

Autistic spectrum disorder

By
Vidya Bhushan Gupta, MD, MPH
Associate Professor of Clinical Pediatrics
New York Medical College

Vidya Bhushan Gupta, MD, MPH

History



Leo Kanner, in 1943 described 11 children with "Autistic disturbances of affective contact"

- Poor social skills
- Quantitative and qualitative defects of communication
- Professional, high achieving parents
Coined the term, Refrigerator mothers"

Vidya Bhushan Gupta, MD, MPH

History (continued)

Hans Asperger, in 1944, described "autistic psychopathy"

Poverty of social interaction

Failure of communication

Oddities of non-verbal communication – gaze aversion, prosody

Attractive appearance

Similarities between the parents and children

Resistance to change

Vidya Bhushan Gupta, MD, MPH

Prevalence

- Prevalence rising
 - Reported vs. true
 - Diagnostic shift from MR to autism
 - Broader definition
- 4-8 per 10,000 in 1980's
- 10-40 per 10,000 now
- 273% increase in California from 87-98

Vidya Bhushan Gupta, MD, MPH

M.I.N.D. Institute, UCLA study, 2002

- California-wide sample of 684 children
- Two birth cohorts – 83 to 85, 93-95
- Increased prevalence
 - Not due to loosening of diagnostic criteria
 - Not due to misclassification of MR
 - Not due to migration to California
 - Diagnosis of MR with autism has declined

Vidya Bhushan Gupta, MD, MPH

Psychogenic versus neurogenic

Kanner's refrigerator mothers
Bruno Bettelheim's Empty Fortress
Feral children- the Wild Boy of Aveyron.

Bernard Rimland
Rutter

Vidya Bhushan Gupta, MD, MPH

Terminology

Childhood psychosis

Kanner's syndrome

Autism

Pervasive developmental disorder

Autistic spectrum disorder

Vidya Bhushan Gupta, MD, MPH

DSM-IV CRITERIA OF AUTISTIC DISORDER

- A. A total of ≥ 6 items, at least 2 from (1), and 1 each from (2) and (3)**
- (1) qualitative impairment in social interaction, at least two of the following:
 - a) marked impairments in the use of nonverbal behaviors such as eye-to-eye gaze, facial expression, body posture, and gestures to regulate social interaction
 - b) failure to develop peer relationships appropriate to developmental level
 - 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 to other people)
 - d) lack of social or emotional reciprocity (note: in the description, it gives the following as examples: not actively participating in simple social play or games, preferring solitary activities, or involving others in activities only as tools or "mechanical" aids)

Vidya Bhushan Gupta, MD, MPH

DSM-IV CRITERIA OF AUTISTIC DISORDER (CONT.)

(2) qualitative impairments in communication, 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
- c) stereotyped and repetitive use of language or idiosyncratic language
- d) lack of varied, spontaneous make-believe play or social imitative play appropriate to developmental level

Vidya Bhushan Gupta, MD, MPH

DSM-IV CRITERIA OF AUTISTIC DISORDER (CONT.)

(3) restricted repetitive and stereotyped patterns of behavior, interests, and activities, as manifested by at least two of the following:

- a) preoccupation with a few stereotyped and restricted patterns of interest that is abnormal either in intensity or focus.
- b) apparently inflexible adherence to specific, nonfunctional routines or rituals
- c) stereotyped and repetitive motor mannerisms (e.g., hand or finger flapping or twisting, or complex whole-body movements)
- d) persistent preoccupation with parts of objects

- B. Delays or abnormal functioning in at least one of the following areas, with onset prior to age 3 years: (1) social interaction, (2) language as used in social communication, (3) symbolic or imaginative play

- C. The disturbance is not better accounted for by Rett's disorder or childhood disintegrative disorder.

Vidya Bhushan Gupta, MD, MPH

PERVASIVE DEVELOPMENTAL DISORDERS (DSM-IV)

- Autistic disorder
- PDD (NOS) including atypical autism
- Asperger's syndrome
- Childhood disintegrative disorder
- Rett's

Vidya Bhushan Gupta, MD, MPH

Social deficits in autism

- Lack of affective attunement
 - Failure to engage in vocal interactions and nonverbal social communication interactions with mother
- Lack of joint attention
 - Failure to engage in attention-sharing behaviors, such as pointing or showing objects
- Theory of mind
 - Inability to guess other's perspective and emotions
- Lack of social referencing
 - To follow their mother's line of sight to an object
 - To look to their mother's face to determine what they should do. If their mothers show interest, the children will look; if the mothers pose fear or anger, the child will not look.

