

Defining Autism Spectrum Disorder in Children and Adolescents

James Miles, MD
NDAFP Family Medicine Update
January 18, 2024



Improving Health. Enriching Life.

1

Disclosures

Relevant Financial Relationship(s)

None

Off Label Usage

None



Improving Health. Enriching Life.

2

Learning Objectives

- Appreciate how common autism spectrum disorder (ASD) is by discussing the epidemiology.
- Review the current understanding of the pathogenesis of ASD.
- Identify clinical features and associated conditions of ASD.
- Summarize the surveillance and screening of ASD, as well as next steps.



Improving Health. Enriching Life.

3

Autism Spectrum Disorder

- DSM-5 2013
- Neurodevelopmental disorder
 - Deficits in social communication and interaction
 - Restrictive repetitive behaviors, interests, and activities
- Must be present in early development
- Must substantially impair functioning



Improving Health. Enriching Life.

4

Epidemiology

- Prevalence 1/40 to 1/500
- Increased over time, esp. since 1990s
 - Changes in definitions
 - Increased awareness
 - Earlier detection
 - More specialized developmental services
 - Diagnostic substitution
 - True increase



Improving Health. Enriching Life.

5

Epidemiology

- More common in US
- 3-4 x more common in males
- 10-20% siblings
- 33-45% intellectual disability
- 50% ADHD
- 30% Epilepsy
- 25% Genetic cause



Improving Health. Enriching Life.

6

Pathogenesis: Genetics

- Incompletely understood
- Genetic factors that alter neural connectivity
- Environmental modifiers
- Polygenic variants, single nucleotide variants, copy number variants, rare inherited variants, tandem repeats, noncoding variants



Improving Health. Enriching Life.

7

Pathogenesis: Genetics

- Supported by unequal sex distribution, increased prevalence in siblings, high concordance in monozygotic twins, increased risk with increased relatedness
- Linkage studies and WES has identified many genetic variations, no individual variation accounts for >1% and no specific mutation is unique to ASD



Improving Health. Enriching Life.

8

Pathogenesis: Neurobiologic Factors

- Neuroimaging, electrophysiology, autopsy studies
 - Brain abnormalities, particularly atypical neural connectivity
- Accelerated head growth during infancy and increased overall brain size



Improving Health. Enriching Life.

9

Pathogenesis: Environmental Factors

- Toxic exposures, teratogens, perinatal insults, prenatal infections
- Second-hit: modulating existing genetic factors predisposing to ASD



Improving Health. Enriching Life.

10

Pathogenesis: Parental Age

- Advanced parental age
 - 30 and older for mothers
 - 40 and older for fathers
 - De novo spontaneous mutations and/or alterations in genetic imprinting



Improving Health. Enriching Life.

11

Pathogenesis: Perinatal Factors

- Little evidence to implicate any single factor
- Broad class of conditions that compromise perinatal and neonatal health may increase risk
 - Abnormal presentation, LBW, meconium aspiration
 - Prenatal meds



Improving Health. Enriching Life.

12

Immunizations

- Increase in ASD and timing of ASD symptoms correlate with vaccine schedule
- Epidemiologic evidence does not support an association between immunizations or thimerosal and ASD
- Benefit outweighs risks of vaccines



Improving Health. Enriching Life

13

Clinical Presentation

- Heterogenous neurodevelopmental disorder
- Atypical social communication and interaction
- Restricted, repetitive patterns of behavior



Improving Health. Enriching Life

14

Impaired Social Communication and Interaction



Improving Health. Enriching Life

15

Social and Emotional Reciprocity

- Social attention
 - Absent or limited interest in social interaction with other children
 - Lack of understanding of “personal space” and boundaries
 - Indifference/aversion to physical contact and affection



Improving Health. Enriching Life

16

Social and Emotional Reciprocity

- Joint attention
 - Awareness of social attention of others
 - 8-10 months of age
 - Pointing by 14-16 months of age
 - Content playing passively by themselves



Improving Health. Enriching Life

17

Social and Emotional Reciprocity

- Nonverbal communication
 - Poor eye contact
 - Poor or scripted facial expressions
 - Fail to notice others nonverbal communications



Improving Health. Enriching Life

18

Social and Emotional Reciprocity

- Pragmatic language
 - Echolalia
 - Scripted language
 - Metaphors, humor, sarcasm, teasing, jokes, deception (6 to 7 years of age)



