

Autism Overview

- ‘Explosion’ of medical / psychological reports
- Media interest / celebrities
- ? Epidemic / changing prevalence
- Cost – estimated \$35 billion annually*
- Affects many fields, all ages
- Many health and educational ramifications

* Ganz, 2006

Autism 'Myths'

- Caused by 'bad parenting'
- Never affectionate
- Defined by self-stimulation and behaviors
- Cannot feel or express emotions
- Never care about others
- Cannot be treated

Definition of Autism

- A ‘moving target’
- Wide range of symptoms
- No single pathonemonic symptom or feature
- Spectrum of characteristic with blurred endpoints

Autism Definition

- Autism spectrum disorder (ASD) describes set of three neurodevelopmental conditions consisting of one or more of:
 1. Qualitative impairment in social interaction
 2. Qualitative impairment in communication
 3. Restricted interests/ repetitive motor mannerisms

Autism Definition

ASD includes:

- Autistic Disorder (AD)
- Asperger's Disorder (Syndrome) (AS)
- Pervasive Developmental Disorder, Not Otherwise Specified (PDD – NOS)
(Excludes Rett Syndrome, Childhood Disintegrative Disorder)

Autism Definition

- Criteria for Autistic Disorder (AD)
- Explanation with reference to normal development for each broad category
- Criteria for Asperger's Disorder (AS)
- Criteria for PDD – NOS

Autistic Disorder

I. Qualitative impairment in social interaction, as manifest by at least two of the following:

A. marked impairment in the use of multiple nonverbal behaviors such as eye-to-eye gaze, facial expression, body postures, and gestures to regulate social interaction

B. failure to develop peer relations appropriate to developmental level

Autistic Disorder

I. Social interaction, continued

C. a lack of spontaneous seeking to share enjoyment, interests, or achievements with other people (e. g. by a lack of showing, bringing, or pointing out objects of interest)

D. lack of social or emotional reciprocity

Autistic Disorder

II. Qualitative impairments in communication as manifested by at least one of the following:

A. delay in, or total lack of, the development of spoken language (not accompanied by an attempt to compensate through alternative modes of communication such as gesture or mime)

B. in individuals with adequate speech, marked impairment in the ability to initiate or sustain a conversation with others

Autistic Disorder

II. Communication, continued

C. stereotyped and restricted use of language or idiosyncratic language

D. lack of varied, spontaneous make-believe play or social imitative play appropriate to developmental level

DSM-IV-TR, 2000

Autistic Disorder

III. Restricted repetitive and stereotyped patterns of behavior, interests, and activities, as manifested by at least one of the following:

A. encompassing preoccupation with one or more stereotyped and restricted patterns of interest that is abnormal either in intensity or focus

B. apparently inflexible adherence to specific, nonfunctional routines or rituals

Autistic Disorder

III. Restricted repetitive of behavior, continued

C. stereotyped or repetitive motor mannerisms (e.g. hand or finger flapping or twisting, or complex whole body movements)

D. persistent preoccupation with parts of objects

Autistic Disorder

- Delays or abnormal functioning in at least one of the following, with onset prior to age 3:
 1. Social Interaction
 2. Language as used in social communication
 3. Symbolic or imaginative play
- Not accounted for by Rett's Disorder or CDD

Asperger Syndrome

- Same social (at least 2) and restricted interest (at least 1) criteria as for AD
- No ‘clinically significant general delay in language’:
 - single words by age 2 years
 - communicative phrases by age 3 years

from DSM-IV-TR, 2000

Asperger Syndrome

- No clinically significant cognitive delay
- No clinically significant delay in:
 - age appropriate self help skills
 - adaptive behavior, aside from socialization
 - curiosity about environment in childhood
- Not better accounted for by any other pervasive developmental disorder or schizophrenia

from DSM-IV-TR, 2000

PDD - NOS

- “Severe and pervasive impairment” with social interaction and either....
 1. Deficits in communication AND /OR
 2. Restricted interests / repetitive behaviors
- 2-5 criteria from list for AD (“sub-threshold” number of symptoms or “atypical autism”)
- Impairment *not* need to be present before age 3

Other Pervasive Dev Disorders

- Rett Syndrome – discussed later
- CDD – apparently normal 1st 24 months
 - Regression (at least 2 areas) by 10 yr: language, social/adaptive, bowel/bladder, motor, or play
 - Deficits in at least 2 of the 3 ASD categories
 - Not explained by another PDD or schizophrenia

from DSM-IV-TR, 2000

Social Deficits

- More *specific* to ASD than language impairment, seem to not seek ‘connectedness’
- Deficits in social relatedness – universal
- Seem to not seek ‘connectedness’
- May appear earlier than frank speech defects but may also be subtle

