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Autism Spectrum Disorders

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Upon completion of this chapter, the reader will

- Be familiar with the core features of autism and related disorders
- Distinguish among the diagnostic criteria for Autistic Disorder, Asperger's Disorder, Pervasive Developmental Disorder-Not Otherwise Specified, Childhood Disintegrative Disorder, and Rett's Disorder
- Understand the issues related to prevalence of autism spectrum disorders
- Be familiar with interventions and outcomes

Autism spectrum disorders (ASDs) are a class of neurodevelopmental disorders characterized by an impairment in social reciprocity, atypical communication, and repetitive behaviors. The term *autism spectrum* indicates that the disorders in this category occur along a continuum and is commonly used as a synonym for the category *pervasive developmental disorders*. The *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR)*, American Psychiatric Association [APA], 2000 uses the equivalent term *Pervasive Developmental Disorders (PDDs)*, because symptoms pervade all areas of development. Included in this group of disorders are the specific diagnoses of Autistic Disorder, Asperger's Disorder, Rett's Disorder, and Childhood Disintegrative Disorder (CDD). Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS) is a classification used when symptoms are present but specific criteria for one of the other diagnoses in this category are not met. Because the continuum of disorders is popularly referred to as the autism spectrum disorders (ASDs) rather than the *DSM-IV-TR* terminology of Pervasive Developmental Disorders, this chapter uses the term *ASDs*. Some research studies cited have been done with people with Autistic Disorder. This will be specifically noted in the text because the findings might be different for people with other ASDs.

The symptoms of ASDs are neurologically based. Scientific evidence indicates a genetic predisposition for ASDs, although there is likely to

be gene-environment interaction (Muhle, Trenchocoste, & Rapin, 2004). ASDs may occur in conjunction with other functionally defined diagnoses such as intellectual disability and learning disabilities, biologically based behaviors such as tics, and medical conditions including epilepsy. Advances in understanding the core symptoms and early implementation of educational, communication, and behavioral treatment approaches have positively affected the outcome of children with ASDs (National Research Council, 2001).

CHRISTOPHER

Christopher and Katie are fraternal twins who were born after an uncomplicated pregnancy. The children's parents, both trained as engineers, recall that Katie was somewhat colicky and that Christopher seemed content in comparison. He seemed advanced in the first year of life compared with his sister. Christopher smiled and babbled on time, and his parents remember that from a very early age, he was quite interested in toys with letters or numbers. By the time he was 1 year old, Christopher could identify some letters, and his parents thought he was rather precocious. They noticed that by 15 months of age, however, Katie was using words and beginning to play appropriately with toys. Christopher, conversely, had many words used as labels but never said "momma" or "dadda" and seemed to be consumed with naming and ordering letters and numbers. He could re-

peat phrases from his movies but did not make novel phrases at 2 years of age. At times, Christopher's parents worried that he was deaf because he seemed to ignore them.

The parents took Christopher to the doctor, and the pediatrician referred Christopher to an early intervention program. His hearing was normal, but he had significant delays in receptive and social language. Christopher was diagnosed as having an ASD and began an intense, disorder-specific program.

DIAGNOSTIC CATEGORIES WITHIN THE AUTISM SPECTRUM

ASDs are defined by the presence or absence of behaviors in three areas: social reciprocity, communication, and repetitive behaviors (APA, 2000). The number and distribution of symptoms, the pattern of early language development, the cognitive ability, and the timing of regression all are used to make a specific diagnosis within this category of disorders.

Autistic Disorder

Autism (or Autistic Disorder, per the *DSM-IV-TR*) is a discrete diagnosis within the ASDs. It is defined by a pattern of six symptoms distributed across three areas (Table 23.1). At least two symptoms must be in the area of social reciprocity. Dr. Leo Kanner first described the syndrome of autism (derived from the Greek word for self-absorption) in 1943 (Kanner, 1943). He observed a series of patients in his practice of child psychiatry with social aloofness and a desire for "preservation of sameness." Although Kanner believed autism was an organic condition, through the 1950s most psychiatrists considered autism to be caused by poor parenting. Some thought it was a form of childhood schizophrenia. With better behavioral description, it became clear that the ASDs were discrete from schizophrenia and occurred along a gradient. Progressive modification of the *DSM* (APA, 2000) has altered diagnostic criteria so both younger children or children with lower functioning and children with typical cognitive abilities can be identified as having ASDs.

Asperger's Disorder

Dr. Hans Asperger was a contemporary of Dr. Kanner (Asperger, 1944/1991). Asperger observed children with apparently typical lan-

guage who had difficulties with socialization, could not conform to social demands, and had repetitive behaviors. The *DSM-IV-TR* indicates that Asperger's Disorder (also called Asperger syndrome) can be diagnosed if three symptoms—two related to social reciprocity and one to habitual behaviors—are present. Language development must be grossly within normal limits (two-word phrases by 2 years of age; longer phrases by 3 years of age). Pragmatic language impairments are common, and adaptive behaviors may be delayed. There is considerable overlap between the diagnosis of high-functioning autism (Autistic Disorder in someone with typical intelligence) and Asperger's Disorder (Szatmari, 2000). Children with Asperger's Disorder may not be diagnosed until school age, when the social demands of the classroom make the symptoms functionally apparent.

Pervasive Developmental Disorder-Not Otherwise Specified

The diagnosis PDD-NOS is used to describe children who do not have the number or distribution of symptoms for another diagnosis within the ASDs or have atypical presentation but have functional impairments in the relevant areas. There is no minimum number of symptoms necessary to diagnose PDD-NOS. This results in significant heterogeneity among individuals given this clinical diagnosis. The comorbidity of cognitive, language, and behavioral symptoms with PDD-NOS may result in significant functional impairment, although fewer symptoms of autism are present.

Childhood Disintegrative Disorder

CDD is a very rare condition in which all aspects of development proceed typically until 3–5 years of age, when skills in all domains regress (Hendry, 2000). Language, cognitive ability, social reciprocity, play, motor skills, and basic adaptive functions such as bowel and bladder skills deteriorate. Behaviors subsequently stabilize at a lower level of functioning. CDD probably represents a common final pathway for a number of neurologic insults. Work up for a neurodegenerative disorder is indicated if late regression is documented. Epileptic aphasia (Landau-Kleffner Syndrome) is not the same as CDD, as children with LKS may lose only language. Characteristic electroencephalogram (EEG) findings are present during sleep (Trevithan, 2004) in LKS.

