


Autism: A Medical Primer

CHRISTOPHER D. PRATER, M.D., and ROBERT G. ZYLSTRA, ED.D., L.C.S.W.
University of Tennessee College of Medicine, Chattanooga, Tennessee

Autistic disorder, a pervasive developmental disorder resulting in social, language, or sensorimotor deficits, occurs in approximately seven of 10,000 persons. Early detection and intervention significantly improve outcome, with about one third of autistic persons achieving some degree of independent living. Indications for developmental evaluation include no babbling, pointing, or use of other gestures by 12 months of age, no single words by 16 months of age, no two-word spontaneous phrases by 24 months of age, and loss of previously learned language or social skills at any age. The differential diagnosis includes other psychiatric and pervasive developmental disorders, deafness, and profound hearing loss. Autism is frequently associated with fragile X syndrome and tuberous sclerosis, and may be caused by lead poisoning and metabolic disorders. Common comorbidities include mental retardation, seizure disorder, and psychiatric disorders such as depression and anxiety. Behavior modification programs are helpful and are usually administered by multidisciplinary teams; targeted medication is used to address behavior concerns. Many different treatment approaches can be used, some of which are unproven and have little scientific support. Parents may be encouraged to investigate national resources and local support networks. (Am Fam Physician 2002;66:1667-74,1680. Copyright© 2002 American Academy of Family Physicians.)

 A patient information handout about autism, written by the authors of this article, is provided on page 1680.

See page 1591
for definitions of
strength-of-evidence
levels.

Recognition of the disorder called autism may have its origin in Itard's 1801 description of the "wild boy of Aveyron," a violent child with no language skills who related to other people as if they were objects. It was not until 1943 that Kanner identified a complex set of characteristics (e.g., aberrations in social development, verbal and nonverbal communication, symbolic thinking) for a syndrome he labeled "autism."

Although Kanner theorized that a single, biologically based defect was responsible for the development of autistic disorders, treatment in the 1950s and 1960s was dominated by the psychodynamic theory of the etiology of autism that charged that pathologic parenting was responsible for the withdrawal of children from their environment. Following the 1970s discovery of neuroreceptors, endogenous neurohormones, and the stereospecific binding sites of neuropeptides to neurons, clinicians have discounted the psychodynamic theory of autism and repostulated Kanner's original supposition that biologically based deficits are responsible for the etiology of autism.

See editorial on page 1610.

Definition

Autistic disorder is a pervasive developmental disorder defined behaviorally as a syndrome consisting of abnormal development of social skills (withdrawal, lack of interest in peers), limitations in the use of interactive language (speech as well as nonverbal communication), and sensorimotor deficits (inconsistent responses to environmental stimuli).^{1,2} In this article, the more generic terms autism and autistic refer to the broad spectrum of pervasive developmental disorders that exhibit autistic features as their primary presenting behaviors. The term autistic disorder is used to describe the specific developmental disorder that occurs at the more severely affected end of this spectrum (*Table 1*).¹

The development of impairments in autistic persons is varied (*Table 2*¹) and characteristically uneven, resulting in good skills in some areas and poor skills in others. Echolalia, the involuntary repetition of a word or a sentence just spoken by another person, is a common feature of language impairment that, when present, may cause language skills to appear better than they really are. There may also be deficiencies in symbolic thinking, stereotypic behaviors (e.g., repetitive nonpro-

Early detection and intervention in autistic disorders significantly improve outcomes, with about one third of patients achieving some degree of independent living as adults.

TABLE 1
DSM-IV Diagnostic Criteria for Autistic Disorder

The rightsholder did not grant rights to reproduce this item in electronic media. For the missing item, see the original print version of this publication.

TABLE 2
Impairments Common to Autistic Syndromes

Impairments in social skills
Limitations in the use of interactive language
Sensorimotor deficiencies
Echolalia
Deficiencies in symbolic thinking
Stereotypic behaviors
Self-injury behaviors
Mental retardation
Seizure disorders

Information from the American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed. Washington, D.C.: American Psychiatric Association, 1994:65-78. Copyright 1994.

ductive movements of hands and fingers, rocking, meaningless vocalizations), self-stimulation, self-injury behaviors, and seizures. Mental retardation is not a diagnostic criterion, but it is frequently present in the moderate to severe range.

