Practical Pearls in Managing Pediatric Aggression in Primary Care

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No disclosures

• I will be discussing off label medication use.

Learning Objectives

- Identify core symptoms of Disruptive Mood Dysregulation Disorder, Conduct Disorder, Oppositional Defiant disorder and signs of early onset bipolar disorder
- Categorize treatment options for aggression in pediatric patients
- Evaluate Autism Spectrum Disorder patients with aggressive behaviors
- Treat Impulsive Aggression in ADHD

A patient presents with aggression...

- Most common reason for a psychiatric referral
- 70% of psychiatrically hospitalized 5-12 year olds are referred for explosive outbursts
- Irritability/aggression is a symptom in multiple childhood disorders
 - ADHD
 - Conduct Disorder
 - Bipolar Disorder
 - Autism Spectrum Disorder
 - Anxiety
 - Adjustment Disorder
 - PTSD
 - Schizophrenia
 - Intermittent explosive disorder
 - Borderline personality disorder
 - Antisocial personality disorder

Multifactorial Etiology of aggression

- Media
- Socio-cultural forces
- Interactive family processes
- School and Community influences
- Relationships with parents, caretakers and peers
- Consider limitations in child's cognitive, physical, social and communication skills
- Inborn/genetic anomalies

Types of Aggression

Predatory/ "Cold"/Premeditated	Impulsive, Reactive, Affective			
Conduct Disorder Antisocial Personality Disorder	Change from previous behavior	r or self	Chronic	
	Child: Rule out stressor School: learning problems, bullying Home: family problems, abuse PTSD	Teen: Depression, Mania, Anxiety, Drugs, Psychosis	Irritable Between Outbursts: DMDD	Fine until frustrated: ADHD + ODD, OCD

Treatment/Assessment Approach Guidelines

- T-MAY (Treatment of Maladaptive Aggression in Youth)
 - The Rutgers CERTS Pocket Reference Guide for Primary Care Clinicians and Mental Health Specialists
- Step 1: Thorough Assessment
 - Engage the patient and parents: I can't do it without you- Pills alone won't give your child the skills he needs
 - Medical Evaluation/Work up if needed
 - Contact prior treating physician, review treatment records
 - Medication history
 - Potential etiologies: infections, toxins, substance abuse, seizures
 - Psychosocial history/stressors- losses, exposures to violence, past/recent or ongoing trauma
 - Contact teachers

Assess and Define Target Symptoms and Behaviors

- Understanding the concern- Clinical Interview Approach:
 - **B**: Behavior- In what ways does the child exhibit aggression?
 - O: Onset: When does it happen? What triggers it? Why?
 - L: Location: Where do the symptoms occur- home/school?
 - **D**: Duration: How long does it last?
 - E: Exacerbants: What makes it worse?
 - **R**: Relief: What makes it better?

Aggression Rating Tools

- Assess target symptoms using available scales and rating tools
 - Vanderbilt (Free- online)
 - Emotional Outburst Inventory (EMO-I)
 - Brief screening tool for irritability and severe emotional outbursts in youth
 - Free online: AACAP Emotional Dysregulation Resources for Clinicians
 - Affective Reactivity Index
 - Characterizes and tracks irritability
 - Free online: AACAP Emotional Dysregulation Resources for Clinicians
 - Modified Overt Aggression Scale
 - Severity/Characterizes types of aggression/track over time
 - Free Online: AACAP Emotional Dysregulation Resources for Clinicians
 - Youth Mania Rating Scale
 - Specific Mania symptoms
 - Free- online

Vanderbilt- ADHD, ODD, CD, Anxiety/Depression

14. Is "on the go" or often acts as if "driven by a motor"
--

15. Talks too much

16. Blurts out answers before questions have been completed

17. Has difficulty waiting his or her turn

18. Interrupts or intrudes in on others' conversations and/or activities

19. Argues with adults

20. Loses temper

21. Actively defies or refuses to go along with adults' requests or rules

22. Deliberately annoys people

23. Blames others for his or her mistakes or misbehaviors

24. Is touchy or easily annoyed by others

25. Is angry or resentful

26. Is spiteful and wants to get even

27. Bullies, threatens, or intimidates others

28. Starts physical fights

29. Lies to get out of trouble or to avoid obligations (ie, "cons" others)

30. Is truant from school (skips school) without permission

31. Is physically cruel to people

32. Has stolen things that have value

The information contained in this publication should not be used as a substitute for the

• Questions 19-26: Oppositional Defiance: Positive is 4 out of 8

• Questions 27-40: Conduct Disorder: Positive is 3 out of 14

NICHQ Vanderbilt Assessment Scale—PARENT Informant

Parent's Name: _____ Child's Name: ____

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Today's Date: _____ Date of Birth: _____

Parent's Phone Number:

Symptoms (continued)	Never	Occasionally	Often	Very Often
33. Deliberately destroys others' property	0	1	2	3
34. Has used a weapon that can cause serious harm (bat, knife, brick, gun)	0	1	2	3
35. Is physically cruel to animals	0	1	2	3
36. Has deliberately set fires to cause damage	0	1	2	3
37. Has broken into someone else's home, business, or car	0	1	2	3
38. Has stayed out at night without permission	0	1	2	3
39. Has run away from home overnight	0	1	2	3
40. Has forced someone into sexual activity	0	1	2	3
41. Is fearful, anxious, or worried	0	1	2	3
42. Is afraid to try new things for fear of making mistakes	0	1	2	3
43. Feels worthless or inferior	0	1	2	3
44. Blames self for problems, feels guilty	0	1	2	3
45. Feels lonely, unwanted, or unloved; complains that "no one loves him or he	er" 0	1	2	3
46. Is sad, unhappy, or depressed	0	1	2	3
47. Is self-conscious or easily embarrassed	0	1	2	3

Somewhat

Emotional Outburst Inventory

- Characterizes what the child does
- Helps in the assessment
- Measures outbursts
- What are triggers?
- What does s/he do?
- How long/how often
- How does s/he feel afterwards?

