Article ▸ Update on Autism Spectrum Disorders for Optometry: A Review of the Literature

Kristi A. Jensen, OD, Western University of Health Sciences – College of Optometry, Pomona, California

Elizabeth Hoppe, OD, MPH, DrPH
Western University of Health Sciences – College of Optometry, Pomona, California

Kristy Remick-Waltman, OD
Western University of Health Sciences – College of Optometry, Pomona, California

Frank Spors, EurOptom, MS, PhD
Western University of Health Sciences – College of Optometry, Pomona, California

Donald Egan, OD, Western University of Health Sciences – College of Optometry, Pomona, California

ABSTRACT

Background: The purpose of the paper is to review current literature on Autism Spectrum Disorders (ASD) and to inform doctors of optometry who will provide care for patients with ASD and their families. As primary care providers, it is important that doctors of optometry have the knowledge and skills required to recognize the signs and symptoms of ASD and to contribute to the multi-disciplinary team for diagnosis and treatment.

Methods: A review and synthesis of current relevant literature was conducted.

Results: Publications describing the epidemiology of autism, risk factors, screening, and diagnosis are reviewed. Optometry is not currently listed as one of the multi-disciplinary professions in the ASD team, and this article proposes potential roles of the doctor of optometry to fill in the missing piece in the coordination of care of ASD patients.

Conclusions: Doctors of optometry should play an important role in the care of individuals with ASD. It is time that optometrists assume their role as primary care providers to care for vulnerable populations such as individuals on the autism spectrum.

Optometrists should be aware of current diagnostic criteria and research regarding patterns of autism and potential risk indicators. Familiarity with types of healthcare providers, local community resources, and screening and diagnostic tools that can assist both in making a definitive diagnosis and in managing autism spectrum disorders is important for the optometric provider.

Keywords: autism spectrum disorder (ASD), prevalence, incidence, risk, screening

Introduction

Description of Condition and Definitions

Many optometrists are providing care for an increasing number of patients with diagnoses of autism, pervasive developmental disorders, sensory processing conditions, Asperger's Syndrome, and attention deficits. Today, one in every 88 American children is on the autism spectrum.[1] Numerous publications stress the important role that primary care providers should play in recognizing the early signs of ASD. The evidence suggests that children who are diagnosed early, and who receive appropriate intervention programs, attain better outcomes.[2-5]

Many refer to the "Autism Spectrum" or "Autism Spectrum Disorder" (ASD) in recognition of the multiple manifestations which occur.[6] The term "spectrum disorder" is used to indicate that ASD encompasses a range of behaviorally defined conditions which are diagnosed through clinical observation of development.

Autism, or Autistic Disorder, is considered to be a neurological condition. Classified as a Pervasive Developmental Disorder (PDD), the Diagnostic and Statistical Manual, fourth edition (DSM-IV) in 1994 (and DSM-IV-TR in 2000[7]) describes Autism as "the presence of markedly abnormal or impaired development in social interaction and communication and a markedly restricted repertoire, activity, and interest."[8] The new DSM-5 criteria for Autism diagnosis was adopted in May 2013 at the American Psychiatric Association's meeting and states that the features of Autism Spectrum Disorder involve "persistent impairment in reciprocal social communication and social interaction, and restricted, repetitive patterns of behavior, interests, or activities, present from early childhood and limit or impair everyday functioning."[9]

In the DSM-IV diagnostic criteria, there are five subgroups of pervasive developmental disorders included: autistic disorder, Asperger's disorder (often referred to as Asperger's syndrome), Rett's disorder (often referred to as Rett's

syndrome), childhood disintegrative disorder (CDD), and pervasive developmental disorder – not otherwise specified (PDD-NOS).[2-4] In the DSM-5 criteria, four separate disorders are considered to be a single condition with differing levels of severity in the symptoms manifested. Rett's disorder is excluded from the criteria and considered a separate differential.[9] ASD now comprises the previous DSM-IV categories, as a single condition, encompassing deficits in social-emotional reciprocity, deficits in non-verbal communicative behaviors used for social interaction, and deficits in developing, maintaining, and understanding relationships.[9]