Epidemiology

In general, pervasive developmental disorders are estimated to occur at a rate of 63 per 10,000 persons.³ While the reported incidence of autistic disorder ranges from about five per 10,000⁴ to 20 per 10,000 persons,⁵ a recent meta-analysis reports the median rate for 11 surveys conducted since 1989 to be seven per 10,000 persons.⁶ Male-to-female ratios vary with IQ scores from 2:1 in severely handicapped persons to 4:1 in moderately handicapped persons.⁷ [Evidence level B, non-randomized studies] The occurrence rate in siblings is suspected to be from 3 to 7 percent, representing a 50- to 100-fold increase in risk.⁸

Etiology

No single cause has been identified for the development of autism. Genetic origins are suggested by studies of twins and a higher

incidence of recurrence among siblings.⁹ In addition, an increased frequency of occurrence is noted in patients with genetic conditions such as fragile X syndrome and tuberous sclerosis.¹⁰ Some reports have suggested a possible association with Down syndrome.¹¹

In addition to the implication of neurotransmitters, such as serotonin, in the development and expression of autism,¹² many other disorders may result in brain dysfunction. Possible contributing factors in the development of autism include infections, errors in metabolism, immunology, lead poisoning, and fetal alcohol syndrome.¹³

Concerns have been raised in recent years that immunizations, particularly measles, mumps, and rubella (MMR) vaccine, may precipitate autism. In addition to reports from several parents who first detected autism in their children following an MMR vaccination at 12 to 15 months of age, an anecdotal study¹⁴ reported similar suspicions on the part of physicians who provided care for 12 autistic patients. Subsequent studies in the United Kingdom^{15,16} [reference 16, Evidence level B: epidemiologic study] and the United States¹⁷ [Evidence level B: epidemiologic study] have failed to show an association between any vaccine and the development of autism. Information about ongoing studies being conducted by the Centers for Disease Control and Prevention and the National Institutes of Health (NIH) is available at their Web sites (*Table 3*).

Recognition and Screening

Indications for formal developmental evaluation include no babbling, pointing, or other gestures by 12 months of age, no single words by 16 months of age, no two-word spontaneous phrases by 24 months of age, and loss of previously learned language or social skills at any age.¹⁸ Parental concerns about delayed speech and language development, typically noticed at about 18 months of age, should always be taken seriously.

Including developmental surveillance as a

routine part of the well-child examination can enhance recognition of developmental disorders. While the Denver screening tools¹⁹ have historically been used in primary care settings for routine developmental surveillance, they lack the sensitivity and specificity necessary for use as screening tools for developmental disorders.²⁰ More specific and sensitive screening surveillance tools, such as the Parents' Evaluation of Developmental Status (PEDS),²¹ are available for assessing these conditions. Screening tools that are specific for autism include the Checklist for Autism in Toddlers

TABLE 3
Resources for Management of Autism

Centers for Disease Control and Prevention National Immunization Program Web address: www.cdc.gov/nip
National Institutes of Health, National Institute of Child Health and Human Development Web address: www.nichd.nih.gov
Parents' Evaluation of Developmental Status (PEDS), Ellsworth & Vandermeer Press Telephone: 615-226-4460 Web address: www.pedstest.com/test/peds_manual.html
Checklist for Autism in Toddlers (CHAT) Web address: www.nas.org.uk/profess/chat.html
Pervasive Developmental Disorders Screening Test-Stage I (PDDST), Porter Psychiatric Institute Telephone: 415-476-7385
Association of University Centers on Disabilities, a listing of professionals by state Telephone: 301-588-8252 Web address: www.aucd.org
The National Institute of Child Health and Human Development, a listing of research centers investigating treatment strategies for autism Web address: www.nichd.nih.gov
Autism Society of America Telephone: 800-3AUTISM (800-328-8476) Web address: www.autism-society.org
Center for the Study of Autism Web address: www.autism.org

Indications for formal developmental evaluation for autism include no babbling or pointing gestures by 12 months of age.

