The Ninja's Guide to PRITE:

Child Edition

2021 Study Guide

Loma Linda
Department of Psychiatry

Who We Are

To *Child and Adolescent Psychiatry Fellows*, Psychiatry Residents and Faculty Everywhere: Loma Linda University Medical Center is located in sunny Southern California, about 60 miles east of Los Angeles. A part of the Adventist Health System, we provide patient care in one of the largest non-profit health systems in the nation. Loma Linda's mission is to excel in medical education, global healthcare, and community outreach, all under a central tenant: "To Make Man Whole." As an official World Health Organization Collaboration Center, our department funds resident electives in Global Mental Health at locations around the world. Additionally, our residents can participate in national and international disaster relief on the LLU Behavioral Health Trauma Team.

We were proud to graduate our first group of Child and Adolescent Psychiatry fellows in June of 2021. This was a long awaited milestone and the culmination of countless hours of work and collaboration between Loma Linda University Department of Psychiatry and San Bernardino County. As our department grows, our faculty remain committed to providing a safe space for resident education and professional development. We believe in supporting the goals of our fellows as they help to shape the future of our burgeoning fellowship program. After nearly 14 editions of The Ninja's Guide to PRITE, we are excited to present the 1st Edition of The Ninja's Guide to PRITE: Child Edition, complete with a young ninja drawn by Joy Launio, MD!

Who We Are

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Created The Ninja's Guide to PRITE in 2007 on her kitchen table, when residents converted 6 years of PRITE exams to a Q&A format. She spent her Chief Resident Year writing and organizing the original guide and for the past decade has continued to edit and update the guide

A special thank you to Dr. Ara Anspikian, Dr. Jennifer Minami, Dr. Jamie Snyder, and Dr. Lauren Laddaran for contributing your time and expertise in reviewing content and providing direction for the study guide.

About This Study Guide

This guide provides a review of key topics in child and adolescent psychiatry as it applies to the child PRITE. Our first edition aims to set up a framework that can be built up in future years with new sections and updated material. This structure revolves around the collective voice of diagnosis and treatment recommendations in child psychiatry: The American Academy of Child and Adolescent Psychiatry Practice Parameters and Clinical Guidelines. When possible, we attempt to provide a more concise summary of the current guidelines for ease of review, and we are excited to provide a summary of the most recent Anxiety and Intellectual Disability Clinical Guidelines just released in 2020. In most cases, we have provided an outline of the topic, including several charts and tables, to aid your study of the unique aspects of child psychiatry.

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AACAP Practice Parameter Categories of Endorsement

- **"Clinical Standards" [CS]** is applied to recommendations that are based on rigorous empirical evidence (e.g., meta-analyses, systematic reviews, individual randomized controlled trials) and/or overwhelming clinical consensus.

- **"Minimal Standards" [MS]** are recommendations that are based on substantial empirical evidence (such as well-controlled, double-blind trials) and/or overwhelming clinical consensus. Minimal standards are expected to apply more than 95% of the time, i.e., in almost all cases. When the practitioner does not follow this standard in a particular case, the medical record should indicate the reason.

- **"Clinical Guidelines" [CG]** are recommendations that are based on empirical evidence (such as open trials, case studies) and/or strong clinical consensus. Clinical guidelines apply approximately 75% of the time. These practices should always be considered by the clinician, but there are exceptions to their application.

- **"Options" [OP]** are practices that are acceptable but not required. There may be insufficient empirical evidence to support recommending these practices as minimal standards or clinical guidelines. In some cases they may be appropriate, but in other cases they should be avoided. If possible, the practice parameter will explain the pros and cons of these options.

- **"Not Endorsed" [NE]** refers to practices that are known to be ineffective or contraindicated.

A Ninja's Guide to Child Development

Developmental Theory

Freud's Psychosexual Stages

- **The Oral Stage:** *Birth to 18 Months*
  - Anyone familiar with very young babies and children knows that they are focused on their mouths.
  - A baby's first nourishment is received through suckling, and the sucking instinct is usually strong, even in newborns.
  - Freud theorized that an infant's oral focus brought not only nourishment, but pleasure.
- **The Anal Stage:** *18 Months to Three Years*
  - Freud believed that during this time period, children derive much pleasure from the process of either retaining or eliminating feces, and are quite focused on the process.
  - This is often the time frame in which many parents choose to potty train their children.
- **The Phallic Stage:** *3 Years to 6 Years*
  - From about age 3-6 years, Freud believed that children's pleasure centers focused on their genitals.
  - He further theorized that young boys develop unconscious sexual feelings for their mothers, complicating their relationships with both parents.
  - Struggling with a feeling that they are in competition with their fathers for the attention of their mothers, Freud felt that boys from 3-6 years also fear that their fathers will punish them for these sexual feelings.

- **Latency Stage:** *6 Years to Onset of Puberty*

  - Freud seemed to view this time as the least complicated in childhood, believing that during these years, children focus their energies on their schooling as well as forming friendship bonds with other children of their own gender.

- **The Genital Stage:** *From Puberty On*

  - In this final stage of psychosexual development, Freud theorized that the onset of puberty represented the reawakening of sexual urges.

  - At this more mature age, however, adolescents focus not only on their genitals, but also on developing sexual relationships with members of the opposite sex and on seeking sexual satisfaction.

Melanie Klein

- **Play Analysis:** Child's play seen as equivalent to free association

  - Encouraged early, deep interpretations of play and minimized contact with parents and teachers.

- **Internal conflicts of younger children**

  - Maintained Freud's libidinous drives and fear of punishment, now applied at an early age

    - Shifting between libidinal and aggressive impulses: seeing oneself as "good" or "bad"

    - Experiencing "good breast" (provides nourishment) and "bad breast" (unavailable and abandoning)

- ➢ **Paranoid-Schizoid position:** fear of harm coming to "good breast" and splitting away the "bad breast"

- ➢ **Depressive position:** infant's realization that the "breast" (mother), and infant are who objects and cannot be split into good and bad parts.

Erikson's "Eight Stages" of Psychosocial Development

- ❖ Formulated not through experimental work, but psychotherapy

- ❖ Erikson believed that the stages must be resolved sequentially

1. Basic Trust versus Basic Mistrust (Hope)

- ❖ Infancy through the first one or two years of life

  - ➢ If nurtured and loved: develops trust and security and a basic optimism

  - ➢ If badly treated: becomes insecure and mistrustful

2. Autonomy versus Shame (Will)

- ❖ Between about 18 months or 2 years and 3½ to 4 years of age

- ❖ The "well-parented" child emerges from this stage sure of himself, elated with his new found control, and proud rather than ashamed. (Works on self-care & toileting)

3. Initiative versus Guilt (Purpose)

- ❖ Occurs during the "play age," or the later preschool years (from about 3½ to, in the United States culture, entry into formal school).

- ❖ **The healthy child learns:**

  1) To imagine, to broaden his skills through active play of all sorts, including fantasy

2) To cooperate with others
3) To lead as well as to follow

- **Alternatively the child is immobilized by guilt, he is:**

1) Fearful

2) Hangs on the fringes of groups

3) Continues to depend unduly on adults

4) Restricted both in the development of play skills and in imagination.

4. Industry versus Inferiority (Competence)

- "School age" possibly including some of junior high school.

- Here the healthy child learns to master the more formal skills of life:

1) Relating with peers according to rules

2) Progressing from free play to play elaborately structured by rules and demanding formal teamwork, such as baseball.

3) Mastering social studies, reading, and arithmetic. Homework is a necessity, and the need for self-discipline increases yearly.

- The child who is trusting, autonomous, and full of initiative will easily learn to be industrious.

- However, the mistrusting child will doubt the future. The shame-and guilt-filled child will experience defeat and inferiority.

5. Identity versus Identity Diffusion (Fidelity)

- Adolescence (from about 13 or 14 to about 20), learns to answer "Who am I?"

- **In successful early adolescence:**

1) Mature time perspective is developed
2) Acquires self-certainty as opposed to self-consciousness and self-doubt

3) Experiments with different roles- usually constructive - rather than adopting a "negative identity" (such as delinquency).

4) Anticipates achievement, and succeeds rather than being "paralyzed" by feelings of inferiority or by an inadequate time perspective.

    - Even the best-adjusted of adolescents experiences some role identity diffusion: most teens experiment with minor rebellion and are flooded with self-doubts at times.

❖ **In later adolescence:**

1) Clear sexual identity is established.

2) The adolescent seeks leadership (someone to inspire him)

3) Gradually develops a set of ideals (hopefully socially congruent and desirable)

    - Erikson sees adolescence as a "psychosocial moratorium" for most youth.

    - They do not have to "play for keeps," but can experiment, trying various roles, and hopefully find the one most suitable for them.

Piaget's Cognitive Development Stages

❖ **The Sensorimotor Stage:** Birth to approximate age two

➢ Sensory perceptions and motor activities

➢ Simple motor responses caused by sensory stimuli

- ➢ Use skills, such as looking, sucking, grasping, and listening, to learn more about the environment

- ❖ **The Preoperational Stage:** Ages two to six

  - ➢ Language development is one of the hallmarks of this period

  - ➢ Do not yet understand concrete logic

  - ➢ Cannot mentally manipulate information (no conservation)

  - ➢ Unable to take the point of view of other people, which he termed "egocentrism"

  - ➢ Become increasingly adept at using symbols, as evidenced by the increase in playing and pretending. Role playing also becomes important

- ❖ **The Concrete Operational Stage:** Age seven until approximately age eleven

  - ➢ Begin thinking logically about concrete events

  - ➢ Good at the use of inductive logic

    - ■ Inductive logic involves going from a specific experience to a general principle

  - ➢ Difficulty using deductive logic, which involves using a general principle to determine the outcome of a specific event

  - ➢ Understanding of reversibility, or awareness that actions can be reversed

    - ■ For example, being able to reverse the order of relationships between mental categories. For instance, recognizing that his or her dog is a Labrador, that a Labrador is a dog, and that a dog is an animal

  - ➢ Problem-solving is Trial & Error

- **The Formal Operational Stage:** Age twelve into adulthood

  - **Deductive logic:** requires the ability to use a general principle to determine a specific outcome
    - This type of thinking involves hypothetical situations and is often required in science and mathematics

  - The ability to think about abstract concepts emerges

    - Instead of relying solely on previous experiences, children begin to consider possible outcomes and consequences of actions

    - This type of thinking is important in long-term planning

  - The ability to systematically solve a problem in a logical and methodical way emerges.

    - Able to quickly plan an organized approach to solving a problem.

Margaret Mahler: Attachment/Separation-Individuation Stages

- **Normal Autistic Phase:** *Birth to 1 Month*

  - A newborn infant is blissfully unaware of anything but its own needs.

  - At this stage, the mother needs to be available to lovingly meet the baby's needs and introduce tender, caring interaction.

- **Normal Symbiotic Phase:** *1 to 5 Months*

  - During these first few months, babies begin to learn about their world and develop their very first human bond -- that which they share with their mothers.

- ➢ Positive stimuli (cuddling, smiling, engaged attention) and relief of discomfort (feeding promptly when hungry, changing of soiled nappies, providing an appropriate sleep environment) all help the infant to develop a trust that their needs will be met, building a basis for security and confidence.

❖ Sub-phase One: Differentiation - *5 to 10 Months*

- ➢ As the baby matures, they develop an increased interest in both the mother and the outside world.

- ➢ Parents often first notice their baby's first outward signs of separation anxiety during this time as the baby continually "checks back," looking at other things but then looking for the mother as a reassurance that she is still present.

- ➢ Often, babies are most comfortable to express interest in outside stimuli when they feel safe in their mother's arms during this phase.

- ➢ Consistent access to the mother aids the baby's emotional well-being and while it first appears about this time, this need may continue well into the practicing sub-phase

❖ Sub-phase Two: Practicing - *10 to 16 Months*

- ➢ As children's mobility increases, they are able to explore their environment with an autonomy that was previously impossible

- ➢ Still not ready for extended separation from their mothers, crawlers and beginning walkers will sometimes choose to separate briefly from their mothers, but will typically return quickly for assurance and comfort

- ➢ Some independent play time is enjoyed, but often the baby is only comfortable to play on their own when the mother is within the child's line of sight

- ➢ Mothers who are able to release their children to a beginning level of independent exploration whilst staying nearby will provide their baby with the ability to take pleasure in their growing world

    - ■ Mahler described this **"hatching"** as the true birth of the individual, with the child beginning to have a basic sense of self not directly connected to the mother

❖ Sub-phase Three: Rapprochement - *16 to 24 Months*

- ➢ As parents of toddlers know, they can be a confusing bunch. One minute, they are running from their mothers, refusing her attention or wishes, and the next they are anxiously clinging to her

- ➢ Mahler referred to this as **"ambitendency"** and explained that this behavior is representative of a toddler's sometimes opposing desires and needs

    - ■ It is during these months that children first get a real sense that they are individuals, separate from their mothers, which is both an exhilarating and frightening discovery

- ➢ Toddlers continue to take pleasure in exploring their environment, but during this phase, much of their growth comes from socialization

    - ■ Imitation of others is common (much to the amusement and sometimes dismay of parents!), as is the tendency to want the things that others have, taking them by force if necessary

- ➢ Mahler also observed that toddlers often become a bit "low key" when they are not around their mothers, and may withdraw a bit into themselves.

- ➢ Unlike when they were babies, toddlers learn that their emotional needs are not automatically sensed or tended to, so they may be especially demanding of their mother's attention.

- ➢ When they don't get their way, frustrated toddlers often resort to throwing temper tantrums.

❖ **Sub-phase Four: Consolidation and Object Constancy** - *24 to 36 Months*

➢ At some point around the second birthday, children begin to be more comfortable separating from their mothers, knowing that they will return (object constancy).

➢ This ability makes it possible for two year olds to accept that they are unique from their mothers without anxiety, allowing the child to engage substitutes for the mother when she is absent

Comparison of Developmental Theories

<table>
<tr><th colspan="2">Approximate Age Ranges</th><th>Freud
Psychosexual</th><th>Erikson
Psychosocial</th><th colspan="2">Mahler
Bridge Ego Psych to Object Relations</th><th>Piaget
Cognitive</th><th>Kohlberg
Moral</th></tr>
<tr><td rowspan="5">Birth to 2 yrs
(Infancy)</td><td>0 - 4 wks</td><td rowspan="5">Oral Stage:
The mouth, tongue, and gums are the focus of pleasurable sensations in the baby's body, and feeding is the most stimulating activity.</td><td rowspan="4">Trust vs. Mistrust:
Babies learn either to trust that others will care for their basic needs, including nourishment, warmth, cleanliness, and physical contact, or to lack confidence in the care of others.</td><td colspan="2">I. Autistic:
Survival, not Relatedness</td><td rowspan="5">Sensorimotor Period:
Most action is reflexive. Perception of events is centered on the body. Objects are extensions of self. Acknowledges the external environment.</td><td rowspan="4"></td></tr>
<tr><td>1 - 5 mo</td><td colspan="2">II. Symbiotic Relatedness:
Smile, visual following, Mother - baby as duality, Attachment to mother forms - trust that needs will be met</td></tr>
<tr><td>5 - 10 mo</td><td rowspan="2">III. Separation - Individuation</td><td>A. Differentiation:
"Hatching", Mother is a separate person
Transitional object</td></tr>
<tr><td>10 - 16 mo</td><td>B. Practicing:
Increase in motor skills
Explore away from mother, Return for refueling</td></tr>
<tr><td>16 - 24 mo</td><td rowspan="2">Autonomy vs. Shame and Doubt:
Children learn either to be self-sufficient in many activities, including toileting, feeding, walking, exploring, and talking or to doubt their own abilities.</td><td rowspan="2"></td><td>C. Rapprochement:
Increased awareness of separation
Increased vulnerability to separation</td><td rowspan="2"></td><td rowspan="2"></td></tr>
<tr><td>1.5 to 3 yrs
(Toddler)</td><td>24 - 36 mo</td><td>Anal Stage:
The anus is the focus of pleasurable sensations in the baby's body, and toilet training is the most important activity.</td><td>D. Object Constancy:
Consolidation of Individuality
Integration of split views of mother
Internalization of soothing presence</td><td>Preconceptual:
Self-centered. Asks many questions. Explores the environment. Language development is rapid. Associate words with objects.</td></tr>
</table>

Approximate Age Ranges	Freud Psychosexual	Erikson Psychosocial	Mahler Bridge Ego Psych to Object Relations	Piaget Cognitive	Kohlberg Moral
3 to 6 yrs (Preschool)	**Phallic Stage:** The phallus, or penis, is the most important body part, and pleasure is derived from genital stimulation. Boys are proud of their penis, and girls wonder why they don't have one. (Oedipal Conflict)	**Initiative vs. Guilt:** Children want to undertake many adult-like activities, sometimes overstepping the limits set by parents and feeling guilty.		**Preoperational:** Egocentric thinking diminishes. Includes others in the environment. Enjoys repeating words, may count to 10. Words express thoughts.	**Preconventional:** Morality is a matter of good or bad, based on a system of punishments. 1. Punishment and obedience orientation. 2. Instrumental relativist orientation
7 to 11 yrs (Middle Childhood)	**Latency:** Not a stage but an interlude, when sexual needs are quiet and children put Psychic energy into conventional activities like schoolwork and sports.	**Industry vs. Inferiority:** Children busily learn to be competent and productive in mastering new skills, or feel inferior and unable to do anything well.		**Concrete Operations:** Solves concrete problems. Begins to understand relationships such as size. Understands right and left. Cognizant of viewpoints.	**Conventional:** Morality seen as following the rules of society. tries to be "good." 1. "Good boy, good girl." 2. Law - and - order orientation.
12 to 18 yrs (Adolescence)	**Genital Stage:** The genitals are the focus of pleasurable sensations, and the young person seeks sexual stimulation and sexual satisfaction in heterosexual relationships.	**Identity vs. Role Confusion:** Adolescents try to figure out "Who am I?" They establish sexual, political, and career identities or are confused about what roles to play.		**Formal Operations:** Uses rational thinking. Reasoning is deductive and futuristic.	**Postconventional:** Morality consists of standards beyond a specific group or authority figure. 1. The social contract orientation. 2. The universal ethical principle orientation. 3. Mystical and religious reflection.

Approximate Age Ranges	Freud Psychosexual	Erikson Psychosocial	Mahler Bridge Ego Psych to Object Relations	Piaget Cognitive	Kohlberg Moral
18 to 40 yrs (Adulthood)	Freud believed that the genital stage lasts throughout adulthood. He also said that the goal of a healthy life is "to love and to work well."	**Intimacy vs. Isolation:** Young adults seek companionship and love with another person or become isolated from others by fearing rejection or disappointment.			
40 to 65 yrs (Middle Years)		**Generativity vs. Stagnation:** Middle-aged adults contribute to the next generation by performing meaningful work, creative activities, and/or raising a family, or become stagnant and inactive.			
65+ yrs (Late Adulthood)		**Integrity vs. Despair:** Older adults try to make sense out of their lives, whether seeing life as a meaningful whole or despairing at goals never reached and questions never answered.			

Theory of Attachment

❖ John Bowlby:

- ➢ Attachment behaviors (crying and searching) were adaptive responses to separation from a primary attachment figure

- ➢ A motivational system, what he called the attachment behavioral system, was gradually "designed" by natural selection to regulate proximity to an attachment figure

    - ■ This system essentially "asks" the fundamental question: Is the attachment figure nearby, accessible, and attentive?

    - ■ If yes, then feels loved, secure, and confident, and will be more likely to explore his or her environment, play with others and be sociable

    - ■ If no, then experiences anxiety, and is likely to exhibit behaviors ranging from simple visual searching on the low extreme to active following and vocal signaling on the other

❖ Mary Ainsworth:

- ➢ Studied individual differences in infant attachment patterns and studied infant-parent separations, developed **"the strange situation"**

    - ■ **Strange Situation:**

    - ■ **Secure = parents who are responsive to needs**

        - ○ Infants who become upset when the parents leave the room, but actively seeks the parent and easily comforted when the parent returns

- **Anxious-Resistant = parents who are insensitive to needs or inconsistent or rejecting in care**
    - Children are ill-at-ease initially, so when there is a separation, they become extremely distressed,
    - When reunited, have a difficult time being sooth, exhibiting conflicting behaviors that suggest they want to be comforted, but also want to "punish" the parent for leaving
- **Avoidant**
    - Those who do not appear distressed by the separation, and upon reunion, actively avoid seeking contact with their parent, sometimes turning their attention to play objects

❖ Maternal deprivation studies: Harry Frederick Harlow

➢ Studied by **Harlow** with rhesus monkeys:

- Separated from their birth mothers and reared by surrogate mothers
- Placed in cages with two **wire-monkey mothers**
    - One held a bottle from which the monkey could obtain nourishment
    - Second was covered with a soft terry cloth
- monkeys went to wire mother to obtain food, but spent most of their days with the soft cloth mother

➢ *Demonstrated that early attachments were result of receiving comfort and care from a caregiver, rather than simply the result of being fed*

❖ Stages of attachment - Developed by Schaffer & Emerson:

- ➢ **Pre-attachment stage** = birth to 3 months
  - ■ Do not show any particular attachment to specific caregiver
  - ■ Infant's signals of crying and fussing naturally attract attention of the caregiver, baby's positive responses encourage caregiver to remain close
- ➢ **Indiscriminate attachment** = 6 weeks to 7 months
  - ■ Show preferences for primary and secondary caregivers, develop trust that caregivers will respond to their needs
- ➢ **Discriminate attachment** = 7 to 11 months
  - ■ Shows strong attachment and preference for one specific individual
    - ○ Will protest when separated from primary attachment figure (separation anxiety)
    - ○ Display anxiety around strangers (stranger anxiety)
- ➢ **Multiple attachments** = 9 months
  - ■ Strong emotional bonds with other caregivers beyond the primary attachment figure

❖ Patterns of attachment:

- ➢ **Ambivalent** = Distressed when parent leaves
  - ■ Due to poor parental availability, children cannot depend on their primary caregiver to be there when they need them
- ➢ **Avoidant** = Avoid parents or caregivers

        - Showing no preference between caregiver and a complete stranger
            - Result of abusive or neglectful caregivers
            - Children who are punished for relying on a caregiver will learn to avoid seeking help in the future

- **Disorganized** = Display a confusing mix of behavior, seeming disoriented, dazed, or confused, avoid or resist the parent
    - Lack of clear attachment pattern is likely linked to inconsistent caregiver behavior
    - Parents serve as both a source of comfort and fear
- **Secure** = show distress when separated and joy when reunited
    - Comfortable seeking reassurance from caregivers

Kohlberg's Stages of Moral Development

- **Lawrence Kohlberg**: American psychologist, studied how children came to their moral decisions, but also why.
    - Developed an interview process with a number of scenarios, each with a moral dilemma and then gauged the answers.
    - Believed that development of moral reasoning happens in a particular sequence, that each step of the way is a precursor to the next, and not all people are able to reach the highest levels of moral reasoning.

❖ Preconventional Level (Self-Focused Morality)

- ➢ **Stage One (punishment and obedience orientation):** Morality is as simple as obeying rules because of the negative consequences of disregarding them. Avoiding punishment is most influential.

- ➢ **Stage Two (instrumental relativist orientation):** Appropriate behavior is motivated by what best satisfies a person's needs, or occasionally, the needs of another.

    - ■ Elements of fairness and equality begin to come into play, but there is still self-motivated reasoning involved.

    - ■ Actions evolve from "what will this do for me?" rather than from loyalty, justice, or a sense of fair play.

❖ Conventional Level (Other-Focused Morality)

- ➢ **Stage Three (interpersonal concordance or "good boy-nice girl" orientation):** Good behavior is deemed by the child to be meeting what they believe their parents and teachers expect from them.

    - ■ Striving to be "nice" is the goal.

- ➢ **Stage Four ("law and order" orientation):** Obeying rules, respecting authority, and fulfilling perceived obligations provide motivation for behavior.

❖ Postconventional Level (Higher-Focused Morality)

- ➢ **Stage Five (social-contract legalistic orientation):** Appropriate behavior seems to be based on societal norms, with emphasis on upholding the values of the people.

    - ■ Laws are still deemed important, but the rationale allows for seeking to change laws that seem unjust.

- **Stage Six (universal ethical-principle orientation):** A deep understanding of your own beliefs allows stage six morality to consider not only society's viewpoint, but also the notion that extenuating circumstances can alter moral choices.

    - Basics of morality, such as justice, human dignity, and fairness provide the starting point for decisions, but independent thought and reasoning are major factors in final evaluations.

Infant and Toddler Development:

❖ First 3 years of postpartum life

- **Infancy:** Time before the beginning of expressive verbal communication

- **Toddlerhood:** Period of increasing autonomy, child using skills to explore their world physically, cognitively, and socially

- This period has the most rapid and contextually transactional period of neurodevelopmental change throughout postpartum life span

❖ Normative Developmental Forces

- Development is characterized by processes by which each individual uniquely adapts and integrates his or her own nature with the opportunities and limitations of his or her experience across time

- So, developmental psychopathology is characterized by patterns of behavioral adaptation over time and in context, rather than static, isolated, or domain-specific problems

❖ Factors in development:

- Maturational processes - progressive unfolding and differentiation of intrinsic capacities

- Important to draw distinction between developmental processes that are primarily delayed vs. those that represent a qualitative deviation from the typical progression of skills

❖ Relationships with others

➢ Relationships and interactions with primary caregivers **directly** affect and dynamically interact with multiple domains of child development

- Attachment, social-emotional development, behavior, cooperation, development of morality, early learning, exploration, cognitive and language development, health and physical development

➢ Parents can **indirectly** transmit to their children, through impact on caregiving behaviors

- Poverty, parental life circumstances, parental beliefs and attitudes

➢ Parents can also **shape** their child's environment indirectly

- Providing stimulating and supportive social and material resources at home, choice of neighborhood, decisions regarding nonparental child care

➢ Infants are strongly motivated and primed to develop attachments with adult caregivers to ensure close, protective, and nurturing contact

❖ Critical sensitive periods

➢ **Prenatal development = during pregnancy**

- Exposure to toxins, rate of maternal weight gain, ease or difficulty of delivery, immediate postnatal complications
- Parental expectations and wishes for unborn infant
- Timing of pregnancy, major life events during the pregnancy

- **Infant, stage 2 = 0-2 months**
    - Work primarily toward achieving homeostasis/maintaining physiological equilibrium
- **Infant, stage 3 = 3-7 months**
    - Increases social reciprocity between infant and caregivers
    - Increased awareness of the external world (possible by greatly enhanced visual abilities) and improved coordination of sensory input and non reflexive/voluntary motor output
    - Beginning to show an understanding of object permanence and rudimentary understanding of principles of cause and effect
- **Infant, stage 4 = 7-18 months**
    - Develop a sense of intersubjectivity (understanding that their thought, feelings, gestures, and sounds can be understood by others)
    - Begin to demonstrate means-end reasoning leading to goal-directed behavior
    - Separation anxiety appears, peaking at 14-18 mo, then declining afterwards
    - Learning to walk → increased independence and a broadening worlds
    - Trial and error problem solving begins to replace condition response learning; develop rudimentary communicative speech
- **Infant, stage 5 = 18-36 months**
    - Increased ability to use symbolic representation, indicated greatly increased language proficiency
        - Marked by a move from direct imitation to deferred imitation (behaviors of others are remembered and practiced later)

- Internal problem solving begins to replace trial-and-error problem solving

- Expressive vocabularies increase

Important Milestones

Age	Receptive Language	Expressive Language	Social Emotional	Gross Motor	Fine Motor	Cognitive Problem Solving
2 mo	Turns to voice	Cooing	Attachment (child to parent), social smile	Head steady when held	Bats at objects	Attends to moderate novelty, follows past midline
4 mo	Respond to "no", responsive to tone of voice	Laugh, squeal	Explores parent's face, turn taking conversation	Sits with support, rolls front to back	Palmar grasp, reaches and obtains items	Anticipates routines, purposeful sensory exploration, stares at own hand
6 mo		Babble (nonspecific)	Express core emotions	Sits tripod, rolls both ways	Raking grasp, transfers hand to hand	Stranger anxiety, looks for dropped objects
9 mo	Listens when spoken to	Mama/Dada (specific), gestures	Separation anxiety	Sits well (hands free), crawling, pulls to stand	Inferior pincer grasp	Object permanence, “peek-a-boo”, bangs two cubes
12 mo	Responds to their name	1 word with meaning, Inhibits with "no"	Points at wanted items, explore from secure base	Walks a few steps	Fine pincer grasp, throws objects	Cause and effect, trial and error, imitation, egocentric pretend play
15 mo	Pointing to body parts, parents, pictures	5 words, jargon	Shared attention	Walks well	Tower 2 blocks, uses spoon	Looks for hidden objects (if seeing it moved)
18 mo	1 Step: Put down your toy	25 words, labels familiar objects	Parallel play	Runs	Tower 4 blocks, scribbles	Symbolic play
2 yo	2 Step: Put down your toy and pick up your backpack	50+ words, 2 word sentences	Testing limits, Tantrums	Jumps on two feet	Tower 6 blocks, draws line, uses fork	New problem-solving strategies without rehearsal
3 yo	3 Step: Put down your toy, pick up your backpack, and meet me outside	200 words, Repeats 3 word phrases	Empathy, Cooperative play, Pretending	Ride a Tricycle	Draws circle and cross, can undress	Simple concept of time, Counts to 3
4 yo	Understands "who, what, where"	Tells a story, 100% intelligible	Fantasy play, has preferred friend	Hop on one foot	Copies square, cuts shape with scissors, buttons shirt	Opposites, Counts to 4
5 yo	Can answer simple questions about stories	500 Words, phonemic awareness	Group of friends, games with rules	Balance on one foot, ride a bicycle	Copies Triangle, Draw person, Independent ADLs	Pre-literacy and numeracy skills

Milestone Red Flags

Age	Missed Milestone Requiring Intervention
2 mo	Lack of Visual fixation No social smile
4 - 6 mo	Fails to track person or object No steady head control No response/turn to sound or voice
6 mo	Decrease/absence of vocalizations
9 - 12 mo	Fails to sit independently
18 mo	Fails to walk independently Does not seek shared attention to object/event with caregiver
24 mo	No single words
36 mo	No 3 word sentences Cannot follow simple commands
> 3 yo	Speech unintelligible Dependence on gestures to follow commands

❖ Forces that may compromise normative development:

- ➢ **Regulatory disturbances:**
  - ■ Including disturbances in sleep or eating (food refusal, night terrors, repeated wakings, problems in impulse control)
    - ○ Indicated in low frustration tolerance
  - ■ Self-stimulatory behaviors, like rocking or head-banging, also indicates a variety of social or regulatory difficulties
- ➢ **Social/environmental disturbances:**
  - ■ Can lead to serious or profound problems in differentiating mother or caregiver (--> PDD, infantile autism)
  - ■ Prolonged separations or neglect, abuse, and exposure to violence leads to increased risk of social and affective disturbances
- ➢ **Psychophysiological disturbances**
  - ■ Includes failure to thrive, recurrent vomiting, wheezing, or chronic skin rashes
- ➢ **Developmental delays**
  - ■ More common in children with complicated perinatal courses
- ➢ **Genetic and metabolic disorders with known neurodevelopmental sequelae**
  - ■ Exposure to toxins (FAS, lead poisoning)
  - ■ CNS damage (TBI, IVH)
  - ■ Prematurity and early illnesses

- May result in hospitalizations or other restrictions of appropriate stimulation early in child's life

- Can lead to altered parent-child interaction and adversely affect development

Preschool Child Development

- **Basic developmental areas:**
  - Robust language learning
  - Emerging thinking and learning capacities (executive functioning, emerging skill of mentalizing)
  - Emerging peer relationships and capacity for imaginary play
  - Separation and individuation
- **Language**: Learns on average about **9 words/day**
  - Sensitive period of language proficiency
  - Specific language and linguistic qualities, such as morphology, grammar, phonology, verbal expression of emotions, and conveyance of information about the past, present, or hypothetical events are best learned in the preschool period
    - **Ease of learning these skills begins to decline at about age 6-7 yo**
- **Emerging minds - starting at 2 yo**
  - Begin to form more stable concepts of the world around them, **begin to think symbolically**
  - Intrinsically motivated to explore, try, and learn
  - Marks the beginning of a concerted attention to a child's skills and abilities that are considered basic to school readiness, as well as basic self-care skills

- Children acquire skills best when caregivers present them with tasks that are just a little too difficult to accomplish independently, but possible with assistance = **"scaffolding"**

- Requires a certain degree of sensitivity to the child's developmental level, referred to as the child's **"zone of proximal development"**

➢ **By age 4-5**, now understands that their thoughts, beliefs, and feelings are their own and that others may feel differently = **theory of mind**

❖ **Play**: Developmental maturity defines the type of play they are capable of creating

➢ Starts around age 2, when able to let a real object stand in for another or something imaginary

➢ **Peer play** = considered to be one of the major developmental tasks of early childhood, starting at **age 3-4,** influenced by caregivers

- Secure attachment, providing peer play opportunities, monitoring peer interactions, modeling and coaching acceptable behaviors, discouraging unacceptable behaviors

➢ Impacted by child's temperament (inhibition vs. excessive exuberance)

➢ Clinical use - those who are traumatized or stressed, unable to use play adaptively and unable to engage in imaginative fantasy play

- Considered a special language for communication with younger children

- Can be used as a means of expression as play may reflect what is concerning to them

❖ **Separation:** Typical for preschool-aged children to struggle between independence and dependence

➢ **Emerging symbolic capacities also help them cope with separations - transitional objects and object constancy**

- Need help in mastering the experience of parting with people outside the family, need to be reassured that their caregiver did not leave because of them

- **Fears and anxiety:** More evident in children **age 2-3** - this is **normative**
  - Keeps very young, small child from straying too far
  - Feels apprehensive not just about new things they encounter, but also about what appears in their thoughts or fantasies
    - Often show their worry and fears in ways that seem unexpected (more anxious they are, the more active and uncontrollable they become)

- **Aggression:** Complex set of behaviors
  - **Reflect a balance between response to frustration vs. assertiveness and individuation**
    - Always express some needs and feelings of the child
    - Those with few words may exhibit greater levels of physical aggression as compared to those who are more verbose, because they have no other means to express their frustration
    - Might be modeled off their parents, other adults, peers, siblings, and screen media
    - Might be a way of **expressing independence** - temper tantrums are expressions of frustrations
    - Must consider the motive/intent of or triggers for aggressive behaviors
      - Important to consider how it might be linked to his **fears or worries**

- For most, physically aggressive behaviors begin to subside by 3rd or 4th birthdays, but verbal aggression increases as they gain more language skills

School Age Child Development:

❖ Primary school through adolescence onset, ages 5-12

➢ Period when child enters society and begins to establish the basis for contributing member of his/her community

❖ Erikson: Industry vs. Inferiority

➢ Attempting to master the basics of industry of our society, to build on academic abilities

➢ Failure to progress in school and in peer context can establish a sense of inferiority, rather than a momentum of a drive for competence

❖ Maturation of CNS:

➢ Brain undergoes a period of rapid growth through age 2

- Then develops at a much slower rate until puberty
- Significant modification of anatomical structures and myelination, almost completed around age 7
- Synaptic pruning in PFC continues as an ongoing process through adolescence

➢ Boys brains are about 10% larger than girls, and this total volume difference persists into adulthood

- Boys have a relatively greater size in the amygdala, while girls have more growth in the hippocampus

- **Speed of processing increases significantly between 6 and 12 yo, which parallels synaptic pruning and myelination**

❖ Major lines of development:

- **Psychosexual:**
  - Per Freud, psychoanalytic theory posits sexual development as biphasic, with "latent" period during the school-age years
  - Contemporary studies of sex hormones do NOT support this biphasic theory
    - Sexual hormones begin a gradual upsurge around age 8 and continues through the pubertal peak
    - Children engage in sexual play with self and others
  - Around age 8, same-sex groupings become polarized
    - Children adopt a firm gender identity by age 3
- **Cognitive:**
  - **Piaget and "Concrete Operations"**
    - Must master important operations that increase their objectivity and their ability to be conventional
    - Two crucial achievements of concrete operational thinking
      - **Classification** (ability to group objects or concepts)
      - **Conservation** (ability to recognize constant qualities and quantities or material even when the material undergoes changes in morphology)

        - Enable the child to deal systematically with hierarchies and categories, series and sequences, alternative and equivalent ways of getting to the same place, and reciprocal relationships

- **Social cognition and morality:** Age 7-8

    - Social comparisons becomes an important component of self and social cognition

    - Sense of morality (appreciation of consequences and justice)

        - Evolves from an egocentric idiosyncratic and often harsh system of evaluations of behavior by punishment to adopting internalized rules for evaluation behavior

    - **Piaget - school age children's morality is in the "interpretation of the rules"**

        - Stage where child understands the spirit of the rule and **can make subjective moral judgments**

    - **Kohlberg** - moral development most children reach as the level of "**conventional morality**"

        1) **Interpersonal Concordance**: Measures behavior and judges it based on whether is please those he looks up to (good girl/boy)
        2) **Orientation toward authority**: Reflect on societal values of duty, respect, and law and order (moral compass now set by social system, rather than immediate social context of family, school, or neighborhood)

- **Emotional**:

    - Most significant emotional issues at this time concern personal worth that is **determined by a sense of competence and place**

        - Competence is not just experience by the child succeeding at a task, but by others' evaluation of his or her performance

- **Erikson -** Emotional risk for school-aged child is the possibility of feeling inferior if the child evaluates him or herself as not being able to accomplish tasks

- By end of middle school, each child has constructed a composite evaluation of his or her own relative areas of competence and weaknesses

- **Fears:** More likely to witness or hear about catastrophic events that could happen to them, and their vulnerability increases as they develop an understanding of irreversibility and inevitability of death

❖ Self in society:

➢ **Kohut** - development of self occurs through a **process of mirroring and idealization**

- In order to develop healthy narcissism, child needs grown-ups to admire him and demonstrate attunement to his feelings (mirroring)

- Needs to be able to look up to his parents and other role models, and aspire to be like them without being unduly distracted by their faults and shortcomings (idealization)

➢ **Baumrind** - classified parenting styles according to **responsivity and demandingness**

1) Authoritative - high responsivity and high demandingness, tend to have the best outcome

2) Neglectful/uninvolved = low responsivity and low demandingness

3) Permissive = high responsivity and low demandingness

4) Authoritarian = low responsivity and high demandingness

➢ **Goodness of fit between parent and child's temperament is constantly in flux**

- Child encounters new challenges and develops new competencies

- Parallels the parental challenge to be sensitive to the child's every changing needs, providing progressive responsibility and supervised autonomy as appropriate

➢ **Peers can be one of the most facilitating influences** in children's development, **or** it can be **disastrously inhibiting**

- Regardless of relative weight placed on these factors, seems that the drive for inclusion and acceptance, and the judgments of other children that the child selects as his peer group

- Impact heavily on the school-age child's development of his own self-image and values

➢ **Schooling:**

- **Vygotsky and zone of proximal development** = distance between the actual developmental level as determined by independent problem solving and level of potential development as determined through problem solving under adult guidance or in collaboration with more capable peers