Individuals who demonstrate autistic impairments demonstrate the characteristics of the disorder on a continuum, or a spectrum. Patients range from lower-functioning with significant developmental compromise to a higher-functioning group with higher cognition and relatively fewer autistic symptoms.[6] Persons with Asperger Disorder have fewer diagnostic symptoms which tend to be of milder severity.[2] Individuals with autistic disorder are considered to have lower function, and a review of published studies suggests that the PDD-NOS category is not operationalized by clinically observed data.[6] Signs of ASD are frequently present before the age of 3 and are often accompanied by abnormalities in cognitive functioning, learning, attention, and sensory processing.[3] Impairments are considered to be chronic and life-long.[8] At the most severe end of the spectrum, individuals may be non-verbal, have serious intellectual deficits, and demonstrate aggressive and self-injurious behavior.[8]

The Cost of Autism

The cost to society of ASD is currently estimated to be $35 billion to $90 billion annually, which rivals that of Alzheimer's disease.[10,11] The impact of ASD on the individual and family can be devastating to their quality of life, with consequences in virtually all areas ranging from physical to psychological to financial. Adults with ASD struggle with basic needs such as employment and housing, while parents of ASD children are often forced to leave the workforce to care for their child, thus losing valuable income needed to live and pay for therapies. According to the American Autism Society, approximately 1.5 million Americans live with the effects of Autism Spectrum Disorder.[13] It is estimated that it can cost about $3.2 million to take care of an autistic person over his or her lifetime.[14]

Prevalence and Incidence Rates

From the first published estimates of the rates of Autism Spectrum Disorder (ASD), researchers have reported gradual increases in both the prevalence (the number of existing cases) and the incidence rates (the number of newly diagnosed cases per time period). The first U.S. multisite collaborative study to monitor ASD prevalence reported data from six areas in the year 2000. The Centers for Disease Control and Prevention organized the Autism and Developmental Disabilities Monitoring Network. This network established a multi-site,

records-based surveillance program to study the prevalence of ASD. Identification of children aged 8 years with a diagnosis of ASD was determined through screening and abstraction of evaluation records at multiple sources, with clinician review of abstracted sources to confirm documentation consistent with the American Psychiatric Association's criteria for diagnosing autistic disorder, pervasive developmental disorder – not otherwise specified, or Asperger's syndrome. It is important to note that this network system relies on systematic screening rather than existing medical or educational labels of ASD. The overall prevalence of ASD ranged from 4.5 per 1,000 to 9.9 per 1,000 with an average estimated prevalence across all 6 sites of 6.7 per 1,000 children.[15]

In 2002, the prevalence of ASD in the United States was estimated using a systematic retrospective review of evaluation records in multiple sites participating in the Autism and Developmental Disabilities Monitoring Network from 14 locations (increased from six in 2000) around the country. The investigators selected an index age of 8 years to monitor the peak prevalence and to compare with the data collected in 2000. The Centers for Disease Control and Prevention reported the estimated ASD prevalence at approximately one child in every 150, or a rate of 6.7 per 1,000, as essentially unchanged from the report 2 years prior.[16]

Another strategy to estimate the prevalence of Autism Spectrum Disorder utilized parent reporting in the National Health Interview Survey (NHIS) and the National Survey of Children's Health (NSCH). The Centers for Disease Control and Prevention estimated the population-based prevalence of diagnosed autism in the United States for 2003-2004 at a rate of 5.7 per 1,000 based on the NHIS and 5.5 per 1,000 based on the NSCH.[17]

A study of children born in Massachusetts between 2001 and 2005 found an increase in the incidence rate of Autism Spectrum Disorders (ASD) in children less than 3 years of age from 56 per 10,000 (5.6 per 1,000) children born in 2001 to 93 per 10,000 (9.3 per 1,000) children born in 2005. The study also found that the increased incidence rate varied by gender, with a 70% increase among boys and a 39% increase among girls.[18]

More recently, in 2006, using data from the same Autism and Developmental Disabilities Monitoring Network, the overall average prevalence was calculated as 9.0 per 1,000 population, ranging from 4.2 in Florida to 12.1 in Arizona and Missouri. This data was compared with rates from data collected in 2002 from 10 of the same sites, yielding an increase of 57% over the four-year time span.[20]

In March 2012, surveillance reports from data captured in 2008 revealed a prevalence rate of 11.3 per 1,000, or one in every 88 children affected.[1] In March 2013, the Centers for Disease Control and Prevention released new estimates showing that the prevalence of parent-reported ASD among children aged 6-17 was 2.0% (20 per 1,000) in 2011-2012. This represents an increase from 1.16% in 2007.[19] The estimates

further increased with a new release of data in March 2014 that shows a prevalence rate estimated at one in 42 boys and one in 189 girls living in the surveillance area as having ASD.