(CHAT)²² (Table 4²³) and the Pervasive Developmental Disorders Screening Test-Stage I (PDDST).²⁴ For a comprehensive review of available screening tools, the authors recommend an article by Filipek and colleagues.¹⁸

When an autistic disorder is suspected, referral should be made for further developmental evaluation and cognitive testing. Although there is currently no cure for autism, early diagnosis and initiation of structured multidisciplinary intervention can significantly enhance functioning in later life.²⁵ Experienced clinicians can reliably diagnose autism in children younger than three years and, frequently, as young as two years. Presently no biologic markers are available to identify patients with autistic disorders. Useful resources for identifying clinicians with exper-

tise in the diagnosis of autism include the University Affiliated Program system and the National Institute of Child Health and Human Development (Table 3).

Once an autistic disorder is suspected, certain medical evaluations should be performed. A family history of limited cognitive abilities or the presence of dysmorphic features may suggest the need for genetic evaluation. Wood's light examination of the skin should be performed to help identify the depigmented macules of tuberous sclerosis. Lead screening and metabolic testing should be considered if there is a history of lethargy, cyclic vomiting, early seizures, dysmorphic features, or mental retardation. Electrophysiologic testing such as electroencephalography and central nervous system imaging studies are warranted to evaluate neurologic features that cannot be explained by the diagnosis of autism alone.¹⁸ Because deafness or profound hearing loss can cause symptoms mimicking autism, a formal hearing evaluation should be given if the diagnosis of autism is being considered.

Autistic disorders should be distinguished from other psychiatric and pervasive developmental disorders. Table 5¹ lists a differential diagnosis for several similar disorders.

Clinical Course

The typical presenting symptoms of autistic disorder are delayed speech or challenging behavior before three years of age.⁷ Although parents frequently see these signs and suspect that something is wrong with their child by 18 months of age, a diagnosis of autism is frequently delayed by two to three years because of reluctance on the part of clinicians and families to incorrectly label a child as autistic.²⁵ Seventy-five percent of autistic persons have some level of mental retardation.¹ Developmental gains in childhood and adolescence are common, but some persons have behavioral regression during adolescence.

Low IQ scores and failure to develop communicative language by five years of age correlate positively with a poor prognosis for

TABLE 4

The Five Key Items on the CHAT Screen

Ask the parent:

Does your child ever pretend (for example, to make a cup of tea using a toy cup and teapot) or pretend with other things?

Does your child ever use an index finger to point, to indicate interest in something?

Health practitioner observation:

Gain 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?

Gain child's attention, then give child a toy cup and teapot and say "Can you make me a cup of tea?" Does the child pretend to pour out tea, drink it, etc.?

Say to the child "Where's the light?" or "Show me the light." Does the child point with an index finger at the light? To record "yes" on this item, the child must have looked up at your face around the time of pointing.

CHAT = Checklist for Autism in Toddlers.

Reprinted with permission from Baird G, Charman T, Cox A, Baron-Cohen S, Swettenham I, Wheelwright S, et al. Current topic: screening and surveillance for autism and pervasive and developmental disorders. *Arch Dis Child* 2001;84:471.

response to treatment.¹ About one third of autistic persons can achieve some degree of independent living,¹ although fewer than 5 percent go on to become self-sufficient adults.¹³ Development of stereotypic behavior, self-injury behavior, and selective attention toward distracting stimuli (e.g., a ticking clock) markedly interfere with structured learning and working environments.¹³

Many autistic persons develop seizures in their first year of life in the form of infantile spasms, a particularly severe form of seizure that is difficult to treat. There is also a significant incidence of first occurrence of seizures during adolescence,²⁶ and as many as 35 percent may develop seizures by adulthood.¹⁸ Comorbid anxiety is common,²⁷ as are depression and obsessional behavior.²⁸