    - Cooperative learning

Adolescent Development

❖ Definitions

- ➢ **Early Adolescence:** pubescence/prepuberty (may occur as much as 2 yrs. before puberty) through puberty
- ➢ **Middle Adolescence**: approximately 15-18 years old
- ➢ **Late Adolescence:** 18 years old to achievement of a stable adult identity
    - ■ Prolonged education and economic dependence on the family can extend adolescence well into middle/late 20's

❖ Importance of Adolescence

- ➢ Helps us understand adult development and psychopathology, as well as phase-specific reactions to illness
- ➢ Formation of adult character structure begins-organizing/crystallizing personality/qualities
- ➢ Constitutes an increasingly large percentage of the average life cycle (10-15 years in this stage)
- ➢ Exerts a strong influence on the cultural tone of our society - dress, language, music have a marked impact on the adult world

Early Adolescence

- **Physical changes**: Hormonally mediated changes = primary and secondary sexual characteristics

    1) **Adrenarche** - steady increase in adrenal produced androgens, begins as early as ages 6-8, leading to increased skeletal growth and body hair

    2) **Gonadarche** - puberty proper

        - Pulsatile release of GRH produces increased pituitary release of FSH and LH, which then drives the production of gonadal hormones (testosterone in boys, estrogen in girls)

        - Girls begin the process on average at age 9-11, approx 2 years earlier than boys

        - Various stages as classified by Tanner stages I-V

    3) **Increased growth hormone secretion**

- **Neurobiologic changes:**

    - Massive elimination or "**pruning**" of cortical synapses

        - Estimated loss of up to 30,000 synapses/second during adolescence

        - Occurs throughout the brain with significant regional variation in the volume and time course of pruning

        - Growth in myelination improves the efficiency of neural communication throughout the brain

    - **Brain matter changes:**

        - White matter volumes increase linearly throughout childhood and adolescence

- Frontal gray matter volumes peak between 12-14 years of age
- Cortical thickness of the dorso-lateral prefrontal cortex continues to undergo dynamic changes into young adulthood

➢ Relatively late maturation of the prefrontal cortex (which is involved in social cognition)

➢ Relative to children and adults, **adolescents have GREATER activation of the subcortical reward processing structure** (**nucleus accumbens, NAcc**) in response to receipt of large rewards

- Reward activity in the NAcc has also been linked to an increased likelihood of engaging in risk-taking behavior across development

➢ **Increased reactivity** of subcortical emotional processing region (**amygdala**) to sources of **negative emotions** in adolescents, less able to decrease amygdala reactivity to aversive stimuli

❖ **Other biologic changes**: Sleep and appetite patterns, developmental hyperphagia, sleep phase delay (sleeping later, waking up later)

❖ **Cognitive changes: Piaget's "Formal Operations"**

➢ Growing complexity, ability to think about possibilities, and increased speed and efficiency of information processing

➢ Development of formal operational thinking allows for growth in social perspective-taking and decline in childhood egocentrism

➢ Moral reasoning becomes more complex and expands to include orientation to interpersonal relationships, maintenance of social order, notions of social contract and general rights, and reference to universal ethical principles

❖ Sexual and aggressive drives - beginning at age 10

- ➢ Feelings of sexual awareness and attraction make their conscious appearance, linked to rising adrenal androgens

- ➢ At age 10-11, some children become aware of same-sex attractions and homoerotic fantasy

    - Feelings of gender dysphoria become more distressing

- Transition from childhood masturbation to that of adolescence involves more than an increased physiologic capacity for arousal

    - Orgasm, sexual fantasies become intense and important part of teens' psychological inner life, allow to elaborate or explicate their own idiosyncratic and personal erotic scripts

    - Explore and become aware of what is pleasurable, anxiety provoking, transgressive, or deeply compelling their longings

- **Key task of adolescence is to bring these erotic longings adaptively into the interpersonal arena as a vehicle for intimacy, emotional closeness, and the formation of stable partnership**

❖ Relationship changes

- ➢ One or two close friends/confidants/best friends replace the larger group of "playmates" (often still same-sex)

- ➢ Relationships change from cooperation, competition & compromise to collaboration in reciprocally meeting each other's needs

    - Necessary for developing capacity for interpersonal intimacy

- ➢ Consensual validation of self-worth

    - Helps correct self-deception and leftover egocentrism

    - Downside: Possibility of rejection, ostracism and loneliness

❖ Entering Junior High School

- ➢ New & older peers, new teachers, new location & curriculum
- ➢ Loss of familiar boundaries when they're needed most -> limit-testing
- ➢ Not defiance-based but anxiety-based; lack of limits increase anxiety and behavior problems

Middle Adolescence

❖ Social Cognition/Executive Function

- ➢ Interpret/identify emotions in self & others
- ➢ Discern social rules, cause & effect in relationships
- ➢ Develop social reciprocity
    - ■ Sensitivity to others needs/expectations and understanding others' perspective
- ➢ Risk perception improves: ability to detect intentions and deception
- ➢ Teens tend to seek high levels of novelty & stimulation
- ➢ Self-regulation is highly peer-influenced and sensitive to level of emotional arousal

❖ Coping with changing body image

- ➢ Pathologic eating behaviors are common
- ➢ Body is also a representation of adolescent's self

- ➢ Most express dissatisfaction with one or more physical traits, though less than in Jr. High

❖ **Changing relations with parents:** time spent with family decreasing

- ■ Parents are often de-idealized - allows for easier separation
- ■ May alternate between wishes for autonomy and wishes to receive care from parents

- ➢ **Conflicts with parents:**
  - ■ Intensity of conflict usually reflects the parents' or child's perception that vital issues are at stake
  - ■ For parents, issues of loyalty, respect, responsibility, and dangers of sex, substance abuse, and other risky behaviors
  - ■ For adolescents, issues of autonomy, control of their own body, and connections to friends

❖ **Developing satisfying relationships *outside* the family**

- ➢ Turn to peers for companionship, advice, support, and intimacy
  - ■ Teen's specific choices of friends reflect an important and often fateful aspect of self-definition
- ➢ Friends can also be chosen based on perceived virtues or aspects of the self that the adolescent conscious repudiates or feels that he or she lacks
- ➢ **Choice of friend may be used to try on or borrow self-attributes**

❖ **Romantic relationships**

- ➢ Dating numerous people briefly protects from commitments they're not ready for emotionally

- Breakups often exceedingly painful and cause major emotional crisis (sometimes suicidal ideation)

❖ Sexual impulses

- Sexual impulses remain intense
- Mixed messages from within and without regarding impulse control
    - Resolution of these conflicts important to adult character structure
- Sublimation and impulse control not supported societally as in the past

❖ Middle to Late Adolescence

- Faces difficult task of leaving home, finding a job or college, and a mate
- Responsibility shifts from parent(s) to self → failures more difficult
- Subtle maneuvers by parents to keep them dependent & avoid pain of loss

Late Adolescence

❖ Usually begins with High School graduation

- Ends when person comfortable with adult role in society → Indefinite time
- **Tasks:** College or job training, establishing a stable unique self-identity
- Mastery of this stage necessary for successful marriage and/or relationships and parenthood

- **Erikson's concept of "Identity vs. Role Confusion"**
  - Symptoms of Role Confusion
    - Inability to make decisions, sense of isolation, feeling of emptiness, lack of satisfying relationships, poor time concept
    - Sense of urgency, inability to work or concentrate (movie "High Fidelity")
  - Identity confusion sometimes resolved in a "negative identity"/"black sheep"
    - May be a reaction to demands of overambitious parents or deep-seated parental conflicts

The Adolescent Patient

- **Doctor-Patient relationship:** varies somewhat depending on the age of the adolescent
  - Younger pts. need more limits/paternalism
- **Confidentiality:**
  - Limits must be discussed (harm to self/others)
  - Patient must be seen alone for some portion of the assessment (Abuse history, sexual history, & substance history)
    - May not be completely honest about sexuality or drug use
    - Important to be non-judgmental
  - Don't be afraid to ask about suicide (40% contemplate it seriously)

❖ Mood difficulties and perceived stress:

- ➢ Time of rising incidence for major depression, increasing not only with age, but more specifically with advancing pubertal status

- ➢ Marked increase in emotional lability, depressed mood, and negative emotions

❖ Risk taking behaviors:

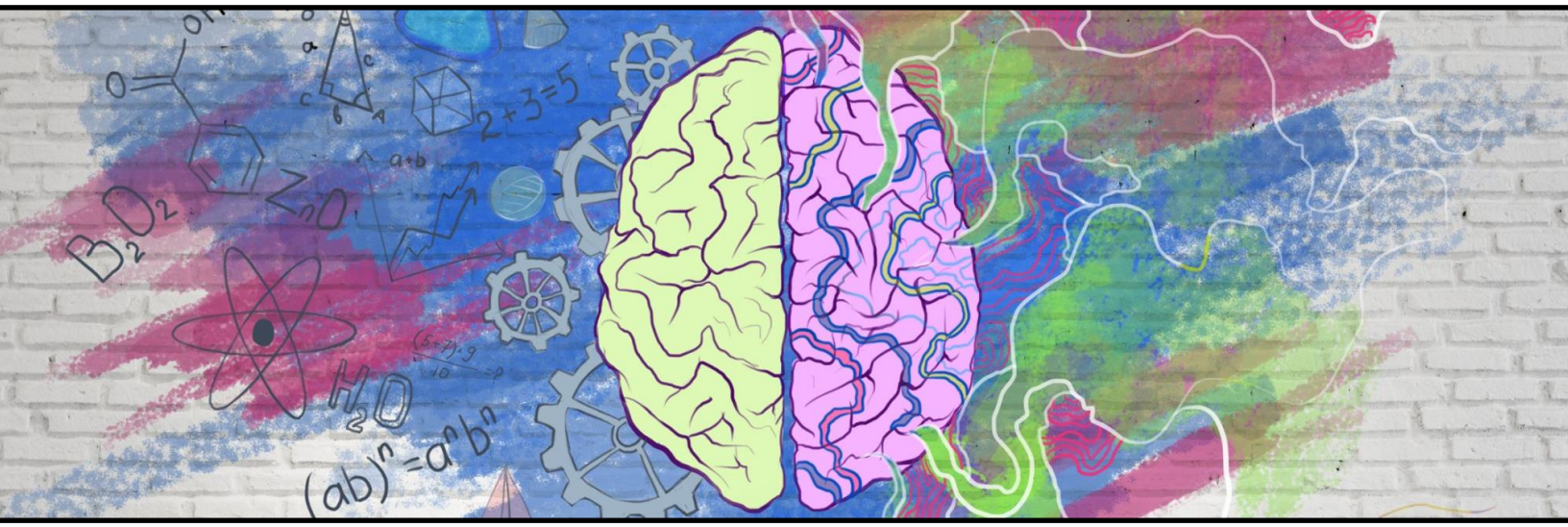
- ➢ Certain patterns of autonomic reactivity may also predispose to increased risk taking under certain circumstances

    - ■ Important to distinguish between occasional experimentation and persistent patterns of dangerous behavior

- ➢ Shifts in reward sensitivity occur early in adolescence, and lead adolescents to seek higher levels of novelty and stimulation

    - ■ More slow-maturing regulatory competencies that might check this novelty and stimulation-seeking do not come online until later in adolescence

A Ninja's Guide to Pediatric Clinical Neurology



Common Neurological Conditions

Disease	Genetics	Diagnostic Test	Clinical Manifestation	Psychiatric Features
Wilsons	• Chromosome 13 • Mutation in ATP7B → Copper accumulation • Autosomal recessive	Serum ceruloplasmin, copper levels; slit lamp exam; 24 hr urinary copper	**Cog:** Rare in early childhood, adults with deficits in attention, executive function, encoding **Phys:** Kayser Fleischer rings, parkinsonism **Med:** Liver disease, seizures, migraines	Dementia, depression, anxiety, psychosis
Neurofibromatosis I (von Recklinghausen)	• Chromosome 17 • Mutation of NF1 tumor suppressor gene (Ras GTPase activating protein neurofibromin) • Autosomal dominant	FISH analysis, direct sequencing, long range RT-PCR, then southern blot	**Cog:** Mild ID, Learning disabilities **Phys:** Cafe-au-lait spots, Lisch nodules, cutaneous neurofibromas **Med:** Optic gliomas, pheochromocytomas	ASD, dysthymia, depression, anxiety, 4x risk of suicide
Neurofibromatosis II	• Chromosome 22 • Mutation NF2 gene (Merlin or schwannomin protein) • Autosomal dominant	FISH analysis, direct sequencing, long range RT-PCR, then southern blot	**Cog:** Weak phonological skills, processing speed, and reading related to hearing loss **Phys:** Juvenile cataracts **Med:** Bilateral acoustic schwannomas, meningiomas, ependymomas	Depression, anxiety
Tuberous Sclerosis	• Mutation of TSC1 (harmartin) or • TSC2 (tuberin)	FISH analysis, direct sequencing, long range RT-PCR, then southern blot	**Cog:** Mild to Severe ID **Phys:** Ash leaf spots, shagreen patches **Med:** angiofibromas, tumors (CNS tubers, retinal hamartomas, cardiac rhabdomyomas, renal angiomyolipoma	ADHD, ASD, aggression, anxiety, depression, sleep problems
Sturge-Weber	• Non-inherited (somatic) developmental anomaly of neural crest derivatives • Activating mutation of GNAQ gene	MRI, CT, Susceptibility weighted imaging (SWI) for brain abnormality	**Cog:** No ID to Severe ID (can be related to seizure d/o), learning disorders **Phys:** Port-wine stain, episcleral hemangioma **Med:** Seizures, headache, glaucoma	Brief ictal and interictal psychosis, behavioral symptoms, mood disorders, inattention, sleep disorders, substance use

Disease	Genetics	Diagnostic Test	Clinical Manifestation	Psychiatric Features
Klinefelter	• Male; 47, XXY • Meiotic nondisjunction	Karyotype	**Cog:** No ID to Mild ID, Deficits in speech, language acquisition, short-term memory, data-retrieval skills, reading, dyslexia **Phys:** Tall, testicular atrophy, long extremities, eunuchoid body, gynecomastia **Med:** Infertility, osteoporosis	ADHD, schizophrenia, depression, anxiety
Turner	• Female; 45, XO • Meiotic nondisjunction	Karyotype	**Cog:** Rare mild ID, Visual-spatial learning deficits - executive function **Phys:** Short stature, shield chest, web neck **Med:** Ovarian dysgenesis, bicuspid aortic valve, coarctation, horseshoe kidney	ADHD, stress-precipitated psychosis, depression

Seizure Disorders in Children

Syndrome	Clinical Features	EEG Findings	Treatment	Prognosis
Infantile spasms	**Onset:** 4-8 months **Description:** Repetitive episodes of brief flexion or extensions of neck, trunk, extremities, lasting 10-30 seconds	High-voltage bilaterally asynchronous, and irregular high-voltage spike and wave	ACTH, Benzos, Vigabatrin, Epilepsy surgery when focal onset	Guarded: Loss of developmental milestones with onset of seizures
Febrile seizures	**Onset:** 6 mo-6 yrs (peak 18-24mo) **Description:** Usually simple, less than 15 minutes, generalized (1/3 may have complex seizures)	Generally normal	Control fever, anticonvulsant prophylaxis not indicated	Excellent: unless signifying underlying sepsis or meningitis
Lennox-Gastaut	**Onset:** Common in preschool children **Description:** Mixture of myoclonic, generalized tonic-clonic, partial, absence, atonic, and status epilepticus, common after encephalopathy	Abnormal background activity, slow spike-waves, and multifocal abnormalities	Valproic acid, Benzos, Ketogenic diet	Poor: High association with behavioral problems and intellectual disability
Landau-Kleffner	**Onset:** 3-5 years, boys more common **Description:** Focal, generalized tonic-clonic, atypical absence, partial complex seizures, Loss of language skills (previously healthy), 70% have seizures and behavioral problems	Independent bilateral high-amplitude spike and wave, more apparent in nonREM sleep	Valproic acid, prednisone, speech therapy	Variable: Significant speech dysfunctions as adults

Syndrome	Clinical Features	EEG Findings	Treatment	Prognosis
Absence seizures	**Onset:** 3-13 years, peak 6-7 years **Description:** Sudden, brief, frequent episodes of unconsciousness, may be accompanied by automatisms, clonic, atonic, or autonomic components	Regular symmetrical generalized spike and wave complexes with a frequency of 3 Hz	Ethosuximide	Good: Spontaneous remission by 12 years
Benign childhood epilepsy with centrotemporal (Rolandic) spikes	**Onset:** peak 9-10 years (avg 2-14 yrs) **Description:** Occur in sleep, child awakened with unilateral tonic-clonic of face, paresthesia of tongue/cheek, then conscious and aphasic for a couple minutes	Repetitive spike discharges confined to centrotemporal area with normal background activity	Frequent seizures controlled by carbamazepine	Good: Spontaneous remission by adolescence
Juvenile myoclonic epilepsy	**Onset:** 12-16 years **Description:** Myoclonic jerks on awakening that decrease later in day, most develop early morning tonic-clonic seizures	4-6 second irregular spike and wave enhanced by photic stimulation	Valproic acid Oxcarbazepine may worsen	Good: Valproic acid required for life
Psychogenic Nonepileptic Seizures	**Onset:** Late adolescence, young adult, girls more common **Description:** Involuntary episodes of movement, sensations, or behaviors that do not result from abnormal cortical discharges, resistance to several AEDs, multiple seizures per day on most days	No abnormal brain activity, Video EEG prefered for observation	Psychotherapy, treat underlying psychiatric disorder	Guarded: Diagnosis may precipitate spontaneous recovery and will prevent morbidity from inappropriate treatment

Neuromuscular Disorders

Type	Age of Onset	Clinical Features	Diagnosis	Genetics	Prognosis
Becker muscular dystrophy	2-16 years, only males	Weakening arms, legs, spine, may cause heart problems	CPK most specific, genetic testing, muscle biopsy	Dystrophin gene, X chromosome	Can live into adulthood
Congenital muscular dystrophy	Presents at birth	weakening muscles, joint stiffness, and shortening of muscles, primarily affects voluntary muscles	CK level, nerve conduction, EMG, brain MRI, muscle biopsy, genetic or metabolic testing	Variable genetic causes	Progression varies, can shorten lifespan
Duchenne muscular dystrophy	2-6 years, only males	Weakening arms, legs, spine, breathing and/or heart issues	CPK most specific, genetic testing, muscle biopsy	Dystrophin gene, X chromosome	Fast progression, usually live to early 20s
Spinal muscular atrophy	Birth-18 mo for Types I-III	Weakness and muscle wasting in limbs, respiratory, bulbar or brainstem muscles	Prenatal and postnatal genetic testing	SMN1 gene deletion	Respiratory infections cause most deaths
Myotonic dystrophy	Anytime from childhood to adulthood	Stiffening and spasms of muscles, overall muscle weakness, can affect CNS	Genetic testing, EMG, muscle biopsy	Trinucleotide repeat expansions in DMPK or CNBP genes	Slow progression, decreased lifespan

Autosomal Trisomies

Disease (Incidence)	Genetics	Diagnostic Test	Clinical Manifestation	Psychiatric Features
Down (1:700)	Trisomy 21 95% Meiotic nondisjunction 4% Robertsonian translocation 1% Mosaicism	Karyotype	**Most Common Genetic ID** **Cog:** Mild/Mod - Severe ID, deficits in: expressive language, auditory processing **Phys:** flat facies, epicanthal folds, single palmar crease, gap between 1st and 2nd toes **Med:** Duodenal atresia, Hirschsprung disease, congenital heart disease (AV septal defect), Brushfield Spots, early onset Alzheimer's, ALL, AML	>50% ADHD, defiance 30% Anxiety, Depression 10% Autism
Edwards (1:8000)	Trisomy 18	Karyotype	**Cog:** Severe ID **Phys:** Rocker bottom feet, micrognathia, low set ears, clenched hands/overlapping fingers, prominent occiput **Med:** Congenital heart disease	Death within 1 year of birth
Patau (1:15000)	Trisomy 13	Karyotype	**Cog:** Severe ID **Phys:** Rocker bottom feet, microphthalmia, microcephaly, cleft lip/palate, polydactyly **Med:** Congenital heart disease, holoprosencephaly, cutis aplasia	Death within 1 year of birth

Microdeletions

Syndrome	Genetics	Diagnostic Test	Clinical Manifestation	Psychiatric Features
Rett	MECP2 Deletion, missense or nonsense mutation	MECP2; del/dep testing	**Cog:** Severe - profound ID, limited language **Phys:** hand-wringing (purposeless hand movement), unusual eye movement/blinking, scoliosis **Med:** Loss of coordination, breathing issues, seizures, irregular heart rhythm	- Stage I: Decreased interactions - Stage II: Social withdrawal, irritability, autistic-like behaviors, sleep disturbance - Stage III: Improvement in alertness, interactions, ongoing sleep disturbance - Stage IV: Persistence of poor communication, irritability
Prader-Willi	15q11-q13; Imprinting-loss of paternal contribution	Methylation PCR followed by FISH	**Cog:** Mild ID, deficits in: short-term memory, auditory processing, socialization, maths, sequential processing **Phys:** Short stature, obese, small hands/feet, dysmorphic facial features **Med:** Obesity, metabolic disease	Hyperphagia, skin picking, OCD, explosiveness, lability, depression, psychosis, social cognitive deficits, cognitive inflexibility
Angelman	15q11-q13; Imprinting-loss of maternal contribution	Methylation PCR followed by FISH, UBE3A sequencing	**Cog:** Severe to profound ID, limited expressive speech **Phys:** Always smiling, Unexpected laughter, hypotonic, dysmorphic facial features, ataxic puppet-like gait **Med:** Seizures	Social disinhibition, fear of crowds, ADHD, sleep problems
Williams	Microdeletion 7q11.23	Locus-specific FISH or CGH microarray	**Cog:** Mild ID, severe visuospatial construction deficits, strong verbal skills **Phys:** "Elfin" facies **Med:** Hypercalcemia (increased Vitamin D sensitivity), cardiovasc problems	ADHD (>50%), attention seeking, tantrums, OCD, fears, anxiety, depression, sleep problems

Syndrome	Genetics	Diagnostic Test	Clinical Manifestation	Psychiatric Features
DiGeorge Syndrome, Velocardiofacial Syndrome, 22q11.2 deletion	Microdeletion 22q11.2, aberrant development of 3rd/4th branchial pouches	Locus-specific FISH or CGH microarray	**Cog:** Mild ID, deficits in: receptive, higher order language skills, abstract reasoning, visuospatial **Phys/Med:** CATCH 22 **C -** Cleft palate **A -** Abnormal facies **T -** Thymic aplasia, T cell def **C -** Cardiac defects **H -** Hypocalcemia 2/2 parathyroid aplasia	Emotional dysregulation, ADHD, anxiety, phobias, ASD, 30% psychosis
Smith-Magenis	Microdeletion 17p11.2	Locus-specific FISH or CGH microarray	**Cog:** Mild to Severe ID, deficits in: short-term memory, visual motor coordination, sequencing, response speed, speech delay (expressive) **Phys:** Broad square face, prominent forehead, deep-set eyes, short nose **Med:** Skeletal abnormality, short stature, hearing loss	Sleep disturbance, self-harm, stereotypy, egocentric, delayed empathy
Cri-du-chat	Microdeletion of 5p	Locus-specific FISH or CGH microarray	**Cog:** Mod to Severe ID, expressive language deficits **Phys:** Cat-like cry, microcephaly, dysmorphic facial features, low set ears, micrognathia, epicanthal folds **Med:** Psychomotor disability (delays in head control, sitting, walking), poor feeding, Cardiac defects (ductus arteriosus, VSD), ear infections, scoliosis	ADHD, Self-harm

Triplet Repeat Expansion

Disease	Genetics	Diagnostic Test	Clinical Manifestation	Psychiatric Features
Fragile X	CGG repeats, X-linked defect affecting increased methylation and decreased expression of the FMR1 gene	FMR1 PCR and Southern blot for CGG repeat length	**Most Common Inherited ID** **Cog:** Mild/Mod to Severe ID, deficits in: abstract thinking, sequential cognitive processing, short-term memory, maths, visual-motor processing **Phys:** Long face, large jaw, large everted ears, postpubertal macroorchidism **Med:** Mitral valve prolapse	Inattention, hyperarousal, social anxiety, social cognition/communication problems 25-50% Autism
Friedreich's Ataxia	GAA repeats, Chromosome 9, FXN gene - encodes Frataxin (iron binding protein), Autosomal recessive	FXN PCR and Southern blot for GAA repeats	**Cog:** poorer performance in verbal fluency, working memory, and social cognition **Phys:** Childhood kyphoscoliosis, staggering gait, frequent falls, dysarthria, pes cavus, hammer toes, DM, HOCM **Med:** Impaired mitochondrial fxn leads to spinal cord degeneration --> muscle weakness, decreased DTRs, loss of vibratory sense, proprioception	Depression
Huntington's	CAG repeats, Chromosome 4 (HTT gene), Autosomal dominant	Family history, MRI, HTT PCR and southern blot for CAG repeats	**Cog:** Mild to Major cognitive impairment **Phys:** Onset 20-50 yo (anticipation), Choreiform movement **Med:** MRI - Atrophy of caudate with ex vacuo dilation of frontal horns	Aggression, Depression, Dementia

Metabolic Disorders

Disease	Genetics	Diagnostic Test	Clinical Manifestation	Psychiatric Features
Lesch-Nyhan	• Deficiency of hypoxanthine-guanine phosphoribosyltransferase (HGPRT) → defective purine salvage • Excess uric acid production and de novo purine synthesis • X-linked Recessive inheritance	Urine urate/creatinine ratio (>2.0 suggestive) followed by HGPRT enzyme activity determination	**Cog:** Mild-Mod ID **Phys:** Self mutilation, dystonia **Med:** Hyperuricemia, gout	Self mutilation, anxiety, vulgar statements, compulsive aggression
Phenylketonuria	• PAH gene, Deficiency of phenylalanine hydroxylase or tetrahydrobiopterin cofactor • Build up of phenylalanine • Autosomal Recessive inheritance	Blood level Phe (>4mg/dL)	**Cog:** If untreated, Mod-Severe ID **Phys:** Growth retardation, fair skin, eczema, musty (mousy) body odor **Med:** Seizures	Early treated children: ADHD, low self-esteem and social competence, depression, anxiety
Tay-Sachs	• HEXA gene, Deficiency of hexosaminidase A • Build up of GM2 gangliosides • Autosomal Recessive inheritance	Blood level hexosaminidase (low/absent)	**Cog:** Mod-Severe ID **Phys:** Onset 3-8 mo, exaggerated startle reflex, retinal cherry-red spot **Med:** Seizures, psychomotor arrest	Death within 3-5 years
Niemann-Pick Type A	• SMPD1 gene, Deficiency of sphingomyelinase • Build up of sphingomyelin • Autosomal Recessive inheritance	Blood level sphingomyelinase	**Cog:** Severe ID **Phys:** Onset 1-6 mo, splenic enlargement, sometimes retinal cherry-red spot **Med:** Psychomotor arrest	Death within 3 years
Metachromatic Leukodystrophy	• Deficiency of cerebroside sulfatase / arylsulfatase A • Build up of sulfatides • Autosomal Recessive inheritance	Blood level cerebroside sulfatase, then urine level sulfatides	**Cog:** Loss of expressive language, then complete communication **Phys:** Progress motor function loss **Med:** Central/peripheral demyelination	Auditory hallucinations, bizarre delusions

Disease	Genetics	Diagnostic Test	Clinical Manifestation	Psychiatric Features
Krabbe Disease	• Deficiency of galactocerebrosidase • Build up of galactocerebroside and psychosine destroys myelin sheath • Autosomal Recessive inheritance	Blood level of GALC enzyme	**Cog:** Developmental regression, severe ID **Phys:** Onset 3-6 mo, irritability, crying **Med:** Seizures, peripheral neuropathy, optic atrophy, globoid cells	Death within 2 years
Galactokinase Deficiency	• Mutation of GALK1 gene • Deficiency of galactokinase • Build up of galactitol • Chromosome 17 • Autosomal Recessive inheritance	Blood level of GALK enzyme	**Cog:** rare cognitive delay **Phys:** Infantile cataracts, failure to track objects, no social smile **Med:** Rare-Pseudotumor cerebri, hypergonadotropic hypogonadism	Rare ADHD, anxiety
Classic galactosemia	• Deficiency of galactose-1-phosphate uridyltransferase • Build up of galactose-1-P • Autosomal Recessive inheritance	Blood level of GALT enzyme	**Cog:** Mild to profound ID, depends on removal of lactose, language and math difficulties **Phys:** Infantile cataracts, Jaundice, hepatomegaly **Med:** Failure to thrive	behavioral disorder
Hurler Syndrome	• Deficiency of alpha-L-iduronidase • Build up of heparan sulfate, dermatan sulfate • Autosomal Recessive inheritance	Urine heparan and dermatan sulfate Confirmed by enzyme deficiency in leukocytes, fibroblasts	**Cog:** Severe ID, developmental regression **Phys:** Gargoylism, corneal clouding, Hepatosplenomegaly **Med:** Airway obstruction, cardiovascular disease	Mild behavioral problems
Hunter Syndrome	• Deficiency of iduronate-2-sulfatase • Build up of heparan sulfate, dermatan sulfate • X-linked recessive inheritance	Testing enzyme activity in skin fibroblasts	**Milder Hurler Syndrome** **Phys:** No corneal clouding	Aggressive behavior

Disease	Genetics	Diagnostic Test	Clinical Manifestation	Psychiatric Features
Acute Intermittent Porphyria	Defect Porphobilinogen deaminase/ hydroxymethylbilane synthase → accumulated porphobilinogen, and urine coporphobilinogen	Spot urine test for porphobilinogen	**5P's:** • Painful abdomen • Port wine-colored urine • Polyneuropathy • Psychological disturbance • Precipitated bydrugs, alcohol, starvadon	Delirium, agitation, psychosis, anxiety, somnolence
Homocystinuria	Mutation on 21q22.3 → cystathionine-B synthase gene → elevated homocystine, homocysteine, methionine	Urine homocysteine or methionine Blood level homocysteine Genetic test - CBS	**Cog:** ID, learning disorder **Phys:** Skeletal abnormalities (tall, long extremities, pectus excavatum, scoliosis) **Med:** Ectopia lentis, risk of thrombus formation	Schizophrenia, depression, OCD
Adrenoleuko-dystrophy	• Mutation of ABCD1 → loss of peroxisomal lignoceroyl-CoA ligase → build up of very long-chain fatty acids (VLCFA) in peroxisome, in myelin of CNS, adrenal cortex, and Leydig cells • X-Linked	Blood test for Very Long-Chain Fatty Acid and Branched-Chain Fatty Acid	**3 presentations:** • Childhood cerebral form: ADHD-like symptoms, cognitive impairment, vision and hearing loss, gait abnormality, dysarthria and dysphagia • Adrenomyeloneuropathy: later onset, slowly progressive; mood and psychotic symptoms • Addison's disease: adrenal findings only	ADHD, mood, psychosis

Tic Disorders

A Ninja's Summary: *Practice Parameter for the Assessment and Treatment of Children and Adolescents With Tic Disorders*

(Updated 2013)

Why Care? Child and Adolescent Psychiatrists are usually the first contact for assessment and treatment of tic disorders; often discovered when treating another psychiatric or neurodevelopmental disorder.

Clinical Presentation and Course:

- **Chronic Tic Disorder:**
  - **Age of onset -** average 7 yo, as young as a few months of age
  - **Severity -** peaks from 9-12 yo, then decreased prevalence afterward
  - **Remission** - 65% have remission (or marked attenuation) by 18-20 yo
  - **Impairments -** daily function, psychosocial distress in family and patients
    - Stress, Anxiety, and Depression associated with worsening tics

Epidemiology:

- **Prevalence:** CTD estimated at 0.5-3%, Transient tics estimated at 5%
  - Gender ratio boys 2:1
  - Higher rates in white compared to African American youth

Etiology:

- **Pathophysiology:** result of dysfunctional cortico-striatal-thalamo-cortical circuits, usually those serving motor function
    - MRI - loss of normal asymmetry of the caudate nucleus
    - Functional MRI - decreased activity in basal ganglia
        - Greater activity in sensorimotor regions (primary motor cortex, putamen) and less activity in anterior cingulate and caudate during tics → deficient engagement of inhibitory circuits
- **Genetics:**
    - 10-100 fold increased risk of CTD among first-degree relatives
    - Twin studies - 77-94% concordance (monozygotic), 23% concordance (dizygotic)
- **Environment:**
    - Sensitivities: temperature changes, stress, illness, fatigue can exacerbate tics
- **Infection:**
    - PANDAS/PANS - childhood acute onset OCD and/or tics following a strep infection
        - Symptoms: separation anxiety, nightmares, personality change, oppositional behaviors, deterioration in math/writing skills

Differential Diagnosis: *See Differential Diagnosis of Repetitive Movements Chart*

- **Drugs that may worsen tics:** SSRIs, lamotrigine, cocaine
    - ***No evidence that stimulants worsen tics***
- **CNS Insults:** Refer for neurological assessment when tics occur in the context of motor and cognitive dysfunction

Tic Disorder Terms and Definitions

Term	Definition
Tic	Sudden, rapid, recurrent, non-rhythmic movement or vocalization
Simple tic	Rapid, meaningless
Simple motor tic	Fast, brief movements, involve 1-3 muscle groups (eye blinking, shoulder shrug, head jerk, facial grimace)
Simple vocal tic	Solitary, meaningless sounds/noises (grunting, sniffing, snorting, throat clearing, humming, coughing, barking, screaming)
Complex tic	Purposeful, elaborate, orchestrated
Complex motor tic	Sequentially and/or simultaneously produced coordinated movements (taping bottom of foot)
Complex vocal tic	Linguistically meaningful utterances or verbalizations, partial words (syllables), words out of context, repeated sentences, coprolalia, palilalia, echolalia
Premonitory urges	Sensory phenomena that precede and trigger the urge to tic
Tic suppression	Volitional suppression of tics for varying periods of time with social pressure or focused tasks (Not associated with tic rebound)
Chronic Tic Disorder	Long-last neuropsychiatric disorder with childhood onset, characterized by multiple motor and/or vocal tics with waxing/waning of severity, commonly comorbid with behavioral problems, ADHD, and OCD
Persistent motor or vocal tic disorder	Tics limited to one of the domains
Tourette's disorder (TD)	Both motor and vocal tics present at some point in the illness
Provisional tic disorder	Tics present for less than 1 year

Differential Diagnosis of Repetitive Movements

Repetitive Movement	Description	Typical Presenting Disorder	Differentiation from Tics
Tics	Sudden, rapid, recurrent, non-rhythmic vocalization or motor movement	Transient tics, TD, CTD	-
Dystonia	Involuntary, sustained, or intermittent muscle contractions that cause twisting and repetitive movements, and/or abnormal postures	DYT1 gene, Wilson's, myoclonic dystonia, extrapyramidal symptoms due to dopamine blocking agents	Sustained muscle contractions
Chorea	Involuntary, random, quick, jerking movements, usually proximal extremities, that flow from joint to joint	Sydenham's chorea, Huntington's chorea	Non-repetitive, variable frequency and intensity
Stereotypies	Stereotyped, rhythmic, repetitive movements or patterns of speech, with lack of variation over time	Autism, stereotypic movement disorder, intellectual disability	No change in body location or movement type over time No premonitory urge
Compulsions	A repetitive, excessive, meaningless activity or mental exercise that a person performs in an attempt to avoid distress or worry	OCD, anorexia, body dysmorphic disorder, hoarding disorder, trichotillomania, excoriation disorder	Age may allow for clear differentiation as introspection improves
Myoclonus	Shock-like involuntary muscle jerk that may affect a single body region, 1 side of the body, or the entire body; may occur as a single jerk or repetitive jerks	Hiccups, hypnic jerks, Lennox-Gastaut syndrome, juvenile myoclonic epilepsy, mitochondrial encephalopathies, metabolic disorders	Arrhythmic twitches of muscles
Habits	Action or pattern of behavior that is repeated often	Onychophagia (fingernail biting)	Goal directed
Akathisia	Unpleasant sensations of "inner" restlessness, often prompting movements in an effort to reduce the sensations	Extrapyramidal adverse effects from dopamine blocking agents; anxiety	Intense desires to walk
Volitional Behaviors	Behavior that may be impulsive or due to boredom like tapping peers, making sounds (animal noises)	ADHD, ODD, sensory integration disorders	Identified function behind behavior

Adapted from Practice Parameter Table 1

Comorbid Psychiatric Disorders: Patients with CTD frequently meet criteria for 2 or more conditions

- **Obsessive-Compulsive Disorder**
  - Bidirectional association between CTD and OCD
  - Difficult to distinguish tapping tics and tics that feel "just right"
- **Attention-Deficit/Hyperactivity Disorder**
  - 50% of children with CTD also meet criteria for ADHD
    - Worse academic achievement and social adjustment than just CTD alone
- **Learning Disabilities**
  - 23% of patients with CTD have learning disabilities (Higher if ADHD present)
    - Risk higher in male patients with hx of perinatal problems and tics
- **Autism Spectrum Disorders**
  - 4.6% of youth with TD have ASD
    - Assess to determine symptom onset, course, language development, and social ability to determine which disorder is primary

Recommendation 1: Routine screening for unusual movements, stereotypies, tics, and family history of tic disorders in Psych Assessment **(CS)**

- **Assessment:** Assess previous meds and dosages before starting medication
  - Parents may attribute sniffing, coughing, blinking as allergies or visual issues

- **Parent-rated screening tools:** Child Behavior Checklist (CBCL) and Swanson, Nolan, and Pelham (SNAP)

Recommendation 2: If screening positive, do a more thorough assessment for tic disorders **(CS)**

- Assessment: age of onset, type, frequency, alleviating and aggravating factors, family history of tics
    - May use several parent-report rating scales for baseline

Recommendation 3: Investigate for general medical conditions and substance etiologies **(CS)**

- **Medical investigation warranted:** sudden onset of severe tics, atypical tics, mental status changes on MMSE
    - Consider complete basic labs, culture, rapid viral tests

Recommendation 4: Look for comorbid psych disorders **(CS)**

- Assess for externalizing/internalizing psych disorders, current social functioning, and developmental delays

Recommendation 5: Include education about course, prognosis, and treatment planning with classroom-based accommodations for those with CTD **(CS)**

- **25% of tics continue into adulthood**
- Review exacerbating factors (illness, stress, heat) and alleviating factors (rest, listening to music), resources in the community for support
    - Classroom accommodations including IEP to guide teachers
        - Most common tool - ignoring tics and leave the room as needed

Recommendation 6: Treatment should address the levels of impairment and distress caused by tics *and* comorbid conditions **(CS)**

- **Mild-Moderate Tics -** may not need intervention beyond psychoeducation
  - Consider risks vs benefits or treatment
  - Comorbid condition may need more treatment and attention than tics

Recommendation 7: Consider behavioral interventions when tics cause impairment, are moderate in severity, or if behavioral-responsive psychiatric comorbidities are present **(CG)**

- **Behavioral Intervention treatment theory:**
  - Most experience tics as voluntary
    - **Premonitory urge:** many describe a tension that builds that is released with tic expression (similar to OCD)
      - Target for behavioral intervention
- **Habit Reversal Training (HRT)**
  - **Components:** awareness training, building a competing response, and social support
  - **Effectiveness:** 50% response rate, 30% reduction in tic severity, 50% reduction in tic-related impairment
- **Comprehensive Behavioral Intervention for Tics (C-BIT)**
  - Training to be more aware of tics and the urge to tic
  - Training to do competing behavior when having the urge to tic
  - Making changes to daily activities to reduce tics

Recommendation 8: Medications should be considered for moderate to severe tics causing severe impairment or when medication responsive psychiatric comorbidities are present that target both tic symptoms and comorbid conditions **(CG)**

- ➢ Results in symptom reduction but not remission
- ➢ FDA approved medications for **Severe** Tourette Syndrome are haloperidol and pimozide
- ➢ Atypical antipsychotics and alpha-2-adrenergic agonists are most commonly used

❖ Tic Disorder and Disruptive Behavior Disorder

- ➢ Antipsychotics → use for aggressive/anger outbursts + tics

❖ Tic Disorder and ADHD

- ➢ Concern about stimulants worsening tics → May occur only at higher doses
- ➢ Alpha-2-adrenergic agonists and Atomoxetine may benefit both conditions
- ➢ **Mechanism of action** - activates the presynaptic auto-receptors in the locus coeruleus, thereby reducing norepinephrine release

<u>Review of Studies for Tic Disorder AACAP Guidelines</u>: See Appendix A

❖ Summary of Studies for Tic Disorders

- ➢ Pimozide and Haldol both showed benefits and are FDA approved for Tic Disorder (Tourette's Disorder)
- ➢ Antipsychotics like Risperidone showed some benefit and may help concurrent mood issues and aggressive behavior

- Monitor for metabolic side effects, hyperprolactinemia

- Aripiprazole has less effect on prolactin and metabolic issues, with some benefit for concurrent OCD

- Alpha-2-Adrenergic Agonists like clonidine and guanfacine have been found to be helpful in tic reduction and concurrent ADHD

- Atomoxetine is a good alternative for ADHD and Tic disorders

- Alternatives include dopamine agonists, tetrabenazine, Antidepressants (MAOIs, TCAs), topiramate, and other agents may be considered for tic disorders.