Many agree with this statement published by Mulvihill, et al: "These results indicate an increased prevalence of identified ASDs among U.S. children… and underscore the need to regard ASDs as an urgent public health concern. … Research is needed to ascertain the factors that put certain persons at risk, and concerted efforts are essential to provide support for persons with ASDs, their families, and communities to improve long-term outcome."[20]

Experts studying ASD have not yet reached consensus about the underlying causes and the relative significance demonstrating the recent increase in the reported prevalence of ASD. Some investigators have suggested that parents are more likely to raise concerns about autism due to heightened awareness by the general public, thereby prompting physicians and school districts to conduct more evaluations.[21-23] Healthcare professionals may have become better prepared to recognize and diagnose ASD due to improvements in the reliability of screening tools and diagnostic instruments.[8]

There is a concern as to whether increased prevalence rates are due to changes in diagnostic practices. Autism was first listed as a specific condition with designated diagnostic criteria in the Diagnostic and Statistical Manual of Mental Disorders (DSM-III) in 1980.[24] Changes in 1987 first broadened the ASD criteria and changed the threshold for diagnosis of PDD-NOS, which resulted in the inclusion of milder cases. These changes were criticized for promoting over-diagnosis. In 1994, the fourth edition of the DSM sought to reduce the perceived over-inclusiveness in the criteria for ASD and PDD-NOS, but Asperger's syndrome was now included for the first time.[8,25,26]

A study published in 2009 evaluated to what extent the increased prevalence of autism in California has been driven by changes in diagnostic practices, diagnostic substitution, and diagnostic accretion. After a retrospective analysis of children born before 1987, 631 individuals with a sole diagnosis of mental retardation who later acquired a diagnosis of autism were identified. This data was used to model the probability of diagnostic change and to estimate the proportion of the autism caseload that resulted from changing diagnostic practices. The investigators concluded that changes in practices for diagnosing autism accounted for approximately one-quarter of the observed increase in prevalence of ASD in California between 1992 and 2005, leaving roughly 75% of the increased rate unexplained by diagnostic trends.[27]

Investigators have also sought to determine whether increased awareness may relate to increased rates of diagnosis and ultimately higher rates of access to services. Rates of ASD that are calculated from statistics captured by school districts are influenced by policies determining access to services. For example, ASD was not a diagnosis for which children became eligible to receive special education services until 1990, with the passage of the Individuals with Disabilities Education Act (IDEA).[28] Before 1990 when IDEA was enacted, in order to obtain eligibility for educational services children had to be "labeled" as having conditions such as mental retardation, learning disability, emotional disturbance, or speech impairment.[29] After the passage of IDEA, the increased number of children who were now "labeled" with ASD included both older children who had previously had a different reason for access to services, indicating a diagnostic substitution, and younger children who were newly diagnosed with ASD, indicating a higher level of awareness.[30]

One example illustrating the complexities that can occur within the educational setting was found based on a review of records in public school districts. Recent research evaluated trends in prevalence of ASD by utilizing changes in access to special education services in public school districts in Wisconsin. The authors found that the overall prevalence of the diagnosis of autism among children enrolled in Wisconsin elementary schools rose from 4.9 to 9.0 per 1,000 from 2002 to 2008. They found that the school districts with the lowest baseline rates for ASD also showed the greatest increase, with the lowest octile growing from 0.5 cases per 1,000 students in 2002 to 7.0 cases per 1,000 students in 2008. Conversely, the school districts with the highest baseline rates showed no statistical difference in the rates reported over the 6-year period, with baseline values at 11.2 per 1,000 and rates at the end of the study calculated as 12.3 per 1,000 students. At the time of the publication, the authors suggested that the prevalence appeared to be leveling off, with the gap between districts narrowing.[31]

The relationship between policies governing access to services and the criteria for diagnosis in the educational setting illustrates the problems with using special education rates to monitor trends in ASD. Experts agree that epidemiological data is a better, and more accurate, source of information.[8] However, for the result to be meaningful over time, the methods for the study and the means for the interpretation of data must remain consistent.