Improving Health, Enriching Life

19

Restricted and Repetitive Behavior, Interests, and Activities

- Stereotyped behaviors
 - Hand flapping, rocking, spinning in circles
 - Tip-toe walking
 - Lining toys up or spinning wheels on toy cars
 - Delayed echolalia
 - Self-stimulative/-injurious behavior
 - New self-injurious behavior should prompt evaluation



Improving Health, Enriching Life

20

Restricted and Repetitive Behavior, Interests, and Activities

- Insistence on sameness and resistance to change
 - Schedules and routes
 - Diet
 - Discussing same topics
 - Scripted play
 - Can be perceived as OCD
 - Unaware of their perseverations



Improving Health, Enriching Life

21

Restricted and Repetitive Behavior, Interests, and Activities

- Restricted interests
 - 1 or more specific topics
 - Preoccupation with unusual objects



Improving Health, Enriching Life

22

Restricted and Repetitive Behavior, Interests, and Activities

- Sensory processing difficulties
 - Overresponsive or underresponsive
 - Textures to touch
 - Food textures or tastes
 - Certain noises
 - PICA
 - Pain insensitivity



Improving Health, Enriching Life

23

Associated Conditions

- Intellectual impairment: usually uneven
- Developmental delay
 - Speech > Fine Motor > Gross Motor
 - Developmental regressions
- Anxiety: 42-55%
- ADHD: 30-50%
- ODD and other disruptive behavior disorders



Improving Health, Enriching Life

24

Associated Conditions

- Mood disorders
- Tic disorders
- Schizophrenia
- Learning disorders
 - Typically 3rd to 4th grade



Improving Health, Enriching Life

25

Associated Conditions

- Sleep disorders
 - Bedtime resistance
 - Sleep anxiety
 - Sleep-onset disturbances
 - Frequent waking
 - Restlessness
 - Abnormal sleep architecture



Improving Health, Enriching Life

26

Associated Conditions

- Feeding problems
 - Textures and tastes
 - GI symptoms: weight abnormalities, diarrhea, constipation
 - Nutritional deficiencies
- Medical conditions (eg seizures)
- Genetic syndromes



Improving Health, Enriching Life

27

Associated Conditions

- Motor deficits
 - Clumsiness
 - Toe-walking
 - Hypotonia
- Macrocephaly 25%, increased rate of head growth 70%
 - PTEN



Improving Health, Enriching Life

28

Associated Conditions

- Special skills ("savant")
 - Memory, math, music, art, puzzles
 - Calendar calculation
 - Hyperlexia



Improving Health, Enriching Life

29

Clinical Presentation

- First 2 years of life
 - Speech/language delays often first thing
 - Poor eye contact
 - Limited interest in socializing
 - Failed ASD screen



Improving Health, Enriching Life

30

Clinical Presentation

- Plateau/regression after typical early development
 - Language, communication, and/or social skills
 - 25-33% of children with ASD
 - 15-24 months of age



Improving Health, Enriching Life

31

Clinical Presentation

- Older toddlers and preschoolers
 - Lack of interest in socializing
 - Absent or delayed speech/language skills
 - Marked resistance to change
 - Restricted interests



Improving Health, Enriching Life

32

Clinical Presentation

- Kindergarten or later
 - Less severe phenotypes
 - Behavior disturbances
 - Coexisting ADHD or anxiety



Improving Health, Enriching Life

33

Benefits of surveillance/screening

- Early individualized intensive interventions
- Earlier education planning
- Family/caregiver support
- Delivery of proper medical care and treatment of associated conditions
- Genetic counseling



Improving Health, Enriching Life

34

Surveillance

- Caregiver concerns important
 - Targeted questions when appropriate
- Maintaining a developmental history
- Observing caregiver-child interactions
- Identifying risk and protective factors
- Routine developmental surveillance
 - 9, **18**, **24**, and 30 months
 - Whenever concerns arise



Improving Health, Enriching Life

35

Screening Tools

- ASD-specific
- Complement general developmental screening tools
 - Poor predictors of ASD
- First- and second-tier screening
- Limited sensitivity and specificity
- Age-specific and validated



Improving Health, Enriching Life

36

Modified Checklist for Autism in Toddlers, Revised w/ Follow-Up

- M-CHAT-R/F
- Two-stage tool
- 16-30 months of age
- Available in many languages
- Validated with sensitivity 85% and specificity 99%, PPV 48%



Improving Health, Enriching Life

37

M-CHAT-R/F: Stage 1

- 20-item yes/no caregiver-report questionnaire
- <5 minutes to administer
- <2 minutes to score
- Scoring
 - 0-2 low risk
 - 3-7 medium risk→Stage 2
 - 8-20 high risk→Referral for diagnosis