Vidya Bhushan Gupta, MD, MPH

Communication impairment

- Delayed language
 - 50% non-verbal
 - 30% regress between 1-2 years
- Qualitatively different language
 - Echolalia
 - Pronomial reversal
 - Do not initiate/maintain conversation
 - Abnormal intonation, volume, rhythm, pitch

Vidya Bhushan Gupta, MD, MPH

Checklist for autism in toddlers

SECTION A: ASK PARENT

- Does your child enjoy being swung, bounced on your knee, etc?
- Does your child take an interest in other children?
- Does your child like climbing on things, such as up stairs?
- Does your child enjoy playing peek-a-boo/hide-and-seek?
- Does your child ever PRETEND, for example, to make a cup of tea using a toy cup and teapot, or pretend other things?
- Does your child ever use his/her index finger to point, to ASK for something?
- Does your child ever use his/her index finger to point, to indicate INTEREST in something?
- Can your child play properly with small toys (e.g. cars or trucks) without just mouthing, fiddling or dropping them?
- Does your child ever bring objects over to you to SHOW you something?

Vidya Bhushan Gupta, MD, MPH

Checklist for autism in toddlers

SECTION B: OBSERVATION

- During the appointment, has the child made eye contact with you?
- Get child's attention, then point across the room at an interesting object and say 'Oh look! There's a (name of toy!)' Watch child's face. Does the child look across to see what you are pointing at? *
- Get the child's attention, then give child a doll and a miniature bottle and say 'Can you feed the doll?' Does the child pretend to feed the doll? **
- Say to the child 'Where's the light?', or 'Show me the light'. Does the child POINT with his/her index finger at the light?
- Can the child build a tower of cubes?

Vidya Bhushan Gupta, MD, MPH

AUTISM RATING SCALES

- Childhood autism rating scale (the CARS)
 - Good screen, easily learned and administered, good interrater reliability, and reasonable sensitivity
- ADI-R and the ADOS/PL-ADOS*
 - Good research instruments, provide a detailed view of social, language, and interpersonal functioning, and restrictive and repetitive behaviors, and they have algorithms for overall diagnosis as well as for each of the 3 *DSM-IV* autism domains.
 - Their drawback is that raters must be fully trained and they are time-consuming to administer

*prelinguistic version

Vidya Bhushan Gupta, MD, MPH

GENETICS OF AUTISM

- Monozygotic concordance rate of 60% for AD and 92% for the broader spectrum of social and communication deficits with stereotypies. Dizygotic twin rates for AD and for the broader spectrum 0% and 10% to 30%.
- Sibling recurrence rate of 3% to 7%
- Heritability of autism approximately 90% (Bailey et al)
- Polygenic model of inheritance with at least 3 (may be 20) gene loci contributing to the wide spectrum of symptoms.
- Gene markers have recently been identified on chromosomes 1p, 7q, 16p, and 17p in linkage studies.
- Autism has been associated with an abnormality of every chromosome except 14 and 20.

Vidya Bhushan Gupta, MD, MPH

Known genetic conditions with autism

- Down syndrome
- Fragile x syndrome
- Prader willi (15q del)
- Angelman syndrome
- 15q duplications, isochromosomes, isodicentric
- Williams syndrome
- XYY syndrome
- Smith-Magenis syndrome
- Duchenne muscular dystrophy
- Cornelia deLange
- Tuberous sclerosis
- Hypomelanosis of Ito
- Neurofibromatosis

Vidya Bhushan Gupta, MD, MPH

HOME OF AUTISM IN THE BRAIN

- CEREBELLUM – Purkinje cells, small vermis
- LIMBIC SYSTEM – Small, closely packed cells
- BASAL GANGLIA – Moebius syndrome
- CEREBRAL CORTEX
 - FRONTAL – executive dysfunction
 - TEMPORAL – language dysfunction
 - PARIETAL – information processing

Vidya Bhushan Gupta, MD, MPH

Autism and MMR vaccination

- Wakefield et al - 12 children with regressive autism with diarrhea and abdominal pain. 8/12 children had the onset of symptoms after MMR vaccination. All had intestinal abnormalities, ranging from ileal lymphoid nodular hyperplasia to aphthoid ulceration. Hypothesis - the altered gut epithelium allowed absorption of toxic dietary (opioid?) peptides or bacterial byproducts, such as endotoxins that damaged the developing brain. The bowel problems caused malabsorption of essential vitamins and nutrients
- Other experts have disputed the validity of the study and whether autistic enterocolitis exists.
- Many of the cases had autistic symptoms before the onset of bowel symptoms.
- Another study in which highly specific laboratory assays for measles virus were negative in patients with inflammatory bowel disease.
- No evidence found for a causal association between MMR (or other measles-containing vaccines) and autism in two epidemiologic studies.