Questions about your child's irritability and anger

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4. HOW OFTEN DOES A SERIOUS TANTRUM	a. Never b. Rarely c. several times a month
OR OUTBURST OCCUR?	d. Weekly e. at least 3 times/week f. Daily
5. HOW LONG DOES A TANTRUM OR OUTBURST LAST?	a. a few minutes b. up to15 minutes c. up to half an hour d. Up to an hour e. Up to half a day
6. IS YOUR CHILD ANGRY OR IRRITABLE	a. Not at all b. Sometimes c. often
BETWEEN OUTBURSTS?	d. very often
7. HOW DOES YOUR CHILD UNDERSTAND	a. Remorseful b. Forgets or denies it
THE OUTBURST?	c. Blames others d. Spiteful
8. WHERE DOES YOUR CHILD HAVE OUTBURSTS?	a. At home/with parents b. at school c. Both home and school d. home, school, public

WHAT HELPS YOUR CHILD CALM DOWN?

Affective Reactivity Index

LEVEL 2—Irritability—Parent/Guardian of Child Age 6–17

*Affective Reactivity Index (ARI)

Child's Name: _____

Sex: 🛛 Male 🖵 Female

Date: _____

What is your relationship with the child receiving care?

<u>Instructions to parent/guardian</u>: On the DSM-5 Level 1 cross-cutting questionnaire that you just completed, you indicated that *during the past 2 weeks* your child receiving care has been bothered by "seeming irritated or easily annoyed" and/or "seeming angry or lost his/her temper" at a mild or greater level of severity. The questions below ask about these feelings in more detail and especially how often your child receiving care has been bothered by a list of symptoms <u>during the past 7 days</u>. Please respond to each item by marking (\checkmark or x) one box per row.

					Clinician Use
In the last SEVEN (7) DAYS and compared to others of the same age, how well does each of the following statements describe the behavior/feelings of your child? Please try to answer all questions.					
		Not True	Somewhat True	Certainly True	Item Score
1.	Is easily annoyed by others.	0	1	2	
2.	Often loses his/her temper.	• 0	• 1	2	
	r				
3.	Stays angry for a long time.	0	1	2	
		I	, , , , , , , , , , , , , , , , , , , ,		
4.	Is angry most of the time.	0	• 1	2	
5.	Gets angry frequently.			D 2	
5.	Gets angly nequently.		U 1	u 2	
6.	Loses temper easily.	0	1	2	
	·		· · · · ·		
7.	Overall irritability causes him/her problems.	0	• 1	2	
Total/Partial Raw Score:					
Prorated Total Raw Score: (if 1 item is left unanswered)					

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- Parent/Child Version (Age 6-17)
- Child Version (Age 11-17)
- How the child feels?
 - Over the last 6 months (assessment)
 - Over the last 2 weeks (follow up)
- Can track change over time

Modified Overt Aggression Scale

- Scale of severity of aggressive behaviors
 - Great for tracking over time
 - Help clinician assess patients' responses to treatment interventions
 - Looking at the last week
 - Scores range from 0-40

INSTRUCTIONS

Rate the patient's aggressive behavior over the past week. Select as many items as are appropriate. Refer to the pocket guide for the full measure.

SCORING

- 1. Add items in each category
- In scoring summary, multiply sum by weight and add weighted sums for total weighted score. Use this score to track changes in level of aggression over time.

Verbal aggression

- 0 No verbal Aggression
- 1 Shouts angrily, curses mildly, or makes personal insults
- 2 Curses viciously, is severely insulting, has temper outbursts
- _____ 3 Impulsively threatens violence toward others or self
- **4** Threatens violence toward others or self repeatedly or deliberately
- SUM VERBAL AGGRESSION SCORE

Aggression against Property

- 0 No aggression against property
- 1 Slams door, rips clothing, urinates on floor
- 2 Throws objects down, kicks furniture, defaces walls
- 3 Breaks objects, smashes windows
- 4 Sets fires, throws objects dangerously
- _____ SUM PROPERTY AGGRESSION SCORE

Autoaggression

- **0** No autoaggression
- Picks or scratches skin, pulls hair out, hits self (without injury)
- 2 Bangs head, hits fists into walls, throws self onto floor
- 3 Inflicts minor cuts, bruises, burns, or welts on self
- 4 Inflicts major injury on self or makes a suicide attempt SUM AUTOAGGRESSION SCORE

Physical Aggression

- 0 No physical aggression
- 1 Makes menacing gestures, swings at people, grabs at clothing
- Strikes, pushes, scratches, pulls hair of others (without injury)
- 3 Attacks others, causing mild injury (bruises, sprain, welts, etc.)
- 4 Attacks others, causing serious injury
- SUM PHYSICAL AGGRESSION SCORE

CATEGORY	SUM SCORE	WEIGHTS	WEIGHTED SUM
Verbal Aggression		x 1	
Aggression against Property		x 2	
Autoaggression		x 3	
Physical Aggression		x 4	
Total Weighted Score			

Youth Mania Scale

- 11-item interviewer rated scale
 - Can include other sources of information.
- The items have five defined grades of severity. Four items are double weighted (irritability, speech, thought content and disruptive/aggressive behavior).
 - Scoring: Less than or equal to 12 = remission
 - 13 19 = minimal symptoms
 - 20 25 = mild mania
 - 26 37 = moderate mania
 - 38 60 = severe mania

Young Mania Rating Scale (YMRS)

Guide for Scoring Items - The purpose of each item is to rate the severity of that abnormality in the patient. When several keys are given for a particular grade of severity, the presence of only one is required to qualify for that rating.