Management of Autism and Comorbid Conditions

The general goals of treatment for autistic patients are to improve language and social skills, decrease problem behaviors, support parents and families in their adjustment to and education of autistic children, and foster independence. Because autistic children who begin treatment at a young age have significantly better outcomes,²⁴ early intervention is

TABLE 5
Differential Diagnosis of Autism

Other pervasive developmental disorders
Rett's syndrome
Childhood disintegrative disorder
Asperger's disorder
Disorders of infancy, childhood, and adolescence
Selective mutism
Stereotypic movement disorder
Schizophrenia with childhood onset

Information from the American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed. Washington, D.C.: American Psychiatric Association, 1994:65-78. Copyright 1994.

The goals of treatment for patients with autism are to improve language and social skills, decrease problem behaviors, support parents, and foster independence.

critical. Public Law 99-457 and the Individuals with Disabilities Education Act²⁹ mandate referral to the special services departments of local preschool or school systems.

Because no treatment protocol meets the needs of every autistic child, it is helpful to get suggestions from a variety of sources. Organizations available to help families and educators are listed in *Table 3*.

NEUROPHARMACOLOGIC TREATMENT

Primary care physicians are commonly asked to address the stereotypic or disruptive behaviors of autistic patients. While numerous medications have been used to treat autistic symptoms, no single medication has been shown to be universally effective. Historically, psychotropic medications have been reserved for use in situations where all attempts at behavior management have failed, and the patients are considered to be harmful to themselves or others.

While use of behavior modification programs is often the primary method of managing challenging behaviors in autistic children, supportive medication use has been found to help reduce behavior problems. Obtaining a correct diagnosis is important before initiating any pharmacologic intervention. For example, attention deficit with or without hyperactivity can coexist with autism and may possibly be managed with the use of methylphenidate (Ritalin)³⁰ [Evidence level C: consensus opinion] or clonidine (Catapres).³¹ [Evidence level C: consensus opinion] It can be difficult to distinguish between the behaviors associated with autism; attention-deficit/hyperactivity disorder; and mania, and an appropriate treatment for one disorder may be ineffective or exacerbate the symptoms of another.

When behavior management programs or the use of supportive medications are unsuccessful in correcting potentially dangerous behavior, the use of sedating medications may be necessary for brief periods while less invasive interventions are attempted. Sedative-hypnotics and neuroleptics such as buspirone (BuSpar), in a dosage of 5 to 20 mg two to three times a day³² [Evidence level C: consensus opinion], or risperidone (Risperdal), in a dosage of 0.5 to 2 mg twice a day³³ are commonly used for this purpose. Benzodiazepines should be used with caution because they can cause disinhibition, resulting in more excitable behavior.³²

Objective data collection and outcome monitoring are important because of the variable nature of individual responses to medication. Information should be collected by persons who have regular contact with the patient—family members, support personnel in day care and residential programs, case managers, and physicians. Given the multiple developmental, behavior, and medical problems associated with autism, coordination of services by a multidisciplinary team is highly recommended.³⁴ [Evidence level C: consensus opinion]

ALTERNATIVE THERAPIES

A number of methods for teaching communication and socialization skills have been developed over the years. One recent example

is augmented communication, a method whereby nonverbal persons are assisted in communication by means of a letter board or a computer keyboard. When a facilitator helps the person choose letters, words, etc., the process is referred to as facilitated communication. While augmented communication devices have markedly improved communication potential in some patients, numerous controlled studies have failed to show that facilitated communication is reliably useful.¹³

Another treatment currently being advocated is auditory integration training (AIT), whereby persons with autism typically spend 10 hours during a two-week period listening to music that has been computer-modified to remove sensitive frequencies and reduce predictable patterns. AIT is said to improve auditory processing capabilities by correcting distortions in hearing and by conditioning patients to focus their attention more appropriately. Unfortunately, this technique also has little supporting scientific documentation.³⁵