Improving Health, Enriching Life

38

M-CHAT-R/F: Stage 2

- Structured follow-up questionnaire administered by provider
- Same questions, probes for more info
- 5-10 minutes to administer



Improving Health, Enriching Life

39

Other Screening Tools

- Screening Tool for Autism in Toddlers and Young Children (STAT)
 - 24-36 months
 - Second-stage or enhanced screening
 - 20-minute play-based (language comprehension unnecessary)
 - Sensitivity 92%, Specificity 85%



Improving Health, Enriching Life

40

Other Screening Tools

- Infant-Toddler Checklist (ITC)
 - 24-item questionnaire part of the CSBS-DP (6-24 mo)
 - Sensitivity and specificity 88.9%
- Parent's Observations of Social Interactions (POSI)
 - 7-item caregiver-report for 16-35 mo
 - Sensitivity 83%, specificity 75%



Improving Health, Enriching Life

41

Other Screening Tools

- Social Communication Questionnaire (SCQ)
 - Second-stage screen 4 yrs and up
- Autism Spectrum Screening Questionnaire (ASSQ)
 - High-functioning, 27-item checklist
 - 7-16 yrs



Improving Health, Enriching Life

42

Other Screening Tools

- Autism Spectrum Quotient (AQ)
 - Self-administered for adults with normal intelligence
 - 50 questions
- AQ-Child
 - 4-11 years
 - Sensitivity and specificity 95%, further studies ongoing



Improving Health. Enriching Life.

43

Other Screening Tools

- Developmental Behaviour Checklist-Autism Screening Algorithm
 - 4-18 yrs w/ intellectual disabilities
 - Sensitivity 86%, specificity 69%
 - False positives with significant behavioral problems
- Developmental Behaviour Checklist-Early Screen
 - 18-48 mo w/ dev delay



Improving Health. Enriching Life.

44

Positive Screen

- Caregiver education
- Referrals and medical evaluation
 - Diagnostic evaluation
 - Developmental services
 - Early intervention and public school
 - Speech and language evaluations
 - Audiology
 - Blood lead level



Improving Health. Enriching Life.

45

Resources for Caregivers

- CDC [Learn the Signs. Act Early.](#)
 - Tools and training
- CDC [Autism Information Center](#)
- Autism Society of America
- Autism Speaks



Improving Health. Enriching Life.

46

Resources

- American Psychiatric Association. Autism spectrum disorder. In: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision, American Psychiatric Association, Washington, DC 2022. p.56.
- Autism Society. <https://autismsociety.org/>.
- Autism Speaks. <https://www.autismspeaks.org/>.
- CDC Autism Information Center. <https://www.cdc.gov/ncbddd/autism/index.html>.
- Filipek PA, Accardo PJ, Ashwal S, et al. Practice parameter: screening and diagnosis of autism: report of the Quality Standards Subcommittee of the American Academy of Neurology and the Child Neurology Society. Neurology 2000; 55:468.



Improving Health. Enriching Life.

47

Resource

- Hyman SL, Levy SE, Myers SM, COUNCIL ON CHILDREN WITH DISABILITIES, SECTION ON DEVELOPMENTAL AND BEHAVIORAL PEDIATRICS. Identification, Evaluation, and Management of Children With Autism Spectrum Disorder. Pediatrics 2020; 145.
- Learn the Signs. Act Early. <https://www.cdc.gov/ncbddd/actearly/index.html>.
- Lord C, Elsabbagh M, Baird G, Veenstra-Vanderweele J. Autism spectrum disorder. Lancet 2018; 392:508.
- Mayo Clinic. <https://mayoclinic.org>.
- Modified Checklist for Autism in Toddlers, Revised with Follow-Up. <https://www.mchatscreen.com>.
- Pina-Garza JE. *Fenichel's Clinical Pediatric Neurology*. 7th ed.



Improving Health. Enriching Life.

48

Resources

- Radiopaedia. <https://radiopaedia.org>.
- Swaiman KF et al. *Swaiman's Pediatric Neurology: Principles and Practice*. 5th ed.
- UpToDate. <https://www.uptodate.com>.
- World Health Organization. ICD-11 International Classification of Diseases 11th Revision. <https://www.who.int/classifications/classification-of-diseases>.



Improving Health. Enriching Life.

49

Questions?



Improving Health. Enriching Life.

50