The keys provided are guides. One can ignore the keys if that is necessary to indicate severity, although this should be the exception rather than the rule.

Scoring between the points given (whole or half points) is possible and encouraged after experience with the scale is acquired. This is particularly useful when severity of a particular item in a patient does not follow the progression indicated by the keys.

- 1. Elevated Mood
 - 0 Absent
 - Mildly or possibly increased on questioning
 - Definite subjective elevation: optimistic, self-2 confident; cheerful; appropriate to content
 - Elevated, inappropriate to content; humorous 3
 - Euphoric; inappropriate to content; singing 4
- 2. Increased Motor Activity Energy
 - 0 Absent
 - Subjectively increased 2
 - Animated; gestures increased
 - Excessive energy; hyperactive at times; restless 3 (can be calmed) 4 Motor excitement; continuous hyperactivity
 - (cannot be calmed)
- 3 Sexual Interest
 - Normal: not increased 0
 - Mildly or possibly increased 2
 - Definitive subjective increase on questioning Spontaneous sexual content; elaborates on sexual 3
 - matters; hypersexual by self-report 4
 - Overt sexual acts (towards patients, staff, or interviewer)
- 4. Sleep
 - 0 Reports no decrease in sleep 1 Sleeping less than normal amount by up to one
 - hour
 - 2 Sleeping less than normal by more than one hour
 - Reports decreased need for sleep 3 4 Denies need for sleep
- 5. Irritability
- 0 Absent
 - Subjectively increased 2
- Irritable at times during interview; recent 4 episodes of anger or annoyance on ward
- 6 Frequently irritable during interview; short, curt throughout
- Hostile, uncooperative; interview impossible 8
- 6. Speech (Rate and Amount)
- 0 No increase
- 2
- Feels talkative 4 Increased rate or amount at times, verbose at times
- 6 Push; consistently increased rate and amount; difficult to interrupt
- Pressured; uninterruptible, continuous speech 8

- 7. Language Thought Disorder
 - 0 Absent
 - 1 Circumstantial; mild distractibility; quick thoughts
 - 2 Distractible; loses goal of thought; changes topics frequently; racing thoughts
 - 3 Flight of ideas; tangentiality; difficult to follow; rhyming; echolalia
 - 4 Incoherent; communication impossible
- 8 Content
 - 0 Normal
 - Questionable plans, new interests 2
 - 4 Special project(s); hyperreligious Grandiose or paranoid ideas; ideas of reference
 - 6 8 Delusions: hallucinations
- Disruptive Aggressive Behavior 9
- Absent: cooperative 0
- 2 Sarcastic; loud at times; guarded
- Demanding; threats on ward 4
- 6 Threatens interviewer; shouting; interview difficult
- 8 Assaultive; destructive; interview impossible
- 10. Appearance
 - 0 Appropriate dress and grooming
 - Minimally unkempt
 - 2 Poorly groomed; moderately disheveled; overdressed
 - Disheveled; partly clothed; garish makeup 3
 - 4 Completely unkempt; decorated; bizarre garb
- 11. Insight
 - 0 Present; admits illness; agrees with need for treatment
 - Possibly ill
 - Admits behavior change, but denies illness 2
 - Admits possible change in behavior, but denies 3 illness
 - 4 Denies any behavior changes

Name:	
Rater:	
Date:	
Score:	

Assessment of Aggression

- Step 1: Thorough Assessment
- Step 2: Make the DSM Diagnosis: Don't rush to make a DSM diagnosis, diagnoses may unfold over time while working with the family
 - Attention Deficit Hyperactivity Disorder
 - Oppositional Defiance Disorder
 - Anxiety
 - Depression
 - Obsessive Compulsive Disorder
 - Post Traumatic Stress Disorder
 - Disruptive Mood Dysregulation Disorder
 - Conduct Disorder
 - Bipolar Disorder
 - Autism Spectrum Disorder

Treatment Approaches for Aggression

- Psychoeducation
- Setting realistic expectations
- Parent- Management training
- School Based Social Skills training
- Need for ongoing family, community and school support
- Flexibility in planning, multiple changes likely needed throughout treatment.
- Pharmacotherapy: Last resort
 - Treat comorbidity to maximum effect 1st, then add on an agent just for the aggression.
 - Atypical Antipsychotics (Second Generation Antipsychotics- SGAs)
 - Typical Antipsychotics
 - Stimulants
 - Mood Stabilizers
 - SSRIs

Psychosocial Interventions for Emotional Dysregulation- they all work!!