Table 23.1. Diagnostic criteria for Autistic Disorder

A. A total of six (or more) items from the following groups:		
Group 1 ^a	Group 2 ^b	Group 3 ^c
<ol style="list-style-type: none"> 1. 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 2. Failure to develop peer relationships appropriate to developmental level 3. 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) 4. Lack of social or emotional reciprocity 	<ol style="list-style-type: none"> 1. 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) 2. In individuals with adequate speech, marked impairment in the ability to initiate or sustain a conversation with others 3. Stereotyped and repetitive use of language or idiosyncratic language 4. Lack of varied, spontaneous make-believe play or social imitative play appropriate to developmental level 	<ol style="list-style-type: none"> 1. Encompassing preoccupation with one or more stereotyped and restricted patterns of interest that is abnormal either in intensity or focus 2. Apparently inflexible adherence to specific, nonfunctional routines or rituals 3. Stereotyped and repetitive motor mannerisms (e.g., hand or finger flapping or twisting, complex whole-body movements) 4. Persistent preoccupation with parts of objects
<p>B. Delays or abnormal functioning in at least one of the following areas with onset prior to age 3 years:</p> <ol style="list-style-type: none"> 1. Social interaction 2. Language as used in social communication 3. Symbolic or imaginative play 		
<p>C. The disturbance is not better accounted for by Rett's Disorder or Childhood Disintegrative Disorder.</p>		

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^aQualitative impairments in social interaction, as manifested by at least two criteria from Group 1.

^bQualitative impairments in communication as manifested by at least one criterion from Group 2.

^cRestricted, repetitive, and stereotyped patterns of behavior, interests, and activities, as manifested by at least one criterion from Group 3.

Rett's Disorder

Rett's Disorder (also called Rett syndrome) is a specific neurogenetic syndrome that is classified as an ASD because it involves the loss of previously obtained language and social milestones. Rett's Disorder is predominantly seen in girls. The deterioration in function is accompanied by the development of a set of mid-line stereotyped hand movements. Rett's Disorder is associated with a mutation in the methyl-CpG-binding protein 2 (MeCP2) gene on the X chromosome (Happke & Gartner, 2005). Affected children have a history of a normal birth and infancy, with slowing of head growth and a loss or plateauing of cognitive, language, and motor skills in the second year of life (Nomura & Sagawa, 2005). Spasticity in the lower extremities, seizures, constipation, and hyperventilation/breathholding are also common findings. Although affected children lose language and social interest with their initial deteriora-

tion, social approach and interest often returns. Understanding the relationship between the genetic mutation and developmental regression may help direct future research examining brain development in children with ASDs and Rett's Disorder.

Broader Autism Phenotype

The term *broader autism phenotype (BAP)* reflects the current conceptualization that each symptom of the autism phenotype exists along a continuum with typical behavior (Dawson et al., 2002). Subtle differences in pragmatic language organization and psychiatric symptoms such as anxiety (Piven et al., 1997) or mood disorders (deLong & Nohria, 1994) may occur with greater frequency in family members of people with ASDs. Understanding that there is a gradient of symptoms is an important step in understanding how multiple genes must interact to result in an ASD.

with socialization, social demands, and had the DSM-IV-TR individual disorder (also called Asperger's Disorder) is diagnosed if three to four social reciprocity behaviors—are present. Must be grossly within phrases by 2 years of age). Pragmatic communication is common, and adaptive. There is considerable prognosis of high-functioning Disorder in someone with Asperger's Disorder until school years of the classroom are usually apparent.

Diagnosis Specified

is used to describe the number or distribution of other diagnosis with relevant number of symptoms PDD-NOS. This heterogeneity among individual diagnosis. The communication, and behavior PDD-NOS may result in impairment, although are present.

Autism Disorder

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DIAGNOSTIC FEATURES OF AUTISM SPECTRUM DISORDERS

There is significant heterogeneity among people diagnosed with ASDs given the number of symptoms and possible patterns. Core symptoms are divided into the three areas, which are discussed next.

Qualitative Impairments in Social Reciprocity

The deficits in social reciprocity that are critical to the diagnosis of an ASD reflect an intrinsic inability to read and comprehend the feelings, experiences, and motives of others. These basic social understanding skills allow interpretation of the verbal and nonverbal messages of others, including nuanced facial expression, vocal inflection, gesture, social intention, and emotional tone. Because of these symptoms, children with ASDs have social difficulties with peers (Travis & Sigman, 1998). Infants with typical development learn that eye contact with adults and vocalizations are associated with attention. They learn to look at their parents when their name is called, as well as to distinguish their parents' facial expressions and the inflection in their voices (Bruinsma, Koegel, & Koegel, 2004). Some infants with ASD are quiet and content babies with decreased gaze.

Understanding that other people have a different point of view is referred to as theory of mind. This basic difference interferes with the capacity of people with ASDs to understand social language and intent of others (Rogers, 1998). Although individuals with ASDs have varying degrees of difficulty in initiating, responding to, and maintaining social interactions, they may be highly responsive to specific individuals or situations. Patterns of relating to other people may be atypical. They may have diminished eye contact, decreased use of facial expression, and exaggerated or absent gestures. People without ASDs generally look at the eyes of a person to whom they are speaking, whereas most people with ASDs tend to look at the person's mouth (Klin et al., 2002). Some people with ASD have intense eye gaze without the social awareness of when to look away. People with ASDs may have difficulty in integrating verbal and nonverbal components of communication. Although some are aloof, many children with ASDs respond to affection and are affectionate with their families (Travis & Sigman, 1998).

There is a broad range of social skills in individuals with ASDs. Symptoms related to atyp-

ical social reciprocity are closely tied to the presence or absence of symptoms in the area of language.

Atypical Communication Development

Difficulty with social communication is present in varying degrees in all people with ASDs (Rapin & Dunn, 2003). Language delays may relate to intellectual disability or exist in isolation. Delays in language are the first area of concern identified by most families whose children are later diagnosed with ASDs. Typical early language is often reported, including the emergence of single words; however, when early milestones are scrutinized, it becomes apparent many children with ASDs have had atypical development in receptive and expressive language (Mars, Mauk, & Dowrick, 1998). Language milestones are lost between 18 and 24 months by at least half of children with autistic disorder (Rogers, 2004). Loss of social milestones is less often reported but occurs with some frequency (Richler et al., 2006).

Early language of children with ASDs is often characterized by imperative labeling (using words for naming instead of communicating); echolalia (echoing speech); abnormal prosody, or inflection; and improper use of pronouns. Echoing adult words is common in typical development, as toddlers gain vocabulary and learn to process what is said to them. In children with ASDs, however, echolalic speech may persist in a perseverative fashion. Perseverative language may occur to provide structure and a known outcome in a social situation that the child with an ASD does not understand. Once functional language is established, prosody may be sing-song, robotic, or imitative of the inflection used by the original speaker. Young children with ASDs also may have difficulty assigning pronouns because they may not see how words need to be rearranged to have meaning to another person (Rapin & Dunn, 2003).

Communication requires a synthesis of many behaviors that are nonverbal. Children with ASDs may have a basic inability to both perceive and imitate facial expression (Dawson, Webb, & McPartland, 2005). Studies have shown that the brains of people with Autistic Disorder process faces as if they were objects. As a result, every time the facial expression of the communication partner is changed, the person with an ASD must reidentify the face (Schultz et al., 2000). This neurobiologic finding

closely tied to the symptoms in the area of

Development

Communication is present in children with ASDs (Rapin & Allen, 1983). Delays may relate to the child's environment. The most serious area of concern is the area of communication whose children are affected. Typical early language development, including the emergence of words, however, when early language becomes apparent, children who have had atypical development may have expressive language delays (Rapin, 1998). Language development at 18 and 24 months in children with autistic disorder is less than typical. Language milestones are less frequent.