❖ Alternative treatments for tic disorders

- Deep brain stimulation, repetitive magnetic stimulation (TMS), special diets, and dietary supplements lack empirical support for the treatment of chronic tic disorder (CTD)/ Tourette's Disorder (TD) and are not recommended

Enuresis

A Ninja's Summary: *Summary of the Practice Parameter for the Assessment and Treatment of Children and Adolescents with Enuresis*

(Updated 2004)

Why Care? Enuresis is a frequently encountered symptom presenting both alone and with other disorders in child psychiatric evaluations.

Etiology & Clinical Presentation

- Genetic Component: children have about 44% incidence if one parent has enuresis, and 77% with two parents
    - 15% incidence in children from non enuretic families
- Clinical Presentation:
    - No arousal to bladder distention, sleep apnea, developmental immaturity, regressive symptom following stress or trauma

Assessment

- Interview both child and parents with great sensitivity to the emotional consequences
- Routine laboratory tests - need only include urinalysis and sometimes urine culture
    - First morning specific gravity may help predict who will respond to desmopressin acetate (DDAVP) treatments.
- 2-week baseline record of wet and dry nights

Treatment

- Urologic referral and treatment indications include daytime wetting, abnormal voiding, history or evidence of infection, and genital abnormalities.

- Mechanical pressure on the bladder is suggested by constipation, encopresis, or palpable stool impaction.

    - A healthy bowel regimen in these cases will often eliminate enuresis.

- Individual psychotherapy, crisis intervention and family therapy may be helpful if psychological problems are present

- **Uncomplicated monosymptomatic primary nocturnal enuresis** - suspected when the history and physical examination do not point to a specific etiology and urinalysis is normal

    - **Supportive approaches**: education, demystification, ensuring that no punishment is administered for episodes, journal keeping, fluid restriction, and night awakening

    - **First line treatment is behavioral**: **Bell and Pad**, use of a written contract, thorough instruction, frequent monitoring, overlearning, and intermittent reinforcement before discontinuation

- Bladder-stretching exercises have not shown consistent effectiveness.

- No empirical evidence suggests efficacy of hypnotherapy, dietary manipulation, and desensitization to allergens.

Pharmacology

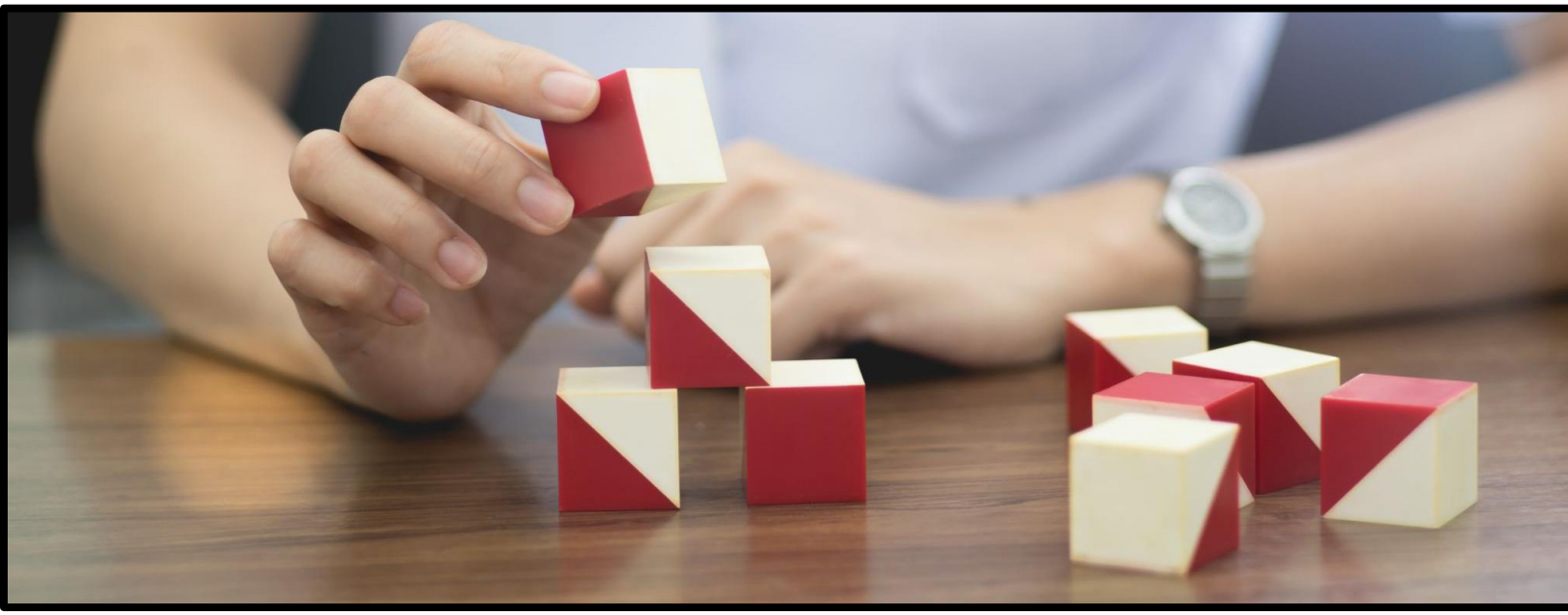
- **Imipramine:**

    - A single dose of imipramine 1 to 2.5 mg/kg can be used if conditioning treatment fails or is not feasible.

- ➢ Documented effectiveness is 40-60%, but the relapse rate is as high as 50%
    - ■ A pretreatment EKG may be obtained because of the possibility of cardiac arrhythmia associated with TCAs including imipramine.

- ❖ **DDAVP:** a synthetic analog of the antidiuretic hormone (ADH) vasopressin that, when taken at bedtime, decreases nightly urine production
    - ➢ It is available both as an intranasal spray dosed 10-40 μg (1-4 sprays) nightly, or in 0.2 mg tablets for doses of 0.2-0.6 mg nightly.
    - ➢ If intercurrent illness is part of the picture, electrolyte monitoring may be merited, as water intoxication is a rare side effect.
    - ➢ Documented success rates are 10-65% with relapse rates as high as 80%.
    - ➢ Combining DDAVP with a sustained-release anticholinergic agent may be more effective.

A Ninja's Guide to Psychological and Neuropsychological Assessment



Objectives of Psychological & Neuropsychological Assessment:

To provide a detailed description of a child's behavioral, emotional, and cognitive functioning, assist with diagnosis, and provide direction for intervention.

- **Final Analysis:** Takes into account test selection, administration, and interpretation of the objective/standardized measures with consideration of the developmental and environmental context.

Psychological Assessment: Designed to measure individual differences by categorizing and classifying individuals based on observations under uniform conditions.

- **Domains:** intellectual, social, emotional, neuropsychological, and adaptive behavior

- **Intelligence Testing:** Debate surrounds the definition of intelligence, interpretation of testing, and use of those results.

  - **Ultimately, intelligence is a construct that is not unified or fixed**

  - **Intelligence: a Multifaceted Entity** → New emphasis on analysis of individual strengths and weaknesses and identifying cognitive processes, rather than report of a single IQ number.

- **Indications:**

  - Diagnosis and/or differential: focus on diagnostic ambiguity, levels of functioning, or development of a specific skill

  - Gain information regarding cognitive, academic, behavioral, and emotional functioning with a focus on designing education and treatment interventions targeted at a child's strengths and weaknesses.

  - Clinical or Research: assess pre and post functioning over time (as in relation to brain trauma or treatment)

Neuropsychological Assessment: Comprehensive assessment of a broad range of skills and abilities designed to describe and understand the relationship between the brain and behavior.

- **Basic Neuropsychological Framework:** Understanding of the dimensions related to behavior reflect the functional systems of the brain, represented as cognitive, emotional, and control processes (all having reciprocal influence on one another)

- **Domains of Assessment:** Alertness/arousal, sensory perception, motor activity, attention, memory, information processing, goal-directed activity

  - Impact of motivation and emotional capacity should be considered

- **Indications:**

  - Clarify child's lack of response to education and therapeutic intervention

    - Are the problems with adaptation a result of compromised brain function (versus, result of psychiatric disturbance?)

  - Identify the cognitive and control processes (how information is received, processed, and expressed) behind the child's psychosocial behavior

  - Determine functional significance of a brain abnormality

  - Determine deterioration of cognitive function or document changes in functioning over time (as in relation to brain trauma or treatment)

  - Determine strengths (assets) and weaknesses (deficits) in the child's presentation to strategize behavioral and education interventions

- **Contraindications:**

  - Acute illness with unstable mental status

  - Uncontrolled ADHD or other psychiatric disorder

  - Recent or current medication changes that may affect cognition

  - Previous similar evaluation has been completed (or currently in process)

Learning and Language Disorders

A Ninja's Summary: *Practice Parameters for the Assessment and Treatment of Children and Adolescents with Language and Learning Disorders*

(Updated 1998)

Why Care? Language and learning disorders (LLDs) are among the most common developmental disorders, and many children referred for evaluation because of behavioral difficulties related to academics have unrecognized LLDs.

Background:

- Children with LLDs may also struggle with performance anxiety, poor peer relationships, family conflicts, and decreased self-esteem.

- Sometimes parents and teachers fail to recognize how important LLDs are in emotional or behavioral problems.

- As children develop, academics become more complex,, and peer interactions increase in importance, emotional or behavioral problems become more likely to manifest.

- The Individuals with Disabilities Education Act (IDEA) delineates the level of disability associated with eligibility for special education services in public schools and mandates the creation and use of an Individual Education Plan (IEP).

Definitions:

- Controversy exists over including LLDs among mental disorders

  - They do fit the DSM-IV definition of mental disorder: "a clinically significant behavioral or psychological syndrome or pattern that occurs in an individual and

that is associated with present distress...or disability...or with a significantly increased risk of suffering…" (p xxi).

- Similarities between disorders and language and learning:
  - Essential and associated features
  - Risk factors
  - Prevalence in epidemiological samples
  - Possible etiological factors
  - Assessment techniques needed
  - Outcomes
  - Natural history
- Central to an LLD is the "lack of normal development of a particular developmental skill, either cognitive or linguistic," examples:
  - Developmental expressive language disorder = impairment in acquiring language production ability
  - Developmental reading disorder = "impairment in reading acquisition not due to a physical neurological, or environmental cause"
- LLDs vary in type and severity: some readily observable, others diagnosable only by standardized testing
- Per the current IDEA, learning disabilities are defined as processing disorders resulting in significant discrepancy between potential and actual acquisition of different academic or language skills
- Specific language impairment: per DSM-IV: delays in excessive or receptive language, not as a result of sensory or motor deficit or environmental deprivation, which exceed that based on nonverbal intelligence scores

- ➢ Consider all children showing age-discrepant language skills for an assessment and possible intervention.

- ❖ Per DSM-IV, learning disorders also necessitate a discrepancy between IQ and achievement

- ❖ Challenges to the IQ-achievement discrepancy requirement:

  - ➢ Research has failed to demonstrate differences between children with or without the discrepancy

  - ➢ Most children with a reading disability show a deficit in phonological-processing skills, which are used to detect and manipulate individual speech sounds or phonemes

  - ➢ Bright children overidentified with disability and low achievers underidentified

- ❖ Domain-specific assessment and remediation for LLDs supported by research

Epidemiology & Clinical Course:

- ❖ It is estimated that 10-20% of children and adolescents have an LLD.

- ❖ Children with early language disorder are at risk for learning disorders.

- ❖ Many children with LLDs outgrow their problems, but many never completely develop a normal skill level in the area of impairment.

- ❖ Recovery can be complicated by secondary difficulties such as anxiety, low self-esteem, or poor peer relationships.

- ❖ About 50% of children with developmental expressive language disorder obtain normal expressive language development.

- ❖ About 25% of children with developmental mixed receptive-expressive language disorder show improvement over 4 years.

Comorbidities: Approximately 50% of children with LLDs have a comorbid Axis I psychiatric disorder.

Etiology:

- Family, genetic, cognitive, environmental, and neuroanatomical factors have been suggested as etiologies.

- Reading to children has been documented as beneficial, but there is only a weak relationship between reading to children and their success at learning to read.

- Language disorders are heritable, and deficits in phonological awareness are the basic component of reading disability.

- Research suggests that children with language impairments cannot process rapid, transient stimuli.

Clinical Presentation:

- Children may present with school refusal, agoraphobia, somatic symptoms on school days they are expected to present that may progress to refusal to do homework, oppositional defiant symptoms, etc.

Assessment:

- Diagnosis should begin with a description of the child's symptoms and areas of difficulty as well as a detailed history of the chronology of the symptoms, developmental history, and family history.

- Delayed speech and language development are often associated with expressive language difficulties, while problems with articulation may be associated with phonemic difficulties.

- Receptive language difficulties may be more subtle

- If an LLD is suspected after the initial examination, psychoeducational testing is essential.

Differential Diagnosis:

- Possible causes for academic problems include physical or sensory deficits, concurrent emotional or behavioral disorders, or environmental factors such as abuse, frequent school changes, etc.

- Differential diagnoses include intellectual disability, motor skills disorders, medical or neurological disorders, and primary psychiatric disorders.

Treatment:

- A multimodal treatment approach with education and consultation is necessary

- The need for psychotherapy, other psychosocial interventions and medication therapy for associated psychiatric diagnoses should be determined

- Parent support may be needed, as well as helping parents and teachers appreciate the connection between the LLD and behavioral and emotional problems.

- Ensuring that parents understand their rights under the IDEA is also important.

Intelligence Assessments			
Measure	**Age range**	**Domains Evaluated**	**General Notes**
Wechsler Intelligence Scale for Children, Fifth Edition (WISC-V)	6-16 years	Full Scale IQ, Verbal Comprehension, Visual Spatial, Fluid Reasoning, Working Memory, Processing speed	Provides information on relative strengths and weaknesses
Stanford-Binet Intelligence Scale, Fifth Edition	2 yo - Adult	Verbal IQ, Nonverbal IQ, Full Scale IQ, Fluid Reasoning, Knowledge, Quantitative Reasoning, Visual Spatial Processing, Working memory	Provides information on relative strengths and weaknesses
Leiter International Performance Scale, Third Edition	3 yo - Adult	Nonverbal test of intelligence	Used for those who are hearing impaired, autistic, or do not speak English
Differential Ability Scale	2.6-17 years	General Cognitive Ability; Verbal, Nonverbal, Spatial Ability	

Academic Achievement Assessments			
Measure	**Age Range**	**Domains Evaluated**	**General Notes**
Kaufman Test of Educational Achievement, Third Edition (KTEA-3)	4 years through adulthood	Academic mastery of reading, writing, math and oral language skills	
Wide Range Achievement Test, Fourth Edition (WRAT-4)	5 years through adulthood	Academic mastery of reading, writing, math and oral language skills	Efficient administration time, alternate forms for repeated testing
Woodcock-Johnson Tests of Achievement, Fourth Edition (WJ IV)	2 years through adulthood	Academic mastery of reading, writing, math, academic knowledge and oral language skills	
Wechsler Individual Achievement Tests, Third Edition (WIAT-III)	4-50 years	Academic mastery of reading, writing, math and oral language skills	Co-normed with WISC to facilitate estimates of ability-achievement discrepancies

Speech and Language Assessments			
Measure	**Age Range**	**Domains Evaluated**	**General Notes**
Peabody Picture Vocabulary Test, Fourth Edition (PPVT-4)	2.6 years through adulthood	Receptive Vocabulary, estimates verbal intelligence	Useful in those with expressive difficulties
Test of Auditory Comprehension of Language-Revised	3 years to 9 years, 11 months	Auditory comprehension, single words, grammatical features, sentence structures	
Token Test for Children	3 years to 12 years, 5 months	Oral direction to subject to manipulate tokens varying in color, shape, size	Useful to identify mild receptive disturbances
Clinical Evaluation of Language-III	5 years and older	Aspects of receptive and expressive language	
Test of Language Development	Version 2P - 4 years to 8 years, 11 months Version 2I - 8 years, 6 months to 12 years, 11 months	Expressive and receptive syntax, semantics, phonology	No phonology in Version 2I
Expressive Vocabulary Test	2-6 to 90+	Expressive Vocabulary, Word Retrieval	Co-normed with PPVT-III

Visuographic & Visuoperceptual Assessments			
Measure	**Age Range**	**Domains Evaluated**	**General Notes**
Beery Developmental Test of Visual Motor Integration	2 years to 99 years, 11 months	visual perception, fine motor skills , and hand-eye coordination	Culture-free, non-verbal assessment
Rey-Osterrieth Complex Figure test	6 - 89 years	visual memory, working memory, and executive planning	Used to study cognitive development

Memory and Learning Assessments			
Measure	**Age Range**	**Domains Evaluated**	**General Notes**
Children's Memory Scale	5 - 16 years	learning, attention and memory	Processing skills screening instrument
Wide Range Assessment of Memory and Learning	5 years to 90 years, 11 months	short- and long-term memory, ability to learn new material, attention/concentration, working memory	Has screener, brief, or full administration options
California Verbal Learning Test	16 -90 years	episodic verbal learning	Tests degree to which one can live independently

Executive Functions			
Measure	**Age Range**	**Domains Evaluated**	**General Notes**
Wisconsin Card Sorting Test	6 years, 5 months to 89 years	Perseveration, working memory, abstraction, executive function	Sensitive to frontal lobe dysfunction
Delis-Kaplan Executive Function System	8 - 89 years	Higher level cognitive functions	Assess the frontal system of the brain

Sustained Attention and Effort			
Measure	**Age Range**	**Domains Evaluated**	**General Notes**
Conners' Continuous Performance Test	8 years and over	inattentiveness, impulsivity, sustained attention, and vigilance	PC software administration
Tests of Variables of Attention	4 to 80+	attention and inhibitory control	Culture- and language-free computerized test

Fine Motor Dexterity and Speed			
Measure	**Age Range**	**Domains Evaluated**	**General Notes**
Grooved Pegboard test	5 years and over	complex visual-motor coordination	Both hands tested separately

A Ninja's Guide to Neurodevelopmental Disorders

Attention-Deficit Hyperactivity Disorder

A Ninja's Summary: *Practice Parameter for the Assessment and Treatment of Children and Adolescents with Attention-Deficit Hyperactivity Disorder*

(Updated 2007)

Why Care? ADHD is one of the most common childhood psychiatric conditions and causes significant functional impairment in children.

Epidemiology & Clinical Course:

- Prevalence of ADHD approximately 6.7 to 10%, while those with ADHD taking medication ranges from 6-7%.
    - The rate of lifetime childhood diagnosis of ADHD was 7.8% and only 4.3% (55% of those with ADHD) had ever been treated with medication.
    - 60-85% of children with ADHD will continue to meet criteria as teenagers
    - Persistence of full syndrome of ADHD thought to range from 2-8% (by self report)
    - Adults with childhood ADHD had higher rates of antisocial/criminal behavior, injuries, accidents, employment/marital issues, health problems, and teen pregnancy.

Comorbidities: 54-85% of those with ADHD may meet criteria for ODD, and may develop conduct disorder.

- Other Comorbidities: Smoking/Substance use (15-19%), Learning/Language disorder (25-35%), Anxiety (33%)

- ❖ Depression and mania comorbidities remain a contentious issue

Etiology: Neuropsychological studies show deficits in executive function, including: response inhibition, vigilance, working memory, and planning.

- ❖ Heritability factors: estimated to be 76% (based on twin studies)
    - ➢ Genes affected: Dopamin 4 & 5 receptors, dopamine transporter, enzyme dopamine β-hydroxylase, serotonin transporter gene, serotonin 1B receptor, and the synaptosomal-associated protein 25 gene
- ❖ Neurobiological factors: Perinatal stress, low birth weight, traumatic brain injury, maternal smoking during pregnancy, severe early deprivation (institutional rearing or child maltreatment)
- ❖ Neuroimaging: Reduced cortical white and gray matter volume in children with ADHD
    - ➢ Low volume is more pronounced in those who have never received long-term medication treatment
    - ➢ Decreased volume in frontal and temporal lobes compared to controls
    - ➢ **fMRI preliminary date:** differences in brain activation relative to controls in caudate, frontal lobes, and anterior cingulate.

Recommendation 1: Screening should be a part of all mental health assessments **(MS)**

- ❖ Consider incorporating into clinic/office registration

Recommendation 2: Evaluation for ADHD should include interviews of parent and patient, assessment of school and/or daycare functioning, comorbid psychiatric disorders, and medical, social, and family history of the patient **(MS)**

- Determine age of onset, duration, severity, frequency of ADHD symptoms
- Must have impairment in at least two settings, but severe impairment in one setting should still be treated.
- Use a validated rating scale for parents and teachers, but do not diagnose ADHD by themselves
- Use samples of school work or report cards if rating scales are not filled out
- Assess family history of ADHD as it is highly heritable
- Assess developmental milestones in preschoolers due to overlap with developmental disorders
- Complete a thorough evaluation for other psychiatric disorders

Recommendation 3: If patient's medical history is unremarkable, no indication for laboratory or neurological testing **(NE)**

- Serum lead levels should not be part of routine screening

Recommendation 4: No Psychological or Neuropsychological testing needed for diagnosis unless low cognitive ability or low achievement in language and mathematics relative to intellectual ability **(OP)**

Recommendation 5: Clinician must evaluate for comorbid psychiatric disorders **(MS)**

Recommendation 6: Create a comprehensive treatment plan **(MS)**

- The patient's treatment plan should take account of ADHD as a chronic disorder and may consist of psychopharmacological and/or behavior therapy

- The short-term efficacy of psychopharmacological intervention for ADHD is well established. However, behavior therapy alone can produce improvement in ADHD symptoms relative to baseline symptoms

- It seems established that a pharmacological intervention for ADHD is more effective than a behavioral treatment alone.

Recommendation 7: Initial psychopharmacological Treatment should be FDA approved **(MS)**

Stimulants

- Stimulants are highly efficacious in the treatment of ADHD

    - In double-blind, placebo-controlled trials in both children and adults, 65%-75% of subjects with ADHD have been clinical responders to stimulants vs. with 4-30% with placebo

    - Effect size about 1.0, one of the largest effects for any psychotropic medication

- There have not been any studies examining the effects of doses of MPH or amphetamine in adolescents of more than 60 mg/day or 72 mg of Concerta

Immediate Release (IR)

- **Advantages:**

    1) Less expensive than long-acting, especially if patient doesn't have insurance

    2) Usually better initial treatment for small children in small children (<16 kg in weight), for whom there are no long-acting forms in a sufficiently low dose

- **Disadvantage:**

    1) Must be taken 2-3x per day to control ADHD symptoms throughout the day

Long-Acting Formulations (extended release, ER)

- **Advantages:**
  - More convenient, less frequent dosing and well-tolerated
  - Better Compliance
  - Single daily dosing is associated with greater compliance
    - Long-acting methylphenidate may improve driving performance in adolescents
  - No need to titrate to appropriate dose on short-acting formulation, can begin with long-acting initially
- **Disadvantage:**
  - More expensive if patient doesn't have insurance

First-line ADHD Medications: FDA Approved

Amphetamine Preparations					
Generic Class Brand Name	**Dose Form**	**Typical Starting Dose**	**FDA Max/Day**	**Off-Label Max/Day**	**Considerations**
SHORT-ACTING	Short-acting stimulants are often used as initial treatment in small children (<16 kg), but have the disadvantage of BID-TID dosing to control symptoms throughout day				
Dextroamphetamine/ Amphetamine (e.g., Adderall)	5, 7.5, 10, 12.5, 15, 20, 30 mg tablets	3–5yo: 2.5mg daily ≥6yo: 5mg Daily-BID	40 mg	>50 kg: 60 mg	
Dextroamphetamine (e.g., Dexedrine)	5 mg capsule	3–5 yo: 2.5 mg Daily	60 mg		
LONG-ACTING	Longer acting stimulants offer greater convenience, confidentiality, and compliance with single daily dosing but may have greater problematic effects on evening appetite and sleep				
Dextroamphetamine (e.g., Dexedrine)	5, 10, 15 mg capsules	≥6 yo: 5–10 mg Daily-BID	40 mg	>50 kg: 60 mg	
Adderall XR	5, 10, 15, 20, 25, 30 mg capsules	≥6 yo: 10mg Daily	30 mg	>50 kg: 60 mg	Adderall XR cap may be opened and sprinkled on soft foods
Lisdexamfetamine (Vyvanse)	30, 50, 70 mg capsules	30 mg Daily	70 mg		Prodrug must be converted in GI tract

Methylphenidate Preparations					
Generic Class Brand Name	**Dose Form**	**Typical Starting Dose**	**FDA Max/Day**	**Off-Label Max/Day**	**Considerations**
SHORT-ACTING	Short-acting stimulants are often used as initial treatment in small children (<16 kg) but have the disadvantage of b.i.d.-t.i.d. dosing to control symptoms throughout day				
Dexmethylphenidate (Focalin)	2.5, 5, 10 mg capsules	2.5 mg BID	20 mg	50 mg	
Methylphenidate (Methylin)	5, 10, 20 mg tablets	5 mg BID	60 mg	>50 kg: 100 mg	
Methylphenidate (Ritalin)	5, 10, 20 mg	5 mg BID	60 mg	>50 kg: 100 mg	
INTERMEDIATE-ACTING	Longer acting stimulants offer greater convenience, confidentiality, and compliance with single daily dosing but may have greater problematic effects on evening appetite and sleep				
Methylphenidate (Metadate ER)	20 mg capsule	20 mg QAM	60 mg	>50 kg: 100 mg	
Methylphenidate (Metadate CD) (30%IR/70%ER)	10, 20, 30, 40, 50, 60 mg	20 mg QAM	60 mg	>50 kg: 100 mg	Metadate CD and Ritalin LA caps may be opened and sprinkled on soft

Methylphenidate Preparations (Continued)					
Generic Class Brand Name	**Dose Form**	**Typical Starting Dose**	**FDA Max/Day**	**Off-Label Max/Day**	**Considerations**
LONG-ACTING					
Methylphenidate (Concerta)	18, 27, 36, 54 mg capsules	18 mg QAM	72 mg	2/mg/kg/day	
Methylphenidate (Ritalin LA) (50%IR/50%DR)	10, 20, 30, 40 mg	20 mg QAM	60 mg	2mg/kg/day	- Swallow whole with liquids - Nonabsorbable tablet shells may be seen in stool
Methylphenidate patch (Daytrana patch) (lasts 9 hours)	10, 15, 20, 30 mg patches	Begin with 10 mg patch QAM, then titrate up by patch strength 5mg QAM	30 mg mg/day patch	30 mg/day patch	
Dexmethylphenidate (Focalin XR)	5, 10, 15, 20 25, 30, 35, 40 mg capsules	5mg PO QAM	30 mg	40 mg	
Selective Norepinephrine Reuptake Inhibitor					
Atomoxetine (Strattera)	10, 18, 25, 40, 60, 80, 100 mg capsules	<70 kg: 0.5 mg/kg/day for 4 days; then 1 mg/kg/day for 4 days; then 1.2 mg/kg/day	Lesser of 1.4 mg/kg/day 100 mg/day		Not controlled*** -BBW: Increased risk for suicidal ideation

Recommendations for Prescribing Stimulants

- Start with methylphenidate due to less abuse potential and better to start in younger patients
- **Titrating upward:** Every 1-3 weeks until the max dose is reached, symptoms of ADHD remit, or side effects prevent further titration, WHICHEVER COMES FIRST
- Office visits monthly to monitor progress and side effects
- Regardless of comorbid conditions, patients respond well to stimulants

Preschool Children: Treatment with Stimulants

- Stimulants widely prescribed for ages ~3-5 years old
  - IR Methylphenidate is preferred, up to 30mg daily
- Caution with use in preschoolers with developmental delays
  - Prone to higher rates of side effects, like social withdrawal, irritability, crying
- Dose titrated more conservatively in preschoolers than in school-age patients
  - Lower mean doses may be effective.

Atomoxetine

- Less pronounced effects on appetite and sleep than stimulants
  - May produce relatively more nausea or sedation
- Greatest effects were at week 6 → Patient should be maintained at the full therapeutic dose for at least several weeks to obtain the drug's full effect

- ❖ Atomoxetine has been studied in the treatment of patients with ADHD and comorbid anxiety
    - ➢ May consider atomoxetine for the treatment of ADHD with comorbid anxiety is a viable alternative approach
    - ➢ Less evidence for depression treatment

Selection of Agent in ADHD

- ❖ Stimulants as the first line of treatment for ADHD, particularly when no comorbidity is present
- ❖ Atomoxetine is less effective than stimulants, but may be considered as the first medication for ADHD in individuals with an active substance abuse problem, comorbid anxiety, or tics
- ❖ Atomoxetine is preferred if the patient experiences severe side effects to stimulants such as mood lability or tics
    - ➢ When dosed twice daily, positive effects on late evening behavior may be seen

Recommendation 8: If no FDA approved medications are effective, consider behavior therapy or off label medications **(CG)**

Alpha-2 α-Agonists (clonidine and guanfacine)

- ❖ Clonidine ER (Kapvay) and Guanfacine ER (Intuniv) are FDA approved for 6 years old and older for ADHD
    - ➢ Target more hyperactivity
- ❖ Widely prescribed for comorbid aggression, or to combat side effects of tics or insomnia

- ❖ Medication should be tapered gradually over 1 to 2 weeks to avoid a sudden increase in blood pressure

Bupropion

- ❖ Noradrenergic antidepressant that showed modest efficacy
- ❖ Contraindicated in patients with a current seizure disorder
- ❖ No pill sizes small enough for children who weigh <25 kg.

Tricyclic Antidepressants

- ❖ Imipramine and nortriptyline have been most commonly used
    - ➢ Desipramine associated with sudden death in adolescents
- ❖ EKG must be performed at baseline and after each dose increase
- ❖ Once the patient is on a stable dose of the TCA, a plasma level should be obtained to ensure the level is not in the toxic range

Alternative ADHD Medications

Antidepressants				
Generic Class Brand Name	**Dose Form**	**Typical Starting Dose**	**Max/day**	**Considerations**
Bupropion IR (Wellbutrin)	75, 100 mg tablets	Lesser of 3 mg/kg/day or 150 mg/day	Lesser of 6 mg/kg or 300 mg, with no single dose >150 mg	Lowers seizure threshold; contraindicated if current seizure disorder
Bupropion (Wellbutrin SR)	100, 150, 200 mg tablets	Lesser of 3 mg/kg/day or 150 mg/day	Lesser of 6 mg/kg or 300 mg, with no single dose >150 mg	Usually given in divided doses, BID for children, TID for adolescents, for safety and effectiveness
Bupropion (Wellbutrin XL)	150, 300 mg tablets	150 mg QAM	300 mg/day	Daily dosing
Tricyclic Antidepressants (TCAs)				
Imipramine (Tofranil)	10, 25, 50, 75 mg tablets	1 mg/kg/day	Lesser of 4 mg/kg or 200 mg	Obtain baseline ECG
Nortriptyline (Pamelor)	10, 25, 50, 75 mg capsules	0.5 mg/kg/day	Lesser of 2 mg/kg or 100 mg	Obtain baseline ECG

Alpha-2-Adrenergic Agonists				
Generic Class Brand Name	**Dose Form**	**Typical Starting Dose**	**Max/day**	**Considerations**
Clonidine (Catapres)	0.1, 0.2, 0.3 mg tablets	<45 kg: 0.05 mg QHS; titrate up to QID >45 kg: 0.1 mg QHS; titrate up to QID	27-40.5 kg: 0.2 mg 40.5-45 kg: 0.3 mg >45 kg: 0.4 mg	- May be used alone or as adjuvant to another medication for ADHD - Effective for impulsivity and hyperactivity; modulating mood level; tics worsening from stimulants; sleep disturbances
Clonidine (Kapvay)	0.1 mg ER	0.1 mg, titrate up 0.1 mg QWeek	0.4 mg in divided doses BID	-FDA approved for >6 yo
Guanfacine (Tenex)	1, 2 mg tablets	27-40.5 kg: 0.5 mg QHS 40.5-45 kg: 0.5 mg QHS >45 kg: 1 mg QHS	27-40.5 kg: 0.5 mg/dose up to 2mg/day 40.5-45 kg: 1 mg/dose up to 3mg/day >45 kg: 1 mg/dose up to 4 mg/day	- May not see effects for 4-6 wk - Review personal and family cardiovascular history - Taper off to avoid rebound hypertension
Guanfacine (Intuniv)	1, 2 mg tablets	<45 kg: 0.5 mg QHS; titrate up to QID >45 kg: 1 mg QHS; titrate up to QID	27-40.5 kg: 2 mg; 40.5-45 kg: 3 mg; >45 kg: 4 mg	FDA approved for >6 years old

Recommendation 9: Monitor for medication side effects **(MS)**

Stimulant Common Adverse Events

- Appetite decrease, weight loss, insomnia, or headache
    - Less common side effects: tics and emotional lability/irritability
- Growth restriction ~1/2-inch difference with continued use
    - drug holidays on weekends and summer breaks recommended
- **Monitor weight, height, and vitals in patients on stimulants**
- **Stimulant-induced Insomnia**
    - Melatonin 3 mg has recently been shown to be helpful in improving sleep in children with ADHD treated with stimulants
    - Low doses of clonidine, trazodone (risk of priapism), or an antihistamine
    - Risk of paradoxical excitement when treated with antihistamines
- **Children with comorbid ADHD and tic disorders:**
    - On average, show a DECLINE in tics when treated with a stimulant… ESPECIALLY longer term over a year of treatment
    - If a patient has treatment-emergent tics during a trial of a given stimulant, then an alternative stimulant or a nonstimulant should be tried
    - If the patient's ADHD symptoms RESPONDED adequately ONLY to a stimulant medication that INDUCES tics…THEN combined pharmacotherapy of the stimulant and an α-agonist (clonidine or guanfacine) is recommended.

Less Common Effects of Stimulants:

- Aggression, Mood Lability, and Suicidal Ideation
  - NOT been shown to induce aggression, AND overall aggressive acts and antisocial behavior decline when ADHD patients are treated with stimulants
  - Stimulants may be associated with increased emotional lability
    - HOWEVER, must distinguish between emotional lability when stimulant is active vs rebound effects when stimulant wears off
    - Giving a dose of IR stimulant in the late afternoon may be helpful

Rare effects (for all stimulants, atomoxetine, and modafinil):

- Toxic psychotic symptoms (e.g., visual and tactile hallucinations of insects)
- Symptoms of aggression and suicidality (but no completed suicides) were reported

Cardiovascular Considerations in Stimulants

- Risk of sudden death
  - The rate of sudden death of children taking ADHD medications do not appear to exceed the base rate of sudden death in the general population
- No evidence currently indicates a need for routine cardiac evaluation before starting any stimulant treatment in otherwise healthy individuals
- General advice is to avoid use with pre-existing heart disease or symptoms suggesting significant cardiovascular disease
  - Obtain cardiologist consultation and possible electrocardiography and/or echocardiography should be obtained

Alternative Agents Adverse Effects

Atomoxetine

- Gastrointestinal distress, sedation, and decreased appetite, usually improved with dose adjustment, but other adverse effects like headache may persist
- Caution as rare risk of developing severe liver disease, monitor LFTs
- Increased suicidal thinking has BBW by FDA and possible risk of pushing into mania due to antidepressant nature of medication (SSRI/SNRI)

Bupropion

- Adverse Effects include mild insomnia or loss of appetite
- HIGH SINGLE doses (>400 mg) of bupropion may induce seizures even in patients without epilepsy, especially with immediate-release dosing

Tricyclic Antidepressants

- May cause anticholinergic side effects such as dry mouth, sedation, constipation, changes in vision, or tachycardia
- Less anticholinergic side effects with Nortriptyline and Desipramine

Alpha-2-Adrenergic Agonists

- May include sedation, dizziness, and possible hypotension
- Blood pressure and pulse should be assessed during use and abrupt discontinuations avoided.

Recommendation 10: Psychopharmacological treatment alone may be satisfactory if there is normative functioning in Academic, Family, and Social Functioning. **(OP)**

- Pharmacological treatment may be adequate monotherapy if sufficient response.