- Parent-directed therapy
 - Parent management training- any of them work!
- Cognitive Behavioral Therapy
 - DBT
 - Emotional regulation intervention
 - Social skills training
 - Exposure and Response Prevention for irritability

- Social Emotional Child-Directed therapy
 - Identifying and regulating emotions with parents trained to a be an emotion coach for the child
- Multimodal
 - Integrative Group Based therapy
 - Multi Family Psychoeducation Groups

Disruptive behaviors in preschoolers

- Normal toddler behaviors/Consider Developmental Context:
 - Biting
 - Temper tantrums
 - Daily angry outbursts are typical from age 1-3
 - Usually decreases with age
- Oppositional Behaviors are the most common presenting symptom in preschoolers
- Primary Care providers have the most contact with this age group
- Parents trust their PCP

Treatment for Preschoolers

- Medication is NEVER First Line!
- Consider evidence-based options:
 - Incredible Years program for teachers, parents and children
 - Positive Parenting Program (aka Triple P)
 - \$90 for a parent online course
 - MATCH: Evidence based treatment of childhood anxiety, depression, trauma, and conduct problems.
 - Combines aspects of CBT and parent training
 - ABA: Applied Behavioral Analysis (Autism)
 - PCIT (Parent Child Interaction Therapy- Emotional Development

Parenting Resources/Books

- Raising your Spirited Child- Mary Sheedy Kurcinka
- How to Talk so your Kids will Listen and Listen so your Kids will Talk-Adele Faber
- 1,2,3 Magic- Thomas Phelan
- Your Defiant Child--8 Steps to Better Behavior-Russell Barkley
- The Explosive Child- Ross Greene
- The Incredible Years- Parent Book: www.incredibleyears.com
- Touchpoints: Your Child's Emotional and Behavioral Development-T. Berry Brazelton: <u>http://www.brazeltontouchpoints.org/</u>
- <u>https://centerforparentingeducation.org</u>

Psychoeducation in Primary Care- Parental Guidance

- Engage the caregiver- validate their concerns. Give them "expert status" Parent have such great influence on their child's lives
- Goal: Parent gains skills to increase child's positive behaviors, therefore decrease negative behaviors.
- Childproof home: remove harmful objects from each room
- Improve attention given to the child
 - More regular one on one time, child led
- Praise!! Often and quickly when child shows any positive response, follow through
- Active ignoring of negative behaviors
 - No eye contact
 - Don't show anger in your voice or face
 - Try not to argue or scold
- Instructions: Follow through, eye contact, calm, have them repeat back
- **Rewards:** list desired rewards, desired behaviors, praise is a reward too!
- Time outs

Disruptive Mood Dysregulation Disorder

- Dx not made before age 6 or after age 13, symptoms started before age 10
- Symptoms:
 - Severe temper outbursts, average 3+ times/week, inconsistent with developmental age, impairing
 - Irritable/angry/sad mood when not having outbursts, easily angered, annoyed, but stays angry
 - Easily annoyed
 - Chronic- 1 year + symptoms
- Occurs in at least 2 of 3 settings (home, school, and peers); severe in at least one
- Not explained by another condition (mania: no history of elevated mood, MDD, PTSD, anxiety, autism)
- Use aggression rating scales: Emotional Outburst Inventory, Affective Reactivity Index or Modified Overt Aggression Scale
- These children more likely present later with depression/anxiety, less likely bipolar.

Comorbid Disorders in Children with DMDD

- ADHD + ODD (77-86%)
- ADHD only (79- 81%)
- ODD only (78-100%)
- Anxiety (31-49%)
- Depression (20-41%)
- Manic Symptoms (28-68%)
- Bipolar 1 Manic (3-9%)
- Autism Spectrum Disorder (3-31%)

DMDD Treatments

- Psychotherapy
- Pharmacotherapy: No approved medications and very little data.
 - Methylphenidate + citalopram
 - Vyvanse +fluoxetine
- Principle: rule out other disorders- and treat those first- maximize that treatment first
 - ADHD/ODD, anxiety, depression
- Record frequency, intensity, number and duration of outbursts using a rating scale
- If no improvement, then add on an SGA or mood stabilizer

Oppositional defiant disorder- 8 symptoms/3 groups

ANGRY/IRRITABLE

- Loses Temper
- Touchy/Easily annoyed
- Angry/resentful

*Overlap with DMDD, Progression to Anxiety, Irritability/ Depression, Non-aggressive Conduct Disorder

VINDICTIVENESS/HURTFUL

- Has been spiteful/vindictive at least 2 times in the past 6 months
- *Progression to Aggressive Conduct Disorder

ARGUMENTATIVE/DEFIANT/ HEADSTRONG

- Argues with authority figures/adults
- Defies or refuses to comply with requests from adults or rules
- Deliberately annoys
- Blames other for mistakes or misbehavior

*Overlap/Progression to ADHD, Non aggressive Conduct Disorder

ODD Assessment

- Use multiple informants- child, parents, teachers
- Differentiate areas of functional impairment- home, school, peers, all kids argue with their parents- is it impairing?
- Evaluate parenting strategies
- Rule out ADHD!
- Rating Scales
 - Vanderbilt Rating Scale
 - Behavior Assessment for Children BASC-2
 - Connors Child Behavior Checklist
- Clinical Interview:
 - Probing for "Moody, Temper tantrums, Argue a lot?"

- DSM Criteria:
 - 4+ symptoms
 - < 5 years: behaviors occur most days
 - ≥ 5 years: behaviors occur at least 1/week
 - Associated distress in the individual or immediate social context and impacts functioning.
 - Mild: symptoms present in 1 setting
 - Moderate: 2 settings
 - Severe: 3+ settings

Oppositional Defiant Disorder

- Lifetime prevalence 10.2%, higher in males
- Comorbid with other disorder 92%
 - 40% ADHD
 - 14% Anxiety
 - 8% Depression
- Heritability 50-70%, Brain Imaging Differences (Chicken/Egg?)
- Risk Factors- inconsistent parenting, harsh discipline
- Pathway/Developmental Progression:
 - ADHD -> ODD -> CD -> Anxiety -> Depression

ODD Psychosocial Risk Factors

- Low SES (NOT a RISK FACTOR <1 % Variance)
- Family, school, neighborhood
 - Lack of structure
 - Lack of parental supervision
 - Lack of Parental involvement
 - Community Violence
 - Poor Peer Relationships
 - Bullying

