

The autistic spectrum disorder¹

Any person, talented or handicapped, whose social skills have been severely deficient since very early childhood, who started to talk late or whose communicative use of language is inadequate, and who perseverates and lacks cognitive and behavioral flexibility meets the diagnostic criteria for an autistic-spectrum disorder. The *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition (DSM-IV), published by the American Psychiatric Association, and the *International Classification of Diseases*, 10th Revision (ICD-10), published by the World Health Organization, use the term «pervasive developmental disorder» to encompass the broad spectrum of developmental disorders with these characteristics (see Table). Pervasive developmental disorders are more common in boys than girls. Autistic disorder is classic autism, one of the more severe disorders on the spectrum. Persons with autistic disorder have substantial impairment in social skills, verbal communication, and cognitive and behavioral flexibility. About 70 percent of such persons are mentally retarded, and a third have had at least two unprovoked epileptic seizures by the time they reach late adolescence. About half are nonverbal or have grossly impaired speech. Most persons with autistic disorder are not able to live independently as adults.

As long as autistic disorder was the only recognized subtype on the spectrum of autistic disorders, autism was considered to be rare (0.4 case per 10,000 persons). In

the early 1940s, however, Kanner and Asperger independently described children whose speech was notable for its stilted quality and unusual vocabulary and who had many autistic characteristics despite average or superior intelligence. Since then, widespread use of improved, standardized questionnaires and observational scales has resulted in the identification of many persons with less severe disorders on the autistic spectrum, some of whom have received a diagnosis such as developmental language disorder, attention-deficit disorder, or obsessive-compulsive di-

sorder. Their cognitive skills are typically uneven. The least severely affected may not come to medical attention at all or not until midchildhood or adolescence, despite aberrant types of behavior that are evident to family members, educators, and peers. According to the DSM-IV and ICD-10 classifications, such children who are not retarded and who started to speak at the expected age have Asperger's disorder, and those who do not meet the criteria for either autistic disorder or Asperger's disorder have pervasive developmental disorder not otherwise specified.

Table: **Characteristics of Pervasive Developmental Disorders**

Disorder	Characteristics
Autistic disorder (classic autism)	<ul style="list-style-type: none"> • Presence of > 6 of 12 potential deficits involving all three behavioral domains that define the autistic spectrum: <ul style="list-style-type: none"> ≥ 2 deficits in sociability, empathy, and insight into other persons' feelings and agendas ≥ 1 deficit in communicative language and imagination ≥ 1 deficit in behavioral and cognitive flexibility • Detectable before the age of 3 years • Diagnosis not excluded by the level of cognitive competence or the existence of other handicaps
Asperger's disorder	<ul style="list-style-type: none"> • Troublesome social ineptness, lack of insight • Behavioral inflexibility with a narrow range of interests • IQ ≥ 70 (affected children may be normally intelligent or gifted) • No delay in the emergence of speech • Often clumsiness
Pervasive developmental disorder not otherwise specified	<ul style="list-style-type: none"> • Applies to less severely affected children who do not meet criteria for either autistic disorder or Asperger's disorder
Disintegrative disorder	<ul style="list-style-type: none"> • Early development entirely normal, including speech • Severe regression between the ages of 2 and 10 years, affecting language, sociability, cognition, and competence in skills of daily life
Rett's syndrome	<ul style="list-style-type: none"> • Severe global regression in infant girls (rarely in boys), resulting in lifelong severe mental retardation, lack of language and purposeful hand use, and other neurologic deficits

¹ This article was published in the *New England Journal of Medicine* 2002; 347(5) 302–303. Copyright © 2002 Massachusetts Medical Society. All rights reserved. Reprint with the permission of the editor and completed (references) by the author.

DSM-IV and ICD-10 list two other rare, very severe disorders with a poor prognosis. The first, disintegrative disorder, is diagnosed in previously normal children who do not have a degenerative disease yet inexplicably undergo a catastrophic global regression, with or without epilepsy, and become autistic, most often between the ages of three and six years. Mutations of the *MECP2* gene on Xq28, identified in 1999, cause the second disorder, Rett's syndrome, which affects girls almost exclusively. This disorder is characterized by postnatal reduction in brain growth, with hand stereotypy, seizures, sensorimotor and autonomic deficits, and curtailment of social, language, cognitive, and neurologic development.