Vidya Bhushan Gupta, MD, MPH

Multifactorial etiology

- Genetic susceptibility → viral infection (rubella) or teratogen exposure (thalidomide/valproic acid) in early gestation → neuronal damage
- Genetic susceptibility → viral infection → Immune dysfunction → cross-reacting neuroantibodies → neuronal damage
serotonergic dysfunction

Vidya Bhushan Gupta, MD, MPH

DIFFERENTIAL DIAGNOSIS

AUTISM

1. Normal SES
2. History of normal development for a few months followed by regression common
3. Normal or large head
4. Social withdrawal and flat affect common
5. Motor stereotypies common
6. Marked deficit in receptive language
7. Marked deficit in pretend play, nonverbal communication, and joint attention

MENTAL RETARDATION

1. Low SES
2. Development delayed since birth
3. Small head common
4. Immature behavior
5. Self-abusive or aggressive behavior common
6. Receptive and expressive language equally affected
7. Delays in these domains are congruent with IQ

Vidya Bhushan Gupta, MD, MPH

DIFFERENTIAL DIAGNOSIS (CONT.)

- Asperger syndrome: poor peer relationships, lack of empathy, and a tendency to overfocus on certain topics. typical IQ and relatively typical language skills.
- Semantic-pragmatic language disorder
- Obsessive-compulsive disorder
- Right hemisphere learning disorder (nonverbal learning disorder)
- Rett syndrome, a neurodegenerative disorder due to mutation in the gene *MECP2*). Occurs in girls, onset during the first or second year of life after a period of typical development. Loss of purposeful hand skills accompanied by stereotypic hand movements, particularly hand wringing; gross motor and coordination skills associated with ataxia and tremor; language and cognitive skills; and social interaction skills. Abnormal EEG.
- Childhood disintegrative disorder. Extremely rare, later onset (older than 2 years), profound losses in language, social, play, and motor skills than those seen in AD or PDD-NOS.

Vidya Bhushan Gupta, MD, MPH

There is no routine work-up for autism!

- **Audiological in all, birthmarks, HC, dysmorphism**
- **No routine MRI, only if unexplained focal seizures**
- **No routine EEG, only if seizures, suspicion of seizures, regression -? Prolonged sleep EEG**
- **Karyotype if has MR, and is dysmorphic**
- **DNA and FISH testing based upon clinical exam. And family history. Fragile X hype, chromosome 15**
- **Metabolic testing if lethargy, cyclic vomiting, regression, coarse features**
- **Lead screen if pica or environmental risk**

Vidya Bhushan Gupta, MD, MPH

MANAGEMENT

- COPING
 - Educating and supporting parents
- CARING
 - APPLIED BEHAVIOR ANALYSIS (LOVAAS)
 - DIRECTIVE-RELATIONAL THERAPY
 - TEAACH
 - SENSORY- INTEGRATION
- CURING
 - PHARMACOTHERAPY OF TARGET SYMPTOMS

Vidya Bhushan Gupta, MD, MPH

Social and Behavioral Therapies

- Goals: improving social, interpersonal, emotional, communicative skills, and pragmatic skills, decrease the intensity of stereotypic and bizarre behaviors.
- Early intervention- refer before evaluations are completed.
- One size does not fit all.

Vidya Bhushan Gupta, MD, MPH

Intensive behavioral interventions

- Therapist-directed discrete trial teaching
 - Applied behavior analysis (Lovaas)
 - New York State Guidelines, min 20 hr/wk
 - Starts with functional behavior analysis: **EATS**
(escape, attention-seeking, tangible gain, sensory stimulation)
- Child-directed social-pragmatic teaching
 - Developmental, Individual Difference, Relationship or DIR model or floor time (Greenspan)

Vidya Bhushan Gupta, MD, MPH

Comprehensive Educational Curricula

- Treatment and Education of Autistic and Communication Handicapped Children (TEACCH) developed by Schopler in North Carolina. Emphasizes parent training, teaching according to the child's strengths, use of structured learning situations, and the importance of visual strategies and supports

Vidya Bhushan Gupta, MD, MPH

Educational approaches (cont.)