Recommendation 11: If response to ADHD medication is not optimal, or has a comorbid disorder, or has stressors in family life, then consider adjunct of psychosocial treatment **(CG)**

- ❖ No clear additive effect of behavioral and pharmacological treatment
    - ➢ Strong evidence that patients with ADHD and comorbid disorders benefit from adjunctive psychosocial intervention
- ❖ Comorbid anxiety predicted a better response to behavioral treatment, particularly with anxiety and a disruptive behavior disorder (Oppositional Defiant Disorder or Conduct Disorder)
- ❖ Children receiving public assistance and ethnic minorities also showed a better outcome with combined treatment

Recommendation 12: Patients should be reassessed periodically and treatment should continue as long as symptoms remain present and cause impairment **(MS)**

- ❖ Regular follow-ups to ensure that the medication is still effective, the dose is optimal, and side effects minimal
    - ➢ Follow-up at least several times per year assessing behavioral and academic functioning
    - ➢ Periodically assess height, weight, blood pressure, and pulse; and assess for the emergence of comorbid disorders and medical conditions
- ❖ If they have been symptom free for at least 1 year, consider if medication is still needed
    - ➢ Remitted ADHD: Lack of any need to adjust dose despite robust growth, lack of deterioration when a dose of stimulant medication is missed, or new-found abilities to concentrate during drug holidays
- ❖ **Drug Holidays:** Low-stress times such as vacations are a good time to attempt a withdrawal from medication

- ➢ Parents should assign some cognitively demanding tasks (reading a book, practicing mathematics problems) to be sure that remission has occurred

Recommendation 13: Monitory height and weight during medication treatment for ADHD **(MS)**

- ❖ Stimulant treatment may be associated with a reduction in expected height gain, at least in the first 1 to 3 years of treatment
  - ➢ No height deficits relative to controls in childhood, some small decrease during adolescence, but no difference in height in adulthood
- ❖ Higher doses of stimulants and extended use without drug holidays contribute to higher risk of long-term effects on height

Autism Spectrum Disorder

A Ninja's Summary: *Practice Parameter for the Assessment and Treatment of Children and Adolescents with Autism Spectrum Disorder*

(Updated 2014)

Why care? Autism Spectrum Disorder has a distinctive course, impact, and treatment. Early intervention is key, yet individuals with autism spectrum disorder can present at any point of their development. It is important to understand the deviance in the development of social, communicative, and cognitive skills that arise in the first parts of life to organize multidisciplinary care, coordinate services, and advocate for the patient and their family.

Background

- Autism was first described by Kanner in 1943, who had a congenital inability to relate to other people (lack of interest in people in infancy) and was sensitive to change in their environment.
- If language developed - characterized by echolalia, pronoun reversal, concreteness
- Motor symptoms present with repetitive, stereotypic purposeless activities
- First thought to be a form of childhood psychosis - later identified as distinct and added to DSM-III in 1980

Defining the Diagnosis

- **DSM-IV-TR:** Disturbances of 3 domains - social relatedness, communication/play, restricted interests and activities, onset by 3 years of age
    - **Social Relatedness** - marked impairment in nonverbal communication, peer relationships, and social-emotional reciprocity

- **Communication/Play** - delay or lack of spoken language; If verbal - difficulty sustaining/initiating conversation, stereotyped/repetitive language; lack of appropriate social/imaginative play

- **Impaired interest/activity** - preoccupations, adherence to routines, rituals, stereotypies, motor mannerisms, and preoccupation with parts of objects

Variability of Presentation

- **Preschool:** marked lack of interest in others, failures in empathy, absent/delayed speech and communication, resistance to change, restricted interest, stereotyped movements

    - Parental Concerns - Lack of language, inconsistent responsiveness, concern child is deaf

- **School Age:** Social/communication skills improved; difficulty with transitions and self-stimulatory (self-injury) more prominent

- **Adolescence:** Some with marked developmental gains; others behaviorally decompensate with tantrums, self-injury, and aggression; Increased risk of accidental death

- **Prognosis:** Presence of communicative speech by 5 years old, overall IQ; Earlier detection and services improve long-term prognosis

Early Classification: Autism included in Pervasive Developmental Disorder Category (PDD) in DSM-IV-TR

- **Rett's disorder:** More common in females, Head circumference and development normal until age 4, then head growth slows, purposeful hand movements lost, stereotypic hand movements (wringing/washing) develop. Mutation in MeCP2 gene (methyl-CpG-binding protein 2).

- **Childhood disintegrative disorder (CDD):** At least 2 years of normal development, then clinically significant loss of 2 skills in areas of receptive or expressive language, social skills, toileting skills, play, or motor skills. Typically presents age 3-4, abruptly or gradual, may be preceded by anxiety or dysphoria. Course of disorder leads to child being mute.

- **Asperger's Disorder:** Typically no developmental concerns in first years of life from parents. Usually precocious in learning to talk, but then talked in a formal, 1 sided way, about finite interests that provided social difficulties.

- **Pervasive Developmental Disorder NOS:** Milder impairment than autism

- **All prior categories were subsumed under Autism Spectrum Disorder in DSM-5**

Epidemiology: CDC estimates prevalence of ASD in the US to be 11.3 in 1,000.

- Higher rates of ASD in recent years can be linked to changing diagnostic criteria/practices, age of children screening, and location of study

- 4x more common in males than females, no difference of prevalence due to family education level, yet may be underdiagnosed in low socioeconomic status.

Etiology:

- Neurobiology: EEG and seizures comorbid in 20-25%, suggesting a neurobiological role, likely a large distribution of neural systems affected.
    - Postmortem studies show limbic system abnormalities
    - fMRI: Difficulties in tasks involving social and affective judgments, differences in processing of facial and non facial stimuli
    - MRI: overall brain size increase - aberrations in white matter tract development seen on diffusion tensor imaging

- ➢ Neurotransmitters: elevated peripheral levels of serotonin - unclear significance, likely also role for dopamine given overactivity and stereotypic behaviors

- ➢ Vaccines: Preponderance of evidence does not support this hypothesis

- ➢ Neuropsychological correlates: impaired executive function, weak central coherence (integration of information), and deficits in theory of mind

❖ Genetic Factors: High recurrence in siblings (18.7% for ASD)

- ➢ Risk factors: closer spacing of pregnancies, advanced maternal/paternal age, <26 weeks gestational age.

- ➢ High rates of language/learning, social disabilities, mood/anxiety disorder in family members

Differential Diagnosis: Developmental disorders, sensory impairments (deaf), RAD, OCD, ID, anxiety (selective mutism), childhood onset schizophrenia, and organic causes.

❖ ASD Development: Most commonly no period of normal development. Less common to have normal development and then developmental regression (such as in Rett's)

❖ Language Disorders: differentiated from ASD by observation of pointing for interest and use of conventional gestures (20 and 42 months respectively)

❖ Developmental Delay:

- ➢ Differentiation at 24 months, observe directing attention (showing) and attention to voice

- ➢ Differentiation at 36 months, observe use of other's body, attention to voice, pointing, and finger mannerisms

- ➢ Differentiation from 38-61 months, observe children with ASD having impaired nonverbal behaviors (eye contact) in social skills

- ❖ Reactive Attachment Disorder: Differentiates as poor social responsivity is improved with adequate caretaking.
- ❖ OCD: Later onset than ASD, no social or communication deficits
- ❖ Anxiety: Less prominent social and communicative impairments, and have social insight
- ❖ Schizophrenia: rarely see delusions or hallucinations in autism
- ❖ ADHD: Diagnostic overlap, difficult to differentiate

Comorbidities: Profound intellectual disability (50%), moderate intellectual disability (35%), hyperactivity, OCD phenomena, self-injury, aggression, stereotypies, tics, affective symptoms

Recommendation 1: Screen for ASD symptoms during developmental and psychiatric assessments of infants, young children, and when indicated, older children **(CS)**

Recommendation 2: If screening indicates significant ASD symptoms, perform a diagnostic evaluation **(CS)**

- ❖ Standard psychiatric assessment - interview child and family, review past records, historical information (past/current educational & behavioral intervention, family history, psychosocial issues), and comorbid diagnoses.
- ❖ Observe broad areas of social interaction and restricted, repetitive behaviors.
- ❖ Child's age, developmental level should be taken into account, along with sensitivities to ehtnic, cultural, and SES factors.
- ❖ Use of assessment instruments (e.g. ADOS) should not replace clinical judgement.

Recommendation 3: Coordinate a multidisciplinary assessment, including: physical exam, hearing screen, wood's lamp exam (s/s of tuberous sclerosis), genetic testing (G-banded karyotype, fragile X, chromosomal microarray). **(CS)**

- Chromosomal microarray: standard of care for initial evaluation of ASD or developmental disabilities
    - Detect known abnormalities associated with increased rates of ASD: 15q11-13 maternal duplications, duplications and deletions of 16p11.2
    - Yield of genetic testing with clinical suspicion is around ⅓ of cases
    - IQ not a strong predictor of positive chromosomal findings
- Additional Evaluation when history of regression, dysmorphology, staring spells, family history are present.
    - Organic: infectious (encephalitis/meningitis), endocrinology (hypothyroid), metabolic (homocystinuria), traumatic (TBI), toxic (FAS), or genetic
        - Landau-Kleffner syndrome - distinctive EEG associated with aphasia
- Psychological Assessment: cognitive ability, adaptive skills for treatment planning and identifying areas of strength and weakness. Include instruments valid for nonverbal population.
    - "Splinter Skills": unusual islets of ability - areas of interest or special talent
- Communication Assessment: receptive and expressive vocabulary and language use for diagnosis and treatment planning.
- Consider Occupational Therapy and Physical Therapy evaluations for sensory/motor
- Assessment for sleep

Recommendation 4: Help family obtain appropriate, evidence-based structured educational and behavioral treatment (comprehensive treatment approaches) - associated with better outcomes **(CS)**

- **Behavioral:** Applied Behavior Analysis (ABA) - widely used ABA program, Early Intensive Behavioral Intervention for young children (Lovaas et al.) - one-to-one direct teaching, discrete trials to teach simple skills → more complex skills
  - Functional analysis (ABCs) identify patterns of reinforcement for problem behaviors
  - Effective for: academic tasks, adaptive living skills, communication, social skills, and vocational skills
- **Communication:** Typically addressed in IEP with speech therapist, while those without language yet can be helped with sign language, communication boards, visual supports, and picture exchange.
  - Fluent speech: focus on pragmatic language skills training, social reciprocity
- **Educational:** structured educational approach with explicit teaching - involves interdisciplinary team and family involvement.
  - Individual Education Plan (IEP): includes strengths, vulnerabilities, explicit description of services, goals, objectives, and procedures for monitoring effectiveness. Focus on enhancing verbal and nonverabl communication, academic skills, social, motor, and behavioral capabilities.
  - Effective models: Early Start Denver Model and Treatment and Education of Autism and related Communication handicapped Children program.
- **Other Interventions:** CBT (anxiety/anger), auditory integration training, sensory integration therapy, touch therapy/massage
  - Psychiatric Hospitalization: likely only effective for psychiatric units that specialize in the ASD population.

Recommendation 5: Medication may be offered to treat a target symptom or comorbid disorder. **(CG)**

- **Primary Goal:** Facilitate the child's ability to adjust or engage in education intervention
- Targets: anxiety/depression, aggression, self-injurious behavior, hyperactivity, inattention, compulsive behaviors, repetitive/stereotypic behaviors, and insomnia.
- Risperidone & Abilify: FDA approved for treatment of irritability - specifically physical aggression and severe tantrum behavior
- Parent management training + Medication
    - Moderately more efficacious than medication alone for serious behavioral disturbances
    - Modestly more effective than medication alone for adaptive functioning

Recommendation 6: Clinicians should remain active in long-term treatment planning and family support. **(CG)**

- **Young children:** Diagnosis and treatment programing
- **School age:** Medication and behavioral support
- **Adolescent:** Vocational and prevocational training → independence if possible
- Parental divorce - NOT higher among parents with ASD

Recommendation 7: Clinicians should ask about use of complementary and alternative medicine (CAM) treatments and prepare to discuss risk/benefits **(CS)**

- Most cases, have no benefit, yet also have little risk

- **Treatments without efficacy:** IV secretin, oral vitamin B6, magnesium, gluten free, casein-free diet, omega-3 fatty acids, oral human immunoglobulin

- **Potential risk:** chelation, diversion of financial and psychosocial resources

Medications for Autism Spectrum Disorder

Alpha 2 Agonists				
Medication (Drug Class)	**Targeted Symptoms**	**Age**	**Adverse Effects (Primary)**	**Main Benefits**
Guanfacine	Hyperactivity, Irritability, Inappropriate speech, Stereotypy	>5 yo	Hypotension Drowsiness	-Hyperactivity -Irritability
Clonidine	Hyperactivity, Irritability, Inappropriate speech, Stereotypy	>5 yo	Hypotension Drowsiness	-Hyperactivity -Irritability
Antipsychotics				
Aripiprazole	Irritability, Hyperactivity, Stereotypy, Social withdrawal, Inappropriate speech	>6 yo	Somnolence, weight gain, drooling, tremor, fatigue, vomiting	-Irritability -Hyperactivity -Stereotypy subscales
Haloperidol	Multiple behavioral symptoms, global functioning	>2 yo	Sedation, Extrapyramidal symptoms* (>25% for 2-7 years)	-Behavioral symptoms
Olanzapine	Global functioning, Aggression, Compulsions, Irritability	>6 yo	Weight gain, Sedation	-Global Functioning
Risperidone	Irritability, Hyperactivity, Stereotypy, Social Withdrawal, Inappropriate speech	>5 yo	Weight gain, Increased appetite, Fatigue, Drowsiness, Drooling, Dizziness	-Hyperactivity -Stereotypy

Mood Stabilizers				
Valproic Acid	Irritability (global), Repetitive Behavior	>5 yo	Increased appetite, Skin rash, Irritability	-Repetitive behavior -Irritability
Lamotrigine	Irritability, Social Behavior	>3 yo	Insomnia, Hyperactivity	**No significant improvements**
Levetiracetam	Irritability, Global functioning	>5 yo	Aggression	**No significant improvements**
Norepinephrine Reuptake Inhibitor				
Atomoxetine	Hyperactivity, Attention	>5 yo	Nausea, Anorexia, Fatigue, Early wakening, Racing heart	-Improved hyperactivity and attention
Serotonin Reuptake Inhibitors				
Citalopram	Repetitive behavior	>5 yo	Hyperactivity, Insomnia, Inattention, Impulsivity, Diarrhea, Stereotypy	**No significant improvements**
Fluoxetine	Repetitive behavior	>5 yo	No significant adverse effects	-Improved repetitive behaviors
Clomipramine	stereotypy, Repetitive behavior, compulsions, hyperactivity, irritability	>6 yo	Insomnia, constipation, twitching, tremors, lethargy, tachycardia, diaphoresis, nausea	Decrease in repetitive behaviors
Stimulants				
Methylphenidate	Hyperactivity, Inattention	>5 yo	Decreased appetite, insomnia, irritability, emotionality, social withdrawal	Hyperactivity Inattention

Miscellaneous				
Amantadine	Hyperactivity, Irritability	>5 yo	Insomnia	-Some improvement in inappropriate speech and hyperactivity
Cyproheptadine **in combination with haloperidol**	Hyperactivity, Autism rating scale (relationships, emotional response, communication)	>3 yo	Trend towards increased appetite	-Hyperactivity -Improvements on Autism rating scale
Donepezil	"autistic behavior", expressive-receptive communication *Child Autism Rating Scale (CARS)	>2 yo	Diarrhea, stomach cramping, irritability	-Improved autistic behavior
Naltrexone	"social behavior", irritability, discriminant learning, hyperactivity, communication (initiation), Self-injurious behavior	>3 yo	Transient sedation, Increased aggression and stereotypy	-Possible hyperactivity and self-injurious behavior
Pentoxifylline **in combination with risperidone**	Irritability, hyperactivity, stereotypy, social withdrawal, inappropriate speech	>4 yo	Sedation, GI effects, increased appetite	-Irritability -Social withdrawal
N-Acetylcysteine **(Cetylev, Acetadote)**	Breaks disulfide bonds, decreasing mucus viscosity; replenishes glutathione	Used at all ages	Nausea, vomiting, rash, tachycardia, flushing	-Mucolytic -Self-harming behavior

Intellectual Disability

A Ninja's Summary: *Practice Parameter for the Assessment and Treatment of Psychiatric Disorders in Children and Adolescents with Intellectual Disability (Intellectual Developmental Disorder)*

(Updated 2020)

Why Care? In the DSM-5, Intellectual Disability/Intellectual Developmental Disorder is now recognized as a psychiatric disorder, emphasizing the role of the psychiatrist in assessment and diagnosis of these patients, including a workup for etiology and determination of severity using the new table focused on adaptive reasoning and functioning, as opposed to IQ number in previous editions.

Background: There has been historical movement away from pejorative language and gradual replacement with terms that emphasize disability. Disability occurs when a person's environmental demands exceed their abilities. The idea would be to provide social support and environmental modifications to enhance the ability for a person to function. Person first language was adopted by the field and federal law to further elevate the person over the disability.

Etiology: Complex interaction of genetics, environment, and developmental vulnerability.

- **Genetic Risk Factors:**
  - Single gene disorders/syndromes - found only in child or inherited by dominant, recessive, or X-linked, leading to brain malformations (lissencephaly, abnormal layering of cortex), neurocutaneous syndromes (tuberous sclerosis, neurofibromatosis), and inborn errors of metabolism (disrupted enzyme to metabolize carbs, amino acids, etc)
    - Most common inherited single gene disorder, Fragile X, repeat variant in FMR1 gene on X chromosome.

- ➢ Chromosomal - missing copy or entire segment - trisomy 13, 18, 21
    - ■ Most common genetic cause of ID, trisomy 21

- ❖ **Prenatal/Perinatal Risk Factors:**
    - ➢ Environmental risk factors - Malnutrition, vitamin/mineral deficiency, placental insufficiency, drugs, alcohol, toxins, teratogens, maternal hypothyroidism.
        - ■ Most common preventable cause of ID, Fetal alcohol spectrum disorder
    - ➢ Prenatal/Perinatal infections - toxoplasmosis, syphilis, varicella-zoster, parvovirus B19, rubella, CMV, herpes - timing of infection determines impact to fetus
    - ➢ Delivery - most important risk factor for brain damage in delivery, asphyxia (prematurity, low birth weight), in addition hypoglycemia, intracranial hemorrhage, eclampsia, premature rupture of membranes.
- ❖ **Postnatal Risk Factors:**
    - ➢ Brain trauma, near-drowning, loss of consciousness, lead poisoning, environmental deprivation, child abuse, neglect, brain tumors, epilepsy, surgical, radiation, chemotherapy, TBI (tumor, hypoxemia)

Epidemiology:

- ❖ Overall prevalence is estimated at 10.37 per 1,000, about 1%, and about 18.3 per 1,000 in children, higher in males than females.
- ❖ Primary risk factor - equal distribution across prenatal, perinatal, postnatal causes, yet unknown in half of cases
- ❖ Higher prevalence in low to mid-income countries - related to access/quality of maternal and child health care, and prenatal screening

Clinical Presentation/Course:

- Three Domains of adaptive reasoning affected: Appreciate areas of strength and weakness in each domain
    - Conceptual - reading, writing, language, maths, knowledge, memory, problem solving, novel judgment
    - Social - theory of mind, social judgment/understanding, interpersonal communication, social problem solving
    - Practical - self management (personal care, responsibilities, transportation, finances, school, work, occupational skills)
- **Clinical Presentation:** delays in meeting milestones and/or frustration, poor self-esteem, behavioral disturbance due to capacity for an individual to meet expectations.
    - Severe ID found within first 2 years, mild ID may be identified when learning problems appear
    - Not a static disability - cognitive impairments/adaptability may change with time or environment.
    - Early intervention improves functioning throughout lifetime, sometimes to the point of not meeting ID criteria.
    - Improvement may be seen with treatment of medical illness, or worsen as disease/syndrome process progresses.

Differential Diagnosis: Differentiate from specific learning disorder, communication disorder, major/mild neurocognitive disorder, ASD, affective disorder, psychosis. Note linkage of ID/IDD with genetic or medical condition.

Psychiatric Comorbidities: 3x more common in ID/IDD

- High rates of ODD, ASD, ADHD - behavioral problems 2.5-4x more frequent
- ADHD: similar presentation, yet inattentive symptoms do not decrease with age
- Anxiety: separation anxiety can persist over a longer period of development

- Risk Factors: severity of impairments, low SES, single bio parent as caregiver

Assessment:

- **Screening:** Recommend standardized screening, such as Ages and Stages Questionnaire (ASQ), and Parent's Evaluation of Developmental Status (PEDS).
    - AAP recommends regular screening at 9, 12, 18, 24, 30 month well child visits
    - Refer children for testing who have academic or behavioral challenges
- **Diagnostic Evaluation:** Positive screening should be followed by a clinical diagnostic evaluation and standardized testing using validated measures (both needed to meet criteria)
    - Role of Child and Adolescent Psychiatrist - Identify 1) intellectual deficits, 2) adaptive deficits, and 3) use severity table
    - Standardized scales for adaptive behaviors need to be clinically correlated
    - Individual cognitive profiles from neuropsych testing are more useful for understanding ID than a single IQ score
    - IQ testing can be limited in cultural/linguistic minorities, motivation, cooperation, temperament, behavior, physical health, mental health, testing environment, and even attitude of tester. Reliability limited in severe ID or language impairment due to a low level of these persons in the standardized population.
    - Global Developmental Delay: significant limitations in 2+ domains, under 5 year old
    - Unspecified Intellectual Disability: older than 5 yo and have other impairments limiting ability to obtain reliable assessment
    - Federal law requires re-evaluation every 3 years in school-age children
    - If improved adaptive skills after intervention are not contingent on ongoing supports/intervention, may consider ID/IDD no longer appropriate

- **Etiological Assessment:** completed by CAP, clinical geneticist, developmental pediatrician, pediatric neurologist

    - Help predict functional impact, prognosis, anticipatory guidance, identify comorbid medical and behavioral problems, determine recurrence risk, allow access to support groups, and research studies.

    - Multidisciplinary approach to obtain detailed history, physical, neuro exam (most critical), and genetic testing

        - History: prenatal/perinatal history, behavioral history, 3 generation family history of medical problems, learning disorders, psychiatric disorders, ID/IDD

        - Physical: physical features, growth, minor abnormalities, vision/hearing screening

        - If history + physical suggest etiology → confirm by specific testing

    - Focused metabolic testing for serum amino acids, urine organic acids for those with clinically suggestive features (developmental regression, hepatosplenomegaly, coarse facial features)

    - EEG if seizures or paroxysmal events suspected

    - MRI if history of birth trauma, physical findings, or abnormal neuro exam

    - Chromosomal microarray for all those with undetermined etiology

    - Fragile X testing (male and female) for those with undetermined etiology

    - Rett testing for MECP2 mutation for females

    - Family history suggestive of X-linked inheritance - X-linked intellectual disability panel

- **Factors affecting psychiatric/behavioral symptoms:**

    - **Medical:** Consider common pediatric illnesses and causes of pain when evaluating emotional and behavioral problems.

        - Seizure disorders - consider postictal state

- Hearing/Vision disorders - higher rates of anxiety, behavioral issues, pragmatic language issues, psychosocial adjustment difficulties

- Motor impairments - spina bifida and cerebral palsy have higher rates of inattention and hyperactivity

➢ **Genetic:** Consider associated medical problems related to disorder (Down's syndrome - cardiac, vision, thyroid, hearing problems)

➢ **Medication:** Side effects of medications that are sedating or activating

- stimulants, muscle relaxers, AEDs, Calcium channel blockers, PDE inhibitors, centrally acting antiemetics

➢ **Behavioral:** Complete a behavioral analysis to determine function of problem behaviors

➢ **Communication:** May consult with a speech language pathologist to assess needs for an adequate communication system when spontaneous and efficient communication is limited.

➢ **Cognitive/Sensory/Occupational:** Consider demand-ability matching in home, school, community setting through assessment of strengths and weakness based on testing. May be helpful to have occupational therapy, social workers, and case managers assist with developing supports.

➢ **Environmental/Psychosocial:** Consider sensitivity to changes in environment (education/habilitation) to ensure needs are met.

- Stressful life events (moving residence, serious problem in family/friend, law enforcement problems, unemployment, trauma/abuse, drug or alcohol problem) predict ER use for behavioral health complaints.

- 2.8x more likely to have issues with sleep → behavioral/psych issues

- At increased risk for bullying (esp when combined with ADHD), and trauma/abuse

❖ **Psychiatric Assessment:** Focus on psychiatric and behavioral symptoms, include baseline, current behaviors, and considerations based on developmental age

➢ Attempt to capture all relevant info from caregivers, use open ended questions with child, no leading questions

- ➢ Pay attention to discrepancies in behavior in presence of different caregivers and school systems to determine how presentations change based on support/stressors

- ➢ Expectations should be based on developmental level, not chronological age

- ➢ Avoid diagnostic overshadowing - attributing all symptoms to ID/IDD

- ❖ **Psychiatric Symptom Measures**: utilize measures to support diagnostic decisions that are validated in patients with ID/IDD

  - ➢ Self-report questionnaires are likely unreliable in ID/IDD - use teacher/parent

  - ➢ Assessments for psych/behavioral problems in children with ID/IDD:

    - ■ Developmental Behavior Checklist (DBC), Nisonger Child Behavior Rating Form (NCBRF), Reiss Scales for Children's Dual Diagnosis (RSCDD).

  - ➢ *Diagnostic Manual-Intellectual Disability-2* assists with accurate diagnosis of mental illness in patients with ID/IDD.

- ❖ **Informed Consent/Assent:** Despite historical assumptions that individuals with ID/IDD could not consent/assent (not involved in treatment decisions, denied research participation), it is now recommended to help individuals with ID/IDD understand the consent process for medical decision making.

Statement 1: Psychosocial treatments can be considered to address psychiatric symptoms in children with ID/IDD

- ❖ **Psychotherapy/CBT:** Prout and Nowak-Drabit meta-analysis showed an effect size of 1.01 for psychotherapy (26% were studies of youth). Studies of CBT are mixed, yet do show some improvement (reduced negative interpretation bias, slow pace of breathing).

  - ➢ Encourage accommodations for developmental age and communication ability

- ❖ **Communication Interventions:** Meta-analysis of alternative and assistive communication found an effect size of 0.88. Early intervention and use of Functional Communication Training (FCT) increased effect size.

- ➢ Little evidence for teaching theory of mind skills

- ❖ **Applied Behavioral Analysis:** Generally found to be effective for ID/IDD and ASD.

  - ➢ Differential reinforcement (reinforce desired behavior) shown most effective.

  - ➢ Positive Parenting Program (Triple P) showed a decrease in parental stress, maladaptive parenting, child behavioral issues

- ❖ **Social Support:** Family needs psychoeducation, case manager, educational advocate, local disability advocacy organization support throughout life.

Statement 2: Psychotropic Medications can be considered to address psychiatric symptoms in children with ID/IDD

- ❖ No current FDA approved medication specifically for use in patients with ID/IDD - most children with ID/IDD excluded from trials

- ❖ May be more sensitive to side effects, use more conservative dosing

- ❖ Consider treatment evidence in youth with ID/IDD when possible

- ❖ **Medication Selection and Monitoring:** Consider other factors (ADHD, anxiety, medical issues, and communication deficits) before prescribing a medication for behavior problems and limit use to those who pose a risk of harming self/others, severe impulsivity, at risk of losing services, or other treatments failed.

  - ➢ Not to be a substitute for appropriate support services

  - ➢ Consider consolidation of medications for those with seizure disorders or other medical comorbidities

  - ➢ PRN medication have potential for overuse, monitor frequency

  - ➢ Monitor response with outcome measures (Aberrant Behavior Checklist, Conners Clinical Index, SNAP)

  - ➢ Children with ID/IDD more sensitive to side effects (irritability, cognitive dulling, sedation) - monitor using visual aids to enhance communication.

- ➢ Document baseline movement disorders as Abnormal Involuntary Movement Scale (AIMS) use may be limited in those with stereotypic movement.

Statement 3: Consider specialized treatment setting and providers with patients who have treatment-refractory symptoms

- ❖ Preliminary evidence for decreased LOS and readmission rates for children with ID/IDD and ASD hospitalized in specialized child psych units.

Summary of Psychotropic Medication Treatment in Children with ID/IDD

Medication	Target Symptoms	Evidence/Findings	Side Effect Profile	Treatment Notes
Risperidone	Irritability, Aggression-related to Conduct Disorder and ODD	Two open label, 48 week extension studies: Positive findings within 2 weeks, sustained efficacy	Headache, Somnolence (most common), weight gain, asymp. prolactin elevation	Due to SE profile, consider psychosocial treatment first
Methylphenidate	Hyperactivity, Inattention	Two RCTs, children with ID/IDD included: Effect size of 0.39 - 0.52	Appetite suppression, sleep problems	Lower effect size than typically developing children (0.8 - 0.9)
Risperidone & Methylphenidate	Irritability, Aggression, Hyperactivity	Post hoc analysis of two large RCTs selecting children with ID/IDD and disruptive behavioral disorders on both medications: Better control of hyperactivity than with stimulant monotherapy	No increase in adverse events	Not original aim of study
Risperidone vs Methylphenidate	Hyperactivity, Inattention	Comparison study: more pronounced effects with Risperidone	Risperdone has worse side effect profile	Methylphenidate remains first line
Alpha agonist	ADHD symptoms	Single study in children with ID/IDD: improvement	Potential: depression, poor sleep, sedation, cardiac disturbances, cognitive dulling	Assume that guanfacine equally effective
SSRIs	Anxiety, Depression	***	_	Fluoxetine, Sertraline
Alpha agonist, Beta blockers	Anxiety	No trials in children with ID/IDD	_	_
Benzodiazepines Antihistamines	Anxiety, Sleep problems	_	Heightened sensitivity to disinhibition	_
Mood Stabilizers	Bipolar Disorder	***	_	Valproic acid, Lithium
Antipsychotics	Psychosis	***	increased sensitivity to EPS in 1st gen antipsychotics	Risperidone, Aripiprazole preferred
Melatonin	Sleep problems	One RCT: Effective at improving sleep in adolescents with ID/IDD	_	_

***No new studies in children with ID/IDD since 1999, treatment similar to typically developing children

A Ninja's Guide to Disruptive Disorders

Oppositional Defiant Disorder

A Ninja's Summary: *Practice Parameter for the Assessment and Treatment of Children and Adolescents with Oppositional Defiant Disorder*

(Updated 2007)

Why Care? ODD is one of the most commonly encountered clinical disorders in C/As, creating a disturbance in social, academic, and occupational functioning. It is frequently comorbid with other psychiatric conditions, and can precede substance use, delinquent behavior, and eventual conduct disorder. Early intervention is more likely to succeed and prevent progression to more problematic behavior.

Epidemiology

- **Community prevalence**: 1-16%
  - Depends on criteria, assessment methods, time window considered, and number of informants.
  - More common in lower SES groups
- More common in prepubertal boys
- Usually manifests by age 8

Etiology

- **Most common opinion:** ODD arises out of complex mix of risk and protective factors originating in the biopsychosocial constellation of an individual
    - ➢ Convincing evidence of etiology remains elusive

Biological Risk Factors

- **Familial clustering of disorders:** ADHD, substance use, mood disorders, and disruptive behavioral disorders
- Inconsistent findings related to exposure to toxins or nutrition
- Studies may implicate prefrontal cortex abnormalities, neurotransmitter dysfunction, low cortisol, and high testosterone

Psychological Risk Factors

- **Attachment theory:** ODD seen as a signal to an unresponsive parent
    - ➢ Empirical evidence inconsistent with this theory
- Children with comorbid ADHD/ODD/CD have multiple intraindividual and contextual risk factors that begin in infancy and lead to adverse personality formation in adulthood
- **Aggressive Children:** underutilize social clues, misattribute hostile intent, come up with fewer solutions to problems, and expect a reward for aggression

Social Risk Factors

- **Ecological Factors:** poverty, poor structure, community violence
    - ➢ Although conflicting evidence about risks related to SES exists

- **Intrafamilial social processes:**
    - Coercive family processes, lack of parental supervision, lack of positive parental involvement, inconsistent discipline, and child abuse

Clinical Presentation

- Recurrent patterns of negativistic, hostile, or defiant behavior for at least 6 months in 1 of 3 domains of functioning
    - Behaviors directed at someone (authority figure)
    - No major antisocial violations
    - Behaviors must be present outside of context of mood/psychotic episodes
    - Behaviors must be abnormal or severe for the child's developmental stage
- Most common in late preschool or early school age children
    - 2-3 years earlier than CD
    - Girls may manifest aggression differently than boys
        - Covert aggression - indirect, verbal, relational

Differential Diagnosis

- **Substantial overlap between ODD and ADHD**
    - Those with ODD and ADHD tend to be more aggressive, higher range and persistence of problem behaviors, rejected more often by peers, and perform worse in academics
    - ADHD may facilitate earlier appearance of ODD and increase the transition to CD

- Youth with ODD have higher rates of comorbid psychiatric disorders, greater family and social dysfunction
    - Population-based study: 14% had comorbid ADHD, 14% had comorbid Anxiety, and 9% had comorbid depression
- **Substance abuse:** suspect in teenagers or when interventions are not working
- Comorbid ODD and CD
    - Higher rates of mood disorders and social impairment
- **Oppositional behavior may be used to manage anxiety due to overwhelming demands**
    - Consider developmental disorders, and language/learning disorders

Preventive Intervention

- Early prevention is key in ODD and other behavioral disorders
    - Delivered at school, clinic, or other community locations
    - Head Start programs may prevent future delinquency
    - Home visitation to high-risk families has positive outcomes related to ODD
- Parent management strategies have the most support
    - Social skills, conflict resolution, and anger management psychoeducation
    - **Adolescents:** Cognitive interventions, skills training, vocational training, and academic preparation prevents disruptive behavior
- School-based prevention programs: modest positive effects

- ➢ Focus on bullying, antisocial behavior, and peer group influences
- ➢ Some evidence that group treatment can have bad outcomes for deviant youth
    - ■ Mixing antisocial peers with prosocial peers may lead to more antisocial peers

Recommendation 1: Successful assessment and treatment of ODD requires establishment of therapeutic alliances with the child and family **(MS)**

- ❖ Establish therapeutic alliance with patient and parents separately
- ❖ Don't rely solely on collateral information → alienate patient
    - ➢ Empathize with patient without sanctioning behavior
- ❖ Raise constructive criticism of parenting without making parents feel accused or judged
    - ➢ Compile list of parental strategies being used and how these are achieving long and short term outcomes

Recommendation 2: Cultural issues need to be actively considered in diagnosis and treatment **(MS)**

- ❖ Ethnic subgroups have different standards of parenting, along with efficacy and risk of different parenting practices
    - ➢ Clinicians should be prepared to be educated about differences
    - ➢ Children's obedience and discipline differences are common

Recommendation 3: The assessment of ODD includes information obtained directly from the child as well as the parents regarding core symptoms of ODD, age of onset, duration of symptoms, and degree of functional impairment **(MS)**

- **Differentiation of ODD from normative oppositional behavior, transient antisocial acts, or CD is important**
  - Isolated occurrences of oppositional behavior are common in childhood
    - Usually related to peer-related conflicts or significant stressors
  - Always consider if oppositionality is triggered by abuse
- Oppositional-defiant behavior may be isolated to one setting or person
  - Unrealistic parental demands → reinforce child's maladaptive response
- **Perform a Functional Analysis**: identify antecedents, consequences of behavior
- Consider access to weapons and securing/removal of weapon
- **Bullying:** either as a victim or a perpetrator (or both)

Recommendation 4: Clinicians should carefully consider significant comorbid psychiatric conditions when diagnosing and treating ODD **(MS)**

- First differentiate ODD from an adjustment reaction, then consider if ODD has already progressed to CD
- Treat all comorbid conditions appropriately → may reduce oppositionality
- Disruptive behavior more common in children with Chronic Illness
  - Consider appropriate compliance with treatment

Recommendation 5: Clinicians my find it helpful to include information obtained independently from multiple outside informants **(CG)**

- ❖ Daycares, teachers, other school professionals can be sources for information
    - ➢ Helps determine how many domains of function affected and confirm diagnosis
    - ➢ Can be low rate of agreement among informants
        - ■ Especially between children and parents/teachers
        - ■ Self-reported problem behaviors have better prognosis

Recommendation 6: The use of specific questionnaires and rating scales may be useful in evaluating children for ODD and tracking progress **(OP)**

Recommendation 7: The clinician should develop an individualized treatment plan based on the specific clinical situation **(MS)**

- ❖ **Multimodal treatment**: indicated due to frequent comorbidities
    - ➢ Usually over several months or longer with booster sessions
    - ➢ Combining individual psychotherapy (problem-solving skills training), family psychotherapy, pharmacotherapy, and school-based interventions
    - ➢ **Absence of comparative clinical trials**
- ❖ **Family interventions are the best-studied treatments**
    - ➢ Opportunities for early intervention at different levels of intensity and provide safety (inpatient or residential treatment)
    - ➢ **Preschool:** emphasis on parent training and education
    - ➢ **School-age:** school-based, family-based, and individual approaches

- **Adolescence:** individual and family approaches

- Pharmacological interventions can be useful at all ages

Instruments for diagnosis and tracking behavioral disorders

Instrument	Construct	Ages	Items	Information	Comments
Conners Rating Scales	Oppositional Hyperactivity, Impulsivity	School age +	10	Parent or teacher report	Does not desegregate impulsivity from hyperactivity
Barratt Aggressive Acts Questionnaire	Impulsive and premeditated aggression, mood, and agitation	Late adolescent +	22	Self-report	Desegregates different forms of aggression
Child Behavior Checklist	Internalizing and externalizing behaviors	School age +	118	Parent report	Best in long-term patterns
Youth Self-Report	Internalizing and externalizing behaviors	School age +	102	Self-report	Best in long-term patterns
Overt Aggression Scale	Overt Aggression	Adult Inpatient	21	Observational	Best use in controlled settings
Aggression Questionnaire	Predatory and affective aggression	Child & Adolescents	10	Observational	-Desegregates different forms of aggression -Limited empirical support
Buss-Durkee Hostility Inventory	Overt and covert hostility	Late adolescents - young adults	21	Self-report	-
Spielberger Anger and Expression of Anger Inventory	8 state and trait anger subscales	Late adolescents - young adults	44	Self-report	-

Anger, Irritability, and Aggression Questionnaire	Labile anger, irritability, and assault	Children, some adolescents, young adults	28	Self-report	Use not fully established in youth
Buss-Perry Aggression Questionnaire	Physical and verbal aggression, anger, hostility	School age +	29	Self-report	Update has an expanded age range
Life History of Aggression	Total lifetime aggression	Young adults	11	Interview	
Children's Aggression Scale	Use of weapons, verbal aggression, provoked or initiated physical aggression, aggression towards objects and animals	Children 7-11 yo	33	Parent report	Limited empirical support
Conners/Wells Adolescent Self-Report of Symptoms	Conduct problems and anger control problems	Adolescents	64	Self-report	Epidemiological orientation
Parent Daily Report	Antisocial and problematic behavior	All ages	30	Parent report	-Tested in controlled trials -Antisocial behavior of child in last 24 hours
Interview for Antisocial Behavior	Diverse overt, covert and antisocial behaviors	All ages	23	Parent report	-Antisocial behavior of child in last 24 hours with differentiation of aggression subtype

Adapted from Table 2 in Practice Parameters

Recommendation 8: The clinician should consider parent intervention based on one of the empirically tested interventions **(MS)**

- **Parent Management Training**
  - Reduce positive reinforcement of disruptive behavior
  - Increase reinforcement of prosocial and compliant behavior
    - Parental attention is predominant
    - Punishment usually consists of a form of time out, loss of tokens, and/or loss of privileges
  - Apply consequences and/or punishment for disruptive behavior
  - Make parental response predictable, contingent, and immediate

Parent Management Training Programs

Program	Ages	Subjects	Administration	Level of Evidence
Incredible Years	Up to 8 yo	Parents, Teachers, Children	Group	RCT
Triple P - Positive Parenting Program	Up to 13 yo	Parents		RCT
Parent-Child Interaction Therapy	Up to 8 yo	Parents, Children	Individual family	RCT
Helping the Noncompliant Child: Parenting and Family Skills Program	Up to 8 yo	Parents	Individual family	RCT
COPE	Up to 12-14 yo	Parents	Group	RCT
Defiant Children	Up to 12 yo	Parents	Individual family	RCT
The Adolescent Transitions Program (ATP)	11-13 yo	Parents, Children	Individual family and group	RCT

- **Issues with family or parental approaches**
  - Use of mild forms of spanking
  - High treatment dropout rates (as high as 50%)
  - Parental psychopathology impeding participation and progress
    - Use of techniques to control children
    - May have more severe confrontations

Recommendation 9: Medications may be helpful as adjuncts to treatment packages, for symptomatic treatment and to treat comorbid conditions **(CG)**

- **Medications should not be the sole intervention for ODD**
  - Mostly adjunctive, palliative, non curative
- **Improving efficacy of medication treatment:**
  - Most effective after strong treatment alliance established
  - Enlist support/assent of child
  - If unresponsive to one medication, switch medications instead of adding another medication
- **Pharmacotherapeutic treatment for ODD not well studied**
  - Support from open-label and double-blind placebo controlled studies
- **Stimulants, Atomoxetine:** Improved oppositional behavior with treatment of primary ADHD diagnosis
- **Mood Stabilizers (Lithium, Depakote, Antipsychotics, Stimulants)**

- ➢ Trials targeted aggressive behavior
- ➢ Atypical antipsychotics are most widely used for aggression
- ➢ Recommended to treat after a baseline has been established
    - ■ Improvement can be attributed to drugs instead of improvements from a stabilizing environment

❖ **Target medications to specific comorbid conditions**

- ➢ Limited evidence for SSRI treatment of ODD in context of mood disorders

Recommendation 10: Intensive and prolonged treatment may be required if ODD is unusually severe and persistent **(CG)**

❖ **Considerations driving inpatient/residential placement**

- ➢ Usually considered measure of last resort
- ➢ Lack of progress
- ➢ Safety concerns for patient or those around them
    - ■ Extreme recklessness may be a form of self-injurious behavior
- ➢ Predatory behavior or planned aggressive behavior
    - ■ Emerges in school years
    - ■ Associated with poor outcomes

❖ **Determining level of care**

- ➢ Treatment should be in least restrictive setting, guarantees safety, and allows for regular delivery of interventions

- ➢ Consider day treatment, residential, or hospitalization if parents are unable or unwilling to collaborate with treatment

- ➢ Hospitalizations for crisis management only

- ➢ **Residential placement:** therapeutic foster care, respite care

    - ■ **Risks:** Separation from family and institutional victimization

    - ■ **Goal:** Rapid return to community and family

    - ■ **Alternatives to Residential:** Intensive in-home therapies

Recommendation 11: Certain interventions are not effective **(NE)**

- ❖ **Dramatic, one-time, time-limited, or short-term interventions are not successful**

    - ➢ Boot camp, shock incarcerations

    - ➢ Risk of injury - exposure to frightening situations

    - ➢ Worsen behavior by heightening a fear-aggression reaction or modeling of deviance

Conduct Disorder

A Ninja's Summary: *Practice Parameter for the Assessment and Treatment of Children and Adolescents with Conduct Disorder*

(Updated 1997)

Why care? Caring for patients with conduct disorder can be challenging and nuanced, the prevalence is between 1.5-3.4%, and 40% of youth with CD develop Antisocial PD. The comorbidities associated with conduct disorders are significant and lead to deficits in multiple domains of functioning

Background

Children with conduct disorder are more likely to be male, of low socioeconomic status, with familial aggregation. ODD and antisocial PD are on the same spectrum as CD. There are significant comorbidities with depression and substance use which should be closely monitored. Treatment must be as early as possible, address multiple aspects of life and be for a significant amount of time.