Children with ASDs may have atypical language use, including atypical labeling (using words for communicating); abnormal prosody, such as use of pronouns, and atypical intonation. Common in typical development is the use of a rich vocabulary and learning of new words. In children with ASDs, they may persist in using repetitive language and a narrow range of vocabulary that the child with ASD may use. Once functional language is established, it may be sing-song or have a flat inflection used by children with ASDs. Atypically assigning pronouns and not seeing how words relate to meaning to another person (Rapin, 2003). There is a synthesis of verbal and nonverbal communication. Children with ASDs have a difficulty in both verbal and nonverbal expression (Dawson, 2005). Studies have shown that people with Autistic Disorder were objects. Facial expression of emotion is changed, the child may not reidentify the face and neurobiological finding

may be one factor that influences social processing and pragmatic language in people with ASDs.

Receptive language problems may also affect communication. Learning may be more efficient with visual, rather than auditory, cues. Unusual eye contact, body posture, gestures, and other nonverbal aspects of communication may have an impact on communication. Without specific intervention, nonverbal communication impairments may be problematic even with the development of conversational language.

Atypical Behavior

Although the differences in social "give and take" may be central to the diagnosis of ASDs, repetitive, perseverative, and stereotyped behaviors are often the most visible symptoms. Strict adherence to routines is common among people with ASDs. This can extend to food aversions, rituals related to daily routines, or obsessions. Young children with ASDs may have attachments to unusual items, such as string, rather than to soft or cuddly toys. Children with ASDs may not use toys in their intended manner but may focus instead on a part of a toy—for example, the wheels on a toy truck, which they may spin repetitively. They may line things up, stare out of the corners of their eyes, or visually inspect aspects of objects. Pretend play may not develop spontaneously, and once taught, it may take on a rote quality.

Interruption of a ritual or preoccupation may upset a child with an ASD and lead to distress or a temper tantrum. Stereotyped movements such as pacing, spinning, running in circles, drumming, flipping light switches, rocking, hand waving, arm flapping, and toe walking are common. Self-injurious behavior, including biting and head banging, may also occur. Unusual responses to sensory input are commonly reported. These include insensitivity to pain or heat and overreaction to environmental noises, touch, or odors. For example, although the child may appear "deaf" to the language of others but hear the television, or they may cover their ears and scream because of hyperacusis (unusual sensitivity to certain sounds).

The core symptoms of ASD vary with age and ability. For example, some people may have a total absence of language and communicative intent, whereas others engage in "professorial" speech with no conversational regard for the interest of the listener. Current challenges in-

clude development of more precise ways to elicit and quantify the core symptoms for early and accurate diagnosis.

CAUSES OF AUTISM SPECTRUM DISORDERS

ASDs do not form a single disorder and are without a single etiology. The weight of evidence now points to a genetic predisposition with environmental interactions (see Chapter 16).

The Genetics of Autism

The evidence for a genetic etiology for ASDs comes from both family studies and twin studies. The recurrence risk for an ASD in subsequent siblings of a child with ASD is 3%–5% (Chakrabarti & Fombonne, 2001). This is tenfold higher than what would be expected in the general population. An identical twin of a child with autism, however, has a 65% chance of having an ASD. Almost all identical twins of individuals with ASDs have some symptoms, although fraternal twins have been reported to have no greater rate of autism than other siblings (Folstein & Rutter, 1977). This strongly supports a genetic component of ASDs. It should be emphasized that these rates suggest an interaction of multiple genes (see Chapter 1). It is also likely that as yet unknown environmental factors influence gene expression and brain development in these disorders. Genetic research has followed three strategies, which are discussed next.

Family Studies In family studies, also called linkage analysis, patterns of genes or specific DNA markers in family members with and without Autistic Disorder or an ASD are investigated. This strategy has identified genes that may be related to ASDs on multiple chromosomes, including 2, 7, and 15 (Muhle et al., 2004).

Candidate Genes Studies Identification of a trait of interest allows specific investigation of associated genes in families with individuals with ASDs. A number of genes of interest relate to early brain development (Muhle et al., 2004). The interaction of genes and environmental events in early pregnancy is an area of active study. Candidate genes related to neurotransmitter generation and receptor function are of great interest because of potential for medical treatment of symptoms (Scott & Deneris, 2005).

Association with Genetic Disorders of Known Etiology ASDs tend to be associated with other genetic disorders that have known etiologies. It is understood that brain functioning in certain genetic disorders, such as tuberous sclerosis and fragile X syndrome, places individuals at a greater risk for having ASDs (see Chapter 19 and Appendix B). This knowledge allows for investigation of the relationship between known biologic abnormalities and behaviors symptomatic of autism.

Brain Structure and Function in Autism Spectrum Disorders

Neuroimaging techniques are used to study brain development and function. Although head circumference is normal at birth, children with ASDs (other than Rett's Disorder) have large heads in early childhood. The reason for this is not yet known. Magnetic resonance imaging (MRI) studies of children with ASDs note a greater volume of white matter in cortex and cerebellum in early childhood, but by middle childhood, the head size is in the normal range (Redcay & Courchesne, 2005). There may be abnormal genetic regulation of early brain growth and/or synaptic development. Anatomic findings on MRI, however, do not consistently identify the same structural asymmetries or size differences. Improvements in imaging, such as diffusion tensor imaging (which images specific neural tracts) will advance understanding of brain structure and function.

It is possible to indirectly examine how neurons in different parts of the brain behave in terms of neurotransmitter activity and energy utilization by using functional MRI and spectroscopy. Most studies have been done with higher functioning adolescents and adults. One finding was that theory of mind tasks require the networking of the medial prefrontal cortex, temporoparietal junction, and temporal poles with other brain regions (Vollm et al., 2005). High-functioning adolescents with ASDs demonstrate impairments in processing faces in the fusiform gyrus (Schultz et al., 2000) and in processing the eye gaze of others in the superior temporal sulcus (Pelphrey, Morris, & McCarthy, 2005). In addition, imitation may be impaired because mirror neurons do not communicate properly (Williams, Waiter, et al., 2005).

Few brains of individuals with ASDs have been examined histologically. The findings to date suggest that prenatal events alter cell number and density in the cerebellum and limbic system. Abnormal development of the brain

stem nuclei and the inferior olive, as well as heterotopias (abnormally placed neurons) have been reported in isolated cases (Bailey et al., 1998). Modern techniques have identified additional pathological changes in some individuals' brains, including atypical inflammation and disordered cellular organization in the cortex (Casanova, Buxhoeveden, & Gomez, 2004; Vargas et al., 2005). To further basic understanding of the neurobiology of these disorders, post-mortem study of the brains of individuals with ASDs must occur. Autism Speaks and the National Institutes of Health have sponsored a brain bank to make pathologic material available to researchers (see <http://www.MemoriesofHope.org>).

Obstetric Complications

Epidemiologic studies have not strongly associated any specific prenatal or birth complications with the development of ASDs. Obstetric optimality scores that reflect the overall health of the pregnancy, delivery, and newborn period are lower in children with ASDs (Zwaigenbaum et al., 2002). The prenatal events that predispose a child to develop an ASD may compromise fetal well-being in subtle and inconsistent ways.