- Inconsistent Discipline
- Coercive or abusive parenting
 - Physical punishment
- Abuse

ODD: Treatment

- Primary Prevention- "good parenting"
 - Parent management training
 - School based intervention
- Parent Management Training
 - Promoting positive parent child interactions
 - Decreasing coercive and negative responses to unwanted behaviors
 - Emphasize structure and consistency, reduce harsh/critical parenting, avoid lax or punitive discipline, reasonable consequences
 - Incredible Years
 - PCIT
 - COPE

- School Based interventions
 - Promote compliance with rules
 - Help develop problem solving skills
 - Prevent problem behaviors
 - Avoid reinforcing oppositional behavior
- Individual CBT based anger management
- Pharmacotherapy- no FDA approved medications for ODD
 - Meds that work for ADHD tend to work ODD
 - Stimulants
 - Guanfacine and atomoxetine

Conduct Disorder

- Diagnosis
 - 15 Behavioral Criteria in 4 categories
 - 1. Aggression towards people or animals
 - 2. Destruction of property
 - 3. Deceitfulness or theft
 - 4. Serious violation of rules
 - Pervasive pattern of behaviors with severe consequences
 - Aggression towards animals is a red flag
 - One symptom before age 10: early onsetworse, more insidious, more heritable, more genetic. Higher risk for adult antisocial personality disorder
 - Later onset: more environmental- negative family factors, more likely to resolve by adulthood.

- Callous and Unemotional Traits modifier:
 - Lack of remorse or guilt
 - Callous lack of empathy
 - Unconcerned about performance
 - Shallow or deficient affect
 - Harsh abusive parenting as a cause, soft parenting can help it.
 - More likely to go on to be antisocial personality disorder
 - Over 12-month period in multiple relationships or settings

Conduct Disorder

- Prevalence: 1-10%
- Mean Age of Onset
 - Males: 10-12 years
 - Females 14-16 years
- Comorbidities
 - ADHD- 90%
 - ODD-80-90%
 - Depression 15-31%
 - Anxiety 22-33%

- Environmental Risk Factors
- Prenatal
 - Maternal Smoking
 - Maternal Diet
- Postnatal
 - Low levels parental monitoring
 - Exposure to violence
 - Harsh and inconsistent discipline
 - Poverty

Conduct Disorder

- Assessment: multi-informant
 - Must probe- tendency to under report
 - Under assessed and under reported
 - Assess/address comorbidities
 - Rating Scales
 - Child Behavior Checklist
 - Conners Scales
 - Retrospective Modified Overt Aggression Scale
- Worse outcome with early onset (before age 10) and callous unemotional traits
- High risk for substance abuse and antisocial personality disorder.

Conduct Disorder: Treatment

- 1st line: Multi modal, family based, systems based
 - Parent management training- benefit decreases with age (peak effects age 8)
 - Social Skills Training, problem solving techniques, anger management
 - Incredible Years- robust effects on CD in studies
- Address psychosocial crises
- Treat comorbid conditions with evidencebased treatment (ADHD, anxiety, depression)
- Requires extended treatment period
- High drop out rates in treatment, parent pathology, poor parental involvement

- 2nd Line: Pharmacotherapy- no specific medication/no FDA approved
 - Stimulants can help with aggression apart from effects on ADHD
 - Clonidine effective in 2 controlled trials with children with ADHD and Conduct Disorder
 - SGA: Risperidone (TOSCA study)
 - Lithium and Divalproex Sodium can help with explosive aggression in Conduct Disorder
 - 1st generation antipsychotics: molindone and haloperidol effective but concerning side effects

Bipolar Disorder- Diagnosis

- Kids with severe episodic irritability and severe behavior symptoms
- Depressive Episodes: Depressed/Irritable for at least 2 weeks, with 4+ of the following symptoms
 - Loss of interests/boredom
 - Poor appetite, weight loss/gain
 - Insomnia/hypersomnia
 - Psychomotor agitation/retardation
 - Fatigue/loss of energy
 - Worthlessness/guilt
 - Poor concentration/indecisiveness
 - Suicidal thoughts/plans

Bipolar Disorder: What is Mania?

- Behavior is different than the patient's usual function
 - Elevated, expansive, or irritable mood
- Episodes lasting > 1 week (4 days for hypomania), most of the day, every day
- Concurrent 3+ symptoms (HIPERS)
 - H: Hyperactivity- goal directed or pleasure oriented
 - I: Irritability/volatile
 - P: Psychosis (grandiosity, hallucinations, delusions)
 - E: Elated, Expansive, Energetic
 - R: Racing Thoughts, Rapid Speech
 - S: Sleep (Doesn't need or want any)
- Drugs can produce manic symptoms (Antidepressants)
 - If still having manic symptoms after antidepressant is stopped (at least 5 half lives of the drug has passed- then this is considered Bipolar 1

Pediatric Bipolar Disorder

- Prevalence is 1-2% in Bipolar 1 and 2. Bipolar NOS 3-4%
- Strong family heritability. BPD in 1 parent = 5x odd of BPD in a child
 - Grandparents, siblings BPD history is also meaningful
- Delays in diagnosis are very common (5-10 years)
 - First mood episode in bipolar is often a depressive episode
 - Children with MDD/Depression can present an irritable mood, not a depressed mood
 - Depressed and bipolar children can both have a labile mood: euthymic to depressed (MDD) vs depressed to manic/hypomanic (BPD)
- Substance Abuse can mimic bipolar
- Conduct Disorder- negative behaviors are more calculated vs in bipolar they are 2/2 grandiosity and poor/risky judgement