Statistics

- Prevalence is between 1.5-3.4%
- 40% of youth with CD develop Antisocial PD (which in adults prevalence is 2.6%)

Diagnosis

- must interview multiple people from various settings over time (parent, child, teachers, social workers, juvenile justice workers)

- ➢ **Birth hx**: ask about substance use by mom, infections during pregnancy, or medication use during pregnancy

- ➢ **Developmental hx**: ask about attachment, temperament, aggression, impulse control, focus/attention, oppositional behavior

- ➢ **Abuse**: always ask about all forms of abuse as a victim *and as the perpetrator*

- ➢ **Cognitive function**: review neuropsych/psychoeducational testing or order it if not available Family assessment is an important part of the evaluation

- ➢ **Family**: how they cope, stressors, resources/support, socioeconomic status, discipline style, how they manage conflict, how parent and child interact (coercive cycles leading to reinforcement of noncompliance), amount of supervision

    - ■ thorough family history: any antisocial behavior in family, jail time, violence, abuse, ADHD, substance use, developmental disorders, personality disorders, adoption, foster care, juvenile hall

    - ■ enquire about separation/divorce of parents, death of key figures

- ❖ Assess patient for:

    - ➢ Ability to form attachments, trust others, capacity for empathy or guilt

    - ➢ Impulse control, are they able to show restraint

    - ➢ Ability to take ownership/accept responsibility

    - ➢ Quality of peer relationships and sibling relationships

    - ➢ Mood, self-esteem, suicide risk

    - ➢ Paranoia, dissociation, psychosis

- ❖ Obtain Physical exam with baseline pulse rate

- Ask about head injuries, seizure disorder, chronic illness, environmental exposures (like lead)
- UA and UDS

- Distinguish childhood onset vs adolescent onset
  - Overt vs covert vs authority-conflicted
  - Underrestrained vs overrestrained
  - Socialized vs undersocialized

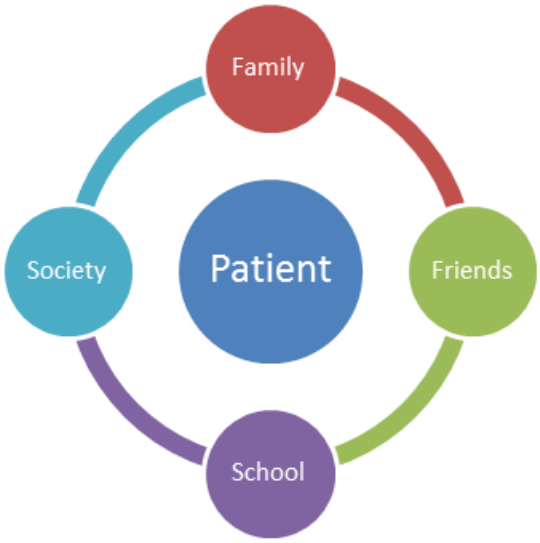
- Differential
  - ADHD, ODD, IED, substance use disorder, mood disorders, PTSD, dissociative disorders, BPD, somatization, organic brain issue, developmental disorders/learning disorders, schizophrenia
    - **How to differentiate** between CD and the above disorders: the *persistent pattern of violating rules and rights of others* along with problems with police is what's unique to CD
  - ADHD most often comorbid

Treatment

- Focus more on interpersonal relationship and psychoeducation over medications and other deeper therapeutic modalities

- Intervention in all aspects of life: family, school, friends, society and patient
  - **Family piece**: parent guidance, training, family therapy, sobriety in family members
    - consistent positive and negative consequences
    - well defined expectation and rules

- **Patient piece:** combination of behavioral approach and cognitive approach along with psychosocial skill building



- **Friend piece**: replace bad influences

- **School piece**: appropriate placement, alliance between parents and school

- **Social piece**: involving judges, probation officers, social services like Big Brother/Big Sister programs, job training and independent living skill

- The diagnosis is chronic, requires extensive treatment and long term follow up

- Meds not enough on their own, mostly useful for comorbid disorders and target symptoms (like stimulants for ADHD, SSRIs for depression, etc)

- Sometimes placement outside the home is needed

A Ninja's Guide to Pediatric Mood Disorders

Depressive Disorders

A Ninja's Summary: *Practice Parameter for the Assessment and Treatment of Children and Adolescents with Depressive Disorders*

(Updated 2007)

Why care? Depression is a familial recurrent illness that impacts every aspect of a child's life (family, social, academics) and leads to an increased risk of suicide, substance abuse, and ongoing depression into adulthood. By early identification and effective treatment, we can help to reduce the psychosocial morbidity and mortality associated with depression.

Epidemiology:

- Prevalence of MDD → 2% in children, 4-8% in adolescents
- Male-to-Female ratio 1:1 in childhood, 1:2 in adolescence (risk increased 2-4x after puberty in females)
- Cumulative incidence by 18 yo is ~20%
- 5-10% of C/A (Child and Adolescents) have subsyndromal symptoms of MDD with psychosocial impairment, high family loading for MDD, and increased risk of SI and later MDD

Clinical Presentation:

- **Differences in Children:**
  - May present with mood lability, irritability, low frustration tolerance, temper tantrums, somatic complaints

- ➢ Social withdrawal → May not verbalize feelings of depression

- ❖ **Atypical Symptoms**

  - ➢ Increased rejection sensitivity, lethargy, increased appetite, carb cravings, hypersomnia

- ❖ **Depression with psychotic features:**

  - ➢ Associated with family hx of bipolar and psychotic depression

  - ➢ More severe depression, higher morbidity, SSRI monotherapy resistance, **increased risk of bipolar disorder**

- ❖ **Seasonal affective disorder:**

  - ➢ Symptoms present in season with less daylight

  - ➢ **Differentiate from school stress** coinciding with the school calendar

- ❖ **Persistent Depressive Disorder (Formerly Dysthymia Disorder):**

  - ➢ Less intense than MDD, but more chronic with higher psychosocial impairment

  - ➢ Symptoms in **children** must be present on most days for most of the day for a period of **1 year**

Comorbidity:

- ❖ 40 to 90% with depression have another psych disorder (50% have 2+ psych disorders)

  - ➢ **Most common comorbidity: Anxiety** >> Disruptive disorder/ADHD (Child) and Substance use (adolescents)

Differential Diagnosis:

- **Psychiatric Disorders:** Anxiety, dysthymia, Premenstrual Dysphoric Disorder, ADHD, ODD, developmental disorders, substance abuse

- **Medical disorders:** hypothyroidism, mononucleosis, anemia, cancer, autoimmune disorders, chronic fatigue syndrome

- **Unipolar Depression vs depressive phase of Bipolar?**

    - Look for high family loading for bipolar, psychosis, history of med induced mania or hypomania

Clinical Course:

- **Duration of MDD episodes:**

    - **8 months** in clinically referred youth

    - 1-2 months in community samples

- **Relapse probability:**

    - 20 to 60% by 1-2 years after remission

    - 70% by 5 years after remission

    - 20 to 40% will develop bipolar disorder

- **Poor outcome probability:**

    - Greater severity, chronicity, multiple episodes, comorbidity, hopelessness, residual subsyndromal symptoms, negative cognitive style, family problems, low SES, ongoing negative events (abuse, family conflict)

- **Duration of PDD episodes:** 3-4 years with increased risk of MDD and substance use disorders

Complications:

- **Untreated MDD:** Affects development of emotional, cognitive, social skills, and family relationships

- **60% have SI and 30% attempt suicide**

    - **Increased risk of SI with:** previous suicide attempt, comorbid psych disorders, impulsivity, aggression, available lethal agents, exposure to violence, physical/sexual abuse, family history of suicide

- **High Risk for:** substance use, legal problems, negative life events, physical illness, early pregnancy, poor work/academic/psychosocial functioning

Risk Factors:

- **Familial Disorder:** shown by high-risk, adoption, and twin studies

    - **Highest predictive factor for MDD =** high family loading

- **Stressors:** effects depend on child's negative attributional styles for interpreting stressors, coping skills, support, and genetic factors

- **Other Factors:** comorbid disorders, **medical illness**, use of medications, biological and sociocultural factors

Recommendation 1: Maintain a confidential relationship with the C/A while collaborating with parents, medical providers, mental health professionals, and school personnel **(MS)**

- Immediately discuss boundaries of confidential relationship (varies by state)

    - Suicide or violence risk communicated to parents

- ❖ Parents will expect info about treatment plan, safety plan, progress toward goals of treatment
    - ➢ Create a way for parents to express concerns about declining function or safety concerns
- ❖ Request permission to communicate with other medical/mental health professionals and school

Recommendation 2: Psych assessment of C/A should routinely include screening for depression **(MS)**

- ❖ Screen for key symptoms of depressed/sad mod, irritability, anhedonia

Recommendation 3: If screening is positive, perform a thorough evaluation for depression, comorbid psych and medical disorders **(MS)**

- ❖ Clinician must be developmentally attuned and build good rapport with C/A
    - ➢ Be attentive to changes in irritability, sleep habits, school performance, withdrawal from activities
- ❖ Evaluate child/families strengths → be **sensitive to racial, cultural, and religious traditions** that may influence presentation, description, interpretation of symptoms and treatment
- ❖ Directly interview child with caregivers, ideally **interview adolescent alone**
- ❖ Build a strong differential diagnosis → may use standardized interviews if there is enough time
- ❖ Consider use of mood diary/timeline to help child and parent visualize course of mood
- ❖ Evaluate child's functioning with rating scales, ie CGAS and GAF

- ❖ Determine the appropriate level of care with patient and family
    - ➢ Can depend on child factors as well as **parental factors** (adherence to treatment, parental psychopathology, family environment)

Recommendation 4: Psych Eval must assess for harm to self or others **(MS)**

- ❖ **Screen at every visit:** may use rating scales, ie Columbia Sucidal Severity Rating Scale
- ❖ Evaluate risk/protective factors, current severity, and highest severity in episode and lifetime
    - ➢ Screen for weapons at home → have parents secure or remove them
- ❖ **Differentiate SI from Non-suicidal self harm to relieve negative affect**
- ❖ Assess for Homicidal ideation:
    - ➢ ⅓ of adolescent suicide victims had HI in week before suicide (in one study)
    - ➢ Restrict access to lethal agents, ie guns

Recommendation 5: Psych Eval should assess for past exposure to negative events, negative environments, support, and family psych history **(MS)**

- ❖ Evaluate for current/past stressors: physical/sexual abuse, familial conflict, neglect, low SES, violence exposure
    - ➢ Ensure patient safety if abuse is current
- ❖ Interpersonal tension cycle: Depression makes the patient more irritable which makes relationships tense, leading patient to feel more depressed
    - ➢ Interpersonal psychotherapy efficacious for improving key relationships

- ❖ Deviant friend groups can lead to antisocial behavior and more stressful life events → increasing depression

- ❖ Evaluate family psychopathology to determine willingness and course prediction of treatment

Recommendation 6: Treatment should always include an Acute and Continuation Phase; some may need maintenance treatment **(MS)**

- ❖ **Treatment of Depression in 3 phases:**
  - ➢ **Acute:** Achieve response and, hopefully, full remission
  - ➢ **Continuation:** Required to consolidate response during acute phase and avoid relapse
  - ➢ **Maintenance:** Avoids recurrences in youth with severe, recurrent, and chronic disorders
- ❖ **Definitions of treatment outcomes:**
  - ➢ **Response:** No symptoms or a significant reduction in depressive symptoms for at least 2 weeks
  - ➢ **Remission:** A period of at least 2 weeks and <2 months with no or few depressive symptoms
  - ➢ **Recovery:** Absence of significant symptoms of depression (e.g., no more than 1Y2 symptoms) for Q2 months
  - ➢ **Relapse:** A DSM episode of depression during the period of remission
  - ➢ **Recurrence:** The emergence of symptoms of depression during the period of recovery (a new episode)

Recommendation 7: Each phase of treatment should include psychoeducation, supportive management, and family/school involvement **(MS)**

- **Psychoeducation:** educate family and patient of causes, symptoms, course, treatment options, risks of treatment and no treatment.
    - Improves adherence to treatment and reduces symptoms
- **Supportive Psychotherapeutic Management:** active listening and reflection, restoration of hope, problem solving, coping skills, strategies for maintaining treatment participation
- **Family involvement:** Need family involvement for treatment to be successful
    - Motivation for treatment comes from parents, involve them in treatment contract
    - Parents may observe aspects of function or symptoms that the child may not share
    - Parents monitor progress and provide a safety net
    - Take into account the family cultural and religious background
    - Facilitate referrals for caregivers and siblings who have psychiatric illness to improve long term success
- **School Involvement:** Psychoeducation for school personal to understand disease model of depression
    - Advocate for accommodations until recovery is achieved
    - After recovery, if still having academic difficulties, consider subsyndromal depression or other comorbid disorders
    - Students with MDD may qualify for Emotional Disturbance Disability IEP under IDEA

Recommendation 8: For depression that is uncomplicated, brief, or has mild psychosocial impairment → education, support, and case management can be sufficient treatment **(CG)**

- ❖ Observe response after 4 to 6 weeks of supportive therapy to determine need for higher level of treatment

Recommendation 9: Children who don't respond to supportive therapy or have complicated depression should have a trial of specific psychotherapy and/or antidepressant **(CG)**

- ❖ **Indications for Psychotherapy and/or Pharmacotherapy:** Mod-Severe depression, chronic/recurrent depression, high psychosocial impairment, suicidality, agitation, and psychosis
- ❖ **Moderate Depression:** May respond to CBT or IPT alone
- ❖ **Severe Depression:** May require antidepressant alone or in combo with therapy
- ❖ **Failed monotherapy previously:** Likely need combo treatment
- ❖ **Psychotherapy contraindications:** previous poor response to psychotherapy, agitation, psychosis, low motivation, poor concentration, sleep disturbance
    - ➢ Use meds alone until able to participate in therapy
- ❖ **Young Children:** May benefit from adaptation of CBT, IPT, family, and psychodynamic therapy modalities

<u>Summary of Evidence for Treatment of Depression with Psychotherapy:</u>
See Appendix B

❖ **Pharmacotherapy:**

- ➢ Selective Serotonin Reuptake Inhibitors (SSRIs) have a relatively good response rate (40%-70%) with NNT of 10
  - ■ Placebo response rate is also high (30%-60%)
    - ○ May be related to studies including patients with mild-mod depression and low medication dosages
- ➢ Fluoxetine is the only medication to be approved by the FDA for the treatment of child and adolescent depression
  - ■ Larger difference between medication and placebo than trials with other antidepressants
  - ■ Long half-life may lessen the impact of poor adherence to treatment
- ➢ Rate of remission is more stringent and clinically relevant endpoint
  - ■ Ranged from 30 to 40% - may be related to need for longer duration of treatment at higher dose, lack of treatment of comorbid conditions, and need for additional psychosocial interventions
- ➢ **TORDIA Study (2010) for resistant depression in Adolescents:** If one SSRI does not work, consider switching to another. If second SSRI doesn't work, may consider SNRI like venlafaxine

❖ **SSRI/SNRI Adverse Effects:**

- ➢ **Common:** Gastrointestinal symptoms, sleep changes (e.g., insomnia or somnolence, vivid dreams), restlessness, diaphoresis, headaches, akathisia, changes in appetite (increase or decrease), and sexual dysfunction.
- ➢ **More specifically IN CHILDREN:** 3-8% may show "behavioral activation" evidenced by increased impulsivity, agitation, irritability, and silliness
- ➢ **Serotonin Syndrome (e.g., hyperthermia, diaphoresis, confusion):**

        - Antidepressants used with other serotonergic agents (ie MOAIs)

    - Increased predisposition to bleeding (e.g., easy bruising, epistaxis)

    - Hyponatremia

    - **Discontinuation syndrome:**

        - Venlafaxine and paroxetine, least with fluoxetine

            - May induce withdrawal symptoms, some of which may mimic a relapse or recurrence of a depressive episode.

            - May include emergent suicidal symptoms with abrupt withdrawal

- **Suicidal Ideation/Attempts:**

    - **FDA/Columbia Meta-analysis:** Evaluated effects on suicidality of 9 antidepressants used in 24 acute RTCs.

        - 17 out of 24 studies showed no significant onset or worsening of suicidality

        - Venlafaxine had a statistically significant increase in suicidality (Ideation and not behavior)

        - 1-3:100 treated with an antidepressant had a suicide adverse event

            - Few suicide attempts and no completion

    - **Bridge et al., 2007 Meta-analysis:** extended included studies

        - NNH for spontaneous suicidality found to be 112

        - NNT previously found to be 10 → meaning **11x** more depressed patients may **respond favorably** than spontaneously report suicidality.

- ➢ ***In fact, there was a dramatic decrease in adolescent suicide with increased use of SSRIs***

- ➢ **Explanation of spontaneous suicidality:**

    - ■ Patients taking medication have more side effects, therefore have more contact with Psychiatrists and have more opportunity to hear about suicidality

    - ■ Improvement from the antidepressant may result in the patient talking about suicidality for the first time

- ➢ ***The risk/benefit ratio for SSRI use in pediatric depression appears to be favorable with careful monitoring***

❖ **Clinical Use:**

- ➢ **Start with low dose and increase it slowly:** Avoid side effects and improve adherence to treatment

    - ■ Doses are similar to those used in adults

- ➢ **Monitor for withdrawal when dosed once daily:**

    - ■ Half-life of sertraline, citalopram, paroxetine, and bupropion SR are much shorter in adults

- ➢ **Monitor clinical response and adjust dose at 4 week intervals**

    - ■ Consider weekly visits for first 4 weeks to monitor for side effects (if the system allows)

        - ○ Specifically risk of suicide and mania symptoms

- ➢ **Consider alternative treatment:**

    - ■ Minimal or no response at 8 weeks

    - ■ Remission not achieved by 12 weeks

Psychopharmacology for Treatment of Depression in Children and Adolescents

SSRIs	**Bleeding risk, Hyponatremia BBW: suicidal ideation**			
Medication	**Pediatric Dosing**	**FDA Indications (*Off-label Use)**	**Evidence**	**Notable Considerations**
Citalopram (Celexa)	10-40 mg	*MDD (>7yo)	-	-Can cause QT prolongation, avoid in long QT syndrome -Consider baseline EKG -Least drug-drug interaction, CYP 450: 2C19 (primary); 2D6, 3A4
Escitalopram (Lexapro)	5-20 mg	MDD (>12 yo) *MDD (>7-11 yo)	-	-Less risk of QT prolongation -Least drug-drug interaction, CYP 450: 2C19 (primary); 2D6, 3A4
Fluvoxamine (Luvox)	25-200 mg	OCD (>8 yo) *MDD (>7 yo)	-	-Generally avoided due to multiple drug interactions and less data supporting - Discontinuation syndrome, CYP 450: 2D6 substrate (primary); 1A2
Fluoxetine (Prozac)	10-60 mg	MDD (>8 yo) OCD (>7 yo) Bipolar 1 Disorder, Acute Depression (>10 yo)	RCTs: Larger difference from placebo than other antidepressants	-Can be activating, consider dosing AM -Long half-life w/ least risk of discontinuation syndrome -CYP 450: 2D6 (primary) *Significant interaction
Paroxetine (Paxil)	10-60 mg	Not indicated	-	-Generally avoided in youth due to discontinuation syndrome, weight gain, and anticholinergic effects -CYP 450: 2D6 substrate *Significant interaction
Sertraline (Zoloft)	25-200 mg	OCD (>6yo) *MDD (>6yo)	-	-Can be more sedating, consider dosing QHS -Give w/ food to increase absorption by 40%, helps w/ GI discomfort -Discontinuation Syndrome, CYP 450: 2C19 (primary); 2D6, 3A4

SNRIs	Risk of elevated BP and HR (Monitor) Can be helpful for chronic pain BBW: suicidal ideation			
Medication	**Pediatric Dosing**	**FDA Indications (*Off-label Use)**	**Evidence**	**Notable Considerations**
Duloxetine (Cymbalta)	30-120 mg	GAD (>7 yo) *MDD (>7 yo)	No RCTs at time of practice parameter	-Associated with hepatic failure, cholestatic jaundice -Associated with Stevens-Johnson and erythema multiforme -May cause weight gain, CYP 450: 1A2, 2D6
Venlafaxine (Effexor)	12.5-225 mg (IR 75 mg max) (ER 225 mg max)	*MDD (>7 yo)	RCTs: Better than placebo in adolescents, no difference from placebo in children	-Serotonergic at lower dose, NE at higher doses. -Abrupt discontinuation syndrome (IR formulation) -Greater risk of suicide than other SRNIs, overdose fatalities -CYP 450: 2D6 (primary); 3A4; active metabolite (desvenlafaxine)
Misc	**Can be used as adjunct to other SSRI/SNRIs**			
Mirtazapine (Remeron)	7.5-45 mg	*MDD (>7yo)	RCTs: No difference from placebo	-Antagonizes Alpha-2 Adrenergic and Serotonin 5-HT2 receptors -Oral disintegrating tablet (ODT) form -Lower doses antihistaminergic effects (<15 mg) w/ weight gain/somnolence, Higher doses more NE
Trazodone (Oleptro)	25-400 mg	*MDD (>6 yo)	-	-Antagonizes Serotonin 5-HT2A/C and Alpha-1 Adrenergic Receptors; Inhibits serotonin reuptake -To be effective for depression need higher consistent doses -Can cause priapism
Bupropion (Wellbutrin)	37.5-450 mg IR: immediate SR: 12-hour XL: 24-hour	*MDD (>6 yo for IR) *MDD (>11 yo with SR and XL)	Open-label study: effective for treating MDD + ADHD No RCTs at time of practice parameter	-Inhibits reuptake of norepinephrine and dopamine -Higher doses >400 mg, risk of seizures -Caution with use with history eating disorders

TCAs	**RCTs/Meta-analysis: TCAs no more efficacious than placebo**			**May cause anticholinergic effects Consider EKG due to risk for QT prolongation Caution with history of suicidality due to lethal overdose Caution with 2D6 agents (fluoxetine/paroxetine) *Should not be used as first-line treatment***
Medication	**Pediatric Dosing**	**FDA Indications (*Off-label Use)**	**Evidence**	**Notable Considerations**
Secondary Amines	**Inhibits norepinephrine (NE) reuptake**			
Desipramine	25-150 mg	MDD (>13 yo)	-	CYP 450: 2D6 (primary); 2C19
Nortriptyline	10-150 mg	*MDD (>6 yo)	-	-CYP 450: 1A2, 2C19, 2D6 (primary), 3A4
Tertiary Amines	**More Anticholinergic effects Inhibits Serotonin and Norepinephrine Reuptake**			
Amitriptyline	10-200 mg	*MDD (>9 yo)	-	-CYP 450: 1A2, 2C19, 2D6 (primary), 3A4; active metabolite
Clomipramine	25-200 mg	OCD (>10 yo)	-	-CYP 450: 1A2, 2C19, 3A4
Imipramine	10-100 mg	Nocturnal Enuresis (>6 yo) *MDD (>6 yo)	-	-CYP 450: 1A2, 2C19, 2D6 (primary), 3A4; active metabolite
Trimipramine	25-100 mg	*MDD (>13 yo)	-	CYP 450: 2D6 (primary), 3A4 -Rarely used

Recommendation 10: Treatment should be continued for 6 to 12 months to consolidate response to acute treatment and avoid relapses **(MS)**

- Rate of relapse after treatment with CBT or SSRI is high
  - Studies show lower rates of relapse with SSRI and/or CBT continuation therapy
- **Continuation Phase:** patients seen monthly (or sooner as needed) and psychotherapy consolidates skills learned during acute phase

Recommendation 11: To Avoid Recurrences, Some Depressed Children and Adolescents Should Be Maintained in Treatment for Longer Periods of Time **(CG)**

- Once asymptomatic for about 6 to 12 months, the clinician must decide whether maintenance therapy is indicated and the type and duration of therapy
- **Maintenance Phase:** Lasts about 1 year or longer, patients seen monthly or quarterly
  - **Duration of Treatment:**
    - >3 episodes of recurrent depression require longer periods of treatment (3-5 yrs in adults)
    - At least 2 episodes → maintenance treatment for at least 1 year
- **General rule:** the longer it takes for a patient to recover or the higher the number of recurrences, the longer the period of maintenance
  - Those who do not achieve full remission of symptoms are more vulnerable to relapse
- "Double Depression" (Depression + Dysthymia): Describe themselves as being depressed "as long as they can remember" may need treatment indefinitely

Recommendation 12: Depressed Patients with Psychosis, Seasonal Depression, and Bipolar Disorder May Require Specific Somatic Treatments **(CG)**

- **Depression with Psychosis (MDD with psychotic features)**
  - The combination of antidepressants with (atypical) antipsychotics may be helpful
    - See Schizophrenia section for chart of Antipsychotics
  - Vague or mild psychotic symptoms in a depressed child may respond to antidepressants alone.
  - Goal to taper off antipsychotic slowly with the eventual goal of keeping the child on monotherapy with an antidepressant.
  - In adults, electroconvulsive therapy is particularly effective for this subtype of depression but may also be useful for depressed psychotic adolescents

- **Seasonal Affective Disorder (SAD)**
  - A small study showed bright light therapy is efficacious for youths with SAD
    - Patients respond better to treatment during the morning hours,
      - Difficult on school days and for youths who refuse to wake up early in the morning
  - **Bright light therapy side effects:** headaches and eye strain
    - An ophthalmological evaluation may be considered before initiating light therapy
  - **Treatment with light may induce episodes of hypomania or mania in vulnerable patients.**

- **Depression vs. Bipolar Disorder**

  - **Similar early course of illness:**

    - If indicators of risk of bipolar disorder are present → discuss with the patient and family the pros and cons of initiating a prophylactic mood-stabilizing agent

    - Patients with a psychotic depression may be at greater risk of developing bipolar disorder

  - **Mild to moderate unipolar depression:**
    - May be best to start with psychotherapy because the risk of manic conversion with the use of antidepressants is substantial

    - Consider mood-stabilizing agent if depression presents with mood lability

Recommendation 13: Treatment should include the management of comorbid conditions **(MS)**

- Failure to treat comorbid conditions reduces probability of treatment response, increases risk of suicide, reduces function in school, and worsens interpersonal relationship problems

Recommendation 14: During All Treatment Phases, Clinicians Should Arrange Frequent Follow-up Contacts That Allow Sufficient Time to Monitor the Subject's Clinical Status, Environmental Conditions, and, If Appropriate, Medication Side Effects **(MS)**

- Determine treatment response, overall improvement, functional improvement using appropriate scales

Recommendation 15: During All Treatment Phases, for a Child or Adolescent Who Is Not Responding to Appropriate Pharmacological and/or Psychotherapeutic Treatments, Consider Factors Associated with Poor Response **(MS)**

- **Consider reasons for treatment failure:**
  - Misdiagnosis, unrecognized or untreated comorbid psychiatric or medical disorders, ongoing life stressors, and compliance
- **Failure to respond to adequate trial of SSRI:**
  - Switch to another antidepressant plus CBT
- May augment with alternative agents
  - **In extreme cases**: electroconvulsive therapy (ECT) may be considered

Recommendation 16: Children with Risk Factors Associated with Development of Depressive Disorders Should Have Access to Early Services Interventions **(CG)**

- Successful treatment of mothers with depression → significantly fewer new psychiatric diagnoses and higher remission rates of existing disorders in their children
- Early-onset dysthymia is associated with an increased risk of MDD
- **Evidence that anxiety disorder is a precursor of depression**
  - Treatment of this disorder may reduce the onset and recurrences of depression
  - SSRIs have greater efficacy for anxiety than for depression
    - Vigorous detection and treatment of anxiety disorders may reduce the risk of subsequent depression

Bipolar Affective Disorder

A Ninja's Summary: *Practice Parameter for the Assessment and Treatment of Children and Adolescents with Bipolar Disorder*

(Updated 2007)

Why care? About 20% of bipolar patients experience their first episode during adolescence. Peak age of onset is between 15 and 19 years old. In the United States, the number of bipolar diagnoses in children and adolescents has markedly increased during the past decade.

Background:

- There has been a shift in diagnosing based on pattern recognition or template to diagnosing based on individual symptom criteria
- Based on periods of elated, expansive, or irritable mood, children may be characterized as "atypical cases" which may be caused by developmental differences in manic symptom expression
- In children, patterns of illness and symptoms vary from the classic description of bipolar disorder in adults.

Definitions:

- **Bipolar I**
  - Requires ≥ 7 days of a manic or mixed episode, unless hospitalization is required
  - ICD-10 description: episodic illness with episodes of depression and mania, the latter lasting ≥ 1 week
  - DSM_III_R criteria did not specify duration criteria for mania
- **Mixed episode:** symptoms for both manic and depressive episodes met during a period lasting ≥ 7 days
- **Bipolar II:** periods of major depression and hypomania (lasting at least 4 days), but no full manic or mixed episodes
- **Rapid cycling:** ≥ 4 mood episodes in 1 year
- **Bipolar NOS:** cases not meeting full criteria for other bipolar diagnoses, used to describe many youth who do not have the classic adult presentation
- **Ultrarapid cycling:** Brief, frequent manic episodes lasting hours to days, but less than 4 days
- **Ultradian cycling:** Repeated brief cycles lasting minutes to hours that occur daily.

Historical Review:

- Early-onset mania often unrecognized during the early 20th century
- Studies of bipolar adults showed evidence of illness before age 19 in about a fifth of the cases.
- Presenting symptoms in childhood were often depression and hyperactivity

- There has been diagnostic confusion between schizophrenia and bipolar disorder, as **mania in adolescence often presents with psychosis**

Epidemiology:

- Estimated lifetime prevalence ranges from 0.4% to 1.6%, with about 0.5% with bipolar II
    - One survey showed an estimated lifetime prevalence of 0.6% in 14 to 16-year-olds
- Affects both sexes equally, but early-onset, especially before age 13, cases are predominantly male.

Risk Factors:

- Strong genetic component - 4 to 6 fold increased risk in first-degree relatives
- Dysthymic, cyclothymic or hyperthymic temperaments
- Premorbid psychiatric problems, particularly with disruptive behavior disorders, irritability, behavioral dyscontrol
- Premorbid anxiety and dysphoria - About 20% of youths with major depression later develop manic episodes
- Factors predicting development of mania
    - Rapid onset, psychomotor retardation, psychotic features characterizing depressive episode
    - Family history of affective disorders, especially bipolar
    - History of mania or hypomania after antidepressant treatment

- Although not supported by all studies, youths with psychotic depression are considered at greater risk of switching to mania with antidepressants.

Clinical Presentation:

- **Children**
  - Labile and erratic changes in mood, energy levels, behavior
  - Irritability, belligerence, mixed features more common than euphoria
  - High rates of comorbid disruptive disorders
- **Prepubertal and early-adolescent bipolar disorder (PEA-BP) phenotype**
  - Manic cycle as short as 4 hours, at least one cycle daily for 2 weeks
  - High rate of comorbid ADHD, other disruptive behavior disorders
  - Reported to be reliable, with stability over 4 years
  - Low maternal warmth → shorter time to relapse, psychosis → greater chronicity
- **Adolescents**
  - Mania associated with psychotic symptoms, labile moods, and/or mixed manic and depressive symptoms
  - Early course more chronic, refractory to treatment than adult onset disorder

Diagnostic Controversy:

- Are explosiveness, dysregulation and emotional lability in youths best characterized as bipolar disorder?

- **Is juvenile mania the same as adult mania?**
    - Adult: cyclical disorder with acute onset of clearly demarcated mood phases; marked reduction in need of sleep
    - Juvenile: chronic difficulties with regulation of moods, emotions, and behaviors; **≤50% of cases with sleep disturbance**
    - Prevalence rates in adults and children are both 1%, not showing the expected increase in adults
    - **Juvenile mania not yet shown to progress into classic adult mania**
- Overlap between mood and personality disorders: mood dysregulation in youths often associated with borderline personality disorder features

Recommendation 1: Psychiatric Assessments for Children and Adolescents Should Include Screening Questions for Bipolar Disorder **(MS)**

- Ask about distinct, spontaneous episodes of mood changes with associate sleep disturbance and psychomotor activation.
- Ask about history of depression, family histories of mood disorders
- Important but not specific: symptoms of irritability, reckless behaviors, increased energies
- Remember that emotional and behavior difficulties are often context dependent.

Recommendation 2: The DSM-IV-TR Criteria, Including the Duration Criteria, Should Be Followed When Making a Diagnosis of Mania or Hypomania in Children and Adolescents **(MS)**

- **Symptoms**
  - Rather than situational reactions, temperamental traits, negotiation strategies, or anger outbursts, manic grandiosity and irritability are distinct changes in the individual's mental and emotional state.
  - Diagnostic clues include pattern of illness, symptom duration, presence of psychomotor, sleep, and cognitive changes
  - Acute psychosis in adolescence may be the initial presentation of mania.
- Incorporate both current and past history of symptomatic presentation, treatment response, psychosocial stressors and family psychiatric history
  - A life chart may be helpful for this.
- Helpful structured diagnostic interviews and questionnaires
  - KSADs and WASH-U-KSADS - most commonly used diagnostic tools in research
  - YMRS, assesses severity of symptoms, treatment responses, but not diagnostic

Recommendation 3: Bipolar Disorder NOS Should Be Used to Describe Youths With Manic Symptoms Lasting Hours to Less Than 4 Days or for Those With Chronic Manic-Like Symptoms Representing Their Baseline Level of Functioning **(CG)**

- Significant impairment caused by manic episodes that last hours to less than 4 days or chronic manic-like symptoms, and youths with such symptoms should be classified as having bipolar disorder NOS.
- High rates of comorbid disorders, moods generally volatile and reactive

- ❖ Examine for environmental triggers, event patterns reinforcing outbursts, pragmatic language impairment, risk factors

Recommendation 4: Youths with Suspected Bipolar Disorder Must Also Be Carefully Evaluated for Other Associated Problems, Including Suicidality, Comorbid Disorders (Including Substance Abuse), Psychosocial Stressors, and Medical Problems **(MS)**

- ❖ Thorough workup recommended for other confounding illness and comorbid disorders
    - ➢ High rates of suicide attempts and substance abuse
    - ➢ Assess for developmental, cognitive, or speech and language disorders

Recommendation 5: The Diagnostic Validity of Bipolar Disorder in Young Children Has Yet to Be Established. Caution Must Be Taken Before Applying This Diagnosis in Preschool Children **(MS)**

- ❖ Assess for contributing factors to mood and behavioral concerns, such as developmental disorders, psychosocial stressors, temperamental difficulties, parent-child relationship conflicts.
- ❖ A diagnosis of a bipolar spectrum disorder in very young children can expose them to aggressive psychotherapy, for which safety has not been established.