Environmental Exposures

It is likely that environmental factors interact with genes to cause the symptoms of ASDs. To date, the only established environmental risk factors for ASDs are a few medications (discussed in the next section) that a mother might have been prescribed early in pregnancy (Hyman, Arndt, & Rodier, 2005).

Teratogens Substances that result in an increased risk of birth defects in the developing fetus are termed *teratogens*. These include maternal medications, drugs of abuse, chemicals, and radiation. Thalidomide is a drug that was used to treat nausea in pregnant women in the 1960s. It was associated with limb deformities in exposed fetuses (see Chapter 2). Many years later, ophthalmologists studying the abnormalities of eye movement in adults who were exposed to thalidomide in utero found that these adults also had a very high prevalence of ASDs. In addition, increased rates of ASDs have been reported in children who were exposed during early pregnancy to valproic acid (used to treat seizures and bipolar disorder) and mesoprostol (which may fail when used to in-

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No known environmental or chemical exposures have been associated with an increased risk for ASDs to date. The epidemiologic study that compared the rates of ASD in Brick Township, New Jersey, to other communities in New Jersey did not identify increased risk in that locale (Bertrand et al., 2001). Recent reports of increased airborne mercury in locations with higher rates of children with ASDs require further study with more rigorous methodology that includes actual air sampling (Palmer et al., 2006). Although existing data do not implicate specific chemical agents, it is certainly plausible that substances to which mothers and newborns are exposed may affect brain development in a way that leads to ASDs in susceptible individuals.

Vaccinations There has been significant controversy about the alleged association of the measles, mumps, and rubella (MMR) vaccine, developmental regression, and ASDs (Wakefield et al., 1998). Population-based studies do not demonstrate an increase in the rate of diagnosis of ASDs with the introduction of MMR (Demicheli et al., 2005). Madsen et al. (2002) compared the rate of ASDs in more than 400,000 children in Denmark who received the MMR vaccine with about 100,000 children who did not get the vaccine. There was no difference in the rate of ASDs. Epidemiologic data does not support an association of the MMR vaccination with autism.

A second hypothesis relates the ethylmercury-based preservative, thimerosal (used as a preservative in pediatric vaccines prior to 2001) to symptoms of ASD in genetically susceptible children (Bernard et al., 2001). The rate of diagnosis of ASDs actually increased after removal of thimerosal from vaccines in Denmark (Madsen et al., 2003), although this was attributed to the broadened diagnostic criteria and increased awareness of ASDs in families and providers. The neurologic symptoms that are known to be associated with specific types of mercury toxicity depend on the type of mercury and age at and length of exposure. Neurologic symptoms of ASDs and acute, chronic and prenatal mercury toxicity affect sensory functions, motor abilities, and learning, but the specific symptoms are not the same (Nelson & Bauman, 2003). Methylmercury, the type of mercury ingested in fish and marine mammals, has not yet been associated with autism in populations with high pre- and postnatal exposure (Davidson, Myers, & Weiss, 2004).

In sum, no studies provide scientific documentation of a causal association of thimerosal containing vaccines and ASDs. In addition, current vaccines administered to children in the U.S. other than some influenza vaccines are typically thimerosal free (see <http://www.fda.gov/cber/vaccine/thimerosal.htm#t1>). Despite these factors, chelation therapy to bind and excrete heavy metals is pursued as a clinical intervention by families of children with ASDs. No clinical trials have been published to date that examine the safety and efficacy of this practice (Levy & Hyman, 2005).

Infections Prenatal infection with rubella increases the risk for cerebral palsy, intellectual disability, visual impairments, and ASDs, depending on the timing of infection (Chess, 1971). Vaccination-based immunity in women has all but eliminated this cause of ASDs in the United States. Other virus and bacterium that commonly infects pregnant women are not routinely associated with ASDs in the offspring, although rare cases of ASD have been reported in children with congenital CMV. A mother's own immunologic response to infections such as influenza might cause subtle differences in brain development, which might predispose a susceptible fetus to an ASD (Shi et al., 2003).

Another issue that has been raised is the possibility of infections in early childhood being associated with ASDs. Children who have severe neurologic injury after meningitis or encephalitis may have symptoms of ASDs. There is no evidence to indicate overgrowth of intestinal yeasts or bacteria (Levy & Hyman, 2005) cause ASDs.

Gender and Autism Spectrum Disorders

There is a 4:1 male to female predominance of ASDs. The gender ratio is closer to 1:1 for children with ASDs who have IQ scores of less than 50 (Yeargin-Allsopp et al., 2003). The excess of identified males may be the result of differential genetic or hormonal susceptibility, teratogenic effects, or application of the diagnostic criteria.

EARLY IDENTIFICATION OF AUTISM SPECTRUM DISORDERS

By *DSM-IV-TR* definition, the symptoms of ASDs must be present by 3 years of age. Even when parents are concerned about a child's early development, the diagnosis of an ASD may not

be made for 2–3 years (Mars et al., 1998). As with many other disorders, the more severe the symptoms, the earlier the child is referred for evaluation. The age of diagnosis has decreased with increased awareness by pediatricians, parents, and preschool teachers. Children with Asperger syndrome and high-functioning autism, however, tend to be diagnosed at school age.

Delayed language development, repetitive behaviors, and atypical social responsivity are common early parental concerns. Systematic review of videotapes from the first of year life demonstrates differences in infants with ASDs by 1 year of age. They may not respond to their name and are less interested in faces and voices than other infants. Infants later diagnosed with ASDs may have had poor eye contact, absence of a social smile, irritability, and a dislike of being held. As toddlers, they may have had sleep difficulties, limited diets, tantrums, and inattention to language. Because of limited response to the language of others, initial concerns may have been around hearing impairment. Overall, ASDs cannot be thought of in terms of age of onset of symptoms but rather in terms of age of recognition (Volkmar, Stier, & Cohen, 1985).

Early diagnosis is based on the recognition of the core features of ASDs as they appear in early childhood. Atypical development of pretend play, pointing to share interest, use of eye gaze to engage another person in communication, and social interest can distinguish toddlers at high risk for ASD as young as 18 months of age. These observations are the basis for the Checklist for Autism in Toddlers (CHAT; Baron-Cohen et al., 2000) and the Modified Checklist for Autism in Toddlers (M-CHAT; Robins et al., 2001). The M-CHAT is a brief parent questionnaire suitable for screening toddlers prior to 3 years of age. Other tests that can be used to screen for ASDs in toddlers include the Screening Tool for Autism (STAT; Stone et al., 2004) and the Pervasive Developmental Disorder Screening Test-II (PDDST-II; Siegel, 2004). The routine use of general developmental and behavioral screening tests by primary care providers, however, is likely to be the best screening mechanism to identify children with ASD. This approach identifies general delays and results in earlier referral for diagnostic and treatment services. Because of the importance of early diagnosis in leading to early intervention, there has been much interest in the accurate screening and diagnosis at younger and younger ages. (See Table 23.2 for more information about screening tools.)