Investigators analyzing the trends evident in the data from the National Survey of Children's Health concluded that parent-reported ASD prevalence is not subject to survey measurement error over time and that this source can be used to accurately measure changes in prevalence. They assert that the increase that has been observed results from newly diagnosed children with previously unrecognized ASD.[19]

One factor that has been consistently cited as contributing to the level of disagreement and uncertainty is the lack of population-based data. Kim, et al. recently reported on a population-based sample of 7-12 year olds in a South Korean community. The study examined both a low-probability sample from the general population and a high-probability sample drawn from special education schools and a disability registry. The prevalence of ASD was estimated to be 2.64% (26.4 per 1,000). Surprisingly, the prevalence was higher in the general population sample at 1.89% (18.9 per 1,000) compared with 0.75% (7.5 per 1,000) in the high-probability group. The

Table 1: Reported Trends in Autism Prevalence

Year of Report	Source	Average Rate per 1,000
	Rates in the United States	
2000	Autism and Developmental Disabilities Monitoring Network	6.7
2001	Massachusetts Review of registry	5.6
2002	Autism and Developmental Disabilities Monitoring Network	6.7
2002	Wisconsin public school records	4.9
2003- 2004	National Health Interview Survey Parent report	5.7
2003- 2004	National Survey of Children's Health Parent report	5.5
2005	Massachusetts Review of registry	9.3
2006	Autism and Developmental Disabilities Monitoring Network	9.0
2008	Wisconsin public school records	9.0
2008	Autism and Developmental Disabilities Monitoring Network Surveillance	11.3
2013	National Survey of Children's Health Parent Report	20.0
	Rates in Other Countries	
1996-2001	Taiwan National Health Insurance Program	3.0
1999-2000	Portuguese Mainland Portuguese Azores Islands Screening administered to teachers in randomly selected schools followed by team-based diagnostic assessment	0.92 1.56
2001	Sweden Medical Record Review	5.34
2004	Israel Review of disability benefits	0.19
2003	Montreal, Quebec, Canada School records	6.5
2005	Hong Kong Registry	1.61
2006	South Thames, U.K. Screening	11.6
2011	South Korea Population-based sample with diagnostic evaluation	26.4

investigators concluded that since two-thirds of the ASD cases were found in the mainstream school population and had not been previously diagnosed or treated, more rigorous screening and comprehensive population coverage would be necessary to provide more accurate ASD prevalence estimates. Furthermore, the investigators cite this research as an indication of the need for better detection, assessment, and services.[32]

A number of other countries have been evaluating rates of Autism Spectrum Disorder. In addition to the research recently published from South Korea, trends in the reported numbers

of people with ASD were analyzed in Israel by reviewing disability benefits registered with the National Insurance Institute from 1972 to 2004. As recently as 1982-1984, the reported incidence rate was zero. The peak occurred in 2004 with an incidence rate of 0.19 per 1,000.[33] Epidemiological data for ASD was evaluated in China over a period from 1986 to 2005 using a registry in Hong Kong. The prevalence was calculated at 1.61 per 1,000.[34] Researchers in Taiwan evaluated newly diagnosed cases of ASD from the National Health Insurance Research Database from 1996-2004. The peak of the cumulative incidence rate was found in the year 1998, at a level of 0.41% or 4.1 per 1,000. Investigators noted a 14% increase in ASD comparing the birth cohorts from 2000-2004 with cohorts from 1996-1999. The overall cumulative incidence rate for the time period studied was 0.30% or 3.0 per 1,000.[35] The Special Needs Autism Project quantified the prevalence of ASD among children residing in South Thames, United Kingdom. Children with a current clinical diagnosis of ASD, and those who were deemed to be at risk for being an undetected case, were screened, with a subset receiving a comprehensive diagnostic evaluation. The total prevalence for all ASD was calculated to be 11.6 per 1,000.[36] Analyzing data that was collected during the 1999-2000 school year, researchers in Portugal noted regional differences in the prevalence of ASD between the mainland and the Azores Islands, with a rate of 0.92 per 1,000 in the mainland increasing to 1.56 per 1,000 in the islands.[37] A population-based study conducted in Göteborg, Sweden screened the total population born in 1977-1994 and still residing in the city in 2001. The rate for any autism spectrum disorder over the entire 18-year period was 53.3 per 10,000, with a sharp increase among the last 6-year cohort to a rate of 80.4 per 10,000.[38]