Another popular behavior-based intervention is the Lovaas program,³⁶ sometimes referred to as DTT because of its use of positive reinforcement through a series of intensive discrete trial training sessions. While initial reports suggested a 47 percent recovery rate from autism when preschoolers were treated,³⁶ subsequent studies have been unable to document long-term gains.³⁷ Studies using similar behavior interventions, however, have been able to document short-term improvements.³⁷ Verification of long-term success becomes important in view of the cost of such intensive treatment programs, which typically require extensive one-on-one training with autistic children for 40 hours a week for a minimum of two years—a cost of approximately \$40,000 a year.³⁸ Controversies about fiscal responsibility are ongoing because some parents feel local school systems should make this level of care available for their children.³⁸

Other interventional strategies include deep pressure therapy, nutritional supplements, and specialty diets.³⁹⁻⁴² [reference 40, Evidence

The Authors

CHRISTOPHER D. PRATER, M.D., is assistant clinical professor in the Department of Family Medicine at the University of Tennessee College of Medicine, Chattanooga Unit. He also serves as medical director for the Orange Grove Center, a treatment facility in Chattanooga for developmentally delayed children and adults. Dr. Prater received his medical degree from the University of Tennessee College of Medicine, Memphis, and completed a family practice residency at the University of Tennessee in Knoxville.

ROBERT G. ZYLSTRA, ED.D., L.C.S.W., is assistant professor and director of behavioral science in the Department of Family Medicine at the University of Tennessee College of Medicine, Chattanooga Unit. Dr. Zylstra earned a master's degree in social work at the University of Michigan, Ann Arbor, and a doctorate in education at the University of Memphis.

Address correspondence to Robert G. Zylstra, Ed.D., L.C.S.W., Department of Family Medicine, Chattanooga Unit, University of Tennessee College of Medicine, 1100 E. Third St., Chattanooga, TN 37403 (e-mail: zylstrrg@erlanger.org). Reprints are not available from the authors.

TABLE 6

**Behavior Modification
in the Management of Autism**

Structuring the environment
Providing consistent responses to behaviors
Positive reinforcement—rewarding a desired behavior
Negative reinforcement—not rewarding an undesirable behavior
Punishment—application of an adverse stimulus to deter an unwanted response
Shaping—reinforcing closer and closer approximations to the desired behavior

Information from Farber JM. Autism and other communication disorders. In: Capute AJ, Accardo PJ, eds. *Developmental disabilities in infancy and childhood*. 2d ed. Baltimore, Md.: Brookes, 1996:347-64.

level A: randomized controlled trial (RCT); reference 42, Evidence level C: consensus opinion] Anecdotal reports of success with alternative or complementary interventions are common, but efficacy in most cases remains clinically unproven. Generally speaking, most successful programs have several common components: (1) recognition of the importance of early identification and intervention; (2) use of behavior-oriented strategies (Table 6³³); (3) development of social communication; and (4) active involvement of parents and families.

Recently, there has been discussion about a possible role of the gastric hormone secretin as a pharmacologic intervention in the treatment of autism. This information was based on one study of three autistic persons.⁴³ Unfortunately, a subsequent study involving 56 autistic persons failed to support the initial findings.⁴⁴ [Evidence level B: lower quality RCT] At present, most investigators do not see a role for secretin in the treatment of autism, an opinion supported by ongoing research at the NIH.

The authors indicate that they do not have any conflicts of interest. Sources of funding: none reported.