Evaluation of the Child with an Autism Spectrum Disorder

Assessment for ASDs requires time, collaboration among health care and educational professionals, and knowledge of the disorders. The evaluation follows directly from the diagnostic criteria that focus on impairments in social reciprocity, language, and restricted patterns of behavior (Filipek et al., 2000).

Multidisciplinary Assessment Most children are initially referred to school-based assessment teams or early intervention services by their primary care providers or by parents because of language delays (see Chapter 33). Initial multidisciplinary evaluation of developmental concerns should involve formal assessments of 1) receptive and expressive language, 2) cognitive function, 3) hearing, 4) fine and gross motor function, 5) social and emotional skills, and 6) adaptive skills.

If an ASD is suspected, referral should be made to a professional experienced in making diagnoses, such as a neurodevelopmental or developmental-behavioral pediatrician, child neurologist, child psychiatrist, child psychologist, or speech-language pathologist. The assessment should include a detailed medical history, with particular attention paid to 1) social development; 2) developmental milestones, especially in language; 3) other medical conditions; 3) family history, including behavioral, medical, neurologic, developmental, and psychiatric illnesses; and 4) current family functioning and circumstances. As noted previously, more than one quarter of children with Autistic Disorder have a reported loss of language and/or social milestones in the second year of life. An underlying medical condition needs to be considered in these cases. Ten percent of children with ASDs are reported to have medical conditions that might be etiologic (Chakrabarti & Foinbonne, 2001). A general physical and neurological examination for intercurrent medical conditions that might exacerbate behavior and for underlying causes of the ASD should take place. The physical examination should include an examination of the skin, as children with neurocutaneous syndromes (e.g., tuberous sclerosis) are at higher risk for ASDs. Head circumference should be monitored and with conventional neurologic assessment of macro and microcephaly.

Diagnostic Measures Diagnosis of an ASD is based on the application of the *DSM-IV-*

Id with Disorder

res time, collabora- educational profes- the disorders. The from the diagnostic ments in social rec- icted patterns of be-

Assessment Most ed to school-based ervention services iders or by parents (see Chapter 33). luation of develop- olve formal assess- xpressive language, earing, 4) fine and cial and emotional

, referral should be rrienced in making velopmental or de- atrician, child neu- child psychologist, ogist. The assess- ed medical history, d to 1) social devel- milestones, espe- medical conditions; ehavioral, medical, and psychiatric ill- y functioning and viously, more than . Autistic Disorder uage and/or social r of life. An under- ls to be considered of children with medical conditions akrabarti & Fom- ical and neurolog- rent medical con- e behavior and for should take place. ould include an ex- ldren with neuro- iberous sclerosis) Head circumfer- and with conven- of macro and mi-

Diagnosis of an on of the *DSM-IV*

TR criteria (APA, 2000). The history and clinical observation requires input from parents, therapists, and teachers who are familiar with the child in multiple settings. Because many children with ASDs are anxious in new settings, it may take multiple visits to obtain a reliable assessment. Structured history through the Autism Diagnostic Inventory (Lord, Rutter, & Le Couter, 1994) and observation of symptoms through the Autism Diagnostic Observation Schedule (Lord et al., 2000) are used primarily in research settings to standardize application of the *DSM-IV-TR* criteria.

Laboratory Testing and Neuroimaging There is no standard medical workup for children with ASDs. Etiologic workup is determined by history and physical examination (American Academy of Pediatrics [AAP], 2001). DNA analysis for fragile X syndrome is often recommended in children with cognitive limitations and symptoms of ASDs. Karyotyping should also be considered. A chromosomal abnormality is identified in up to 5% of children with ASDs and cognitive limitations. Advances in chromosome analysis such as subtelomeric analysis (see Chapter 1) has not increased diagnostic yield to date. As the genes for ASD are identified, it is likely that testing for specific gene alterations will be routinely recommended.

Although abnormalities may be seen on MRI in children with ASDs, the yield for diagnostic or treatable conditions identified by routine neuroimaging studies is low. Similarly, in the absence of a history of seizures, routine screening with EEGs is not indicated (Filipek et al., 2000). General metabolic screening rarely has positive results if the history and physical examination is negative. Although additional medical and biological evaluations are often pursued, there is no scientific evidence to support measurement of heavy metal levels in hair, blood, or urine; immunologic parameters in blood; stool flora; urine peptides; or yeast metabolites in urine in children with ASDs (Levy & Hyman, 2005).

ASSOCIATED CONDITIONS

ASDs may be associated with intellectual disability, as well as many other conditions. These are discussed next.

Intellectual Disability

Most studies report that up to three quarters of individuals with Autistic Disorder also have in-

Table 23.2. Screening and diagnostic tests for autism spectrum disorders (ASDs)

Screening tests for ASDs in toddlers

Modified Checklist for Autism in Toddlers (M-CHAT; Dumont-Mathew & Fein, 2005): ages 18–36 months

Screening Tool for Autism in Two-Year-Olds (STAT; Stone et al., 2004)

Pervasive Developmental Disorder Screening Test (PDDST; Seigel, 2004)

Screening tests for older children

Social Communication Questionnaire (SCQ; Berument et al., 2002): older than 3 years of age
Social Reciprocity Scale (Constantino, 2004): school age

Standardized tests that support a clinical diagnosis of autism

Childhood Autism Rating Scale (CARS; Schopler, Reichler, & Renner, 1993): older than 2 years of age

Gilliam Autism Rating Scale, Second Edition (GARS-2; Gilliam, 2005): older than age 3

"Gold standard" companion measures designed to elicit symptoms of ASDs for diagnostic purposes
Autism Diagnostic Interview (ADI; Lord et al., 1994): semistructured interview with the caregiver that allows for scoring whether autism is present

Autism Diagnostic Observation Schedule (ADOS; Lord et al., 2000): structured interactions for children of different language abilities to allow for observation of symptoms of ASDs per the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR; American Psychiatric Association, 2000)* criteria for both Autistic Disorder and Pervasive Developmental Disorder

The above two measures are often used together to characterize cases for research related to autism.

Note: Clinical application of the diagnostic criteria from *DSM-IV-TR* by an experienced clinician is the mainstay of diagnosis.

tellectual disability. Yeargain-Alsop et al. (2003) reported that 68% of the children between 3 and 10 years of age identified with ASDs in the Atlanta area also had intellectual disability. Only 40% of preschool children diagnosed with ASDs were found to have comorbid intellectual disability at the time of the first evaluation (Chakrabarti & Fombonne, 2001). With more inclusive diagnostic criteria for ASD, it is likely that increasing numbers of individuals with typical cognitive abilities and with significant intellectual disability will be identified as having ASDs. Brain insults responsible for causing ASDs can disrupt other neurologic functions and result in intellectual disability.

Overlap of symptoms between intellectual disability and the ASDs also complicates the diagnostic process. Careful clinical assessment is necessary to determine if social development is atypical for the child's mental age. Symptoms of ASD such as a lack of interest in peer play, lack of pretend play, and repetitive behaviors may also be seen in people with severe intellectual disability without ASDs (de Bildt et al., 2004).