Many of the studies reporting the prevalence rates for ASD do not differentiate the specific type of disorder. Researchers in Montreal, Canada analyzed the overall prevalence and the results by sub-type in 2003. They found the overall rate to be 6.5 per 1,000 with rates for autistic disorder at 2.2 per 1,000 and Asperger's syndrome at 1.0 per 1,000. The most common sub-type was PDD-NOS with a rate of 3.3 per 1,000.[39]

The reported trends and the sources of data are summarized in Table 1. As can be seen by the summary, rates per 1,000 vary over time, location, and methods used to collect the data. In response to the apparent trends and varying interpretations of data, researchers at McGill University conducted a comprehensive and systematic review of the literature, published in 2009, that attempted to put information gained from numerous epidemiological studies into perspective.[40] Their work had three specific aims: to clarify how cases of pervasive developmental disorders are defined and identified in epidemiological surveys; to develop the best estimates for the prevalence of autism and related pervasive developmental disorders while factoring in the methodological implications; and to interpret trends observed in prevalence rates. The investigators reviewed 57

Table 2: Summary of Prevalence Rates
*rates are reported per 1,000

Condition	Number of Studies Evaluated	Highest Reported Prevalence Rate	Lowest Reported Prevalence Rate	Median Prevalence Rate
Autistic Disorder	47	7.26	0.07	1.27
Asperger Syndrome	12	4.84	0.03	1.1
Childhood Disintegrative Disorder	11	0.092	0	0.02

studies published between 1966 and 2009 from 17 different countries. Table 2 summarizes the results from their in-depth review. The authors note many methodological limitations and potential for lack of reliability but summarize their analysis with a best estimate of 6 to 7 per 1,000 for the prevalence of autism spectrum disorders.

Risk Factors

A myriad of researchers have been investigating possible risk factors for the development of ASD, with the ultimate goal of understanding and ameliorating the underlying cause. Risks may be grouped into factors associated with maternal characteristics and pre- and peri-natal influences; intrinsic factors associated with race, ethnicity, and gender; genetics; and environmental risks.

Maternal Factors, Complications with Pregnancy, Timing of Conception, Environmental Factors

Increased maternal age, advanced paternal age,[41,42] use of fertility drugs, and maternal autoimmune disorders have all been linked with increased risk of ASD. Autism diagnosis is more likely in children born to older mothers, especially those over the age of 45.[18] Evidence from the Nurses' Health Study II suggests that a history of fertility problems and the use of ovulation-inducing drugs is associated with nearly a 2-fold increase in the odds of having a child with autism spectrum disorder (Odds Ratio 1.9).[43] Maternal history of rheumatoid arthritis and celiac disease and a family history of type 1 diabetes were positively associated with increased rates of ASD, suggesting that familial autoimmunity may play a role in the pathogenesis of autism.[44]

Complications during pregnancy have also been studied for association with ASD. A case-control study evaluating twenty-eight different pre-, peri-, and neonatal factors found a statistically significant higher incidence of uterine bleeding, a lower incidence of maternal vaginal infection, and less maternal use of contraceptives during conception as compared with the general neuro-typical population.[45] A study of children born in Western Australia between 1980 and 1995 who were later diagnosed with autism found a variety of obstetric risk factors based on characteristics of the mother, as well as higher rates of labor and delivery complications. Children with ASD were more likely to be born to older parents and were more often firstborn. Mothers of children with ASD had greater frequencies of threatened miscarriage, epidural anesthesia during labor, labor induction, and a labor duration of less than one hour. Children with ASD were more likely to have had fetal distress, delivery by an elective or emergency cesarean section, and an Apgar score of less than 6 at one minute. Because of the large number of factors identified, the investigators suggest that ASD is unlikely to be the result of a single obstetric factor. Instead, they hypothesize that the increased rates of obstetrical complications may in fact be due to underlying genetic factors or perhaps due to an interaction of a variety of risk factors with environmental triggers.[46]