Social Milestones

- Begins in utero with attachment
- 2 months – social smile
- 3 months – initiates interaction with wiggles, smiles, cooing; searches room for caregiver
- 3-5 months – preference for primary caregiver and social referencing
- 7 months – responds to emotion of others, may respond to own name

Zucherman et. al 1999

Joint Attention

- Desire + ability to draw the attention of another for the purpose of enjoying a shared experience
- Comes in stages, begins around 8 months with gaze monitoring
- Follows a point by 10-12 months
- After a year more at child's initiation
- Point to object and look back at parents (protoimperative pointing) – not yet true JA

Johnson and Myers, 2008

Joint Attention

- Points simply to comment by 14-16 months (protodeclarative pointing) – seeking the social experience with the parent
- Showing objects to parents to look at
- *Mastery of joint attention often reliably predicts functional language acquisition*

Johnson and Myers, 2008

Social Deficits in ASD

- 6-9 months of age
 - Poor social smiling
 - No gaze, little or no eye contact
 - Little facial expression
- 9-12 months of age
 - Not orienting well to name
 - Orienting to environment > human voice
 - Not following point well

Social Deficits in ASD

- 12-15 months of age
 - Rare point, may just open/close hand
 - Using hand as tool – very common
 - Failure to reference parents during stress
- *Therefore* the child is left with fewer building blocks for more advanced socialization as expected for older children...

Social Deficits in ASD

- Difficulties with ‘theory of mind’ skills – understanding the perspective of others (may start in typical developing children age 4)
- Few friends, may revolve around child’s interests
- Impaired central coherence ‘missing the big picture’
- Difficulty with empathy, sharing, comforting

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Communication Milestones

- Definitions *:
 - communication: ‘ the process’
 - language: ‘the contents of the message’
 - speech: ‘ the mode of delivery’
- Complex interaction of cognition, social, physical, and environmental factors
- Receptive generally precedes expressive

*Modified from Matthew Braun, MA, CCC-SLP

Communication Milestones

AGE	RECEPTIVE	EXPRESSIVE
0-1 m.	Startles	Cries
5-7 m	Turns to sound/name	Babbles
8-10 m	Link action-word	Mama/Dada
11-14 m	Simple ? / command	few words/jargon
15-18 m	Point to 3 body part	20+ word / needs
By 24 m	you / me, “show me” in / on / under	100 words 2-word sent.

Communication Milestones

- Preschoolers will begin to answer “w” questions, become 100% intelligible by age 4, may have some dysfluency lingering
- By age 4 may tell a story, use past tense, vocabulary of *thousands* of words
- By age 8, all sounds of English language articulated correctly spontaneously
- Language typically commensurate with cognition

Communication Deficit

- Infants with ASD, compared to peers, may
 - Lack gaze / fewer expressions with gaze
 - Lack to-fro interaction that occurs at 6 months
 - Seem to not recognize caretaker's voice
 - Delayed onset babbling (past 9 months)
 - Lack of expressions such as 'oh oh' or 'huh'

Johnson and Myers, 2007

Communication Deficit

- 25-30% of toddlers with ASD may have language *regression*
 - Gradual or sudden
 - Often occurs ages 15-24 months
 - May lose gestures and social skills
 - *Should always raise the question of ASD*

Johnson and Myers, 2007

Communication Deficit

- In older children, speech may
 - Be absent
 - Lack communicative intent
 - Echolalic = ‘parroting’, immediate or delayed
 - Monotone with ‘chunks’ of language
 - May be better at rote labeling objects than pointing to them when asked
- Hyperlexia without accompanying comprehension

Johnson and Myers, 2007

Play Skills

- Based on representation – one thing stands for another (hence very related to communication)
- Pretend play builds on social and communicative skills:
 - More detached from real life objects
 - Less centered on self
 - More complex, more prolonged

Play Milestones

- 9-12 mos: peek-a-boo as object permanence emerges, visual-motor inspection
- 12-18 mos: symbolic play based on self
- 18-24 mos: symbolic directed toward another; Simple pretend play
- 24-30 mos: truly imaginative play, more symbolic
- 36 mos: role playing, beginning to take turns
- 48 mos: group games with simple rules

Play Deficit

- Play in children with ASD may differ as:
 - In some not progress beyond sensory-motor
 - Mouth, twirl, bang repetitively
 - Repetitive wheel spinning on cars, line up toys, arranging instead of truly playing
 - Common objects may be preferred
 - Puzzles and constructive activities favored