Learning Disabilities

Learning disabilities are common among individuals who have ASDs. Specific impairments in **executive function**—the cognitive tasks related to taking in, organizing, processing and acting on information—also may be present in people with ASDs (Ozonoff et al., 2004).

Epilepsy

Overall, epilepsy is reported in about one quarter of individuals with ASDs and most commonly presents in infancy and adolescence (Tuchman & Rapin, 2002). There is also an increased likelihood of having an abnormal EEG without seizures in people with ASDs. The implications of this finding are unclear, and the role of anticonvulsant treatment in the absence of seizures has not been evaluated.

Tic Disorders

Up to 9% of children with ASDs also have tics or brief involuntary motor movements. Tourette syndrome can be diagnosed when both vocal and motor tics last 6 months. Tourette syndrome may be associated with inattention and hyperactivity, obsessions, and learning disabilities. Individuals who have Tourette syndrome but not an ASD have appropriate social reciprocity (Ringman & Jankovic, 2000).

Sleep Disorders

Sleep disturbances are reported in 50%–70% of children with ASDs. Although often considered most problematic in the preschool years, symptoms persist in many children. Night waking, delayed sleep onset, and early morning waking are all reported (Wiggs & Stores, 2004). Poor sleep may be associated with daytime inattention and irritability. Underlying biologic causes may relate to abnormal melatonin synthesis and release or disordered sleep cycles. Until the etiology is better understood, the mainstay of

treatment is behavioral intervention. Medical treatment with melatonin, antihistamines, and other sedating agents may be used to augment behavioral treatment.

Gastrointestinal Symptoms

Increased prevalence of abdominal pain, gastroesophageal reflux, diarrhea, constipation, and bloating among children with ASDs has been suggested (Erickson et al., 2005). Although high rates of gastrointestinal symptoms are reported among children with ASDs attending subspecialty clinics, no increased rate of complaint was identified in studies examining primary care records in the United Kingdom for children prior to diagnosis. In a clinical series of children with ASDs who were referred for evaluation of accompanying gastrointestinal (GI) concerns, the children were reported to have a greater than anticipated rate of lymphonodular hyperplasia on intestinal biopsy (Wakefield, Anthony, & Murch, 2000). Additional study is necessary to determine if this evidence of inflammatory response represents a specific disease state. Abdominal discomfort may be responsible for acute behavioral changes. Children with ASDs often have specific food aversions and rituals and are at risk for nutritional compromise. Symptoms of GI disease need to be assessed and treated in children with ASDs as with any other children.

Psychiatric Conditions

Children with ASDs are at greater risk for depression, mood disorders, symptoms of attention-deficit/hyperactivity disorder, and anxiety. Comorbid diagnosis may be most evident in adolescents with adequate language and insight to allow standard application of diagnostic criteria.

Genetic Disorders Associated with Autism Spectrum Disorders

ASDs occurs with greater frequency among children with specific genetic disorders. Children with these disorders need to be monitored for symptoms of ASDs.

Tuberous Sclerosis Tuberous sclerosis is an autosomal dominant disorder caused by a defect in the TSC2 gene that codes for the protein tuberin. This neurocutaneous condition results in characteristic skin lesions (depigmented oblong patches called ash leaf spots),

intervention. Medical antihistamines, and be used to augment

ptoms

lominial pain, gastro- a, constipation, and with ASDs has been l., 2005). Although al symptoms are re- ith ASDs attending reased rate of com- idies examining pri- nited Kingdom for In a clinical series of re referred for eval- astrointestinal (GI) e reported to have a e of lymphonodular biopsy (Wakefield, Additional study is this evidence of in- sents a specific dis- omfort may be re- al changes. Children cific food aversions or nutritional com- isease need to be as- dren with ASDs as

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greater risk for de- symptoms of atten- disorder, and anxiety. e most evident in nguage and insight n of diagnostic cri-

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frequency among tic disorders. Chil- ed to be monitored

Tuberous sclero- disorder caused by that codes for the cutaneous condi- c skin lesions (de- lled ash leaf spots),

acne-like adenoma sebaceum, and benign growths (**tubers**) in the brain (Smalley, 1998). Common features are intellectual disability and seizures. Although, only 1%–4% of people with ASDs are likely to have tuberous sclerosis, a substantial number of children with tuberous sclerosis have symptoms of autism. All children being evaluated for an ASD should be examined to rule out neurocutaneous conditions.

Fragile X Syndrome At one time fragile X syndrome, the most prevalent cause of inherited intellectual disability, was believed to be a common genetic cause of ASDs. With careful clinical diagnosis, it has become clear that a large number of individuals with fragile X syndrome have many symptoms of ASDs but do not meet full criteria for the diagnosis. Up to 2% of boys with an ASD also have fragile X (Wassink, Piven, & Pitel, 2001).

Chromosome 15 Deletion Prader-Willi syndrome and Angelman syndrome share a common region for chromosomal deletion on chromosome 15 (15q11-q13). People with Prader-Willi syndrome have profound obesity, short stature, skin picking behaviors, and mild cognitive limitations. Angelman syndrome is characterized by intellectual disability, a happy affect, ataxic movements, hand clapping, and a characteristic facial appearance. A subgroup of children within ASD has been identified who also have a deletion or duplication in this region on chromosome 15 (Muhle et al., 2004).

Other Syndromes Associated with Autism Spectrum Disorders An increased rate of ASDs has been reported in Moebius syndrome (facial diplegia) and Joubert syndrome (cerebellar hypoplasia). Both of these syndromes may involve disruption of early embryologic brain development. Other genetic syndromes that have been associated with ASDs include Down syndrome, CHARGE syndrome, and Smith-Lemli-Opitz syndrome. The co-occurrence of these syndromes and the behaviors of autism may help researchers learn more about the neurobiology of ASDs (Muhle et al., 2004).

TREATMENT APPROACHES

It is important to diagnose children with ASDs early and accurately. Early educational programs focus on teaching social language and enhancing appropriate behaviors to children with ASDs. It is believed that treatment is most ef-

fective if started early. The National Research Council (2001) recommended intervention that is intensive, multidisciplinary, and continuous. Goals of autism treatment include 1) fostering development, 2) promoting learning, 3) reducing rigidity and stereotypy, 4) eliminating maladaptive behaviors, and 5) alleviating family distress (Rutter, 1985). A comprehensive approach usually requires a combination of an **individualized educational program**, behavioral supports, social and pragmatic language skills development, and family support.

Educational Approaches

The mainstay of treatment is education (National Research Council, 2001). Disorder-specific programs should be instituted as soon as a diagnosis is made. There are many different approaches to preschool education for children with ASDs. Successful programs share the characteristics of early entry, active participation in an intensive program offered daily throughout the year, planned teaching opportunities organized with the attention span of the child in mind, and sufficient adult staffing to meet the needs of the individual child and his or her program. An increase in tested IQ scores has been documented in young children with autism who participate in disorder-specific interventions (Harris et al., 1991). This finding may be in part the result of maturation, and increased motivation to participate in testing. In the absence of well-designed studies, one must be careful in ascribing treatment effects to either educational or complementary interventions that are instituted during early childhood.