Bipolar Cross Over Symptoms

Bipolar	ADHD	MDD	ODD	Anxiety
Elated/Elevated Mood				
Grandiosity				
Self Injury/Suicidal		Severe Cases		
Poor Judgement/Risky Hypersexuality	Impulsive			
Flight of Ideas/Racing thoughts/Pressured Speech	Talking excessively			
Reduced Need for Sleep/Activity in the middle of the night	Trouble settling down, early wake up	Poor Sleep/Insomnia		Insomnia
Irritability (Rages 4-5x day for hours)	Easily frustrated (Shorter, known triggers)	> 50%	Lose Temper/Touchy/Easily Annoyed	Very Common
Hyperactivity	Hyperactivity	Agitation		Restlessness
Distractibility	Distractable	Poor Concentration		Poor Concentration

Bipolar Assessment and Treatment

- Rating Scales
 - Youth Mania Rating Scales
 - PHQ-9
- Clinical Interview
- Tracking symptoms, taking time
- Psychoeducation
- Psychotherapy
 - CBT, social skills, problem solving

Pharmacotherapy

- Atypical Antipsychotic
 - Risperidone
 - Aripiprazole
 - Olanzapine
 - Quetiapine
- Mood Stabilizers
 - Lithium (ages 12+)
 - Target Dose of 30mg/kg/day
 - Start outpatients 25mg/kg/day
 - Serum Level 0.9-1.1 mEq/L
 - Divalproex/Valproate
 - Serum level 60-90
 - Carbamazepine
 - Lamotrigine
 - Good for maintenance, not for acute mania

ADHD and Impulsive Aggression

- Impulsive aggression
 - Reactive, Overt, outside of acceptable social context
 - Impulsive in nature, triggered by environmental precipitants
 - "Outbursts" "Rages" "Tantrum"
 - Presence in several mental health diagnoses
- Very common in ADHD!
- These patients are more symptomatic and impaired than those without mood dysregulation. Must weigh the pros/cons of treating aggression vs side effects
- Assessment
 - Vanderbilt, Conners Scales, Modified Overt Aggression Scale

ADHD and Impulsive Aggression-Treatment

1) Maximize response of ADHD, usually with a stimulant

- Adjust doses, alternate formulations (different peak onset or duration of coverage)
- Switch stimulant class (MPH vs AMP)
- May consider an alpha 2 agonists or atomoxetine (no data for impulsive aggression)
 - See improvement in children with ADHD and ODD
 - Guanfacine XR: either monotherapy or adjunctive therapy

2) Then add on 2nd treatment meant to address the mood (or aggression symptoms

- Stimulant + Risperidone
- Stimulant + Mood stabilizer (lithium or divalproex)
- Stimulant + Antidepressant (SSRI)

Studies in ADHD and Aggression

- MTA Study: Impulsive aggression decreased from 54% to 26% with stimulant and behavioral therapy
- TOSCA Study: Severe Aggression (ODD/CD) in ADHD: Optimize stimulant + Behavioral therapy
 - Stimulant Refractory?
 - Boys (more conduct/ODD/mood)
 - Higher baseline depressive and manic symptoms
 - No worsening of mood symptoms with the stimulants
 - Divalproex (mean level 77.75mL/L) vs Risperidone (mean dose 1.65mg) vs Placebo
 - Risperidone works better, but causes more weight gain (> 2kg in 8 weeks)
 - Consider up to 6 month treatment period if working, then taper off
 - 5-64% Stimulant Responsive (High variance)- Aggression Remitted
 - Highest remission with longest therapy lead in (~9 weeks)- THERAPY WORKS FOR AGGRESSION!

Non-Stimulant Treatment in ADHD: Alpha Agonists

- They do work? Yes- evidence based data! FDA approved for ADHD
 - Showed Improvement in ADHD and ODD compared to placebo
 - Combination with stimulant > stimulant alone > alpha agonist alone
 - Long-Acting Alpha 2 Agonists- Guanfacine XR and Clonidine XR
- Mechanism of action
 - Exert their effects primarily through Norepinephrine activity- true mechanism is not known
 - Up to 2 weeks in long-acting forms to see effect
- Helps with associated motor/vocal tics, <u>aggression</u>, sleep and <u>behavioral</u> <u>dysregulation</u>
- Adjunct for ASD

ADHD and DMDD Diagnosis

- Stimulants alone work- MPH/MPH OROS (Concerta)
 - Improve irritability
 - Emotional lability
 - Anger
 - ADHD and ODD symptoms
- Stimulant + Aripiprazole
 - Significant improvement in irritability
- Risperidone only
 - Significant improvement in irritability
- Stimulant + SSRI (Citalopram: 5-40mg)
 - Helped with temper outbursts but not with chronic irritability
- Lithium
 - Behavioral therapy vs lithium (300mg BID) showed no differences. Behavioral therapy works!