Recommendation 6: For Mania in Well-Defined *DSM-IV-TR* Bipolar I Disorder, Pharmacotherapy Is the Primary Treatment (No updates including DSM-V yet established) **(MS)**

- ❖ Standard therapy, inspired by adult literature, includes lithium, valproate, and/or atypical antipsychotic agents, with other adjunctive medications used if indicated.
- ❖ Medication choice should be influenced by:

- ➢ evidence-proven efficacy
- ➢ illness phase
- ➢ confounding presentations (e.g., rapid cycling mood swings, psychotic symptoms)
- ➢ side effect spectrum and safety
- ➢ the patient's history of responding to medication, and
- ➢ patient and family's preferences

Considerations in Pediatric Populations

- ❖ **Lithium** is approved down to age **7 years and older** (Immediate release) and **12 years or older** (Extended Release) for acute mania and maintenance therapy
  - ➢ **It is the only medication approved for Bipolar disorder in youth.**
- ❖ **In adults**, the following medications are approved:
  - ➢ **For acute mania:** aripiprazole, valproate, olanzapine, risperidone, chlorpromazine, quetiapine, and ziprasidone, (Chlorpromazine is not generally used first-line.)
  - ➢ **For maintenance:** lamotrigine and olanzapine
  - ➢ **For bipolar depression:** the combination of olanzapine and fluoxetine other agents with some support for efficacy in adult studies include carbamazepine and antipsychotic agents.
- ❖ Evidence has *not shown* **gabapentin or topiramate** *to be helpful*
  - ➢ One study of topiramate in children and adolescents was equivocal
- ❖ Due to its side effects, **clozapine** should only be used for **treatment-refractory cases** with a well-established diagnosis.

- **Benzodiazepines** can stabilize the manic acute agitation and sleep disturbance but may **disinhibit younger children.**

- **Antidepressants** (SSRIs, non tricyclics) may be used adjunctively for depression, if the patient is also on at least one mood stabilizer.

    - Antidepressants may destabilize the patient's mood or lead to a manic episode

        - The event would be classified as Substance-Induced Manic Episode, even though it may be unmasking the disorder.

- **Less rate of relapse** seen with **antipsychotics combined with lithium** in youth in few trials conducted as opposed to lithium monotherapy in acute psychotic mania.

- **Mood stabilizers:** Lithium > Valproate > Carbamazepine for mania; Lamotrigine considered for maintenance therapy and depression

- **Antipsychotics** that can be effective in pediatric bipolar disorder: Aripiprazole, Olanzapine, Quetiapine, Risperidone (especially in combination with mood stabilizer)

    - Metabolic side effects including weight gain have been a particular concern for atypical antipsychotics, especially in youths.

    - **Response to therapy is generally low** even with atypical antipsychotics and mood stabilizers

        - **Rates of relapse were high**

- **Comorbid ADHD:** Stimulant medications may be helpful for ADHD symptoms once the patient's mood is stabilized on a mood stabilizer regimen

    - Comorbid disruptive behavioral disorders and ADHD are associated with poorer response to treatment

Pharmacology of Mood Stabilizers

Medication	Dose	Age	Indication(s) *Off-label	Notable Considerations
Carbamazepine (Tegretol, Equetro)	IR liquid (20-40 mEQ) IR (400-1200 mg) ER (400-1200 mg)	>6 years old	Seizure Disorder *Off-label for Bipolar disorder (Adults)	-Agranulocytosis -HLA-B1502 allele (esp Asian heritage); SJS -Monitor levels, pregnancy (teteragenic), CBC w/diff, Bun/Cr, LFTs, UA, eye exam -Autoinducer: decrease effectiveness of OCP and other meds
Lamotrigine (Lamictal)	25-400 mg	>2 years old	Seizure Disorder Bipolar 1 Disorder, maintenance (Adults)	-Slower titration with valproate -Caution with rash and SJS/TEN
Lithium (Lithobid-BID) (Eskalith-QD)	IR liquid (16-32 mEQ) IR (600-1800mg) ER (900-1200 mg)	>7 years old, 20-30 kg >12 years old	Bipolar 1 Disorder (Maintenance) Bipolar 1 Disorder, acute manic/mixed	-QHS dosing (for any formulation) to limit renal exposure -Monitor Cr, TSH, Electrolytes, CBC, UA, pregnancy, Li levels -Nephrogenic Diabetic Insipidus -Toxicity (tremor, N/V, seizures) higher risk with dehydration -DDI: **Increases** ACEI/ARBs , NSAIDS, Diuretics; **Decrease** Caffeine, Theophylline
Oxcarbazepine (Trileptal)	150-1800 mg	>2 years old	Seizure Disorder *Bipolar Disorder (Adults)	-Monitor for SIADH (hyponatremia), Cr, Na at baseline -Decrease effectiveness of OCP -NOT EFFECTIVE FOR BIPOLAR DISORDER
Valproic Acid Depakote DR BID dosing, ER once daily, Depakote Sprinkles, PO liquid, IV formulation	125 mg to maximum 60mg/kg/day	>10 years old	Seizure Disorder *Bipolar Disorder, Acute mania (Adults)	-Monitor VPA levels -LFTs, CBC (Platelets), Coagulation factors, Lipids, A1C, pregnancy, NH3 (usually elevated with VPA),

Recommendation 7: Most Youths with Bipolar I Disorder Will Require Ongoing Medication Therapy to Prevent Relapse; Some Individuals Will Need Lifelong Treatment **(CG)**

- In the adults, >80% of patients who have had a manic episode will have ≥1 relapse
    - Stopping maintenance lithium therapy predicts an increased relapse risk, especially within the 6-month period following lithium discontinuation.
- **Valproate** has some benefits and may be used in combination with lithium to help prevent relapse and one study in 2003 showed more effective than either alone.
- Attempts to discontinue prophylactic therapy should be gradual
    - The regimen that stabilizes acute mania in youth may need to be **maintained for 12-24 months** and sometimes even lifelong.
- Stimulants for comorbid ADHD have not affected relapse rates

Recommendation 8: Psychopharmacological Interventions Require Baseline and Follow-up Symptom, Side Effect (Including Patient's Weight), and Laboratory Monitoring as Indicated **(MS)**

- A **6- to 8-week trial of a mood-stabilizing agent** is recommended before adding or replacing with other mood stabilizers.
- Phase of illness is important to consider.
- Avoid unnecessary polypharmacy, in part by discontinuing agents not showing significant benefit.

Recommendation 9: For Severely Impaired Adolescents with Manic or Depressive Episodes in Bipolar I Disorder, Electroconvulsive Therapy (ECT) May Be Used If Medications either Are Not Helpful or Cannot Be Tolerated **(OP)**

- In adults, ECT is effective for mania, but usually offered only in treatment-resistant cases.

- **ECT is seen as the treatment of choice for bipolar disorder in the following clinical contexts:**

  - pregnancy

  - catatonia

  - neuroleptic malignant syndrome

  - medical conditions in which more standard medications are contraindicated

- Limited data has shown that ECT may help youths with bipolar disorder in different phases.

  - Only to be considered for adolescents with well-characterized bipolar I disorder with severe manic or depressive episodes and lack of response to standard medications

  - Potential adverse effects such as short-term cognitive impairment, anxiety reactions, disinhibition, and altered seizure threshold

Recommendation 10: Psychotherapeutic Interventions Are an Important Component of a Comprehensive Treatment Plan for Early-Onset Bipolar Disorder **(MS)**

- Bipolar disorder affects academic, social, and family development and functioning

- Medications alone do not address functional and developmental impairments or need for support and skills.

- **Psychotherapeutic interventions** help promote medication compliance and relapse avoidance as well as help those affected with the development impact of the disorder.

- Adult data on psychoeducational, family, individual interpersonal and social rhythm therapies

    - **Family dynamics can affect treatment response and relapse rates.**

        - Family-focused therapy can enhance problem-solving and communication skills.

    - Interpersonal and social rhythm therapy help reduce stress and vulnerability through stabilizing social and sleep routines.

    - The combination of individual and family interventions helps decrease relapse and depressive symptoms.

- **Areas in which psychotherapeutic interventions should be directed:**

    1. **Psychoeducational therapy:** Information about the disorder's symptoms, course, treatment options, potential impact on psychosocial and family functioning, and treatment options.

    2. **Relapse prevention:** Education about the impact of medication noncompliance, recognizing emergent relapse symptoms and factors that can lead to relapse.

    3. **Individual psychotherapy:** Supports psychological development, skill building, monitoring of symptoms and progress.

    4. **Social and family functioning:** working on family and social relationships, communication, and problem-solving skills

    5. **Academic and occupational functioning:** School consultation and an IEP are often necessary, and some youths may need specialized educational programs. Older teenagers may benefit from vocational training and occupational support.

    6. **Community consultation:** Community, juvenile justice, social welfare programs may be involved. Referral to intensive community-based services is sometimes needed, or foster care or residential services.

Recommendation 11: The Treatment of Bipolar Disorder NOS Generally Involves the Combination of Psychopharmacology with Behavioral/Psychosocial Interventions **(CG)**

- It is unclear how well adult bipolar treatment literature applies to this population.
- Treatment strategies should be inspired by the youth's specific symptoms, comorbid conditions, and family needs, rather than standard bipolar I disorder treatment.
- DBT may be helpful for youths with mood and behavioral dysregulation.
- Mood stabilizers and atypical antipsychotics are often used for severe mood lability and explosive outbursts.
- Other medications for comorbid conditions may be used.
    - When should stimulants be used when there is a question between mania/hypomania or ADHD with mood lability and low frustration tolerance:
        - Two studies showed good response to methylphenidate in ADHD with and without manic-like symptoms and no precipitation of progression to bipolar disorder
    - It can be a challenge to distinguish medication side effects such as irritability and disinhibition from stimulants and SSRIs from an emerging manic episode.
    - In one review, 58% of youths with bipolar disorder experienced manic symptoms emerge after taking a mood-elevating agent.
    - Activation secondary to mood-elevating agents does not equate to a bipolar disorder diagnosis.

Suicidal Behavior

A Ninja's Summary: *Summary of the Practice Parameters for the Assessment and Treatment of Children and Adolescents with Suicidal Behavior*

(Updated 2001)

Why Care? Suicidal behavior in children and adolescents should be considered life-threatening in all cases. Adults may assume that the intention of the youth's reports of suicidal thoughts or their suicidal behavior is not serious or is attention-seeking and may not seek treatment

Background:

- Suicide is among the top 5 leading causes of death among teenagers in the United States
    - Nationwide, 15.8% of students had seriously considered attempting suicide during the 12 months before being surveyed
        - 7.8% of students had attempted suicide one or more times during this time
    - Top methods used included firearms, suffocation, poisoning
        - Firearm is the most common method for suicide among teens in the United States
    - 50% of adolescents report only starting to think about self-harm less than an hour before the act itself
    - Only one-third of suicide attempters are ever referred to a mental health service

- In a US population-based study of 11875 children ages 9-10yo, the risk of child-reported suicidality:
  - **Increased** with higher weekend screen use time
  - **Decreased** with greater parental supervision and positive school involvement
  - In this study, psychopathology was associated with almost five times increase in likelihood of suicidality, and family conflict was associated with 30-75% increase in likelihood of suicidality

Gender Variation in Child and Adolescent Suicide

	Prevalence	Choice of method in completed suicide	Psychiatric history prior to suicide attempt
Males	Male to female ratio of completed suicide attempts: Prepubertal age 3:1 15-24 years of age 5:1	More likely to use firearms	History of suicidal behaviors increase the risk of completed suicide
Females	Female to male ratio in creating a plan, and in attempting suicide: 2:1	More likely to use hanging	History of major depressive disorder is the strongest risk factor for suicide attempt

Evaluation:

- Assess symptoms of mood disorder, substance abuse, impulsive behavior, desire to die, influence of others at the time of the attempt, history of suicide in a friend or family member, amount of preparation and planning, coping skills and social supports
- Consider the lethality and intention to determine the seriousness of the attempt

- ➢ **Lethality** is a measure of the likelihood of death and is based on method, location, and the likelihood of being found

- ➢ **Intention** is a description of what the patient wished to happen. This is based on information by the patient and the interpretation by the clinician

- ❖ Assess risk factors for suicide and current protective factors

Risk Factors for Suicide in the Youth Population

Intrapersonal	Social & Situational	Cultural & Environmental	Adverse life events	Temperament & character
Mental health disorders	Family history of suicide	Access to lethal means *i.e., firearms, pills*	Family conflict	Novelty seeking
Hopelessness, helplessness, guilt, worthlessness	Child abuse or neglect	Stigma associated with asking for help	Academic stressors	Impulsiveness
Prior suicide attempt	Witnessing family violence	Barriers to access *i.e., transportation, financial cost, lack of bilingual service*	Romantic break-up	Neuroticism, pessimism, perfectionism, dependence
Alcohol or other substance use disorder	Lack of social support//social isolation	Cultural or religious beliefs *i.e., belief that suicide is a noble resolution*	Bullying	Low self-esteem
Disciplinary problems	Sense of isolation		Recent or serious loss	External attributional style
High risk behaviors *i.e., sexual activity, self-harm behaviors*	Change of residence			
Sexual orientation confusion	Previous noncompliance with psychiatric treatment			
Medical illness *i.e., epilepsy, CNS damage due to trauma, infection or chemotherapy, etc.*				

Family risk factors for repeat suicide attempt

- Wishes to be rid of child or adolescent
- Does not take child's problems seriously
- Overly angry and punitive
- Depression or suicidality in family member
- Unwilling or unable to provide support and supervision

Additional considerations

- Suicide in elementary school-age children is rare, but is more often associated with attention-deficit-hyperactivity-disorder (ADHD)
- Adolescent suicides are often preceded by stressful events
    - Access to firearms greatly increases risk

Acute Management

- Safety is of primary concern
    - Note that brief hospitalization may be helpful even in youths who deny continuing suicidality
- Consider hospitalization if the patient expresses a persistent wish to die or conveys an abnormal mental state
- Obtain third-party collateral information
- Create a thorough safety plan

- ➢ Identify warning signals, triggers, potential coping strategies, external supports

- ➢ Note that "no-suicide contracts" may be helpful, but the value has not been empirically proven

❖ Treatment of primary and comorbid psychiatric disorders

- ➢ The patient's experience with anxiety, ADHD or other psychiatric or medical condition may play a strong role in their suicidality. Identify all contributing factors and address according to significance/impact

❖ May consider discharge when patient's mental state and level of suicidality has stabilized

- ➢ When the patient will return to a safe home environment

  - ■ i.e., adequate supervision and support will be available over the next few days, the environment is clear of potential vehicles of self-harm

❖ Follow-up with outpatient providers should be established prior to discharge home

Postvention

❖ Consider referral for CBT, interpersonal therapy, DBT, psychodynamic therapy and family therapy

❖ Psychopharmacotherapy

- ➢ SSRIs

  - ■ Reduce suicidal ideation and suicide attempts in nondepressed adults with cluster B personality disorder

  - ■ Safe in children and adolescents, have low lethality, are effective in treating depression in non-suicidal children and adolescents

        - Monitor children and adolescents for new suicidal ideation or akathisia; some reports have been made that SSRIs may have a disinhibiting effect
            - Especially in patients with SSRI-induced akathisia
    - Tricyclic antidepressants
        - Should not be prescribed for suicidal children or adolescents as first-line due to higher lethality (small difference between therapeutic and toxic levels of the drugs) and due to these having not been proven effective in children or adolescents
    - Other medications
        - Use medications which may cause disinhibition or impulsivity with cautions (i.e., benzodiazepines or phenobarbital)

- Referral for families, friends, and teachers of a child or adolescent who has committed suicide to outpatient psychiatric services should be offered to help facilitate grieving, reduce guilt and depression, and decrease the effects of guilt and trauma

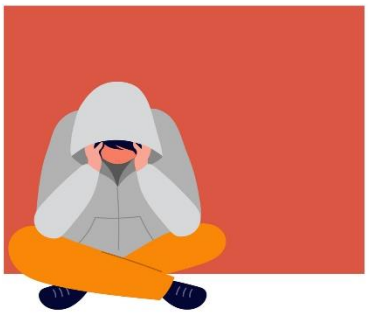
Prevention

- Note that curriculum-based suicide awareness programs disturb some high-risk students; talks and lectures about suicide to groups of children and adolescents drawn from regular classes should be discouraged
    - These interventions may activate suicidal ideation in disturbed adolescents whose identity is not usually known to the instructor
- Screening or suicide education programs for teenagers that do not include procedures to evaluate and refer identified ideators or attempters are not endorsed
- Self-completion questionnaires may be used by primary practitioners, counselors, or others to evaluate a child's or teenager's mental state

- Ample evidence shows that teens in mid-late adolescence will reveal symptoms of depression or suicidal ideation if asked directly

- Those identified as being at risk should be referred for further evaluation and treatment, if necessary, and should receive support and follow-up during the transition period

A Ninja's Guide to Pediatric Anxiety Disorders

A Ninja's Summary: *Clinical Practice Guideline for the Assessment and Treatment of Children and Adolescents with Anxiety Disorders*

(Updated 2020)

Why Care? Effective diagnosis and treatment of anxiety disorders in children and adolescents can be helpful for social and academic functioning over their lifespan.

Epidemiology: One of the most common psychiatric disorders in children

- Prevalence: 7% of children worldwide; lifetime prevalence in US 20-30%
    - Lifetime prevalence for 13-18 yo in US: Specific phobia 20%, Social Anxiety 9%, Separation Anxiety 8%, 2% for agoraphobia, panic, and GAD
- Less than 50% of children needing treatment for anxiety receive treatment, and much of it is not evidence based

Clinical Presentation: Fears and worries are developmentally appropriate for children/adolescents, unless they lead to impaired functioning when they don't subside with age.

- **Developmental phases of Anxiety**
    - Preschool/early school-age - separation anxiety
    - School-age - specific phobia
    - later school-age/early adolescent - social anxiety
    - Later adolescent/early adults - GAD, panic, agoraphobia
- **Foreshadowing symptoms of anxiety disorder**

- Behavioral inhibition, autonomic hyperreactivity, negative affect

- **Contributing factors**

  - Parenting factors, trauma/stress, poor attachment

- **Clinical Course:** Chronic, waxing and waning with homotypic and heterotypic continuity

  - **Homotypic continuity** - prediction of a disorder by the same disorder, ie prediction of social anxiety as an adult in a child with selective mutism

  - **Heterotypic continuity** - prediction of a disorder by another disorder, ie prediction of depressive disorder as an adult in a child with separation anxiety

- **Sequelae of Anxiety Disorders:**

  - Impairments in social, education, occupational, and mental/physical health outcomes into adulthood

  - Adolescents w/ anxiety: 9% have suicidal ideation, 6% attempted suicide

  - Suicide Risk - highest in those with Panic and GAD with comorbid depression

Assessment of Anxiety:

- **Identification:**

  - Employ systematic, standardized general social-emotional screening tools in primary care, schools, other child centered settings

    - Pediatric Symptom Checklist, Strengths and Difficulties Questionnaire

  - Spontaneous parents/youth reports during psych evaluation

- ➢ Standardized self/parent-rated measures during intake and before psych evaluation
    - ■ Level 1 Cross-Cutting Symptom Measure (free from psychiatry.org)

❖ **Evaluation:**

- ➢ Clinical expertise is required to differentiate anxiety from normal human experience (ie, everyday worries and fears)

Comparison of Anxiety Presentation from DSM-5 to Clinical Practice

Anxiety Disorder	DSM-5 Characterization	Clinical Presentation in Children
Separation Anxiety	Developmentally inappropriate, excessive worry or distress with separation from primary caregiver	Worry about parents' safety, can't sleep/bathe alone, nightmares about separation, somatic complaints
Specific Phobia	Excessive worry about specific object or situation	Usually, multiple phobias
Generalized Anxiety Disorder	Excessive uncontrollable worry about everyday situations	Perfectionistic, seek reassurance, high internal distress
Social Anxiety	Excessive worry/fear of negative evaluation by others in a social situation	Won't answer questions or read in class, shy, won't attend parties, refusal to eat in public places
Selective Mutism	Absence of speech in certain social situations with speech in others	Speech usually normal at home
Panic Disorder	Recurrent unexpected abrupt fear or discomfort associated with physical and cognitive symptoms	"Cued" panic attacks commonly seen in adolescence (Low prevalence before age 14, <0.04%)

- **Evaluation Structure:** Diagnostic interview of patient, parent/guardian, separate and together
    - Patient - direct/indirect questioning, interactive/projective techniques, symptom rating scales, behavioral approach test
    - Family - observe for environmental reinforcement of anxiety, parenting styles, collateral from other family, teachers, PCP, social workers
    - Ensure use of appropriate interpretation in the most proficient language for both family and patient
        - Failure to provide interpretation could lead to misdiagnosis and adverse events

- **Differential Diagnosis:**
    - Medical conditions - hyperthyroidism, caffeinism, migraine, asthma, diabetes, chronic pain/illness, lead intoxication, hypoglycemic episodes, hypoxia, pheochromocytoma, CNS disorders, arrhythmias, valvular disease, SLE, allergic reactions, dysmenorrhea
        - Collaborate with PCP for lab testing if needed
        - Note baseline somatic symptoms to prevent false attribution to medication side effects
    - Medications - bronchodilators, nasal decongestants (sympathomimetics), antihistamines, steroids, dietary supplements, stimulants, antidepressants, antipsychotics, benzo withdrawal
        - Complete a medication reconciliation
    - Substance use - marijuana, cocaine, anabolic steroids, hallucinogens, PCP, withdrawal from nicotine, alcohol, caffeine

- ➢ Environmental exposure - organophosphates, lead, arsenic

- ➢ Mental Health - Depression, ADHD, Bipolar, OCD, Psychosis, ASD, learning disorders

- ❖ **Psychiatric Comorbidities:** ADHD, Depression, Bipolar, OCD, eating, learning, language, substance use disorders

  - ➢ Anxiety disorders usually combine with each other, ie, separation anxiety, generalized anxiety, social anxiety disorder frequently co-occur

  - ➢ Comorbidities increase distress, worsen function and treatment outcomes

- ❖ **Medical Comorbidities:** Children with anxiety, more likely to have variety of health problems (can be coincidental or causal)

  - ➢ Headaches, asthma, GI disorders, allergies - each needs separate assessment and treatment

- ❖ **Structured Interview Guides:** infrequently used outside of research, but do enhance reliability of psychiatric diagnosis

  - ➢ Gold Standard: Anxiety Disorders Interview Schedule (ADIS)

  - ➢ Free Structured Interview: K-SADS PL - also includes screening and follow up questions for other disorders

- ❖ **Symptom Rating Scales:** Not diagnostic, yet helpful for baseline function and tracking response to treatment

  - ➢ Screen for Child Anxiety Related Emotional Disorders (SCARED), Spence Children's Anxiety Scale (SCAS), Preschool Anxiety Scale, Generalized Anxiety Disorder-7 (GAD-7), APA Level 2 Cross-Cutting Symptom Measures for those who endorsed anxiety on Level 1 Measure

- ➢ Poor to Moderate agreement between parent and child reports on structured interview guides and rating scales
    - ■ Rule: accept any symptom as present if reported on any informants report (although the child's report is paramount)

- ❖ **Mental Status Examination:** Many signs of anxiety are nonspecific and adjunctive to other diagnostic data.

- ❖ **Clinical Formulation of Anxiety:** Utilize the Bio-Psycho-Social formulation organized to reflect predisposing, precipitation, perpetuating, and protective factors.

Clinical Formulation of Anxiety Disorders

Domain	Vulnerabilities
Biological	Family history of anxiety Brain lesions Autonomic hyperreactivity Negative affectivity temperament Behavioral inhibition Sleep/eating issues Chronic medical conditions
Psychological	Insecure attachment Maladaptive cognitive schemas Information processing errors Negative self-evaluation Disconnects between feelings and behaviors Ego deficits Internalized object relation issues Unconscious conflicts Affect management instability
Social	Stressful/trauma life events Parenting behaviors (overprotective, high rejection, modeling anxious thoughts) Social skills deficits Peer rejection Inappropriate expectations for achievement Lack of support/opportunities for competency development Poor fit in a given environment

- **Safety:**
  - Assess for suicidal thoughts/behaviors, self-harm, risky behaviors, impulsivity - during eval and during treatment
  - Explore history of trauma and report to CPS as required
  - Two Questions: Is the patient safe? Are the patient and family able to adhere to recommendations for safety planning and follow-up care?

- **High-Quality Treatment Planning:** safe, timely, effective, efficient, feasible, equitable, child and family centered

    - Explain treatment at cognitive, linguistic, cultural level of family/patient and prioritize according to acuity, severity, distress, and impairment associated with each disorder

    - Review patient and family preferences of treatment

    - **Level of care -** based on diagnosis, severity of symptoms, comorbid medical/psychiatric disorders, safety assessment, child's illness course/complications, potential supports, and treatment alliance between clinician and child/family

    - **Informed Consent Discussion:**

        1) Diagnosis

        2) Nature/purpose of treatment

        3) Risks/benefits of proposed treatment

        4) Alternative treatment (their risks/benefits)

        5) Risks and benefits of declining treatment

        6) Document informed consent discussion

    - Incorporate cultural/spiritual values, beliefs, attitudes of treatment interventions to enhance families participation and effectiveness of treatment

Treatment of Anxiety

- **AACAP Committee on Quality Issues Treatment Statement Rating/Grading Procedure:** Statements about the treatment of anxiety disorders are based upon empirical evidence derived from a critical systematic review of the scientific literature conducted by the Mayo Clinic Evidence-based Practice Center under contract with the Agency for Healthcare Research and Quality (AHRQ)

  - **Benefit/Harm Grades:**

    - **Recommendation Statement (Numeral 1):** indicates confidence that the benefits of the action clearly outweigh the harms.

    - **Suggestion Statement (Numeral 2):** indicates greater uncertainty, in that the benefits of the action are considered likely to outweigh the harms, but the balance is more difficult to judge.

  - **Strength of Evidence (SOE) Ratings:**

    - **Letter A:** If the preponderance of AHRQ/Mayo SOE ratings across the six key outcomes for a given comparison was high, the SOE rating for the corresponding treatment statement was high

    - **Letter B:** If the preponderance of AHRQ/Mayo SOE ratings across the six key outcomes was moderate, the SOE rating for the treatment statement was moderate

    - **Letter C:** If the preponderance of AHRQ/Mayo SOE ratings across the six key outcomes was low, the SOE rating for the treatment statement was low

❖ **Treatment Statements:**

1) **AACAP Recommends CBT be offered to 6-18 yo patients with social anxiety, GAD, separation anxiety, specific phobia, panic disorder (1C)**

   ➢ **Implementation of Recommendation:**

   - Diverse group of interventions, reinforced with practice, used to make connections among worries, fears, thoughts, behaviors; directing them toward eliminating emotional and physical distress, changing maladaptive coping mechanisms, and reducing avoidance
   - Structured to provide symptomatic relief and functional improvement within 12-20 sessions
   - May use symptom rating scales to assess treatment response
   - Requires specialized education, training, and experience for the CBT to be effective
   - Elements of CBT: education about anxiety, behavioral goal setting with contingent rewards, self-monitoring for connections between worries, thoughts, and behaviors, relaxation techniques, progressive muscle relaxation, guided imagery, cognitive restructuring, graduated exposure, problem solving/social skills
   - Family directed interventions to improve family-child relationships, strengthen problem-solving, communication skills, reduce parental anxiety, teach anxiety reducing parenting skills
   - School-directed interventions that educate teachers about child's anxiety, teach effective problem-solving, coping, management strategies of anxiety at school (May be added to IEP or 504 plan)

Current Research Evidence of CBT Against the Type of Control:

See Appendix C

2) **AACAP Recommends SSRIs be offered to 6-18 yo patients with social anxiety, GAD, separation anxiety, panic disorder (1B)**

- ➢ **Current Research Evidence for SSRIs**
  - ■ **Improvements compared to pill placebo:**
    - ○ **High SOE:** Improved global function
    - ○ Moderate SOE: Improved primary anxiety symptoms (parent & clinician report), Response to treatment, Remission of disorder
  - ■ **No separation compared to pill placebo:**
    - ○ Moderate to low SOE: Short term adverse effects (AEs)
    - ○ Low SOE: Primary anxiety symptoms (child report), secondary measures, social function
    - ○ Insufficient data: Assessment of AEs related to SI or behavior, assessment of AEs related to neurologic or oral (dry mouth) AEs.

- ➢ **Treatment with SSRIs**
  - ■ Serotonergic function thought to play a role in modulation of fear, worry, and stress - also facilitates cognitive processing of these emotions
  - ■ No current FDA approval of any SSRI for the treatment of Anxiety, yet there is substantial empirical support for effectiveness and safety
    - ○ SSRIs with sufficient data: Fluoxetine, Fluvoxamine, Paroxetine, Sertraline

- ➢ **Pharmacodynamics of SSRIs:**
  - ■ Limited data on pharmacodynamics of SSRIs in children - Sertraline and Fluvoxamine likely benefit from twice daily dosing, while the long ½ life of Fluoxetine allows for once daily dosing.

- No current role for pharmacogenomic testing in medication selection

➢ **Anxiety treatment response**

- Logarithmic model showing *statistically* significant improvement in anxiety at 2 weeks, *clinically* significant improvement by 6 weeks, and maximal improvement by 12 weeks, or later

- Supports slow up-titration to avoid exceeding optimal dose

➢ **Adverse Effects of SSRIs:**

- Most common AEs - first few weeks - dry mouth, nausea, diarrhea, heartburn, headache, somnolence, insomnia, dizziness, vivid dreams, changes in appetite, weight loss/gain, fatigue, nervousness, tremor, bruxism, and diaphoresis

- Serious AEs - suicidal thinking/behavior, behavioral activation/agitation, hypomania, mania, sexual dysfunction, seizures, abnormal bleeding, serotonin syndrome

- Black Box Warning: Risk of suicidal thinking and behavior through 24 yo, 1% rate of SI for youth treated with SSRI, NNH = 143
  - Recommend close monitoring first month and with each dose adjustment

- Margin of safety of SSRIs in overdose is high - some reports of death with giant ingestion

➢ **Behavioral Activation (BA) or Agitation:** Motor or mental restlessness, insomnia, impulsiveness, talkativeness, disinhibited behavior, aggression

- More common: in younger children, in anxiety disorders, in early SSRI treatment or dose increases, with drugs that inhibit SSRI metabolism

- Risk reduction - slow up-titration and close monitoring, education of patient and family about potential side effects

➢ **Behavioral Activation vs Mania:**

- Mania appears later in treatment
- BA resolves quickly when SSRI is stopped, mania will continue need further medication intervention

➢ **Serotonin Syndrome:** Usually triggered when serotonergic meds are combined

- Most common when combining with MAOIs
- Symptoms can start within 24-48 hours - mental status changes, neuromuscular hyperactivity, autonomic hyperactivity
- Advanced symptoms - fever, seizures, arrhythmias, LOC → death
- **Treatment:** admission to hospital, discontinue serotonergic meds, continuous cardiac monitoring
- **Prevention:** starting second serotonergic at low dose, slow up titration, monitoring for symptoms (especially in first 24-48 hours)

Serotonergic Agents:

- Antidepressants - SSRIs, SNRIs, TCAs, atypical antidepressants
- Opioids and other pain medications - Tramadol, meperidine, methadone, fentanyl
- Stimulants - Amphetamine and possibly methylphenidate classes
- Cough, cold, allergy medications - Dextromethorphan, chlorpheniramine
- Other OTC products - St. John's wort, L-tryptophan, diet pills
- Illicit drugs - Ecstasy, methamphetamine, cocaine, LSD

- **Discontinuation Syndrome:** Missed dose or abrupt discontinuation
  - Dizziness, fatigue, lethargy, general malaise, myalgias, chills, headaches, nausea, vomiting, diarrhea, insomnia, imbalance, vertigo, sensory disturbance, paresthesias, anxiety, irritability, and agitation
  - Most common in paroxetine (less often with fluvoxamine and sertraline) - need a slow discontinuation taper
  - Fluoxetine has long ½ life, lowest risk of discontinuation syndrome

- **Prescribing considerations:**
  - **Medical education, training, and experience are essential for safe prescribing of SSRIs.**
  - **Mild to Moderate Anxiety -** Start with low dose, increase in smallest increments every 1-2 weeks (shorter ½ life, ie sertraline) or 3-4 weeks (longer ½ life, ie fluoxetine) → until harm outweighs benefit or remission
  - **Severe Anxiety -** quicker up-titration as tolerated
    - No clear correlation with dose of medication and response - may increase side effects (anxiety/agitation)
  - **Best Practice:**
    - Start with subtherapeutic dose
    - Track treatment response with rating scales, monitor adverse effects
    - Adverse effect observed/reported → lower dose
    - Adverse effect does not resolve → discontinue medication

- **Monitoring:**
    - Height and weight only
    - No specific lab tests recommended
- **Duration of Treatment (Generally accepted approach)**
    - Continue effective/tolerated dose for 12 months after remission
    - Begin slow discontinuation during stress free period
    - Severe/Chronic anxiety may need longer treatment
- **Switching from one SSRI to another**
    - Conservative - taper and discontinue 1st SSRI, then start 2nd SSRI
        - Risk of exacerbation of original symptoms
    - Cross-tapering - avoid exacerbation of symptoms - should be closely monitored

3) **AACAP Suggests combination treatment of SSRI + CBT could be offered preferentially, over CBT or SSRI alone, to 6-18 yo patients with social anxiety, GAD, separation anxiety, panic disorder (2C)**

➢ **Implementation:** No definitive evidence for superiority of combination treatment over monotherapy - **Only two studies with conflicting evidence**

- **CAMS (Child-Adolescent Anxiety Multimodal Study)**
    - Youth with combo treatment had higher rates of remission vs CBT, SSRI, or placebo alone at 12 and 24 weeks
- **Naturalistic follow-up of CAMS**
    - No long term maintenance of initial superiority of combo over monotherapy

- Strong predictor of long-term outcome is *initial response to treatment* → **give the most potent treatment as early as possible**

- **Clinical practice:** Combination favored for acute symptom reduction for severe cases or partial response to monotherapy

Current Evidence of Combination (CBT + SSRI) vs Monotreatment for Anxiety

Treatment Arm	CBT + Sertraline	CBT + Fluoxetine
CBT Alone	**Combination Improved:** Primary anxiety (clinician report), global function, response to treatment, remission (Mod SOE) **Combination No Difference:** short-term AEs, SI and behavior (Low SOE) **Combination Increased:** AEs related behavior activation (Mod SOE), any AEs and AEs related to sleep (Low SOE)	**Combination Improved:** Primary anxiety (clinician report), global function, response to treatment, remission (Mod SOE) **Combination No Difference:** Short team AEs (Low SOE) **Combination Increased:** AEs related to behavior activation (Mod SOE) **Combination Reduced:** AEs related to fatigue/somnolence (Mod SOE)
Sertraline Alone	**Combination No Separation:** Global function, secondary measures, response to treatment **Combination No Difference:** Dropouts (Low SOE)	–

4) **AACAP Suggests SNRIs could be offered to 6-18 yo patients with social anxiety, GAD, separation anxiety, panic disorder (2C)**

➢ **Compared to Pill Placebo:**

- SNRIs improved primary anxiety symptoms (clinician report) **(High SOE)**

- SNRIs did not separate for primary anxiety symptoms (parent report) or global function (Low SOE), short term AEs like SI or behavior (Mod-Low SOE)

- Insufficient data precluded assessment of primary anxiety (child report), and assessment of AEs related to infections

- SNRIs increased fatigue/somnolence (Mod SOE)

➢ **Treatment with SNRIs:**

- Noradrenergic neurons typically modulate stress response of alertness, arousal, attentiveness, and vigilance ("fight or flight")

- Paradoxical effect of noradrenergic medications shown to reduce anxiety

    - Likely complex interaction with other neurotransmitters including serotonin

- SNRIs with sufficient data - venlafaxine and duloxetine

    - Duloxetine only SNRI with FDA indication for treatment of GAD in 7-17 yo

➢ **Pharmacodynamics of SNRIs:**

- Venlafaxine IR - short ½ life → require BID to TID dosing to avoid discontinuation syndrome

- Venlafaxine ER, desvenlafaxine, duloxetine - longer ½ life → once daily dosing

➢ **Adverse Effects of SNRIs:**

- **Common AEs:** Diaphoresis, dry mouth, abdominal discomfort, nausea, vomiting, diarrhea, dizziness, headache, tremor, insomnia, somnolence, decreased appetite, and weight loss

- **Less common AEs:** Sustained clinical HTN, increased BP, increased HR

- **Serious AEs:** suicidal thinking and behavior, behavioral activation, hypomania, mania, sexual dysfunction, seizures, abnormal bleeding, serotonin syndrome.

- **Venlafaxine:** Associated with greater risk of suicide than other SNRIs, overdose fatalities (including desvenlafaxine), and discontinuation syndrome

- **Duloxetine:** Hepatic failure (abdominal pain, hepatomegaly, increased LFTs), cholestatic jaundice, Stevens-Johnson and erythema multiforme

    - Discontinue and do not restart if jaundice or rash is reported

➢ **Prescribing Considerations:**

- **Medical Monitoring:** Height, weight, **HR, BP**

- **All other considerations similar to SSRIs above**

Selected SSRIs for the Treatment of Anxiety Disorders

Medication	Pediatric Dosing	CYP 450	Notable Considerations
SSRIs			**Bleeding risk, Hyponatremia** **BBW: Suicidal ideation**
Citalopram (Celexa)	10-40 mg	-2C19 (primary); 2D6, 3A4	-Can cause QT prolongation, avoid in long QT syndrome -Least drug-drug interaction
Escitalopram (Lexapro)	5-20 mg	-2C19 (primary); 2D6, 3A4	-Less risk of QT prolongation -Least drug-drug interaction
Fluvoxamine (Luvox)	25-200 mg	-2D6 (primary); 1A2	- Higher drug-drug interactions - Discontinuation syndrome
Fluoxetine (Prozac)	10-60 mg	-2D6 substrate *Significant interaction	-Can be activating, consider dosing AM -Long half-life w/ least risk of discontinuation syndrome
Paroxetine (Paxil)	10-60 mg	-2D6 substrate *Significant interaction	-Generally avoided in youth due to discontinuation syndrome, weight gain, and anticholinergic effects -Increased risk of SI compared to other SSRIs
Sertraline (Zoloft)	25-200 mg	-2C19 (primary); 2D6, 3A4	-Can be more sedating, consider dosing QHS -Give w/ food to increase absorption by 40%, and helps with GI discomfort -Discontinuation Syndrome

Selected SNRIs for the Treatment of Anxiety Disorders

Medication	Pediatric Dosing	CYP 450	Notable Considerations
SNRIs			**Risk of elevated BP and HR (Monitor)** **Can be helpful for chronic pain** **BBW: Suicidal Ideation**
Duloxetine (Cymbalta)	30-120 mg	-1A2, 2D6	-Associated with hepatic failure, cholestatic jaundice -Associated with Stevens-Johnson syndrome and erythema multiforme
Venlafaxine (Effexor)	12.5-225 mg (IR 75 mg max) (ER 225 mg max)	-2D6 (primary); 3A4 Active metabolite (desvenlafaxine)	-Serotonergic at lower dose, NE at higher doses. -Abrupt discontinuation syndrome (IR formulation) -Greater risk of suicide than other SRNIs -Associated with overdose fatalities

A Ninja's Guide to Obsessive-Compulsive Disorder

A Ninja's Summary: *Clinical Practice Guideline for the Assessment and Treatment of Children and Adolescents with Obsessive-Compulsive Disorder*

(Updated 2012)

Why Care? Obsessive-compulsive disorder (OCD) is a common psychiatric condition that can lead to disability among children and adolescents. There has been increasing evidence about impact of genetics, role of comorbid disorders and related effects, immune-based neuropsychiatric causes (Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcus [PANDAS]) and trials reviewing types of psychotherapy and use of serotonin reuptake inhibitors (SSRIs) in this condition.