Although there are philosophical differences between some of the teaching strategies, most preschool programs utilize the following: 1) structured teaching periods, 2) reinforcement of spontaneous communication, 3) instruction of specific skills using principles of reinforcement, and 4) incidental learning (i.e., use of spontaneously occurring “teachable moments”). Some of the more common approaches are described next.

TEACCH The TEACCH (Treatment and Education of Autistic and related Communication handicapped Children) was one of the initial disorder-specific educational programs that recognized the need for an intensive and coordinated approach to skill building and developing communication abilities (Mesibov, Shea, & Schopler, 2005). It was designed to ad-

dress the needs of the child and family across the school experience and includes classroom teaching, parent training, and other support services. The approach is eclectic and involves the use of behavioral strategies to enhance communication and social interaction, as well as visual organization and cuing; in addition, it emphasizes the parents' roles as co-therapists.

Applied Behavior Analysis The behavioral principles of operant learning (see Chapter 35) were used in a program for preschool children with ASDs developed by Dr. Ivor Lovaas (1987). His initial studies demonstrated that intensive and early intervention that specifically teaches the component skills necessary for development was associated with typical classroom performance in almost half of the 20 children with autism studied from 7–11 years of age (McEachin, Smith, & Lovaas, 1993). This model initially tested a 40-hour-per-week program that was based on individual therapy using discrete trial teaching, prompting, and reinforcement. Goals of the first year of treatment were to develop language skills, increase social use of language, increase social approach, promote play skills, and decrease behaviors that competed with the desired goals of therapy. In the second year of treatment, the goal was to extend intervention to a preschool environment in order to encourage interaction with peers and generalize the acquired skills. Later studies reported qualitative improvement even in children who do not have the dramatic response to behavioral treatment because of comorbid intellectual disability (Smith et al., 1997). Modifications in the delivery of applied behavior analysis (ABA) services have addressed teaching language skills and using a variety of behaviorally based strategies for skill development (Koegel, Koegel, & McNeerney, 2001). Generalization of skills to the home and classroom are an important component of the treatment plan.

Developmental-Individual Difference-Relationship Based Model The Developmental-Individual Difference-Relationship Based model (DIR model) is a treatment strategy described by Weider and Greenspan (2003) that builds on social communication learned in relationships with consistent and responsive adults. "Opening and closing circles of communication" in the context of child directed play is the focus of this intervention. It

depends on participation by the family and educational team. This type of therapy has been demonstrated to contribute to developmental gains when used as part of an early intervention program (Mahoney & Perales, 2005). It seeks to build shared attention leading to engagement. Communication and problem solving are also practiced, and the adults shape the development of appropriate play and interaction.

Relationship Development Intervention Relationship Development Intervention (RDI; Connections Center, 2004) is another relationship development approach that addresses social learning as an apprenticeship model. The adults lead the child through learning how to interact and respond in naturalistic settings. Parents are educated to understand the core deficits of ASDs so they can respond and shape their child's responses to language and social situations.

Classroom-Based Programs For children 3–21 years of age, Autistic Disorder is included as a special category of educational disability under the Individuals with Disabilities Education Improvement Act of 2004 (PL 108-446). This law mandates that specific academic goals should relate to the child's cognitive and functional level, and the program should be provided in the least restrictive environment. The Handicapping Condition under federal law is Autism, although under the diagnostic criteria in the *DSM-IV-TR*, Autistic Disorder is only one of the ASDs (or Pervasive Developmental Disorders per the *DSM-IV-TR*).

Children with ASDs should have their individualized needs addressed whether they are educated in small structured classrooms or in inclusive environments. Inclusive education allows for the child to model appropriate behaviors and learn how to participate in the community. Modifying educational materials may require consultant teacher support or team-taught classrooms. Some children with ASDs may benefit from a more structured environment with fewer sensory distractions. A specialized class setting could potentially be *less* restrictive for some children with ASDs because the predictability may result in less personal distress. Many educational strategies can be used to enhance the success of children with ASDs in the classroom (Harrower & Dunlap, 2001; Myles & Southwick, 1999). Future studies need to determine which programs are most effective and for which students.

Behavioral Intervention

An important goal of educating children with ASDs is to teach skills that extend their ability to communicate and socialize with others. Behavior carries meaning and should not be presumed to be a random act. Painful medical conditions and comorbid psychiatric conditions should be considered in cases of acute behavioral deterioration. If the origin of the behavior is considered, it may be possible to teach more effective ways to achieve a similar result (e.g., comfort, communication) and to expand behaviors that increase social adaptability. Behavioral support can be helpful in establishing daily routines, in extinguishing destructive behaviors, and in responding to tantrums. A functional behavioral analysis is indicated if behaviors interfere with classroom functioning (Dalton, 2002). This formal assessment determines why the behaviors are occurring. A functional behavioral plan can then be developed to alter the environmental factors that precipitate the challenging behaviors or teach the child and staff other means of responding (see Chapter 33).

Pragmatic Language and Social Skills Training

Communication attempts by children with ASDs should be rewarded socially or in other ways to foster language development. Bondy and Frost (1998) demonstrated that organizing visual cues helps children with ASDs associate the spoken word with events. This helps them learn the role of communication in obtaining tangible items and can be built into a Picture Exchange Communication System (PECS). There may be comorbid verbal motor dyspraxia or apraxia. This is when the motor coordination of speech is discordant with language understanding. Therapy may include a visual language system (picture or sign) which, in some cases, scaffolds the development of spoken communication. The use of augmentative and alternative communication (AAC) is different from facilitated communication. In AAC, children who do not have efficient oral speech are taught to independently gain access to written, graphic, or computer-assisted technologies for independent communication. Facilitated communication is a technique whereby a facilitator guides the individual with an ASD to type responses. Subconscious guidance by the facilitator has been demonstrated under experimental condi-

tions, and facilitated communication is not endorsed for clinical use (Mostert, 2001).

For children with spoken language, an important objective is the promotion of language skills used in conversation (Quill, 2000). *Pragmatic language* refers to the integration of gesture, expression, proximity, and inflection of language to enhance interpersonal understanding of communication. It involves both production and understanding of these functions in the conversational partner. These skills can make the difference in independent living, employment, and higher education. Encouraging social and pragmatic language development can be accomplished through a variety of approaches, including modeling by peers in inclusive settings, Social Stories (Gray, 2000), formal social skills curricula, supervised social skills group experiences, and tutoring by typically developing peers (Rogers, 2000). Children with ASDs may not generalize rehearsal in a group to other settings unless specifically taught to do so. Moreover, these techniques may not bridge the gap between social interactions and social relationships (Bauminger & Kasari, 2000). Therefore, educational objectives should address mastery of social skills in different settings and with different people.

Medication

Medication should only be considered as a component of a therapeutic program that includes behaviorally based therapy to teach appropriate behaviors and understanding of the reasons why behaviors might occur. Treatment with medication should be for specific target behaviors or a comorbid psychiatric or medical disorder.