- **Daily Life Therapy** (The Higashi School) originated in Japan. Emphasizes academic, fine art, and physical education skills while using certain behavioral strategies, including prompting, ignoring problematic ones and teaching alternatives, emphasizes group participation rather than an individualized curriculum. The development of language skills and other functional skills is not emphasized.
- **The Bright Start curriculum:** focuses on strategies that improve cognitive skills, such as flexible thinking. The curriculum addresses deficits in attention, social interaction, communication, and motivation.
- **Ecologic approaches:** Emphasize teaching a child functional skills in natural environments. Do not address specific disabilities commonly present in these children.

Vidya Bhushan Gupta, MD, MPH

Communication therapies

- Traditional speech and language therapy
- Augmentative strategies – PECS, signs, devices
- Pragmatic communication therapy- improving functional communication skills
- Language assessment needs to include all areas of communication, including semantics and pragmatics, and should lead directly into intervention. Behavioral techniques can be helpful in teaching language to children with ASD as well.

Vidya Bhushan Gupta, MD, MPH

Miscellaneous

- Occupational therapy using sensory integration techniques to address sensory processing problems is commonly used in children with ASD. Research data to support its effectiveness is scant.
- Occupational and physical therapy may be helpful in addressing coordination and motor planning deficits occurring in some children with ASD.
- Integration - All types of therapy should be interwoven throughout all aspects of a child's program, not just as a "pullout" technique.
- Eclectic approaches

Vidya Bhushan Gupta, MD, MPH

Sensory-integration therapy

- Integration of sight, hearing, smell, taste, touch, position
- Interventions: vestibular (swinging), proprioceptive (touch, message, hug machine), somatosensory (deep brushing)
- Despite little scientific evidence, very popular
- No harm, but costly
- May decrease tactile defensiveness
- Music therapy, auditory-integration therapy

Vidya Bhushan Gupta, MD, MPH

Target symptoms for pharmacological treatment of autism

- hyperactivity
- aggression
- self-abusive behavior
- lability of mood, irritability
- social withdrawal, anxiety
- repetitive compulsive behaviors and stereotypies
- sleep problems

Vidya Bhushan Gupta, MD, MPH

Medications for target symptoms

- Atypical neuroleptics
- Selective serotonin reuptake inhibitors
- Stimulants
- Mood stabilizers
- Opiate antagonists
- Sedatives

Vidya Bhushan Gupta, MD, MPH

Hyperactivity

- Stimulants
 - Less effective and more side effects
- Clonidine
- Atypical neuroleptics - risperidone
- Serotonin reuptake inhibitors
- Anxiolytics - buspar
- Opiate blockers - naltrexone

Vidya Bhushan Gupta, MD, MPH

Risperidone in children with autism and serious behavior problems (NEJM. 347:314-321, 2002)

- Research Units on Pediatric Psychopharmacology Autism Network
- 101 children ages 8.8 ± 2.7 years
- In two thirds a positive response to risperidone at 8 weeks, benefit maintained at 6 months
- Decrease irritability, tantrums, aggression, and self-injurious behavior
- Weight gain, fatigue, dizziness, drooling

Vidya Bhushan Gupta, MD, MPH

COMPLEMENTARY AND ALTERNATIVE TREATMENTS (CAM)

- Innocuous and reasonably priced
- Innocuous but costly
- Harmful and costly
- Harmful but reasonably priced

Evidence based vs. anecdotal/rhetorical

Vidya Bhushan Gupta, MD, MPH

Unproven CAMs

- Nystatin
- Gluten-free /casein-free diet –leaky gut
- Secretin, single dose not effective, multi-dose trials in progress
- ACTH analog ORG 2766, only one study
- IVIG and transfer factor
- Megavitamins- Pyridoxine with magnesium, ascorbic acid, folate
- DMG (demethylglycine)
- Vancomycin

Vidya Bhushan Gupta, MD, MPH

Prognosis

- IQ single most important indicator
- For community living and independence
 - 33% in those with normal IQ and functional language, 20% attend college
- Onset of seizures in adolescence a bad sign
- Overall - 10-20% may outgrow diagnosis but continue to have poor social skills, rarely marry
- Girls have poor outcomes
- Poor prognosis if no meaningful speech by 5