Johnson and Myers, 2007

Play Deficit

- May play alone for extended time
- ‘Chase’ and ‘roughhouse’ for sensory-motor aspects rather than social play
- Difficulty with social rules of complex games
- May be left out, bullied, rejected

Johnson and Myers, 2007

Restricted / Stereotyped Behavior

- May include several behaviors:
 - Unusual mannerisms
 - Unusual attachments / obsessions / compulsions
 - Self injury (esp. with cognitive deficit)
 - Stereotypy – repetitive and nonfunctional
 - Difficulty with transition, insisting ‘sameness’
 - May have strict routines

Johnson and Myers, 2007

Restricted / Stereotyped Behavior

- Not specific for ASD
- Also seen in profound MR, severe sensory defects, typically developing children before onset of functional language
- Rare before age 3, confounding AD diagnosis
- Self injury may have functional cause

Additional (non-DSM) Features of ASD

Cognitive Abnormalities

- Global developmental delay (GDD)/Mental Retardation (MR) or Intellectual Disability
- Term depends on age / assessment
- Once believed to include vast majority of ASD
- More recent studies approx 50%, as low as 26%
- Perhaps result of better assessment - ?
- Uneven skills – splinter skills – savant skills

Johnson and Myers, 2007

Additional (non-DSM) Features of ASD

Sensory

- Hypo / hypersensitivities with same modality (voice / sound)
- Oral aversions
- ‘Tactile defensiveness’ vs. decreased pain sens.
- May have restricted diets as result but rarely globally malnourished
- Not distinguishing features of ASD

Johnson and Myers, 2007

Additional (non-DSM) Features of ASD

Motor

- Poor coordination, praxis
- Hypo- or Hyperactive (may suggest ADHD)
- Motor clumsiness – particularly Asperger
- Again, not distinguishing features of ASD

Johnson and Myers, 2007

Asperger Notes

- Generally not diagnosed until age 4 or later
- May not differ from AD with normal intelligence, may both be ‘high functioning autism’
- Language not severely delayed, but may be
 - Verbal about restricted topics
 - Hard to express feelings
 - Pedantic (overly formal)
 - Difficult pragmatics – carrying on conversation
 - Unique prosody – intonation, pitch, delivery

Epidemiology

- Studies hard to compare – design & definition
- CDC 2007 average 14 sites in US, 8-year olds reported as **1/150**
- Ten fold increase worldwide since 1950's
- Male > Female: 2 – 6.5 to 1 (higher ratio in AS)

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Epidemiology

- Changing / broader criteria
- More awareness
- More PDD-NOS and AS and ‘milder cases’
- More concerns voiced by parent to PCP’s
- Recognition of ASD in certain syndromes
- Diagnostic substitution debate
- ? True epidemic?

Johnson and Myers, 2007

Etiology of ASD

- No known cause
- Biologically based, highly heritable
 - Genetically complex
 - Phenotypically variable
 - Very likely ‘multifactorial’
- May be idiopathic (90%+) or syndromic

Genetics

- More common in monozygotic vs dyzygotic twins (60% vs 3% for AD)
- Strong family clustering
- Male predominance
- Multiple genes implicated, most consistently 2, 3, 7, 15, 17
- X chromosome: Fragile X and Rett's

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Idiopathic ASD

- No known medical condition or known cause
- At least 90% of ASD, possibly all of AS
- No dysmorphic features to suggest syndrome
- Less likely than syndromic to have MR / ID
- Recurrence 5-6 % after one child higher after two (May approach 25%)

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Secondary ASD

- Identifiable syndrome or medical condition believed to be *casually* associated
- Fewer than 10% of children with ASD
- More likely with *severe* MR / ID
- Besides syndromes, other causes of secondary:
 - Advanced maternal and paternal age implicated
 - Environmental, esp. Early gestation (see later)
 - ? Epigenetics – heritable, no changes in DNA

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Fragile X Syndrome

- Most common *known* genetic cause of AD
- Named after CGG repeats seen on DNA
- Most common genetic cause of MR / ID in males
- Macrocephaly, large ears, large testicles, low tone, hyperextensible joints, mitral valve prolapse
- 0 – 8 % of those dx with ASD have Fragile X
BUT 30-50 of those with Fragile X have ASD

Tuberous Sclerosis

- Autosomal dominant, mostly new mutations
- Seizures, mental retardation, renal problems, hypopigmented macules, pits in dental enamel
- Abnormalities on brain MRI (hamartomas)
- 40% may have ASD (small study)