A number of researchers have noted an increased risk of ASD associated with summer conception and spring birth. Earlier research conducted in Israel disputes these findings. A cohort study evaluating data from the Israeli Draft Board's mandatory assessment of 17-year-olds found no association between season of birth and prevalence of ASD.[47] However, more recent studies found that the rate of ASD was calculated at 9.5 per 1,000 conceptions in summer, as compared with rates of 5.1, 4.6, and 5.7 per 1,000 in the spring, autumn, and winter months, respectively. When comparing the odds for ASD in summer conception with autumn conception, the odds were found to be doubled (OR 2.08; 95% CI 1.18 – 3.70). The increased rates associated with summer conception correspond to a peak in ASD in spring births.[48] Researchers from the Johns Hopkins Bloomberg School of Public Health found three peaks in the singleton births of children with ASD in April, June, and October, with similar peaks in multiple births occurring about 2-4 weeks earlier.[49] The evidence suggests that the presence of seasonal trends in ASD birth rates supports the hypothesis that there are non-heritable factors playing a significant role in the development of ASD during the pre- or perinatal period.[49] The investigators urge that further study on the seasonal influences of autism is needed to identify possible environmental risk factors and more clearly to understand their mechanisms and the timing for influencing the development of ASD.[48] Investigators have explored the association between maternal vitamin D deficiency as the underlying risk factor to explain seasonal variation in birth rates. They hypothesize that vitamin D deficiency and wintertime solar ultraviolet B radiation may affect fetal brain development and the maternal immune system during pregnancy.[50]

To further support the possibility of environmental factors playing a role in the development of ASD, there is increasing evidence that people with ASD show higher levels of toxins in their bodies and that they are more likely to have reduced ability appropriately to metabolize and to excrete environmental toxins after exposure. Evidence is growing that links higher rates of ASD near EPA Superfund sites, suggesting a combined effect of genetic predisposition and environmental triggers.[51]

Race, Ethnicity, Gender

A number of studies have found increased rates of ASD among males. Investigators reviewing data collected in Massachusetts for children born between 2001 and 2005 found that boys were 4.5 times more likely than girls to be given an early diagnosis of ASD.[18] In 2007, the Developmental Disabilities Monitoring Network found differential rates in males versus females ranging from 3.4:1, in three reporting states, to 6.5:1 in the state with the highest gender differential.[16] The National Survey of Children's Health also found that the increase in prevalence was greatest for boys.[19] The greater association with male gender is not completely understood but may indicate that causative genes occur more frequently on the X chromosome.[52]

Earlier research found differing rates based on race and ethnicity. In 2000, five of six network surveillance sites reported no statistically significant differences in the rate of ASD between non-Hispanic black and non-Hispanic white children. The exception was found in the state of Georgia, with statistically significant higher rates of ASD among white children. In 2003-2004, the prevalence of autism was found to be lower among children of Latino heritage at rates of 2.6 per 1,000 versus 5.1 per 1,000. The same study found no difference in rates between whites and blacks.[53] In 2007, the Developmental Disabilities Monitoring Network found a higher prevalence among non-Hispanic white children than for non-Hispanic black children.[16]

However, newer work suggests that the variance may, at least in part, be explained by differences in access to care or levels of awareness. Rates for children born in the earlier years of a review conducted between 2001 and 2005 found that white children were 30% more likely than African American children, and 90% more likely than Hispanic children, to be referred for an early-intervention program for ASD. However, by the end of the study period, those differences had disappeared.[18]

Screening and Diagnostic Processes

Screening Process

In 2004, a survey of pediatricians found that 44% of the respondents reported caring for at least ten children with Autism Spectrum Disorders. Despite that level of familiarity with the disorder, only 8% reported that they routinely screened for ASD.[54]

The evaluation process for determining whether an individual has ASD can be considered in three phases: surveillance, screening, and diagnosis. Surveillance is the ongoing process of identifying children who may be at risk for developmental delays, whereas screening is the use of standardized tools at specific intervals to support and refine the risk.[8]

The American Academy of Pediatrics developed a policy statement "Identifying Infants and Young Children with Developmental Disorders in the Medical Home: An Algorithm for Developmental Surveillance and Screening" in 2006.[55] The algorithm provides a step-by-step process for the actions and decisions used in routine surveillance and screening and recommends that developmental surveillance should occur at every well-child and preventive visit throughout childhood. The policy recommends evaluating four areas in the surveillance process: determining whether there is a history of a sibling previously diagnosed with ASD, evaluating parental concern, evaluating concerns raised by other care givers, and checking for attainment of normal developmental milestones.[56] If two or more of these four areas raise a red flag for the possibility of ASD, it is recommended that a formal screening be considered.

