvanse Chew

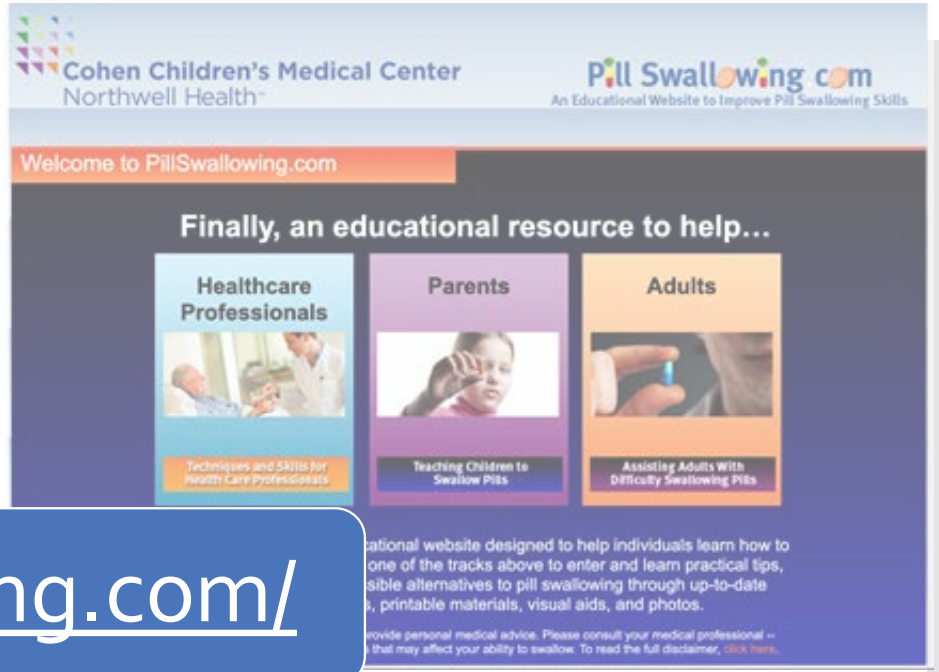
Patch

- Daytrana, Conidine Patch

Liquid

- Adzenyz
- Dynavel
- Methyphenidate solution
- Procentra
- Quillivant XR

Pill Swallowing



https://pillswallowing.com/

Pill glide swallowing spray

Oralflo™ cup

Atomoxetine and Suicidality

- Meta-analysis of 12 RCT
- 6-18 wks, > 2200 patients
- 4/1000 reported suicidal thinking, 0 in the placebo groups
- One suicide attempt, no reported completions

http://www.fda.gov/cder/drug/infopage/atomoxetine/default.htm

Atomoxetine: Warn and Precaution

- Of the two million pa prescribed this medic
  - Two children suffer from reversible but severe liver injury
  - Would not start in patient with risk fo disease

----------WARNINGS AND PRECAUTIONS----------

- Suicidal Ideation – Monitor for suicidality, clinical worsening, and unusual changes in behavior. (5.1)
- Severe Liver Injury – Should be discontinued and not restarted in patients with jaundice or laboratory evidence of liver injury. (5.2)
- Serious Cardiovascular Events – Sudden death, stroke and myocardial infarction have been reported in association with atomoxetine treatment. Patients should have a careful history and physical exam to assess for presence of cardiovascular disease. STRATTERA generally should not be used in children or adolescents with known serious structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, or other serious cardiac problems that may place them at increased vulnerability to its noradrenergic effects. Consideration should be given

Very useful references as resources

1. Southammakosane C, Schmitz K. Pediatric Psychopharmacology for Treatment of ADHD, Depression, and Anxiety. Pediatrics Aug 2015, 136 (2) 351-359.
2. Strawn, Dobson, Giles. Primary Pediatric Care Psychopharmacology: Focus on medications for ADHD, depression and anxiety. Curr Probl Pediatr Adolesc Health Care. 2017 January ; 47(1): 3–14.
3. Sharma, A. (2018). Update on common psychiatric medications for children.*Pediatric Annals*, *47*(8), 311-316.
4. Fung, et al. Pharmacologic Treatment of Severe Irritability and Problem Behaviors in Autism: A Systematic Review and Meta-analysis. Pediatrics Feb 2016, 137 (Supplement 2) S124-S135.

Additional References

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2. Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes. American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists, and North American Association for the Study of Obesity. Diabetes Care February 2004 vol. 27 no. 2 596-601.
3. Margari et al. Tolerability and safety profile if risperidone in a sample of children and adolescents. International Clin Psychopharm 28 (2013) 177-183.
4. Mohatt et al. Treatment of Separation, Generalized, and Social Anxiety Disorders in Youths. Am J Psychiatry 2014;171:741-748.
5. Ceranoglu TA, Wozniak J, Fried R, Galdo M, Hoskova B, DeLeon Fong M, Biederman J, Joshi G. A Retrospective Chart Review of Buspirone for the Treatment of Anxiety in Psychiatrically Referred Youth with High-Functioning Autism Spectrum Disorder. J Child Adolesc Psychopharmacol. 2019 Feb;29(1):28-33.