Rett Syndrome

- Carried on X chromosome – almost all female
- MECP2 gene in 80% of cases
- Autistic like features (100%) with regression followed by plateau of development
- Hand wringing, microcephaly, seizures, peculiar sigh, ataxia, poor weight gain common
- May have subtle motor abnormalities in infancy

Angelman Syndrome

- Loss of maternally expressed UBE3A on maternal chromosome 15
- Global delays – often severe and nonverbal
- Low tone, wide-based gait, seizures, spasticity
- Episodes of laughter, seem very happy

Environmental Issues

- No single factor identified to be fully responsible
- Possibly ‘second hit phenomenon’
- Active area of investigation
- Likely *early* event in fetal brain development

Prenatal / Perinatal Period

- Maternal rubella illness
- Cytomegalovirus
- Valproate (seizure medicine)
- Thalidomide – early
- Threatened abortion
- Advanced maternal / paternal age
- Newborn encephalopathy – perhaps up to 5%
- Warning: findings not always consistent among studies, cannot make 1-1 associations!

Vaccines - MMR

- Study in late 90's proported causal association between MMR vaccine and autism (12 subjects)
- Further reviews fail to support
- 2004 – ten of the 13 authors retracted statement
- 2008 – repeated studies fail to support correlation
- Rise in vaccine preventable disease in some areas where vaccine rates going down

Peacock et al 2009

Vaccines - Thiomersal

- Never was in MMR vaccine, still in flu vaccine
- Removed from all other vaccines 1999
- Contains ethyl-mercury, rapidly excreted
- IOM “ There was inadequate evidence to conclude or discredit a relationship between thiomersal and neurodevelopmental disorders”
- Continues to be actively researched

Peacock et al 2009

Neurological Correlates

- Seizures (30%) and abnormal EEG (50%)
- Likely different brain growth / organization
- No cohesive neurological explanation
 - Changing DSM criteria
 - Broad phenotype
 - Coexisting MR / ID in some children
 - Challenges in study children
 - Limited autopsy data and controls

Neurological Correlates

- Trends in head size have suggested unique brain development – not true for all patients
- Normal or small at birth
- Acceleration in size age 6 months to 2-4 years
- Eventual macrocephaly, then deceleration in size
- Differences in gray to white matter distribution

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Neurological Correlates

- Hypoactivity of fusiform gyrus (part of temporal lobe possibly responsible for face recognition)
- Most consistent finding on functional MRI in autistic children
- Children with ASD have been shown to look less at faces compared to background objects
- May relate to ASD social symptoms and communication characteristics

Johnson and Myers, 2008

Medical Home

- Characteristics from AAP Definition*:
 - Accessible, Family – Centered
 - Continuous, Comprehensive
 - Coordinated, Compassionate
 - Culturally Effective
- A concept where parents can hopefully be empowered to foster healthy growth and development

*www.medicalhomeinfo.org

Medical Home Aspects for ASD

- Surveillance & screening (AAP algorithm ref #)
- Timely referral
- Medical Care
- Transition Planning
- Advocacy

Surveillance

- Part of every preventive visit
- A ‘moving picture’ – ongoing process
- Elicit parent concerns – open ended questions
- Observations of child
- Identify risk factors, protective factors
- Documentation
- “Do you have any concerns about how your child is developing or behaving?”

Surveillance

- Family history
- Attention to siblings
- Red Flags from American Academy of Neurology demand immediate attention*:
 - No babbling, point, or gesture by 12 months
 - No single words by 16 months
 - No two-word phrases by 24 months
 - Loss of language or social skills at any age

* Filipek et al 2000

Screening

- Performed at 18 and 24 (or 30) months *OR*
- Performed when concern arises from surveillance
- “A snapshot in time”
- Use a tool that has the following properties:
 - Reliable: consistency of measurement
 - Valid: measures what it is supposed to
 - Sensitive: those at risk will be positive
 - Specific: those not at risk will be negative

Screening

- No tools routinely used in under 18 months
- Modified Checklist for Autism in Toddlers (M-CHAT) perhaps most common
- Can be downloaded free at www.firstsigns.org
- Series of YES / NO questions (23 total)
- Developed for 16-30 months
- High false positive rate so should include follow-up interview

Evaluation

- Audiology evaluation
- Early intervention / early childhood services
- Physical Exam
 - Head circumference
 - Dysmorphic features
 - Neurological Exam
 - Birthmarks, use Wood's light
 - Often noted for *lack* of physical findings!