Age of Onset of Pediatric Mental Health Disorders

Toddler/Preschool (0-3 Years)	Early School Age (4-7 years)		Adolescent (13-16 years)	Late Teen/Young Adult
ASD	ADHD	Anxiety	Depression	Bipolar/Psychosis Panic Disorder

Autism Spectrum Disorder

- Core Features of Autism
 - Impaired social interaction and communication
 - Repetitive behavior/restricted interests
- No medications to target core symptoms
- All medications in ASD target specific behavioral problems
 - Aggression/Irritability/Self injury
 - Hyperactivity
 - Anxiety
 - Sleep

Aggression in Autism

- The most common chief complaint for a child with Autism is irritability
 - Easily frustrated
 - Temper
 - Anger outbursts
 - Inattentive, hyperactivity
- If it's an acute behavioral change, make sure you take a good history
 - What's the trigger?
 - Medical: pain, infection, seizures, new medication
 - Environmental: trauma, stress, staff/school changes, family stressors

Aggression in Autism- Treatment Approach

- Identify underlying cause and treat (medical work up)
- Appropriate behavioral and education supports. Address psychosocial stressors
- Treat underlying ADHD, Anxiety, depression first
 - Re: stimulants, alpha 2 agonists, atomoxetine
- Mild/moderate- take your time with the above strategies, work with the parents
- Severe symptoms, prevent severe injury to self or others, hospitalizationuse SGAs as a last resort
- Last, Last Resort: Mood Stabilizers- Lithium and Divalproex with some positive data to help aggression

Aggression in Autism

- Why use Atypical Antipsychotics/SGAs?
 - Most studied medications in autism
 - Targets severe irritability and disruptive behaviors in Autism
 - FDA approved, good data
- When to use SGAs?
 - Is someone getting hurt or likely to get hurt?
 - Aggression, self injury, extreme impulsivity (cars, street, running away)
 - Is the child likely to lose access to educational or other resources without the medication?
 - Has everything else failed?

SGA Treatment Guidelines in ASD

- Start low and go slow
- Higher rates of side effects/limitation in patient communication/monitoring challenging
- Monthly Monitoring, use an objective rating scale
- Response may be unpredictable: Usually see response in 4-8 weeks
 - One change at a time
 - One medication at a time
- Collaborate with others treating the patient- Therapists, teachers, parents
- Reduce dosing regularly to establish ongoing benefit

Aggression in Autism: Other medications

- Prolonged and short release melatonin
 - 2-5 mg of prolonged release melatonin
- Vitamin D
- Omega 3 Fatty Acids:
 - Small improvement in ADHD. Improves mood. Ratio of EPA >DHA
- N-Acetyl cystenine for irritability, OCD, ritualistic behaviors
 - 600mg/day for 3 days then increase to 600mg BID. If after 2 weeks, there is some response, can move to 600mg TID

Aggression Pharmacotherapy Overview by Diagnosis

	1st Line	2 nd Line	
DMDD	Treat Comorbidity. Likely ADHD or mood with a stimulant, alpha agonist, atomoxetine or SSRI	SGA or Mood stabilizer	
ODD	Treat Comorbidity. Likely ADHD or mood with a stimulant, alpha agonist, atomoxetine or SSRI	SGA or Mood Stabilizer	
Conduct Disorder	Treat Comorbidity. Likely ADHD or mood with a stimulant, alpha agonist, atomoxetine or SSRI	SGA or Mood Stabilizer	
Bipolar Disorder	*SGA or Mood Stabilizer		*FDA Approved
ADHD	*Stimulant, alpha agonist, atomoxetine	SGA or Mood Stabilizer	*FDA Approved
Autism	Treat Comorbidity. Likely ADHD or mood with a stimulant, alpha agonist, atomoxetine or SSRI	*SGA or Mood stabilizer	*FDA Approved
Anxiety	*SSRI	SGA or Mood Stabilizer	*FDA Approved
Depression	*SSRI	SGA or Mood Stabilizer	*FDA Approved

Methylphenidate Products

Short Acting (3-5 hours)	Medium Acting	Long Acting	
Onset: 20-60 minutes	Onset: 1-3 hours	Onset: 1 hour	
Duration: 3-5 hours	Durations 3-8 hours	Durations: 8-12+ hours	
 Ritalin (Methylphenidate IR) 30 minutes until effect, 90 min peak concentration. ½ life of 3 hours Methylin (Solution or chewable) Focalin (Dexmethylphenidate IR) 5-6 hours D enantiomer is more active pharmacologically Focalin doses 50% lower than Ritalin (mixed d, L enantiomer) doses 	 Ritalin SR (3-8 hours) Ritalin LA (6-8 hours) [50IR/50ER] Metadate ER (3-8 hours) Metadate CD (6-8 hours) [30IR/70ER] Methylin ER (3-8 hours) Quillichew ER (8 hour) [30IR/70ER] 	 Focalin XR (lower doses needed) Concerta Daytrana Transdermal patch Higher rates of adverse effects Quillivant XR (12 hr)- liquid suspension [20IR/80ER] Aptensio XR (12hr) [40IR/60ER] Contempla XR-ODT (10-12 hr) [25IR/75ER] Jornay PM (starts to release 10 hours after taken, can last up to 10-12 hours) 	

Amphetamine Products

Short Acting	Medium Acting	Long Acting
Onset: 20-60 minutes	Onset: 60-90 minutes	Onset: 1 hour
Duration: 6 hours	Duration: 5-8 hours	Duration: 8-12+ hours
 Dexedrine Tablets Evekeo 	 Adderall IR (4-6 hours) Dexedrine IR (4-6 hours) DEXtroamphetamine: d enantiomer- more active pharmacologically- lower doses needed 	 Adderall XR (10-12 hr) [50IR/50ER] Dexedrine SR (6-10 hr) Adenzys-XR-ODT (mixed) [50IR/50ER] Dyanavel XR (suspension) (mixed) Lisdexamfetatamine "Vyvanse" (12+ hr) Mydayis (16 hour) (mixed)

Stimulants side effects

- MPH: Irritability improved 71%, worsened 19%, no change in 10%
- MPH overall reduced risk of irritability
- AMP worsened emotional lability

Atypical Antipsychotics/SGAs

- How do they work?
- Dopamine blockers- reduce dopamine neurotransmission
- Second Generation Antipsychotics also work at 5HT receptors (serotonin)
- Less side effects than the typical antipsychotics