Epidemiology

- High prevalence of OCD became more apparent after the first epidemiological study approximately 20 years ago
    - In part, due to patient lack of desire to seek help, it is often under recognized and underdiagnosed in youth.
- Prevalence of pediatric OCD is about 1-2% in the United States
    - Bimodal distribution in preadolescent children and young adults (mean age 21 years old)
    - Can become less pronounced later in life, thus expected cumulative cases over the lifespan are incrementally increased from childhood.

Etiology

- Family studies have consistently demonstrated that OCD has a genetic basis
    - Monozygotic twin studies show higher rates of OCD than dizygotic twin studies.

- ➢ Higher risk of OCD in first degree family members, especially in those suffering with OCD in childhood.

- ❖ Evidence points toward glutamate receptor/modulating gene association with development of OCD

- ❖ **Pediatric Autoimmune Neuropsychiatric Disorders (PANDAS):** an immune response to group A β-hemolytic streptococcus (GABHS) infections, causing a cross reactivity with, and inflammation of basal ganglia, with a distinct neurobehavioral syndrome.

    - ➢ This syndrome includes Sydenham chorea, a consequence of rheumatic fever; includes OCD, tics, and hyperactivity.

Clinical Presentation

- ❖ **Phenotype:**

    - ➢ Symptoms can progress over childhood with developmental themes that may distinguish them from adults

    - ➢ In young children, often unable to verbalize symptoms and compulsions may be exhibited without clear obsessions and/or rituals other than typical washing, repeating ordering, counting or checking

    - ➢ Majority will have many obsessions and compulsions over lifetime

        - ■ No consistency with nature, age, or gender, but often revolve around catastrophic family event like death of caretaker

        - ■ Higher male to female ratio occurrence in younger ages and usually onset between 7 and 13 years old

    - ➢ **The Dimensional Yale-Brown Obsessive-Compulsive (YBOC) Scale** measures the presence and severity of OCD symptoms within several distinct dimensions that combine thematically related obsessions and compulsions.

- **Psychiatric Comorbidity**
  - >50% of OCD in youth has comorbid psychiatric diagnoses
    - Younger onset more associated with attention-deficit/hyperactivity disorder (ADHD) and anxiety disorders.
- **Neuropsychological Findings**
  - Fronto-striatal systems are involved in OCD
  - Decreases in visual spatial performance and processing speeds typical

Clinical Course and Outcome

- No likely trigger for pediatric OCD, unless PANDAS-related case
- Long-term prognosis is better than previously believed with decreasing symptoms over time
  - **Worse outcomes with younger onset, longer duration, inpatient treatment, and sexual, religious, or hoarding obsessions**
- High levels of social issues with peers leading to isolation, more unemployment and difficulty sustaining a job

Differential Diagnoses

- **Normal Development**
  - Toddlers and preschool-aged children's ritualistic behavior can be part of normal development
  - Routines are part of daily life with deviations not causing severe distress in a child.

Other Psychiatric Disorders

- "Spectrum Disorders" and other neurodevelopmental disorders which include stereotypic and repetitive behaviors, narrow range of interests
    - Behaviors may mimic OCD especially in young children.
    - ~5% of those children with OCD meet criteria for Asperger's
    - Deficiency in social and communication abilities characteristic of the spectrum disorders can help differentiate neurodevelopmental disorders from OCD
    - With OCD, the **obsessions are ego-dystonic** and behaviors driven by anxiety and some recurrent themes, while patients with a neurodevelopmental disorders perform behaviors with gratification and have distress when activities are interrupted
- Obsessional thoughts and compulsions along with anxiety can lead to overvalued ideas and even delusional thinking, presenting as psychosis
    - Rarely associated with schizophrenia spectrum disorders in youth
- Obsessive-compulsive personality disorder (OCPD) is unusual in young children and often associated with PDD in terms of orderliness and perfectionism at expense of flexibility

Recommendation 1: The psychiatric assessment of children and adolescents should routinely screen for the presence of obsessions and/or compulsions or repetitive behaviors. (CG)

- Providers should screen for OCD even when not part of presenting complaint as symptoms may vary in severity and intensity over time
- Screening symptoms should be followed up by more detailed assessment like the **Child Behavior Checklist**

Recommendation 2: If screening suggests Obsessive Compulsive symptoms may be present, clinicians should fully evaluate the child using the DSM-IV-TR **(Now DSM 5)** criteria and scalar assessment. (CS)

- **Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS)** includes the diagnostic criteria of time occupied by OCD symptoms, the level of subjective distress, and functional impairment, in addition to a standardized inventory of symptoms and a scalar assessment of severity.
    - **Limitations of CY-BOCS:** poor insight, indecisiveness, obsessional "slowness"
        - Use "worst-report algorithm" to be most accurate
- Other OCD scales: Leyton Obsessional Inventory; interviews that assess more broadly for internalizing symptoms (Ten Year Review of Rating Scales II: Scales for Internalizing Disorders)and anxiety, such as the Anxiety Disorders Interview Schedule for Children, the Pediatric Anxiety Rating Scale, the Screen for Child Anxiety Related Disorders, and the Multidimensional Anxiety Scale for Children

Recommendation 3: A complete psychiatric evaluation should be performed, including information from all available sources and comprising standard elements of history and a mental state examination, with attention to the presence of commonly occurring comorbid psychiatric disorders (CS)

- Psychiatric comorbidity expected, 74% of youth with OCD met the criteria for at least one comorbid diagnosis
    - **Children with OCD and at least one comorbid diagnosis had lower treatment response and remission rates with CBT treatment**
- **Disruptive behavior disorders** in particular may cause difficulty in treating the patient
- **Mood disorders** like major depressive disorder and bipolar disorder are especially important to identify before the initiation of an SSRI

- ➢ These mood issues may affect CBT treatment effectiveness and overall improvement for patients of all ages

- ❖ **Eating disorders** are less common in children with OCD, but may become more frequent during adolescence

  - ➢ Medical considerations must be stabilized before mental health interventions

- ❖ A "spectrum" of compulsive/impulsive habit disorders include **trichotillomania, compulsive nail biting, skin picking,** and other forms of self-injury have some overlap with OCD

  - ➢ Usually NOT preceded by specific cognitions (obsessions) - more like a sense of tension that is general or localized

  - ➢ Behavior is often a source of (temporary) gratification but may be followed by remorse and shame and mainstay of treatment is **Behavioral therapy not SSRIs.**

- ❖ **Body dysmorphic Disorder** usually starts in adolescence, but possibly sooner, when developmental pressure increases regarding appearance.

Recommendation 4: A full medical, developmental, family, and school history should be included with the psychiatric history and examination (CG)

- ❖ **Family Accommodation:**

  - ➢ Parental efforts to relieve a child's anxiety may inadvertently lead to an accommodation and reinforcement of OCD behaviors due to enmeshment with children

    - ■ Important to consider role of caretakers in providing verbal reassurance or other "assistance" to children

      - ○ Handling objects that children avoid touching

- Difficult for parents to react with the supportive yet detached responses needed for effective behavioral management

➢ Important to assess the role of individual family members in the maintenance and management of OCD symptoms

- Also assess family history of OCD and other anxiety disorders possibly perpetuating the behavior

❖ **Medical History:**

➢ Medical history should focus on the CNS during a review of symptoms (ROS) with attention to trauma and neurologic symptoms

➢ GABHS a potential contributor for a PANDAS-associated OCD

- More concern with acute and dramatic onsets or exacerbations in preadolescent patients or when a child in remission suddenly relapses

- Signs of rheumatic fever may include chorea but less severe signs like coordination difficulties can be signs of PANDAS diagnosis.

- For diagnosis, **GABHS culture is the first choice**, antistreptococcal antibodies titers are not very definitive.

➢ Currently, no neuroimaging procedures have been validated for the assessment or diagnosis of OCD

❖ **Educational Assessment**

➢ School and educational histories provide information about level of function and of illness severity as it can affect multiple aspects of life and may require special accommodations

➢ Pediatric OCD is evidenced by impairments in visual memory, visual organization, and processing speed

- Children with evidence of this pattern often prefer reading to writing, and have stronger language than math skills

- ➢ **Neuropsych assessment, intelligence, and academic achievement testing** consideration should be high in children with OCD who are struggling at school

Recommendation 5: When possible, CBT is the first line treatment for mild to moderate cases of OCD in children (CS)

- ❖ Numerous studies have consistently shown its acceptability and efficacy of CBT with OCD

- ❖ CBT protocol used by March et al. in the National Institute of Mental Health **Pediatric Obsessive-Compulsive Disorder Treatment Study (POTS)**

  - ➢ Consisted of 14 visits over 12 weeks spread across **five phases:**

    - ■ psychoeducation, cognitive training, mapping OCD, exposure and response prevention (E/RP), and relapse prevention and generalization training

- ❖ **Exposure and response prevention (E/RP):**

  - ➢ Anxiety usually decreases after prolonged contact with a feared stimulus
    - ■ Repeated exposure is associated with a decreased anxiety across exposure trials

  - ➢ **Response prevention:** Providing adequate exposure and then blocking the negative reinforcement effect of rituals or avoidance behavior

    - ■ Child that is worried about germs must not only touch "germy things" but also refrain from ritualized washing until his or her anxiety diminishes substantially

  - ➢ **Graded exposure:** Implemented in a gradual manner

- ❖ Positive reinforcement (rewards) do NOT seem to directly alter OCD symptoms, BUT rather helps to encourage exposure and so produces an indirect, clinical benefit
    - ➢ **Punishment is unhelpful in the treatment of OCD**

Recommendation 6: For moderate to severe OCD, medication is indicated in addition to CBT (CS)

- ❖ What meets this threshold as being more severe?
    - ➢ CY-BOCS or Clinical Global Impression Severity Scale scores higher than 23 demonstrate severe impairment based on time occupied, subjective distress, and functional limitations
- ❖ Other indications for early medication treatment: Unable to meaningfully engage in CBT treatment

Recommendation 7: SSRIs are the first-line medications recommended for OCD in children and should be used according to AACAP guidelines to monitor response, tolerability, and safety (CS)

- ❖ **Efficacy:**
    - ➢ Medications for OCD in child and adolescent patients began with clomipramine in 1989
    - ➢ Subsequent trials gained approval for SSRIs including sertraline, fluvoxamine, fluoxetine, and paroxetine
        - ■ No comparative treatment studies between the agents, but agents were superior to placebo with target improvement as >25% decrease in CY-BOCS scores.
    - ➢ Data suggests clomipramine may be better than SSRIs for OCD
        - ■ Adverse drug effects and narrow toxicity index make it less favorable as a first line medication

- **POTS study:**
    - CBT alone did not differ statistically from sertraline alone
        - CBT alone was superior for the remission rate
    - CBT and sertraline were better than placebo
- **Long-term studies on Sertraline suggested a cumulative benefit with gradually decreasing scalar scores and increasing remission rates for up to one year.**

❖ **Safety and Tolerability:**

- SSRI medications are well-tolerated and safer than TCAs, especially in the setting of misuse or overdose
- Increases of initial doses should be done every 3+ weeks
    - Takes 12 weeks for substantial benefits, yet may take 6 to 12 months for full effect
- After stabilization for 6 to 12 months, medication can be gradually withdrawn over several months
    - After 2-3 relapses of at least moderate severity, consider longer-term treatment
- Behavioral side effects are more common in younger children, such as behavioral activation
    - May be late-onset adverse effects appearing in parallel with a decrease in anxiety
- Peripubertal children exposed to antidepressants are at higher risk of conversion to mania
- **Black box warnings (BBW):** Increased risk of increased suicidal behavior remains a concern.

- **Should be noted that no suicides occurred in any of the pediatric randomized controlled trials of SSRIs.**

➢ Clomipramine use should come with an evaluation of the pediatric patient's medical condition and cardiac status, along with investigation of personal or family history of heart disease.

Dosing Guidelines for Treatment of OCD with an SSRI

Drug	Starting Dose (mg)		Typical Dose Range (mg) (Mean Dose in randomized trials)
	Preadolescent	Adolescent	
Clomipramine	6.25–25	25	50–200
Fluoxetine	2.5–10	10–20	10–80 **(25)**
Sertraline	12.5–25	25–50	50–200 **(178)**
Fluvoxamine	12.5–25	25–50	50–300 **(165)**
Paroxetine	2.5–10	10	10–60 **(32)**
Citalopram	2.5–10	10–20	10–60

Recommendation 8: The modality of assigned treatment should be guided by empirical evidence on the moderators and predictors of treatment response (CS)

❖ Psychiatric comorbidity may negatively impact treatment response rate

➢ OCD alone - success rate of over 70% with SSRI use

➢ Decrease in response with patients with comorbid ADHD (56%), tic disorder (53%), or oppositional defiant disorder (39%)

❖ Sertraline was more beneficial in patients with comorbid tic disorders only when combined with CBT

❖ Children with first-degree family members with OCD responded less to CBT only and are better candidates for combined therapy

- ➢ High levels of parental accommodation may lead to treatment resistance

- ❖ **POTS:** Best candidates for CBT only had lower severity scale scores, less OCD-related impairment, fewer comorbid externalizing symptoms, better insight, and less family accommodation

Recommendation 9: Multimodal treatment is recommended if CBT fails to achieve a clinical response after several months or in more severe cases (CS)

- ❖ Combination CBT + medication most efficacious as first-line treatment in moderate to severe OCD

- ❖ Recommendations from the comparative treatment trial: start treatment with CBT alone or CBT + medication

  - ➢ If CBT alone is unsuccessful, medication should be added

  - ➢ Combined treatment has better outcomes with CBT by decreasing anxiety and improving a child's ability to tolerate Exposure/ Response Prevention treatment

Recommendation 10: Medication augmentation strategies are reserved for treatment-resistant cases in which impairments are deemed moderate in at least one important domain of function despite adequate monotherapy (OP)

- ❖ **Treatment Resistance:** refers to a patient who has not responded to interventions known to be effective for the specific condition being treated

  - ➢ Trial of at least two SSRIs or one SSRI and a clomipramine trial + failure of adequately delivered CBT

  - ➢ Children should have a minimum of 10 weeks of each SSRI or clomipramine at maximum recommended or maximum tolerated doses, with no change in dose for the preceding 3 weeks

  - ➢ **CBT non-responders:** child who has not shown any improvement after 8 to 10 total sessions (or six to eight sessions of Exposure/Relapse Prevention) or has substantial residual OCD psychopathology after completing standard CBT

- **Hospitalization**: Not usually indicated for OCD alone, unless having severe mood instability or SI
    - Typical inpatient psychiatric units and staff are not well equipped to deal with youth with OCD
        - Staff may think rituals and avoidance are oppositional behavior, leading to unhelpful behavioral interventions.
- **Medication Augmentation Strategies:**
    - **MAY** consider adding clomipramine to an SSRI
        - Intended to maximize the serotonergic effects of each while minimizing adverse events across different drug classes
        - Caution with fluvoxamine, fluoxetine, and paroxetine with clomipramine → substantially increase serum clomipramine levels
            - Monitor clomipramine levels and EKG
    - **SNRIs:** Consider venlafaxine and duloxetine instead of clomipramine
        - Similar combined monoamine uptake inhibition to clomipramine but with fewer potential cardiovascular adverse effects
    - **Clonazepam:** Used in combination with SSRIs in several small open trials
        - Should be used with caution in younger children
    - **Antipsychotics:** Most Common Augmentation Strategy
        - High-quality randomized controlled trials using antipsychotics have been performed in adults with OCD
            - NO controlled data exist in children
        - **Adult studies:** significant advantage with Haloperidol and Risperidone over placebo

        - Must monitor weight, lipid and glucose

    - **Possible indications for Children:** Treatment-resistant OCD, particularly children with tic disorders, poor insight, pervasive developmental disorder symptoms, and mood instability.

    - **Approaches to augmentation:**

        1) Meta-analysis suggested 12 weeks of treatment with SSRI before antipsychotic augmentation was effective

        2) Consider 2 different adequate SSRI trials or SSRI and clomipramine before antipsychotic augmentation

- PANDAS cases of OCD have tried interventions including antibiotic prophylaxis with penicillin to prevent streptococcal infections

    - mixed results with one year follow up

    - Antibiotic prophylaxis cannot be recommended in children with OCD even if PANDAS is the suspected cause

Recommendation 11: Empirically validated medication and psychosocial treatments for comorbid disorders should be considered (CG)

- CBT treatment can be used with comorbid disorders like oppositional defiant disorder (ODD), major depressive disorder, or family-based therapy for eating disorders patients

- Insight-oriented psychotherapy has not been helpful in OCD symptoms

- Supportive therapy might be helpful for decreased function in aspects of life like relationships or self-esteem.

- Family therapy for dynamics impacting effectiveness of treatments aimed at the primary symptoms of OCD or high parental levels of accommodation

- **OCD and comorbid ADHD:** target OCD first with medications

- ➢ Stimulants may increase anxiety and obsessions in children → impacting ability to pay attention to tasks

- ❖ **OCD and ODD:** target OCD first → decrease anxiety contributing to ODD symptoms

- ❖ Caution with SSRIs in younger children, behavioral activation may mimic ADHD

  - ➢ Consider atomoxetine or clomipramine (Noradrenergic effects)

- ❖ **Tics and OCD:** consider alpha 2 agonists like clonidine and guanfacine along with medication for OCD (prefered over antipsychotic)

- ❖ **Bipolar Disorder and OCD:** Need to address mood disorder first before considering antidepressant

A Ninja's Guide to Trauma Related Disorders

Post-Traumatic Stress Disorder

A Ninja's Summary: *Clinical Practice Guideline for the Assessment and Treatment of Children and Adolescents with Post-Traumatic Stress Disorder*

(Updated 2010)

Why care? At least 25% of children experience a significant traumatic event prior to adulthood.

Epidemiology

- Significant proportions of children who have experienced a traumatic event continue to meet criteria for chronic PTSD despite documentation recording decreases in rates of PTSD over time
- Recent national sample of adolescents (12-17yo) indicated that 3.7% of boys and 6.3% of girls met full diagnostic criteria for PTSD
- Recent meta-analysis (Alisic et al. 2014) estimates a rate of childhood PTSD of 16%
- Rates of both trauma exposure and PTSD is greater in girls than boys
- Risk of developing PTSD after a disaster include:
  - Media exposure
  - Peritraumatic panic symptoms
  - Delayed evacuation

- ➢ Sense of endangerment
- ➢ Premorbid anxiety disorder

Risk and Protective Factors of PTSD

Risk Factors	Protective Factors
Female gender Prior trauma exposure Multiple traumas More intense or longer exposure to the trauma Interpersonal violence *(esp. if parent or caregiver is the perpetrator)* Proximity to trauma Presence of preexisting psychiatric disorder *(particularly anxiety disorder)* Parental psychopathology Lack of social support Having felt one's own or a family member's life was in danger	Parental support Lower levels of parental PTSD Resolution of other parental trauma-related symptoms

Etiology

- ❖ An identifiable etiological agent must be present for diagnosis of PTSD
- ❖ Multiple factors are likely involved, including genetic, psychological, and social factors, contributing to a complicated interaction of neuroendocrine dysregulation
- ❖ Higher rates of acute stress disorder occur in children who have experienced bodily injury, pain, or violence
- ❖ More severe or prolonged symptoms may occur in children who have experienced multiple stressors, prior loss, disturbances in family functioning, psychiatric comorbidity.
- ❖ A sufficiently severe stressor may produce symptoms despite absence of any predisposition

Clinical Description

PTSD encompasses the emotional, cognitive, behavioral, and physiological reactions that may occur after directly experiencing, witnessing, or learning of a loved one's experience of a traumatic event, such as actual or threatened death, serious injury, or sexual violence. Examples of traumatic events that may affect children and adolescents include:

- Child abuse
- Domestic, community, or school violence
- Natural disasters
- Vehicular or other accidents
- Medical traumas
- War, terrorism, or refugee trauma
- The traumatic death of significant others

Defining the Diagnosis

- DSM-IV-TR:
  - Presence of a known etiological factor is *required*, whether reported by child or compelling evidence to suggest the event is available
  - Between 3-30 days of traumatic event -> diagnosis of Acute stress disorder
  - Between 30-90 days of traumatic event -> diagnosis of Acute PTSD
  - 90 days + of traumatic event -> diagnosis of Chronic PTSD
  - Symptoms must cause distress and impairment in important functional areas of life

Diagnostic Criteria for PTSD

Symptom Cluster	Manifestations
Re-experiencing *(at least one symptom)*	Recurrent and intrusive recollections Nightmares Other senses of reliving the trauma
Avoidance *(at least three symptoms)*	Efforts to avoid trauma reminders Inability to recall important aspects of the trauma Decreased interest/apathy Detachment or estrangement from others Restricted affect Expectation of a shortened life expectancy
Hyperarousal *(at least two symptoms)*	Difficulty falling or staying asleep Irritability or angry outbursts Difficulty concentrating Hypervigilance Increased startle reaction

Variability of Presentation

- Intrusive symptoms in children may be expressed through repetitive, trauma-themed play or trauma-themed reenactment
- Children may report "scary" dreams but not be able to fully verbalize nightmares, and dreams may not have trauma-specific content
- Children may experience intense psychological or physiological distress at trauma reminders
- Feelings of guilt may be expressed, especially if they survived the trauma and others in the situation did not
- Avoidance of trauma cues may manifest as increased clinginess, separation anxiety fears, or a diminished capacity to feel emotions

- In some children, hyperarousal may present in a generalized inability to relax with increased irritability, outbursts, and impaired ability to concentrate, physical or verbal aggression, emotional numbing, hypoactivity, sleep disturbance, and increased awareness of the environment

- Negative alterations in mood or cognition may present as confusion, forgetfulness, alterations in concentration, inhibition, sense of foreshortened future, preoccupation with death of self or loved ones, self-blame (that may lead to lack of disclosure in situations of abuse), and behavioral regression

- Sequencing or duration of events on report is often distorted

- Perceptual distortions can occur, including tactile, olfactory, visual and auditory misperceptions

Evaluation and Differential Diagnosis

- Acute Stress Disorder or PTSD should be suspected in any child or adolescent who has had *significant change in behavior or emotional state*; a traumatic event may or may not be known at time of clinical evaluation.

- PTSD can mimic many other disorders (any of which could also be comorbid) including:

    - ADHD, Bipolar disorder, Depressive disorders, Psychotic disorders, ODD, Panic disorder, Social anxiety disorder, Substance use

    - Acute Stress Disorder and PTSD are distinguished from adjustment disorder by the severity and type of stressors and the distinctive trauma-related symptoms (i.e., re-experiencing)

Course and Prognosis

- "Natural recovery" from PTSD is controversial

    - One meta-analysis found that without intervention, 50% of children and adolescent no longer met PTSD symptom criteria 6 months following trauma

- Presence of *dissociation and hyperarousal* symptoms predicted development of PTSD

- Symptoms may be partially ameliorated by a stable, cohesive, and supportive family and safe environment

- Abuse or neglect of children may cause cognitive and developmental delays as well as increased arousal or withdrawal secondary to changes in brain physiology

- Trauma may affect functioning in a more generalized manner, given the high degree of comorbidity with both internalizing and externalizing disorders

- Trauma-reactive symptoms may be prolonged or triggered due to psychosocial complications, including disruption of the family unit, displacement, or repeated exposure to trauma through numerous interviews (i.e., legal and child welfare involvement)

- Prognosis is poor for those with persistent PTSD if left untreated

Biological factors

- Recent research suggests a children's psychological reactions to trauma exposure are to some degree influenced by genetic factors

- PTSD related to child abuse or domestic violence is associated with smaller cerebral volume and a smaller corpora colossum, severity being proportional to duration of trauma exposure

Psychological factors

- Many traumatized children develop a chronic sense of pessimism and hopelessness about the future

- Up to 20% of all adolescent suicide attempts are attributable to sexual trauma

- Childhood sexual abuse alone is a strong predictor of several adverse outcomes in adolescence and adulthood, including substance abuse, conduct disorder, and depression

- Childhood PTSD is associated with increased rates of other anxiety disorders in addition to depressive episodes, substance use disorders, attentional difficulties, and suicide attempts into adulthood

- Maltreatment in childhood significantly increases the risk of adult depression and anxiety

Social factors

- Symptoms of anxiety, depression, inattention, and impulsivity may arise, resulting in *interference with school performance*

- Adolescents with sexual abuse-related PTSD also have high-risk sexual behaviors

- Adults with PTSD related to childhood trauma are more likely to have relationship difficulties compared with anxiety-disordered adults who have a trauma history without PTSD or no trauma history

Treatment

- Trauma-focused psychotherapies should be considered first-line treatments for children or adolescents with PTSD. Refer to trauma-focused psychotherapy including CBT, psychodynamic psychotherapy, and family therapy

- Provide psychoeducation to the child and caregivers, consultation with school personnel, and primary care providers

- Consider psychopharmacological options as appropriate

- Note that children with significant PTSD symptoms who do not meet full criteria for a PTSD diagnosis often have comparable functional impairment to those with the diagnosis; consider this in treatment decisions

- There is evidence that including parents in treatment is helpful for resolution of children's trauma-related symptoms

    - Deblinger et al provided trauma-focused CBT to parents alone, children alone, or to parents and children and compared these three conditions with community treatment as usual. Parental inclusion in treatment resulted in significantly greater improvement in child-reported depression and parent-reported behavior problems

- Incorporate appropriate interventions for comorbid psychiatric disorders

- Consider school-based accommodations as appropriate

- The following are not endorsed: restrictive "rebirthing" therapies, techniques that bind, restrict, withholding food or water; these may lead to serious injury or death

- School or other community-based screening for PTSD symptoms and risk factors should be conducted after traumatic events that affect significant numbers of children

Reactive Attachment Disorder *AND* Disinhibited Social Engagement Disorder

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A Ninja's Summary: *Clinical Practice Guideline for the Assessment and Treatment of Children and Adolescents with Reactive Attachment Disorder and Disinhibited Social Engagement Disorder*

(Updated 2016)

Why Care? Extremely adverse caregiving environments have been linked with aberrant social behaviors in young children for more than a century

Background

- The DSM-5 defines two clinical disorders characterized by disordered attachment behaviors which manifest by consequence of deficient caregiving environments
    - Reactive attachment disorder (RAD)
    - Disinhibited social engagement disorder (DSED)
- History of social neglect must be documented to reliably form a diagnosis of either RAD or DSED
- Diagnosis cannot made prior to the child reaching 9 months of age
- Disorders of attachment have been formally defined since 1980, within the DSM-III
- Most research has been conducted on children ages 1-5yo; there is neither little research about homotypic continuity of these disorders nor a consensus about how they manifest in older children and adolescents

Human Development of Attachment

- Biologically driven
  - Newborns – recognize mother's smell and sound, yet show no preference
  - 2-7 mo – may be more readily comforted by a familiar caregiver, yet generally able to be soothed by unfamiliar adults as well
  - 7-9 mo – a preferred attachment may develop (i.e., infants may protest separation from familiar caregivers and exhibit wariness towards unfamiliar adults)
- Comfort, support, nurturance, and protection is sought through organized behaviors, i.e., creating physical proximity to a preferred caregiver
- Physical contact and regular interaction seem to be required for attachment to form, and infants prefer those who they interact the most and who most consistently provides comfort, support, nurturance, and protection
- It is thought that by 12 months of age, it becomes possible to assess the quality of the infant's attachment to a preferred caregiver
- Strange Situation Procedure
  - Devised by Mary Ainsworth to observe attachment in children
  - Played an important role in the development of Attachment theory
  - Involves observation of a child as they play while caregivers and strangers enter and leave the room. The child is placed in various situations and their behavior is observed (including amount of exploration with toys, reactions to the departure of its caregiver, level of anxiety when alone with the stranger, and reaction to reunion with the caregiver)
- Identification of attachment does not make a diagnosis, nor does it suggest a specific clinical approach
- Patterns of attachment are culturally universal and relationship-specific

Patterns of Attachment

As described in the Strange Situation Procedure

- **Secure**
  - Able to use the caregiver as a secure base for exploration in a novel room
  - Upon separation from caregiver, is distressed, play is affected
  - May be friendly with and be comforted by a stranger, but has clear preference for the caregiver
  - Upon reunion, seeks proximity/contact with the caregiver, is readily comforted
- **Avoidant**
  - Engages with the toys with caregiver presence, yet only for instrumental assistance, and does not show affective sharing (i.e., smiling)
  - In separation from caregiver, unlikely to be distressed
  - Treats the stranger in the same way, or sometimes with more attention, as they do the caregiver
  - Upon reunion, will ignore or move past the caregiver rather than approach
- **Resistant/Ambivalent**
  - Seeks contact prior to separation of caregiver
  - Distressed upon separation from caregiver and not easily calmed by stranger
  - Upon reunion, wants proximity with caregiver, but then resists contact angrily once achieved
  - May continue to cry but fail to seek comfort

- **Disorganized**

    - Unusual, conflicted, or disoriented behaviors; unable to maintain one coherent attachment strategy

    - Behavioral stilling, stereotypies, direct apprehension regarding the parent

- *Both the avoidant and the resistant attachment type involved the infant displaying more anger and noncompliance at home, and mothers were less sensitive, interfered more with the children's behavior, and were less accessible to the children's bids.*

- *In the avoidant attachment, mothers expressed an aversion to physician contact when their children sought it and expressed little emotion during interactions with them.*

Epidemiology

- Limited data is available regarding the prevalence of RAD and DSED

- RAD is more common in children currently living in institutions

    - Exceedingly rare outside of institutional care, yet few data exist about the prevalence of RAD

- DSED occurs only in a minority of children who have been severely neglected and subsequently placed in foster or institutional care, has been reported in fewer than 20% of children in these populations

Clinical Presentation

- Reactive Attachment Disorder (RAD)

    - Social reciprocity is minimal or absent

    - Neither looks for nor accepts comfort from caregivers in times of emotional need

- ➢ Limited or absence of positive affect so that they often appear unresponsive

- ➢ May display episodes of unexplained irritability, sadness, or fearfulness around familiar caregivers

❖ Disinhibited Social Engagement Disorder (DSED)

- ➢ Lack of wariness of strangers, will indiscriminately approach unfamiliar adults

- ➢ Overly proximate/intrusive level of friendliness

- ➢ Episodes of mood lability may occur in the context of attention-seeking behaviors

- ➢ May still exhibit a demonstrated attachment, healthy or aberrant, to a caregiver

Comparison of RAD and DSED

	RAD	Both	DSED
Etiology		Social neglect and deprivation	
Risks		Adverse, neglectful caregiving environment	
Core Presentation	Minimal or absent social reciprocity		Social disinhibition
DDx	ASD Global developmental delay Depression		ADHD Williams syndrome
Comorbidities	Stereotypies and cognitive delays	Intellectual disabilities Language problems Learning difficulties	Inattention/ Overactivity
Prognosis	As the child forms new attachments, signs of RAD seem to disappear		May persist for years, even after the child forms attachments in families

Treatment recommendations

- When assessing the developmental history of a child or adolescent patient raised in an institutional setting, placed in foster care, or adopted, consider:
  - Attachment behaviors towards caregivers as a child
  - Behaviors towards strangers as a child

- ➢ Indiscriminate behaviors with peers as an older child/adolescent (i.e. does the child or adolescent claim "close" friendships with relatively new acquaintances?)

- ❖ Obtain a history of the child's patterns of attachment behaviors with their primary caregivers as well as observe the child interacting with their caregivers

- ❖ Consider observing the child's behavior with familiar and unfamiliar adults in a structured setting

- ❖ Assess for comorbid disorders through comprehensive psychiatric assessment

- ❖ Assess the safety of the current placement, keeping in mind that previously maltreated children with negative behaviors are at high risk for being re-traumatized

  - ➢ Consider family support and stability, caregiver psychopathology, caregiver response to previous interventions and willingness to take responsibility for the plight of the child, as well as the severity and pattern of previous abuse

- ❖ Report any suspicion of previously unreported or current maltreatment to appropriate protective services authorities and/or law enforcement

- ❖ The most important intervention for a child diagnosed with RAD or DSED is to have an emotionally available caregiver. Ensure that effective and appropriate resources are provided to promote the optimal development of the caregiver-child relationship.

- ❖ Recommend adjunctive interventions for children who display aggressive and/or oppositional behavior that is comorbid with DSED.