Evaluation

- 3 generation family history
- Close follow up of families during this time
- Schedule comprehensive evaluation
 - Autism center of excellence
 - Developmental Pediatrics
 - Pediatrics Department

Evaluation – DSM criteria

- Define the condition
- Challenging to apply in young children
 - True stereotypy often not until age 3
 - Often with PDD-NOS or ‘provisional ASD’
- Augmented by observation of free play (e.g. in home or school settings)

Evaluation

- Autism Diagnostic Interview – Revised (ADI-R)
 - Interview lasting 90 minutes to 3 hours
- Autism Diagnostic Observation Schedule (ADOS)
 - Samples of social interaction, communication, play that are coded and scored
 - Considered ‘gold standard’ for research when combined with ADI – R
 - Includes modules useful for Asperger / HFA

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Evaluation

- Childhood autism rating scale (CARS)
 - 15 item structured interview
 - Children aged 2 and older
 - Rated based on level of severity for each question
 - One of most widely used rating scales for autism
 - May over identify young children, under identify older ones esp. With HFA
- Several others also available

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Evaluation – Asperger specific

- Often initiated by school personnel
- Several scales available:
 - Australian, Asperger syndrome diagnostic scale, childhood Asperger syndrome test, Gilliam Asperger disorder scale
 - Krug Asperger disorder index – probably best psychometrics
- None of these to be used in isolation

Evaluation - Genetics

- Several guidelines, often not in agreement
- Must consider family wishes
- Most suggest DNA probe for Fragile X and Chromosome Analysis
 - Comparative Genomic Hybridization
 - High resolution karyotype – may be more available
- Some suggest above only if coexisting MR / ID
- No clear guidelines for Asperger / HFA

Evaluation - Genetics

- SHANK3 – gene on ch. 22, in severe patients
- MECP2 on X chromosome – girls with MR with idiopathic ASD, note will not resemble Rett
- PTEN on ch. 10, in patients with head size 3 SD above normal, may carry cancer risk as adults
- HOXA1 – consanguineous families, patient with deafness and vascular problems
- Genetics consultation

Evaluation - other

- Lead test – esp if mouthing or pica
- EEG – only if suspect seizures
- MRI – microcephaly, midline facial defect, neurocutaneous findings, or abnormal neuro exam
- Metabolic – if clinical signs esp. if not done in nursery

Treatment

- No known cure
- Careful attention to other medical factors:
 - Seizures
 - Sleep disturbance – melatonin may help
 - Behaviors may need medical treatment if severe and not ammenable to behavioral methods
 - Any other childhood illnesses

Treatment

- Intensive Intervention
- Assess family goals
- Low student – teacher ratios
- Inclusion of typically developing peers to extent that such inclusion is helpful to overall goals
- Structure through predictable routines, visual schedules, clear boundaries

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Treatment

- Generalization of strategies across environments
- Functional adaptive skills
- Functional assessment of behaviors
- Symbolic play and perspective taking
- Academic skills as appropriate

- Several strategies including the following...

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Applied Behavior Analysis (ABA)

- Studied for nearly 5 decades
- A process to apply principles for the following:
 - Support positive behaviors
 - Reduce maladaptive behaviors
 - Teach new skills
 - Generalize to new situations
- Organized structure with skills broken to small steps, taught with prompts, repeated opportunities to practice and learn with positive reinforcement

Applied Behavior Analysis (ABA)

- Includes careful observation and modification as needed
- Analysis of why behaviors occur
 - To get attention ?
 - To get a desired object, sensation, etc?
 - Escape?
- Early + intense intervention studies show gains in IQ, language, adaptive skills, and social behavior

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TEACCH

- Aka ‘structured teaching’
- Assessed to identify emerging skills and focus on them, hence flexible to each child versus standard curriculum
- Structured environment with visual supports
- Emphasized both improving skills and accommodating challenges

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Treatment

- Picture exchange communication system (PECS)
- Visual schedules
- Social skills and joint attention training
- Specific attention to self care skills (hygiene, utensils, dressing, etc)
- Some programs integrate Sensory Integration Tx.
- Transition meeting age 14 with consideration of living, vocation, schooling and may take years

Family Support

- Parents more likely to experience stress and depression compared to controls (1)
- Also have found greater meaning in lives, delight in child's accomplishments, and empathy for others (2)
- Support groups, extended family, church
- SSI benefits, Kansas waiver
- Special Needs Trust

(1) Bouma et al 1990

(2) Marcus 2005

Family Support

- American Academy of Pediatrics
 - www.aap.org
- Families Together
 - www.familiestogetherinc.org
- Autism Speaks
 - 1. www.autismspeaks.org
- Many others

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