REFERENCES

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders, 4th ed. Washington, DC: American Psychiatric Association, 1994:65-78.
2. World Health Organization. ICD-10: international statistical classification of diseases and related health problems. Geneva: World Health Organization, 1992.
3. Chakrabarti S, Fombonne E. Pervasive developmental disorders in preschool children. *JAMA* 2001;285:3093-9.
4. Fombonne E, Du Mazaubrun C, Cans C, Grandjean H. Autism and associated medical disorders in a French epidemiological survey. *J Am Acad Child Adolesc Psychiatry* 1997;36:1561-9.
5. Bryson SE. Epidemiology of autism. *J Autism Dev Disord* 1996;26:165-7.
6. Fombonne E. The epidemiology of autism: a review. *Psychol Med* 1999;29:769-86.
7. Bryson SE. Epidemiology of autism: Overview and issues outstanding. In: Cohen DJ, Volkmar FR, eds. *Handbook of autism and pervasive developmental disorders*. 2d ed. New York: Wiley, 1997:41-6.
8. Rutter M, Bailey A, Simonoff E, Pickles A. Genetic influences and autism. In: Cohen DJ, Volkmar FR, eds. *Handbook of autism and pervasive developmental disorders*. 2d ed. New York: Wiley, 1997: 370-87.
9. Szatmari P, Jones MB, Zwaigenbaum L, MacLean JE. Genetics of autism: overview and new directions. *J Autism Dev Disord* 1998;28:351-68.
10. Baker P, Piven J, Sato Y. Autism and tuberous sclerosis complex: prevalence and clinical features. *J Autism Dev Disord* 1998;28:279-85.
11. Howlin P, Wing L, Gould J. The recognition of autism in children with Down syndrome—implications for intervention and some speculations about pathology. *Dev Med Child Neurol* 1995;37:406-14.
12. Anderson GM, Hoshino Y. Neurochemical studies of autism. In: Cohen DJ, Volkmar FR, eds. *Handbook of autism and pervasive developmental disorders*. 2d ed. New York: Wiley, 1997:325-43.
13. Farber JM. Autism and other communication disorders. In: Capute AJ, Accardo PJ, eds. *Developmental disabilities in infancy and childhood*. 2d ed. Baltimore, Md.: Brookes, 1996:347-64.
14. Wakefield AJ, Murch SH, Anthony A, Linnell J, Casson DM, Malik M, et al. Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. *Lancet* 1998; 351:637-41.
15. Miller D, Wadsworth J, Diamond J, Ross E. Measles vaccination and neurological events. *Lancet* 1997; 349:730-1.
16. Taylor B, Miller E, Farrington CP, Petropoulos MC, Favot-Mayaud I, Li J, et al. Autism and measles, mumps, and rubella vaccine: no epidemiological evidence for a causal association. *Lancet* 1999;353:2026-9.
17. DeStefano F, Chen RT. Autism and measles, mumps, and rubella vaccine: no epidemiological