A puzzling feature reported by about a third of the parents of children with autism is stagnation or regression of early language, usually between the ages of 18 and 24 months, and regression of sociability and play, with the appearance of stereotypy. Some parents blame the problem on an intercurrent illness or a traumatic environmental change, but in most cases, it is insidious and unexplained. Clinical or subclinical epilepsy (the latter diagnosed on the basis of epileptiform electroencephalographic features in the absence of clinical seizures) occurs in no more than 10 to 20 percent of children with autism, whether or not they have a history of regression. The value of treatment with antiepileptic medications has not been determined. The natural course of autistic regression is an improvement, although full recovery is rare.

The dramatic increase in estimates of the prevalence of autism – to 2 to 5 cases per

1000 children – has raised the possibility of an «epidemic» of autism, and school systems are hard put to address the problem. More active case ascertainment and changes in diagnostic criteria probably account in large part for the increase. The role of such environmental factors as perinatal injury, vaccines (exposure to minuscule amounts of mercury preservative or the persistence of measles in the enteric lymphatic system), or food allergies is unsubstantiated. In the case of both autism and a broad spectrum of developmental disorders in families, twin and family studies have implicated multigenic influences in the families of many affected persons. Because autism is a behavioral, not a biologic, diagnosis, prenatal diagnosis is not possible except in the rare case in which autism is associated with a single-gene disorder, such as tuberous sclerosis, Rett's syndrome, the fragile X syndrome, or Angelman's syndrome. Research requires brain imaging and electrophysiological, biochemical, and genetic investigations, but the yield of these studies is minimal in the clinic, barring specific indications.

In a distressingly large proportion of children with autistic-spectrum disorders, tantrums, noncompliance, destructiveness, and self-injury impede integration into mainstream social and educational environments. Pharmacologic agents cannot cure autism because, in most cases, the brain has undergone atypical cellular development dating from the earliest embryonic stages. The goal is to alleviate troublesome symptoms that interfere with the most effective intervention – intensive, targeted education. The results of a controlled study of the effecti-

veness of risperidone, reported by the Pediatric Psychopharmacology Autism Network in the *N Engl J Med* 2002; 347 (5): 314–321, are therefore welcome and encouraging, despite the acknowledged limitations of the study. The search for safe and effective psychotropic medications has been frustrating so far. May this study be followed by larger, longer, and equally rigorous trials of interventions in children with autism. Such studies are sorely needed.

References

- American Psychiatric Association (2000). Diagnostic and Statistical Manual of Mental Disorders. Fourth edition, text revision: DSM IV-TR. (4th ed.) Washington, DC.: American Psychiatric Association.
- Filipek, P. A., Accardo, P. J., Ashwal, S., Baranek, G. T., Cook, E. H. Jr., Dawson, G. et al. (2000). 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*, 55, 468-479.
- Fombonne, E. (1999). The epidemiology of autism: a review. *Psychological Medicine*, 29, 769–786.
- Gillberg, C. & Coleman, M. (2000). The biology of the autistic syndromes. (3 ed.) London: Mac Keith Press.
- National Research Council (2001). *Educating Children with Autism*. Washington DC: National Academy of Sciences.
- Rapin, I. (Ed.) (1996) *Preschool Children with Inadequate Communication: Developmental Language Disorders, Autism, Low IQ*. (Clinics in Developmental Medicine # 139). London UK: Mac Keith Press.
- Rapin, I. (1997). Autism. *New England Journal of Medicine*, 337, 97–104.
- Tuchman, R. & Rapin, I. (2002). Epilepsy in autism. *The Lancet Neurology*, 1, 352–358.
- Tuchman, R. F. & Rapin, I. (1997). Regression in pervasive developmental disorders: Seizures and epileptiform EEG correlates. *Pediatrics*, 99, 560–566.
- World Health Organization (1992). *The ICD-10 Classification of Mental and Behavioural Disorders. Clinical Descriptions and Diagnostic Guidelines*. (10 ed.) Geneva CH: World Health Organization.

Isabelle Rapin, New York

Author's address:

Isabelle Rapin, M.D.
Albert Einstein College of Medicine
Bronx, NY 10461