- ❖ Psychopharmacological interventions are not indicated for the core features of RAD or DSED

- ❖ Avoid non-contingent physical restraint/coercion and avoid promotion of regression for "reattachment, as there is no evidence supporting their efficacy and they have been associated with serious harm and death

A Ninja's Guide to Pediatric Schizophrenia

A Ninja's Summary: *Clinical Practice Guideline for the Assessment and Treatment of Children and Adolescents with Schizophrenia*

(Updated 2013)

Why Care? Children and Adolescents with a Schizophrenia spectrum disorder, and their families, often have substantial morbidity and suffering that can be limited by early intervention

Definitions:

- **Early Onset Schizophrenia (EOS):** Onset before age 18
- **Childhood-onset Schizophrenia (COS):** Onset before age 13
- **Adapting DSM-5 criteria to Child and Adolescent (C/A) population:**
  - Decline in function - includes failure to achieve age-appropriate levels of interpersonal or academic development

Epidemiology:

- **Prevalence:** 1% worldwide, Male to Female ratio 1.4:1
  - Onset before age 13, extremely rare
  - Peak age of onset: 15 to 30 years old
  - EOS more common in males
  - No established diagnostic validity of schizophrenia in children under 6 years

Clinical Presentation:

- **Psychosis:** severe disruption of thought and behavior resulting in loss of reality testing
  - Diagnosis based on overt changes in behavior and function on MSE
  - Not confined to Schizophrenia alone
- Misdiagnosis is common
  - Improve accuracy of diagnosis with a comprehensive diagnostic assessment
  - **Most children who report hallucinations do not meet criteria for schizophrenia**
    - **Related to vivid fantasies or overactive imaginations**
  - Difficult to rule out a developmental disorder that impairs speech and language function
- **Symptomatology:**
  - Characterized by positive and negative symptoms
    - Systematic delusions and catatonia occur less frequently
- **Cognitive Delays: Common in EOS**
  - Deficits in memory, executive functioning, attention, global impairments
    - Usually have problems with verbal reasoning, working memory, attention, and processing speed
  - Cognitive decline typically occurs at time of illness onset
    - Stable over time without deterioration

- **Premorbid Functioning**
  - **Premorbid abnormalities more common in COS:**
    - Social withdrawal and isolation, disruptive behavior disorders, academic difficulties, speech and language problems, and cognitive delays
  - **Predicting progression to Schizophrenia:**
    - Familial risk of schizophrenia, recent deterioration in functioning, paranoid thoughts (unusual or suspicious), greater social impairment, history of substance abuse

Etiology: Multifactorial neurodevelopmental model

- **Genetic Factors:**
  - Strong evidence for genetic component from family, twin, and adoption studies
    - 5-20x higher risk if you have a first degree relative with schizophrenia
    - Monozygotic twin rate of concordance: 40-60%
    - Dizygotic twin and sibling concordance: 5-15%
  - Genomic loci/genes: Major histocompatibility complex 6p21.1, MIR137, and ZNF804a
  - EOS associated with large cytogenetic abnormalities and rare structural variants than adults
    - 1q21.1, 15q13.3, and 22q11.2
  - Most affected persons have a unique genetic cause

- **Environmental Exposures:**
  - Genetic and environmental factors interact to affect disease risk and progression
    - Direct neurologic damage, gene-by-environment interactions, epigenetic effects, de novo mutations
  - Impacted by maternal famine, paternal age, prenatal infections, obstetric complications, marijuana use, immigration
- **Neuroanatomic Abnormalities:**
  - Increased lateral ventricle volumes, decreases in hippocampus, thalamus, and frontal lobe volumes
    - EOS abnormalities: Limbic structure, decreased gray matter volume, decreased cortical folding
    - COS abnormalities: Cortical thinning plateaus in early adulthood
- **Psychological and Social Factors:**
  - Psychosocial factors interact to influence onset/exacerbation of acute episodes and relapse rates
  - Potential protection: being raised in a healthy home environment

Course of Schizophrenia

- **Prodrome Phase:**
  - Functional deterioration before the onset of psychotic symptoms
    - Social withdrawal and isolation, idiosyncratic or bizarre preoccupations, unusual behaviors, academic failure, deteriorating self-care skills, and dysphoria

- May be an acute or chronic deterioration

❖ **Acute Phase:**

➢ Prominent positive symptoms with significant deterioration in functioning

- May last several months depending on treatment response

❖ **Recuperative/Recovery Phase:**

➢ Remission of acute psychosis, yet continue to have a several-month period with significant degree of impairment

➢ Negative symptoms predominate with some experiencing a post-psychosis depression

❖ **Residual Phase:**

➢ May have several months between acute phases with impairment due to negative symptoms

➢ Some may never progress to the residual phase and remain chronically symptomatic

❖ **Outcome:** Moderate to severe impairment across lifespan

➢ **Poor long-term outcome predictors:** low premorbid functioning, insidious onset, higher rates of negative symptoms, insidious onset, childhood onset, higher rates of negative symptoms, and low intellectual functioning

➢ **Adulthood progression:** lower levels of employment, greater social deficits, lower likelihood to live independently

- Higher risk of heart disease, obesity, HIV, hepatitis, and diabetes

➢ 5% of individuals with EOS die by suicide related to psychotic thinking

Differential Diagnosis

- Effective treatment of schizophrenia relies on accurate diagnosis and assessment
  - A child's affirmative response to questioning about hallucinations and delusions does not confirm a psychotic illness
    - Diagnosis should be based on characteristic patterns of illness and overt signs on the MSE
  - Psychosis in youth under 12 yo is rare
- **Medical Conditions**
  - CNS infections, delirium, neoplasms, endocrine disorders, genetic syndromes, autoimmune disorders, toxic exposures
  - **Drugs of Abuse:** Dextromethorphan, LSD, mushrooms, psilocybin, peyote, cannabis, stimulants, inhalants
  - **Prescription Drugs:** Corticosteroids, anesthetics, anticholinergics, antihistamines, amphetamines
  - Adolescents with EOS at highest risk of comorbid substance use and eventual development of psychosis
    - Difficult to extract the independent drug effects from an underlying illness that was unmasked by drug use
- **Schizoaffective Disorder**
  - Presence of psychotic symptoms plus prominent mood episodes present for a substantial duration of the illness
    - Reliability of the diagnosis in clinical settings is poor and early-onset schizoaffective disorder is difficult to distinguish from schizophrenia

- **Affective Psychosis**
  - **Mania:** often presents with florid psychosis
  - **Psychotic Depression:** mood congruent or incongruent hallucinations or delusions
    - Negative symptoms may be confused for a mood disorder
    - Longitudinal assessment for confirmation is necessary
- **Atypical Reports of Psychotic Symptoms**
  - **Reasons for high rate of false-positive results in children:** overactive imaginations, cognitive limitations, or misunderstanding the questions
  - **PTSD:** May represent dissociation, anxiety, intrusive thoughts or worries, derealization, depersonalization
    - Higher risk of being diagnosis with a psychotic illness as adults
- **Autism Spectrum Disorder**
  - Differentiated by lack of psychotic symptoms, younger age of onset, absence of a normal period of development
  - EOS premorbid abnormalities are less pervasive or severe
    - Social oddities and aloofness are non-specific

Recommendation 1: Psychiatric assessment for C/As should include screening questions for psychosis **(CS)**

- Probing Questions: Does your mind ever play tricks on you? Do you hear voices talking when no one is there? Does your mind ever feel confused?
- Developmental context should be considered with children under 12 years

- ➢ True psychosis is usually confusing to the patient - a detailed, descriptive, organized account is not likely

Recommendation 2: The diagnosis of schizophrenia in C/As should follow DSM-5 criteria, using the same criteria as adults **(CS)**

- ❖ Consider using a structured diagnostic interview designed for youth
- ❖ Consider a medication free trial to clarify a complicated clinical presentation

Recommendation 3: Youth with suspected schizophrenia should be carefully evaluated for other pertinent clinical conditions and/or associated problems, including suicidality, comorbid disorders, substance abuse, developmental disabilities, psychosocial stressors, and medical problems **(CS)**

- ❖ Psychosis should be prioritized for treatment unless SI or HI are present
  - ➢ Comorbid conditions may respond better to treatment once psychosis is stabilized
- ❖ No neuroimaging, psychological, or lab testing to establish a diagnosis
  - ➢ Medical evaluation should focus on rule out non-psychiatric causes
- ❖ Obtain complete blood count, metabolic panel, Liver, renal, and thyroid functions as a baseline for medication monitoring

Recommendation 4: Antipsychotic medication is a primary treatment for schizophrenia spectrum disorders in C/As **(CS)**

- ❖ Antipsychotic medication efficacy for schizophrenia is well established in adults
  - ➢ Atypical antipsychotics are considered first line in conjunction with psychotherapy

Evidence for use of antipsychotics in youth

Medication	Study	Evidence
Loxapine	Pool D, Bloom W, Mielke DH, et al. 1976	Older study supported use
Haloperidol	Spencer EK, et al. 1992	Older study supported use
Risperidone for EOS	Haas M, Eerdekens M, Kushner S. 2009	RTC supported efficacy
Aripiprazole for EOS	Findling RL, Robb A, Nyilas M, et al. 2008	RTC supported efficacy
Olanzapine vs Placebo	Kryzhanovskaya L, Schulz SC, McDougle C, et al. 2009	Industry sponsored study: Superior to placebo on symptom rating scales, but did not differ for overall response rate
Olanzapine vs Risperidone vs Haloperidol	Sikich L, et al. 2004	- Olanzapine discontinuation rates lower - No significant difference in response at 8 weeks - All with high sedation, weight gain, and EPS
Risperidone vs Quetiapine in first episode psychosis	Swadi HS, et al. 2010	No significant difference in efficacy or tolerability
Olanzapine vs Risperidone vs Quetiapine	Jensen JB, Kumra S, Leitten W, et al. 2008	No significant difference in efficacy at 8 weeks
Atypical comparison	Olfson M, et al. 2012	- All medications discontinued within 18 months of initiating treatment - No difference in hospitalization rates
Olanzapine vs Risperidone vs Quetiapine	Castro-Fornieles J, Parellada M, Soutullo CA, et al. 2008	- No difference in decreased symptom measurements - More weight gain with Olanzapine - More neurologic side effects with Risperidone
Olanzapine vs Risperidone vs Molindone	The Treatment of Early Onset Schizophrenia Spectrum Disorders Study (TEOSS) Sikich L, Frazier JA, McClellan J, et al. 2008	- Less than 50% of participants responded at 8 weeks - No difference in response rates or magnitude of symptom decrease - Higher weight gain with Olanzapine - No difference in EPS (Molindone participants got prophylactic benztropine)
Olanzapine vs Risperidone vs Molindone	TEOSS Safety and Efficacy Findling RL, Johnson JL, McClellan J, et al. 2010	None of the agents worked well and all participants had problems with side effects

- **Approved by FDA for 13+ yo:** Risperidone, Aripiprazole, Quetiapine, Paliperidone, Olanzapine, Haloperidol, Molindone (discontinued)
    - Long term safety data is limited
    - Poor results after 6 weeks, use a different antipsychotic
    - **Ziprasidone should not be used** - Study in 2009 stopped early due to lack of efficacy
- **Long Acting Antipsychotics**
    - Risk of long term exposure to side effects
    - Only consider with documented chronic psychotic symptoms and poor medication adherence

Recommendation 5: Ongoing medication therapy should be provided to most youth with schizophrenia to improve functioning and avoid relapse **(CS)**

- Most patients need long term treatment with significant risk of relapse if medication is stopped
- Maintenance therapy should be at lowest effective dose
    - Should be reassessed over time to minimize side effects
    - Some may be able to discontinue medication without re-emergence of psychosis

Recommendation 6: Some patients with schizophrenia may need adjunctive medications for side effects of antipsychotics or associated symptoms (agitation, mood instability, depression, outbursts) **(CG)**

- **Common Adjuncts:**
  - Antiparkinsonian agents - EPS
  - Beta blockers - akathisia
  - Mood stabilizers - mood instability, aggression
  - Antidepressants - depression, negative symptoms
  - Benzodiazepines - anxiety, insomnia, akathisia
- Not systematically studied in youth

Recommendation 7: Trial of clozapine can be considered for treatment resistant schizophrenia **(CS)**

- Clozapine has established superiority over other antipsychotics
  - Reserved for treatment refractory cases due to side effect profile

Recommendation 8: Baseline and follow-up symptoms, side effects, and lab tests should be monitored as indicated **(CS)**

- **Metabolic function and weight gain monitoring:**
  - Youth at higher risk of diabetes and hyperlipidemia
  - Study of weight gain over 12 weeks: gain 4.4kg on aripiprazole, 5.3kg on risperidone, 6.1kg on quetiapine, 8.5kg on olanzapine
    - Significant increase in cholesterol and triglycerides on risperidone, olanzapine, and quetiapine

- **Consensus Monitoring Guidelines**
    - At baseline, assess patient/family history of obesity, diabetes, CVD, dyslipidemia, and HTN
    - BMI at baseline, 4, 8, 12 weeks, then every 3 months thereafter
    - Fasting glucose, lipid profile, BP at baseline and every 3 months thereafter
        - If BP and glucose normal at 3 months, may monitor every 6 months
        - If Lipid profile normal at 3 months, may monitor every 6 months
- Educate about important of healthy lifestyle, smoking cessation, healthy diet, routine exercise
- Significant weight gain or metabolic syndrome → switch to agent with lower metabolic risk or add metformin

❖ **Side effects:**

- Assess for EPS (dystonia, akathisia), Tardive dyskinesia, NMS
    - Utilize standardized measurements - Abnormal Involuntary Movement Scale or Neurological Rating Scale
- Antiparkinsonian agents
    - Consider prophylactic use in those at risk for acute dystonia or history of dystonic reactions
    - Re-evaluate need after the acute phase of treatment - many patients do not need them long term

- ➢ Other side effects: sedation, orthostatic hypotension, sexual dysfunction, hyperprolactinemia, EKG changes, increased LFTs, and steatohepatitis
    - ■ Sudden death rare in pediatric populations

Recommendation 9: Psychotherapy should be provided in combo with medication **(CG)**

- ❖ Helpful Modalities: CBT, social skills training, cognitive remediation, family interventions
    - ➢ Goal of treatment - symptom reduction, improving social/occupational function, improve quality of life, decrease risk of relapse, address comorbid conditions (substance abuse)
    - ➢ Psychoeducation of patient and family - illness and treatment options, social skills training, relapse prevention, basic life skills training, and problem solving strategies

Recommendation 10: ECT may be used for severely impaired adolescents if medications are not effective or not tolerated **(OP)**

- ❖ Not systematically studied in EOS - balance risk and benefits

Psychopharmacology for use of Antipsychotics in Child and Adolescents

Medication	Dosage	Indications (*Off-label use)	Metabolism	Notable Side Effects	Considerations
Atypical Antipsychotics					
Aripiprazole (Abilify)	2-30 mg	- Bipolar Type 1 Disorder, manic/mixed episode (>10 yo) - Schizophrenia (>13 yo) - Irritability, Autistic Disorder-Associated (>6 yo) - Tourette Syndrome (>6 yo)	CYP 450: 2D6, 3A4; poor metabolizers of 2D6 have 60% increased active metabolite	- May cause akathisia - Less metabolic side effects (weight gain)	- Unique mechanism: partial agonist D2 and 5-H1A receptors; antagonist serotonin 5HT2A - Comes in long-acting injectable - Can be used to TREAT hyperprolactinemia
Asenapine (Saphris)	2.5-20 mg Sublingual use	Bipolar type 1 disorder; acute mania/mixed episode (>10 yo)	-Poor absorption even sublingually	Bad Taste	Few advantages
Clozapine (Clozaril)	12.5-700 mg	*Schizophrenia, treatment resistant (>10 yo)	- Levels decreased by cigarette smoking (1A2) - CYP 450: 1A2, 2D6, 3A4	- Myocarditis - Significant constipation with ileus - Sialorrhea: can use ipratropium and atropine drops - Weight gain/Metabolic syndrome/sedation - Decreased seizure threshold - Orthostatic hypotension/syncope	- REMS registry for agranulocytosis - Protocol for use
Lurasidone (Latuda)	20-80 mg	- Schizophrenia (>13yo) - Bipolar 1 Disorder, Acute Depression (>10 yo)	Give with >350 calories for absorption	Most weight-neutral	- Once daily dosing - Pregnancy Category B

Olanzapine (Zyprexa)	2.5-20 mg	- Schizophrenia (>13 yo) - Bipolar type 1, acute manic/mixed episode (>13 yo)	- Levels decreased by cigarette smoking (1A2) - CYP 450: 1A2 (primary), 2D6 (minor), 2C19, UGT	- Metabolic syndrome - Sedation - Orthostatic hypotension - Constipation	Comes in Long Acting Injectable (2 weeks), not used due to severe hypotension and clinic monitoring
Quetiapine (Seroquel)	12.5-800 mg Comes in IR/ER	- Bipolar Type 1 Disorder, acute mania (>10 yo; max 600 mg) - Schizophrenia (>13yo; max 800 mg)	CYP 450: 3A4	- Metabolic syndrome - Sedation - Orthostatic hypotension - May increase BP and cause diarrhea in pediatric patients	QHS dosing
Risperidone (Risperdal)	0.25-6 mg	- Schizophrenia (>13 yo) - Bipolar Type 1 Disorder, Acute manic/mixed episode (>10 yo) - Irritability, Autistic Disorder-Related (>5yo, max 3 mg) *Tourette Syndrome (>6 yo)	-CYP 450:2D6 (primary); 3A4 substrate - DDI: Fluoxetine, Paroxetine increase Risperidone levels	- One of most notable for QT prolongation - Hyperprolactinemia (gynecomastia) due to stronger D2 blockade at higher doses - Orthostatic hypotension	Long Acting Injectable (2 weeks)
Paliperidone (Invega)	3-9 mg	Schizophrenia	- Active metabolite of Risperdal - Bypasses liver metabolism	- One of most notable for QT prolongation - Hyperprolactinemia (gynecomastia)	Long-acting injectable (1 month, 3 months)
Ziprasidone (Geodon)	20-160 mg	*Bipolar Type 1 Disorder, Manic/Mixed Episode (>10 yo) *Tourette Syndrome (>7 yo, max 40 mg)	- Take with 500 calories for absorption - CYP 450: 3A4 substrate	- One of most notable for QT prolongation - Considered more weight neutral	**Not recommended in youth** 2009 trial terminated early due to lack of efficacy in youth

Typical Antipsychotics					
Chlorpromazine (Thorazine)	2.5-6mg/kg/day <5 yo: 50 mg/day max >5 yo: 200 mg/day max	- Behavioral Disorders, Severe - Nausea/Vomiting - Sedation, preop - Tetanus, Adjunct treatment	CYP 450: 1A2, 2D6 (primary), 3A4 substrate; has active metabolite	- Sedation - Weight gain - Constipation	Commonly used for acute agitation in children
Haloperidol (Haldol)	1-100 mg <12 yo: 0.5 mg/kg/day >12 yo: 100mg/day	- Psychosis - Tourette Syndrome - Behavioral Disorders, Severe *Agitation	-DDI: fluoxetine/paroxetine increase Haldol levels -CYP 450: 3A4 (primary), 2D6 Inhibitor	QT prolongation notable; especially with bolus IV dosing	- Long-acting injectable (1 month) - Comes in IV/IM/PO
Molindone (Moban)	5-225 mg	Schizophrenia	CYP 450: unknown	Antihistaminergic properties	Discontinued
Pimozide (Orap)	1-10 mg	Tourette Syndrome, Severe	- Caution with Poor 2D6 metabolizers - CYP 450: 2D6, 3A4 (primary)	-	-
Prochlorperazine (Compro)	0.5-20 mg	- Nausea/Vomiting, Severe - Schizophrenia	CYP 450: Unknown	Antihistaminergic properties	Injectable in pediatric populations

A Ninja's Guide to Disordered Eating

A Ninja's Summary: *Practice Parameter for the Assessment and Treatment of Children and Adolescents with Eating Disorders*

(Updated 2015)

Why care? Caring for patients with eating disorders is complicated and nuanced. The comorbidities associated with eating disorders are significant and patients need close medical monitoring. A multidisciplinary team is best practice in treating these complex cases.

Background

- Anorexia first described in 1689, described as *nervous consumption*, actually called anorexia nervosa/hysterique in 1874 to describe self-starvation and weight preoccupations.
    - Charcot felt families should be removed from patients due to their "pernicious" influence, even now treatment includes long separation from family
    - Hilda Baruch felt it was a disorder of suppression and neglect in childhood leading to food refusal for self-assertion
    - Minuchin's work re-introduced families into treatment (structural family therapy had good outcomes)
- **Bulimia**: First included in 1980 DSM-III
- **Binge Eating Disorder:** First included in DSM-5, notably rarer in younger patients
- **ARFID (Avoidant-Restrictive Food Intake Disorder):** Involves avoiding food or eating but not associated with shape/weight concerns

Defining the Diagnosis: Anorexia Nervosa (AN)

- **Characteristics**:
  - Restriction of energy intake causing low body weight
  - Fear of gaining weight OR behavior that interferes with weight gain
  - Self-evaluation unduly influenced by weight and body shape
  - Often includes denial of seriousness of malnutrition
  - Patients can have perfectionistic, obsessive, avoidant personality features
    - Also associated with cognitive rigidity and in detail oriented individuals
  - Picky eating early in life associated with later development of AN
- **Subtypes**: restricting type and binge eating/purging type
- Level of severity mild to extreme based on **BMI percentiles**.
  - **Below 10th BMI percentile** or deviations from individual growth trajectories in growth charts
- **Parent reports** about child's behavior are critical
  - Self-report unreliable due to lack of insight, minimization, denial

- ➢ Kids are not abstract, so food refusal could be a nonverbal expression of emotion

- ❖ **Clinical signs**: usually weight concerns and behavior changes start 6-12 months before diagnosis

  - ➢ Patients often claim they are trying to be healthy: eat less, avoid fattening foods, exercise more, other insist they just aren't hungry or complain of abdominal discomfort

  - ➢ Look for avoidance of "fattening" foods or fear of weight gain like repeated weighing, pinching skin

  - ➢ Reduction of calories worsens over time as they limit protein, fats, sweets

  - ➢ When involved in academics, athletics higher risk to become more compulsive and driven

  - ➢ Often have Compulsions to stand or move, exercise in secret

  - ➢ Dress in baggy clothing, layers, feel cold

  - ➢ Could drink lots of water or avoid water

  - ➢ Appear withdrawn, depressed, anxious

  - ➢ Cognitively intact until severe malnutrition

- ❖ **Epidemiology & Facts**

  - ➢ Mortality of 5-7%, as high as 18% in some samples, death is due to medical complications of starvation or suicide

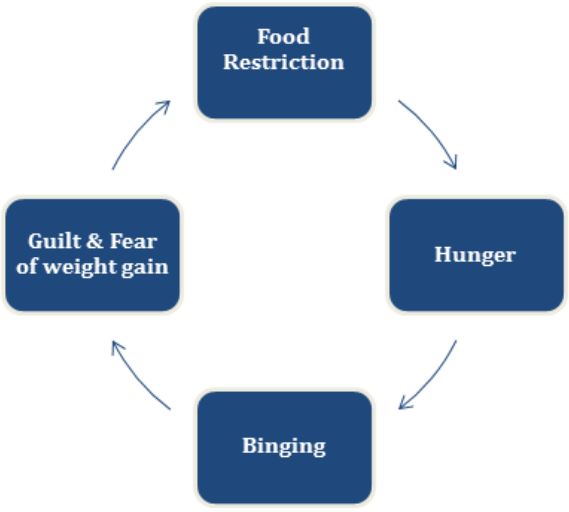
- ➢ Lifetime rate of comorbidity with 1 other psychiatric disorder is 55.2%, commonly depression, social anxiety, OCD, separation anxiety, GAD, substance use, personality disorders (avoidant, dependent, obsessive-compulsive)
    - ■ Differentiate from OCD by looking at focus of preoccupations and compulsions. If they emerge at the same time and are focused on food, eating, weight, more likely to be AN.
- ➢ Better prognosis in adolescents than adults
- ➢ Youth less likely than adults to have binge eating/purging
- ➢ Prevalence 1-2% in females, in teenage girls 0.3%-0.7%
    - ■ For males, studies say 1 male case for every 10 female cases or up to 1:1 ratio
- ➢ Anorexia occurs at 5x the expected rates in affected families, heritability in twin studies from 30-75%
- ➢ Ballet, gymnastics, wrestling, modeling can increase risk for eating disorders

❖ **Differential Diagnosis**

- ➢ ARFID or rumination disorder that leads to low body weight
- ➢ Chronic infection, thyroid disease, IBS, cystic fibrosis, any disease of digestive tract, diabetes, anything that leads to weight loss, appetite loss and refusal to eat
- ➢ Atypical Anorexia means meets all criteria for AN except that despite significant weight loss, their weight is normal

Defining the Diagnosis: Bulimia Nervosa (BN)

- Recurrent binge-eating of a very large amount of food in a discrete period of time and loss of control over eating, at least once a week for 3 months
  - Loss of control more important to look at than calories consumed in binge
- Recurrent compensatory behavior like vomiting, fasting, exercise, laxatives, diuretics, diet pills at least once a week for 3 months
  - Mild, moderate or extreme based on frequency of these behaviors
  - Males more likely than females to have excessive exercise and steroid use
    - Increased risk for males in wrestling, gymnastics, diving, long distance running
- Self-evaluation unduly influenced by weight and body shape (like anorexia)
- **Normal or high normal weight range**
- Often accompanied with secrecy, shame and guilt which interferes with life
  - **Bulimia Behavioral Cycle** (see image): Starvation leads to hunger and promotes binging when food is available, then guilt comes due to binging and fear of weight gain which leads to compensatory behaviors



- **Epidemiology & Facts**
  - Often has varying cycles of remission and exacerbation, average time to treatment is 5 years
  - History of low self-esteem, childhood obesity, personality disorder predict longer duration

- PTSD, impulsive personality, perfectionistic traits are risk factors
- Mood disorders, anxiety disorders, substance use disorders highly associated, **BN patients have lifetime psychiatric comorbidity rate of 88%**
  - 53% have SI, 35% have suicide attempts

➢ Hx of Non-suicidal self injury (NSSI), substance abuse, impulsivity common in adults and older teens

➢ 1-2% of teenage girls and 0.5% teenage boys, male to female ratio from 1:10 to 1:3

➢ Typically begins between 14-22, rarely diagnosed in children and younger teens

➢ Heritability in twin studies 60-83%.

➢ Mortality rate 1%

❖ **Differential Diagnosis**:

➢ AN binge/purge type, purging disorder (no binging, just purging), binge eating disorder, CNS tumors, Kleine-Levin syndrome (rare disorder with excessive sleep), Kluver-Bucy syndrome (rare disorder causes hyperphagia and inappropriate sexual behavior), GI issues like obstruction/gastroparesis

❖ **Treatment**: Adult studies describe CBT, Antidepressants and interpersonal psychotherapy are effective

Defining the Diagnosis: Binge Eating Disorder

❖ Recurrent binge eating episodes with a sense of loss of control over eating during the episode.

- ➢ Associated with at least 3: eating quicker, eating until uncomfortably full, eating when not hungry, eating alone due to embarrassment about amount of food consumed, feelings of disgust/depression/guilt

- ➢ Often patients are overweight or obese

- ❖ At least once a week for 3 months and associated with marked distress

  - ➢ However, if children present with symptoms, should likely use a lower threshold to diagnose since younger kids don't have as much access to food

- ❖ No compensatory behaviors (which distinguishes it from Bulimia)

- ❖ **Most common eating disorder**

  - ➢ In adults: 3.5% of females and 2% of males

  - ➢ In teens: 2.3% of females and 0.8% of males

  - ➢ Serious complications include esophageal or gastric rupture

- ❖ Begins in late adolescence or early adulthood often after significant dieting/weight loss

- ❖ Differential Diagnosis: night eating syndrome (recurrent eating at night causing distress), nocturnal sleep related eating disorder, CNS tumors, Kleine-Levin syndrome, Kluver-Bucy, Prader-Willi and GI pathology

  - ➢ In adults associated with depression, anxiety, PTSD, impulse control disorders, substance use disorder, personality disorders

- ❖ Bulimia Test Revised: BULIT-R is a standardized measure specific to BN

- ❖ Interpersonal therapy supported, but not a lot of data for youth. In adults, CBT, DBT, IPT.

Defining the Diagnosis: Avoidant Restrictive Food Intake Disorder (ARFID)

- ❖ Food restriction or avoidance without shape or weight concerns. Without intentional efforts to lose weight, there is significant weight loss and nutritional deficiencies (no avoidance of high calorie food, patients want to gain weight)
    - ➢ Some patients have highly selective eating, neophobia (fear of new things) related to food types, hypersensitivity to food. Texture, appearance, taste
    - ➢ Some patients have fear of swallowing or choking contributing to food avoidance and an advent can be identified as trigger for that fear
    - ➢ Also can apply to lack of interest in eating or low appetite
- ❖ Anxiety and depression can pre-date ARFID, neglect and abuse and DD can increase risk for chewing/spitting behaviors
    - ➢ Autism patients can have selective eating
- ❖ No studies to guide treatment, treat with individualized behavioral plans, CBT and family involvement can be helpful. Gradual desensitization, behavioral reinforcement can be useful. May progress to hospitalization/medical instability.

Defining the Diagnosis: Eating Disorder NOS

- ❖ Covers sub threshold presentations and other eating problems
- ❖ Female triad syndrome: common in women athletes
    - ➢ Defined as low energy with disordered eating, amenorrhea, low bone density
    - ➢ High risk for eating disorder, monitor closely
    - ➢ 18.2% female high school athletes meet criteria for disordered eating

Treatment overview

- **Family based treatment:** parental management of eating and related behavior until patient improves
    - Evidence: 6 RCTs support it for AN, 2 RCT show its useful for BN
    - Recommendation: useful for most cases of short duration AN and BN in pediatric patients
- Adolescent focused therapy: since its individual the focus is on autonomy and self-efficacy
    - Evidence: 2 RCTs it did worse than Family Based Treatment but still effective
    - Recommendation: useful when FBT not possible
- CBT: focuses on distorted cognitions and behaviors
    - Evidence: 1 RTC and 1 case series for BN, no data for AN
    - Recommendation: may be useful in BN
- Interpersonal therapy: changing problematic relationship that trigger or maintain eating disorder symptoms
    - Evidence: 2 RCTs in adults show its helpful for BN and BED, preliminary studies showing it may be useful for teens with BN
    - Recommendation: useful for BN, BED as alternative to CBT
- Antidepressants: help with obsessions, anxiety, depression, targets binegin eating/purging specifically in BN
    - Evidence: 1 uncontrolled trial says they're helpful for teenage BN
    - Recommendation: use for comorbid disorders, second line treatment for teenage BN
- Atypical Antipsychotics: helps with body image distortion, weight gain fears/anxieties in AN

- ➢ Evidence: 3 RCTs and a case series, not enough evidence for AN
- ➢ Recommendation: not enough data supporting use in AN but useful for comorbid issues

Practice Parameters:

Recommendation 1: Screen all pediatric patients for eating disorders by asking about eating patterns and body satisfaction, track height/weight **(CS)**

- ❖ Short, validated self report measures that can be useful for screening: Eating Disorder Examination-Questionnaire (EDE-Q), Eating Disorder Inventory (EDI), Eating Attitudes Test (EAT)
    - ➢ For young children: Kids' Eating Disorder Survey (KEDS), children's versions available for EDE-Q and EDI. Also Child-Eating Attitudes Test (CHEAT)

Recommendation 2: Positive screen warrants evaluation, labs and imaging **(CS)**

- ❖ Complete psychiatric and physical exam: include weight, height, changes in weight, menstrual history, dieting, calorie counting, body image concerns, thorough exercise history, binge/purge behavior history, depression, anxiety, obsessive thoughts, NSSI, SI, psychosis, substance use, label checking, self weighing
- ❖ BMI percentiles necessary over just BMI, obtain growth charts from pediatrician
- ❖ Eating Disorder Examination: EDE, structure interview for assessing disordered eating. Reliable for those 12 and older
- ❖ Labs: CBC, Chem 13, BUN, Cr, Glucose, AST/ALT, TSH, Ca, Mg, Pho's, total protein, albumin, ESR, amylase (high when patients are vomiting), B12, lipids, LH,, FSH, estradiol, BhCG
    - ➢ EKG for Arrhythmia
    - ➢ DEXA. For bone should. Be done if amenorrhea lasts more than 6 months and. Once a year if it persists
        - ■ All males with significant weight loss should have a DEXA

Recommendation 3: Treat severe or acute physical/medical complications **(CS)**

- Look out for arrhythmia, bradycardia, hypotension, hypothermia, dehydration, CHF, kidney failure, pancreatitis, amenorrhea, irregular menses, low bone mineral density, cognitive impairments, delay in growth, pubertal interruption, hormone imbalances, fluid/electrolyte abnormalities

- Clinical signs: hair loss, lanugo hair, dry skin, dependent edema, muscle weakness, cramps

- Most issues reversible once healthy weight is reached, but growth impairment, bone density, structural brain changes may persist, even infertility

- Physical signs of purging: parotid swelling, calluses on dorsum of hand (called Russell's sign), erosion of dental enamel, esophageal tears, even hypokalemia and other electrolyte issues can cause syncope and orthostatic hypotension.

- When to hospitalize: heart rate changes like bradycardia or orthostatic HR changes), issues with blood pressure, body temperature, electrolyte abnormalities and severe malnutrition

    - Some data suggests NG tube feeding is more efficient than other approaches but long term effects have not been studied

Recommendation 4: Hospitalize, admit to PHP/IOP or residential only when outpatient is unsuccessful/unavailable **(CG)**

- No evidence that psychiatric hospitalization is more effective then outpatient

- No RCTs on residential/intensive treatment compared to outpatient

- There are negative effects of separating from family but sometimes they are clinically necessary

Recommendation 5: Treatment of eating disorders in pediatrics requires a multidisciplinary team that is developmentally aware, sensitive and skilled in EDO treatment **(CS)**

- Usually psychologist, pediatrician, dietician plus child psychiatrist

Recommendation 6: Outpatient psychosocial interventions are initial treatment of choice **(CS)**

- ❖ 6 RCTs looked at family based treatment and found it is effective & superior to individual therapy
    - ➢ 10-20 family meetings over 6-12 months, empowers parents to take charge of weight restoration by taking action to disrupt symptoms of self-starvation and over exercise, its efficient and decreases need for hospitalization
    - ➢ Individual still beneficial, adolescent-focused therapy (AFT) focuses on individuation and self-efficacy, also on tolerating negative emotions
        - ■ CBT helpful for AN
        - ■ CBT group therapy better at decreasing binge eating than family therapy for BN
            - ● Psychoeducational, changing maladaptive behaviors, normalize eating patterns, self-monitoring with diet records, challenge beliefs/fears
            - ● DBT has a role when there are multiple diagnoses

Recommendation 7: Medications should be reserved for comorbid conditions and refractory cases **(CG)**

- ❖ SSRI: Large scale studies do not support SSRIs but none have been done for teens with AN.
    - ➢ Effective for adults with BN, fluoxetine decreases urges to binge/purge (FDA approved), 60mg/day
    - ➢ CBT superior to antidepressants, combination best when also depressed
    - ➢ May not be effective until weight is partially restored due to lower levels of available serotonin
    - ➢ Obsessive thoughts and depression improve with weight gain alone

- ❖ Atypical Antipsychotics: small studies found a few benefits to adding risperidone, quetiapine. Difficult for patients to accept weight gain side effect but can be helpful in eating related thinking

Summary of Eating Disorders

	Anorexia	Bulimia	Binge Eating D/O	ARFID
Defining Features	-Below 10th BMI percentile or deviation from growth chart trajectory -Restriction causing low body weight -Fear of gaining weight -High mortality rate	-Binging with loss of control -Compensating after binge -Normal or high normal weight -High comorbidity rate	-Binging with loss of control -No compensation -Overweight/obese -Most common eating disorder	-Food restriction without weight concerns -Highly selective eating -Associated with anxiety and depression
Treatment	Family based treatment, Adolescent focused therapy	CBT, Interpersonal therapy, Antidepressants	Interpersonal Therapy	Behavioral plans, CBT, Desensitization

APPENDIX A

Review of Studies for Tic Disorder AACAP Guidelines

Treatment (Dosage range)	Weight change	Age of patients	Main Outcome
Haloperidol (0.5-10mg) vs **Pimozide** (1-20mg) vs Placebo (Shapiro, et al. 1989)	-	8-46 years (avg 21.1)	**Both effective**, Haldol > Pimozide
Clonidine (0.05-0.25mg) vs Placebo (Leckman, et al. 1991)	-	7-48 years (avg 15.6 years)	**Small benefit** in tic reduction
Selegiline (5mg BID) vs Placebo (Fiegin, et al. 1996)	-	7-16 years (avg 12 years)	Benefit in tics and ADHD symptoms
Pimozide (3mg) vs Haldol (3mg) vs Placebo (Sallee, et al. 1997)	-	7-16 years (avg 10.2 years)	Some benefit from both. Pimozide had better response
Pergolide (0.025-3mg) vs Placebo (Gilbert, et al. 2000)	-	7-17 years	Some benefit in Parkinson's Disease
Ziprasidone (5-40mg) vs Placebo (Sallee, et al. 2000)	-	7-17 years	Some benefit
Risperidone (0.5-6mg) vs **Pimozide** (1-6mg) (Bruggeman, et al. 2001)	+8.6 lbs +6.5 lbs	10-65 years (avg 21.5)	**Both beneficial for TD** (NNT 6.1)
Guanfacine (1.5-3mg) vs Placebo (Scahill, et al. 2001)	-	7-15 years	**~34% reduction in tic and ADHD** (NNT=3)
Mecamylamine (2.5-7.5mg) vs Placebo (Silver, et al. 2001)	-	8-17 years (avg 11.3 years)	No benefit
Risperidone (1-6mg) vs Placebo (Dion, et al. 2002)	+2.9 lbs	14-49 years (avg 32 years)	**Benefit in 60%** vs 26.1% placebo (NNT=2.9)
Risperidone (1-1.5mg) vs **Clonidine** (0.1-0.2mg) (Gaffney, et al. 2002)	+4.6 lbs +0.2 lbs	7-17 years	Small benefit with **both equally**
Desipramine (150-200mg) vs Placebo (Spencer, et al. 2002)	-	5-17 years	Significantly reduced tics and ADHD

Methylphenidate (1-60mg) vs Clonidine (0.1-0.6mg) vs Combo vs Placebo (Tourette Syndrome Study Group, 2002)	-	7-14 years	Clonidine significantly reduced tics and helped ADHD. **Methylphenidate didn't exacerbate tics**
Pergolide (0.15-0.45mg) vs Placebo (Gilbert, et al. 2003)	-	7-17 years	Small reduction in tics (~25%) and some benefit ADHD symptoms
Risperidone (1.5-3.5mg) vs Placebo (Scahill, et al. 2003)	+6.2 lbs	6-62 years (Avg 19.7)	Some benefit in tic reduction (NNT 6.2)
Atomoxetine (1mg/kg/day) vs Placebo (Allen, et al. 2005)	-2 lbs (active) +3.5 lbs (placebo)	7-17 years	**Some benefit in tic reduction** (50% vs 33% placebo) and benefit ADHD (NNT=6.2)
Metoclopramide (5-40mg) vs Placebo (Nicolson, et al. 2005)	+2.2 (active) +1.1 lbs (placebo)	7-18 years	Some benefit for tic reduction (NNT=5)
Ondansetron (8-24mg titrated over 3 wks) vs Placebo (Toren, et al. 2005)	-	12-46 years; N=30	Some benefit for tic reduction (NNT 3.1)
Levetiracetam (750-3000mg) vs Placebo (Smith-Hicks, et al. 2007)	-	8-16 years (avg 12.2)	No benefit
Clonidine adhesive patch (1-2mg) vs Placebo (Du, et al. 2008)	-	6-18 years	Some benefit in tic reduction (NNT 4.6)
Clonidine (0.15-0.3mg)/ Levetiracetam (250-1750mg) Crossover (Hedderick, et al. 2009)	-	8-27 years (avg 14.9); N=12 pts	Clonidine resulted in a small benefit Levetiracetam had no benefit
Topiramate (25-200mg) vs Placebo (Jankovic, et al. 2009)	-4 lbs weight loss average	7-65 years (average 16.5) of N=29 patients	**Showed significant tic severity reduction compared to placebo**
Pramipexole (0.0625-0.5mg) vs Placebo (Kurlan, et al. 2012)	-	6-17 years	No benefits for suppressing tics, possible help in ADHD
Habit Reversal Training vs Supportive Therapy	-	9-17 years (avg 11.7)	**Greater improvement** in symptom severity over supportive therapy

>50% improvement in tics: Clonidine, Atomoxetine

APPENDIX B

Summary of Evidence for Treatment of Depression with Psychotherapy

Modality	Study Design	Author(s)	Important Notes
Multiple Psychotherapy Modalities	Meta-Analysis	Weisz et al., 2006	- Effects of psychotherapy for acute treatment of youth with depression only modest - Treatments were equally efficacious for all modalities - Outcomes better when youth was the informant - Psychotherapy treatment effective for first few month, but not for 1 year follow-up - Small reduction in suicidality
CBT	Meta-Analysis	Compton et al., 2004; Harrington et al., 1998	- CBT effective for the treatment of youth with MDD
CBT	RCT	Barbe et al., 2004b; Brent et al., 1998; Lewinsohn et al., 1998; Melvin et al., 2006, Rohde et al., 2004	- CBT effective despite comorbidity, SI, and hopelessness - Less effective with history of sexual abuse or one of the parents is depressed
CBT, Fluoxetine	Large RCT	March et al., 2004, 2006b **(TADS Team)**	- No difference between CBT and placebo - Nonexistent or modest difference between combination and med alone, yet **combo still favored** - Limitations: Subjects not blinded to medication assignment and CBT treatment not comprehensive
CBT, Fluoxetine	Large RCT	Kratochvil et al., 2006 **(TADS Team)**	- Combo CBT + Fluoxetine shows more rapid symptom reduction - No difference between combo vs med alone for rates of clinical improvement and symptom ratings

CBT, Fluoxetine	Large RCT	Curry et al., 2006 **(TADS Team)**	- Combo better than med alone for mild-mod depression in teens and for high levels of cognitive distortions, but not severe depression
CBT, Fluoxetine	Large RCT	Kennard et al., 2006 **(TADS Team)**	- Higher remission rate in combo treatment (37%)
CBT	RCT	Asarnow et al., 2005	- CBT delivered in primary care setting can be delivered effectively and has better outcomes than treatment as usual
CBT, SSRI	RCT	Goodyer et al., 2007	- CBT + SSRI no better than SSRI alone
CBT, Sertraline	RCT	Melvin et al,. 2006	- No difference between CBT + Sertraline vs CBT or Sertraline alone for mild-mod depression - CBT superior to sertraline alone after acute treatment - Limitation: Low sertraline dose
CBT, SSRI	RCT	Clarke et al., 2005	- CBT + SSRI in primary care setting shows modest improvement on quality of life, not primary outcomes - Patients on combo treatment more likely to discontinue SSRI
CBT, Systemic behavioral family therapy	RCT	Brent et al., 1997	- CBT superior to systemic behavioral family therapy in short-term reduction of adolescent depression
Attachment Therapy	Uncontrolled Trial (UT)	Diamond et al., 2002	- Superior to waitlist control for relief of depression symptoms
Psychodynamic Psychotherapy	UT, RCT	Crits-Christoph et al., 2002 [ut]; Muratori et al., 2003 [ut]; Trowell et al., 2007 [rct]	- Psychodynamic vs family therapy shows promising results

APPENDIX C

Current Research Evidence of CBT Against the Type of Control

Strength of Evidence (SOE)	Inactive Controls (Waitlist/ No Treatment)	Active Controls (Attention/ Treatment as Usual)	Pill Placebo
High SOE	-	-	-
Mod SOE	**CBT Improved:** Primary anxiety symptoms (child, parent, clinician reports), global function, response to treatment	**CBT Improved:** Only primary anxiety (child report)	-
Low SOE	**CBT Improved:** Reduced dropouts **CBT may have Improved:** Remission **No Separation from CBT:** Satisfaction, secondary measures, short-term adverse events,	**No Separation from CBT:** Improved primary anxiety (parent/clinician report), satisfaction, secondary measures, remission, short-term adverse events	**CBT Improved:** Reduced dropouts due to adverse events **No Separation from CBT:** Primary anxiety (child report), secondary measures, short-term adverse events, reduced dropouts
Insufficient Evidence	Improved social function	Improved global function, social function, response to treatment	Improved primary anxiety (clinician report), global function, social function
Limitations	Publication bias		