Stimulant Medications Hyperactivity and inattention are common symptoms in children with ASDs. If appropriate language and educational interventions are in place and inattention persists, treatment with conventional stimulant medications such as methylphenidate and mixed dextroamphetamine salts can have beneficial effects (Handen, Johnson, & Lubetsky, 2000; see Appendix C). Side effects may include insomnia, decreased appetite, increased moodiness, and repetitive behaviors. Guanfacine and clonidine have been used for treatment of motor hyperactivity with some success (Jaselskis et al., 1992). Potential side effects of these two medications include hypotension and sedation.

Selective Serotonin Reuptake Inhibitors Because of some similarities between perseverative interests and obsessions, selective serotonin reuptake inhibitors (SSRIs) have been used to treat repetitive behaviors, irritability, and self-injury in people with ASDs (Moore et al., 2004). Decreasing anxiety may have additional benefits in enhancing language and social interactions. Side effects may include paradoxical hyperactivity or mood instability. Suicidal behaviors have very rarely been reported with drugs in this class when used to treat adolescent depression, so close monitoring is suggested.

Atypical Neuroleptics Well-designed trials have demonstrated that the atypical neuroleptic risperidone significantly improves irritability, aggression, and self-stimulatory/self-injurious behaviors in children with ASDs and intellectual disability (McCracken et al., 2002; McDougle et al., 2005). Medications in this class, such as olanzapine and aripiprazole, have been used on the basis of small open trials. The major side effect seen is weight gain. Less common side effects from this class of medications include metabolic syndrome (a prediabetic state with elevation of blood lipids), tardive dyskinesia, sedation, and hormonal imbalances. Routine monitoring for side effects is important.

Mood Stabilizers Anticonvulsant drugs used to treat bipolar disorder, such as valproic acid and carbamazepine, are also used in the management of explosive behaviors in people with ASDs (Hollander et al., 2001). Both medications need to be monitored with blood levels. By extension, newer anticonvulsants are sometimes used.

Other Medications Other types of medications are being investigated for symptoms of ASDs. Advances in technology are likely to bring to market other medications designed to affect specific neural systems.

Complementary and Alternative Therapies

Almost two thirds of Americans employ treatments that could fall into the category of complementary or alternative medicine (CAM). Up to one third of families are already using CAM therapies at the time that their child receives the formal diagnosis of an ASD (Levy et al., 2003). The AAP Committee on Children with Disabilities (2001) recognized that CAM treat-

ments are commonly used for chronic conditions. The committee encouraged traditional health care providers to understand the issues that families are dealing with, to help educate families in the interpretation of claims made by CAM providers and literature, and to monitor children for side effects if CAM therapies are utilized. The health care professional should advocate for the child to pursue educational and other therapeutic interventions known to enhance outcome and help the families evaluate data regarding the cost, side effects, plausibility of the claims, and the claimed benefits for the treatment they wish to try.

There are increasing numbers of scientific studies examining CAM therapies for safety and efficacy. The most informative study design is the double-blind placebo-controlled trial with an adequate number of subjects with well-defined ASDs whose treatment response is measured using valid tests. In most behavioral studies, up to one third of participants report benefit from placebo. That is why it is so important that placebo controlled trials be reported for treatment.

Dietary treatment is popular. Elimination of gluten and casein (wheat and milk proteins) has been hypothesized to result in decreased symptoms of autism and in decreased intestinal distress in some children. Although there are many anecdotal reports of improvement, two small studies have not demonstrated marked improvement (Elder et al., 2006; Millward et al., 2005). Despite this, the gluten- and casein-restricted diet remains popular, and families who decide to pursue it need to carefully monitor their child's nutritional needs. For example, when milk is removed, alternative sources of calcium, vitamin D, and protein need to be provided.

Vitamins are often used in doses greater than the recommended daily intake in an attempt to effect behavioral change. Vitamin B₆ taken with magnesium is one such treatment used to enhance attention and language. Although several studies suggested benefit, two double-blind placebo-controlled studies could not demonstrate it (Nye & Brice, 2005). Other nutritional treatments that enjoy popularity at the writing of this chapter include supplementation with essential fatty acids, B₁₂, dimethylglycine, and carnosine (Levy & Hyman, 2005). Children should have target behaviors identified and a monitoring system in place to determine if the intervention has a positive effect. Knowledge of potential side effects is also cru-

cial. Other types of CAM are used to treat hypothesized infectious or immune imbalances such as yeast overgrowth in the colon and intestinal dysbiosis (Finegold et al., 2002). The current scientific literature does not support these treatments.

Sometimes the nontraditional use of a prescription medication becomes a CAM therapy. Secretin is one example. Secretin is a hormone that increases pancreatic secretion into the intestine and is usually employed to evaluate pancreatic function during endoscopy. Anecdotal observation of behavioral improvement in three children after secretin with endoscopy resulted in its widespread use. Subsequently, more than 700 children with ASDs have been studied in double-blind placebo-controlled trials of secretin without confirmation of the original improvement (Williams, Wray, & Wheeler, 2005).

Not all CAM therapies are biologic. Facilitated communication, auditory integration training, and optometric training are nonbiologic examples of CAM. The conventional medical literature does not support the use of these interventions. Sensory integration techniques are often used by occupational therapists to stimulate or calm children who demonstrate altered sensory and motor reactivity (Baranek, 2002). Although popular, there is little data to support general implementation of these strategies. Until appropriately designed scientific studies are completed, each child must be evaluated by the family and therapy team for both positive and negative responses to CAM therapies that families chose to employ.

Family Supports

Families should be connected with appropriate parent support organizations at the time of diagnosis (Chapter 40). The stressors of receiving the diagnosis, making decisions, and addressing the child's needs may require referral for additional counseling services for other family members. The needs of siblings must also be addressed. Most studies indicate that the siblings of children with disabilities are resilient (Kaminsky & Dewey, 2002).

OUTCOME

Measured IQ scores and the presence of language that can be used for conversation remains the best predictor of outcome for children with ASDs (Bilstedt, Gillberg, & Gillberg, 2005). More than half of children diagnosed with au-

tism acquire language that can be used for communication (Howlin, 2003). With the expansion of diagnostic criteria to include a large number of individuals with typical cognitive abilities among those with ASDs (e.g., people with Asperger syndrome), the outcome for successful completion of education and community employment may be more optimistic.

It is as yet unknown how function is altered by educational programs. Diagnosis of an ASD at age 2 seems to be accurate (Lord et al., 2006). It is impossible to predict at the time of diagnosis which children will respond positively to intervention and which children will later also be diagnosed with intellectual disability. Therefore the need to provide an intense and disorder-specific intervention program to all children with ASDs is imperative.

SUMMARY

ASDs are neurodevelopmental disorders with a genetic basis, the presentation of which might be modified by environmental factors. These disorders are characterized by abnormalities in communication, social interaction, and repetitive interests and behaviors. Children with ASDs may have associated intellectual disability and severe communication impairments. Individuals with typical cognitive abilities and high-functioning autism or Asperger syndrome have symptoms related to social reciprocity and repetitive behaviors. Advances in early recognition and intervention have had a positive impact on outcome and quality of life for people with ASDs and their families. Individualized, multidimensional treatment is the standard of care and is associated with notable improvements in symptoms.

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