Atypical Antipsychotics: Dosing/Titration for Aggression

Atypical Antipsychotic	Starting Dose	Titration	Dose Range	FDA Indication
Aripiprazole (most data in aggression)	2-2.5-5mg mg/day	2.5mg-5mg every 7- 10 days	2-15mg/day Psychosis: 30mg/day	Bipolar disorder: 10 years + Irritability with Autism: 5-17 years
Risperidone (most data in aggression)	0.25-0.5mg/day	0.25-1mg every 2 weeks	0.5-4mg/day Psychosis: 6mg/day	Bipolar disorder 10 years + Irritability with Autism: 5-16 years
Olanzapine	1.25-5mg/day	2.5mg every 2 weeks	7.5-10mg	Bipolar Disorder: 13- 17 years
Quetiapine (no data)	12.5mg-25mg/day	25-50mg every 2-3 days	50-200mg/day Psychosis: 800mg/day	Bipolar Disorder: 10-17 years
Ziprasidone EKG Baseline (long QT)	20mg/day	20mg/day every 2 weeks (take with high calorie meal)	40-120mg/day	Bipolar Disorder: 10- 17 years old
Lurasidone	20mg/day	20mg/day every 2 weeks (take with meal)	20-80 mg/day	Bipolar 10-17 years old

Monitoring Guidelines for Antipsychotics

	Baseline	3 months	6 months	Every 6 months	Yearly
Medical History	х				x
BMI	х	x	x	x	
Blood Pressure	х	x	x	x	
Fasting glucose	х	x	x	x	
Fasting lipids	х	x	x	x	
Fasting Insulin	x (not required)				x (not required)
TSH	x		x		x
Prolactin	Only if symptomatic: nipple discharge, gynecomastia				

Molindone (Typical antipsychotic)

- Some evidence to show it helps with aggression in ADHD and CD
- Used as an adjunct to a stimulant and behavioral therapy
- Low dose (12-18mg) and medium dose (24-36mg) helped with aggression. High dose did not help
- Adverse affects: Headache, sedation, increased appetite

Side effects of Antipsychotics

Typical/1st Generation (Haloperidol, Clozapine, Molindone)

- Withdrawal dyskinesias/Tardive Dyskinesia
- Acute dystonic reaction
 - Higher rates in younger males
- Risk for seizures (clozapine)

Atypical/Second Generation (Aripiprazole, Risperidone)

- Weight gain
 - Most rapid during first few weeks of treatment
 - Initial weight gain is an indicator of long-term weight gain
- Metabolic changes (dyslipidemia, diabetes)

Treating the Side Effects of SGAs

- Weight Gain
 - Healthy lifestyle guidance
 - Consider starting with a more weight neutral antipsychotic
 - If greater than 5% weight increase, then consider switching/stopping medications
- Metabolic Syndrome
 - Lifestyle modification
 - Referral to nutritionist or exercise program
 - Lower dose of the SGA if tolerated
 - Switch to more weight neutral antipsychotics
 - Risperidone= Quetiapine > Aripiprazole > Ziprasidone =Lurasidone
 - Metformin for weight gain: 500-850 mg BID
 - Omega 3 treatment for hyperlipidemia

Metabolic Syndrome

- 6-10 years old
 - Can't be diagnosed
 - Obesity > 90% (waist circumference)
 - Higher risk if a strong family history of metabolic syndrome T2Diabetes, dyslipidemia, CV disease, HTN or obesity
- 10-16 years old
 - Obesity > 90% waist circumference
 - Triglycerides > 1.7mmol/L
 - HDL-cholesterol <1.03 mmol/L
 - Blood pressure > 130 systolic 85 diastolic
 - Glucose > 5.6 mmol/L (oral glucose tolerance test) or known T2Diabetes

Mood Stabilizer- when to use?

• Bipolar Disorder

 Side effects or no response from SGAs

	Starting Dose	Titration	Serum Level	Lab Monitoring	FDA Approval
Lithium	15-20mg/kg/day (BID or TID) <25kg: 300mg 25-40kg: 600mg >40kg: 900mg	300mg/day every 3-5 days	0.6-1.2 mEq/L	CBC, BUN, Creatinine, UA, TFS, EKG (Baseline and every 6 months) Lithium Level 12 hours after dose, every 1-2 weeks until stable, then every 1-2 months	Bipolar Disorder > 12 years
Divalproex	<25 kg: 250mg 25-40kg: 375mg >40kg: 500mg	10mg/kg/d every 3 days	50-120 mg/L	CBC and LFTs (Baseline, Month 1, 2, every q4-6 months). Serum level 5 days after starting, 8— 12 hours after dose	

Take Home Points

- Irritability and aggression are common among most pediatric mental health disorders
- DMDD, ODD, CD, ADHD, and Autism have overlapping symptoms and a few key distinguishing features.
- Identify any underlying causes and treat first (medical, psychosocial)
- Parent training is at the core of prevention and treatment.
- Psychosocial support at home and at school is critical.
- Pharmacotherapy is used as a last resort.
- DMDD, ODD, CD have no FDA approved medications for treatment.
- SGAs are used as an off label approach for aggression across most diagnoses.
- Impulsive aggression ADHD should be treated first with maximizing stimulant + behavioral therapy before trying a SGA.
- Aggression in Autism should be treated with SGAs (FDA approved) only if severe.

Racial Issues and Disparities

- Pediatric Psychiatric Studies are mostly with white males
- Black children are less likely to use medication, but more likely to utilize counseling
- Hispanic families are less likely to utilize counseling and medication
- Where are the perceptions coming from?