- evidence for a causal association. *J Pediatr* 2000; 136:125-6.
18. Flipek PA, Accardo PJ, Baranek GT, Cook EH Jr, Dawson G, Gordon B, et al. The screening and diagnosis of autistic spectrum disorders. *J Autism Dev Disord* 1999;29:439-84.
 19. Frankenburg WK, Dodds J, Archer P, Shapiro H, Bresnick B. The Denver II: a major revision and restandardization of the Denver Developmental Screening Test. *Pediatrics* 1992;89:91-7.
 20. Sciarillo WG, Brown MM, Robinson NM, Bennett FC, Sells CJ. Effectiveness of the Denver Developmental Screening Test with biologically vulnerable infants. *J Dev Behav Pediatr* 1986;7:77-83.
 21. Glascoe FP. Collaborating with parents: using parents' evaluation of developmental status to detect and address developmental and behavioral problems. Nashville: Ellsworth & Vandermeer, 1998.
 22. Baron-Cohen S, Allen J, Gillberg C. Can autism be detected at 18 months? The needle, the haystack, and the CHAT. *Br J Psychiatry* 1992;161:839-43.
 23. Baird G, Charman T, Cox A, Baron-Cohen S, Swettenham J, Wheelwright S, et al. Current topic: screening and surveillance for autism and pervasive developmental disorders. *Arch Dis Child* 2001; 84:468-75.
 24. Siegel B. Early screening and diagnosis in autism spectrum disorders: the pervasive developmental disorders screening test (PDDST). NIH State of the Science in Autism: Screening and Diagnosis Working Conference, Bethesda, Md., June 15-17, 1998.
 25. Flipek PA, Accardo PJ, Ashwal S, Baranek GT, Cook EH Jr, Dawson G, 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;55:468-79.
 26. Gillberg C, Steffenburg S. Outcome and prognostic factors in infantile autism and similar conditions: a population-based study of 46 cases followed through puberty. *J Autism Dev Disord* 1987;17: 273-87.
 27. Muris P, Steerneman P, Merckelbach H, Holdrinet I, Meesters C. Comorbid anxiety symptoms in children with pervasive developmental disorders. *J Anxiety Disord* 1998;12:387-93.
 28. Kobayashi R, Murata T. Behavioral characteristics of 187 young adults with autism. *Psychiatry Clin Neurosci* 1998;52:383-90.
 29. Individuals with Disabilities Education Act-IDEA '97. Public Law 1997;105-17.
 30. Arnold LE, Gadow K, Pearson D, Varley C. Stimulants. In: Reiss S, Aman MG, eds. Psychotropic medications and developmental disabilities: the international consensus handbook. Columbus, Ohio: Ohio State University Nisonger Center, 1998: 229-43.
 31. Hagerman R, Bregman J, Tirosh E. Clonidine. In: Reiss S, Aman MG, eds. Psychotropic medications and developmental disabilities: the international consensus handbook. Columbus, Ohio: Ohio State University Nisonger Center, 1998:259-69.
 32. Werry JS. Anxiolytics and sedatives. In: Reiss S, Aman MG, eds. Psychotropic medications and developmental disabilities: the international consensus handbook. Columbus, Ohio: Ohio State University Nisonger Center, 1998:201-14.
 33. Demb HB, Espiritu C. The use of risperidone with children and adolescents with developmental disabilities: effects on some common challenging behaviors. *Ment Health Aspects Dev Disabil* 1999; 2:73-82.
 34. Volkmar F, Cook EH Jr, Pomeroy J, Realmuto G, Tanguay P. Practice parameters for the assessment and treatment of children, adolescents, and adults with autism and other pervasive developmental disorders. *J Am Acad Child Adolesc Psychiatry* 1999;38(12 suppl):325-545.
 35. Rimland B, Edelson SM. Auditory integration training in autism: a pilot study. *Autism Research Institute* 1992;112:1-7.
 36. Lovaas OI, Smith T. A comprehensive behavioral theory of autistic children: paradigm for research and treatment. *J Behav Ther Exp Psychiatry* 1989; 20:17-29.
 37. Sheinkopf SJ, Siegel B. Home-based behavioral treatment of young children with autism. *J Autism Dev Disord* 1998;28:15-23.
 38. Mauk JE, Reber M, Batshaw ML. Autism and other pervasive developmental disorders. In: Batshaw ML, ed. Children with disabilities. 4th ed. Baltimore, Md.: Brookes, 1997:425-47.
 39. Grandin T. Thinking in pictures: and other reports from my life with autism. New York: Vintage Books, 1996:62-81.
 40. Rimland B, Callaway E, Dreyfus P. The effect of high doses of vitamin B₆ on autistic children: a double-blind crossover study. *Am J Psychiatry* 1978; 135: 472-5.
 41. Rimland B. Megavitamin B₆ and magnesium in the treatment of autistic children and adults. In: Schopler E, Mesibov GB, eds. Neurobiological issues in autism. New York: Plenum, 1987:389-405.
 42. Singh NN, Ellis CR, Mulick JA, Poling A. Vitamin, mineral and dietary treatments. In: Reiss S, Aman MG, eds. Psychotropic medications and developmental disabilities: the international consensus handbook. Columbus, Ohio: Ohio State University Nisonger Center, 1997:311-20.
 43. Horvath K, Stefanatos G, Sokolski KN, Wachtel R, Nabors L, Tildon JT. Improved social and language skills after secretin administration in patients with autistic spectrum disorders. *J Assoc Acad Minor Phys* 1998;9:9-15.
 44. Chez MG, Buchanan CP, Bagan BT, Hammer MS, McCarthy KS, Ovrutskaya I, et al. Secretin and autism: a two-part clinical investigation. *J Autism Dev Disord* 2000;30:87-94.