As suggested by this algorithm, screening can be done when a child is at high risk of having an autism spectrum disorder. Screenings may be done in the health care setting or in the educational environment. When screenings are done in the health care setting, they may commonly be performed by pediatricians, nurse practitioners, speech-language pathologists, behavioral health professionals, or other types of healthcare providers. The American Academy of Pediatrics recommends that a standardized screening tool be used at any point when concerns about ASD are raised by a parent without prompting, as a result of observations made by the clinician, or when questions are raised about socialization, communication, or play behaviors. In addition, the American Academy of Pediatrics also recommends administering a standardized screening instrument for ASD on all children at the 18-month preventive care visit. A repeated screening at the age of 24 months is also recommended in an effort to identify children who may regress after age 18 months.[55,57] Doctors of optometry may not typically include screening for ASD in their current practice, but with some additional training and education, screening tests could be incorporated.

In the school setting, screenings for autism spectrum disorder might be performed by educational psychologists, school nurses, or social workers. Teachers may be asked to complete questionnaires or screening evaluations based on their classroom observations.

Accuracy of the screening and diagnostic processes has been reported in the literature for a variety of tests by assessing sensitivity, specificity, predictive value, inter-rater reliability, and test-retest reliability. Confounders can arise when instruments are translated for different languages and different cultures. Accuracy of the screening and diagnosis can be further complicated by commonly occurring co-morbidities such as other neurological or behavioral health disorders. Stability of diagnosis can be called into question, particularly when the diagnosis occurs at a young age.

The literature does describe a number of screening instruments that have been evaluated for their utility in the identification of children with ASD. It is important to consider the age of the child when selecting the correct screening instrument. Reports have identified a number of problems with screening accuracy through rigorous and systematic evaluations

of sensitivity and specificity. Because of the importance of early diagnosis of ASD, and the value of referral for a diagnostic work-up and inclusion in early intervention programs, it is essential that health care providers utilize well established screening instruments to maximize their time and increase the reliability of the assessment.[58]

The Autism Spectrum Quotient-Children's Version (AQ-Child) is a questionnaire that relies on parent reporting to quantify autistic traits in children aged 4 to 11 years. The AQ-Child was evaluated in a population-based study and found to have both sensitivity and specificity levels of 95%.[59]

Another tool is the Social Responsiveness Scale (SRS). The SRS is a brief quantitative measure of autistic traits designed for use in 4- to 18-year olds. The SRS is designed for use by parents, care-givers, or teachers to measure children's social impairments in a natural social setting.[60] The measures include social awareness, social information processing, capacity for reciprocal social communication, social anxiety/avoidance, and autistic preoccupations and traits. Investigators found that internal consistency, long-term stability, and inter-rater reliability were all high. It was noted that the SRS is capable of distinguishing children with ASD from children who have other psychiatric disorders or mental retardation.[61] Another version of the Social Responsiveness Scale was recently developed for three-year-olds in an effort to support earlier diagnosis. Inter-rater reliability comparing mothers' ratings with ratings by teachers and test-retest reliability were both found to be highly correlated (Pearson's r=0.75 for each). The SRS was also found to agree with both the Vineland Adaptive Behavior Composite (Pearson's r=-0.86) and the scores for social impairment on the Autism Diagnostic Interview-Revised (Pearson's r=0.63). The investigators did note that quantitative autistic scores improved over time, regardless of treatment conditions.[62]

A study of children at high risk of ASD aged 20-40 months evaluated the accuracy of three screening instruments: the Social Communication Questionnaire (SCQ), the Autism Diagnostic Interview-Revised (ADI-R), and the Autism Diagnostic Observation Schedule (ADOS). The investigators determined that the SCQ is likely to result in a high number of false-positive findings. The SCQ and the ADI-R were found to be highly correlated, but the agreement with clinical diagnosis was poor for both measures. The authors suggest that the ADOS should be considered the most valid and reliable measure for very young children who are considered at risk for ASD.[63]

Extremely preterm birth (less than 26 weeks gestation) is considered to be a risk factor for ASD that warrants screening. The Social Communication Questionnaire (SCQ) was used to evaluate a birth cohort of preterm survivors at age 11. A cut-off score of ≥ 14 was found to have the optimal utility with a sensitivity of 91% and specificity of 86%. The investigators noted that the screening had a low positive predictive value of 31%, resulting in a high rate of false-positives and over-referrals. They suggest that these children with false-positive results on

the SCQ represent a high-risk group who may have other types of neuro-developmental, cognitive, and behavioral disabilities for whom further assessment would be beneficial anyway.[64]

Infants who are born into families with one or more children who have been previously diagnosed with ASD are considered to be at higher risk and should be screened as early as possible. The Autism Observation Scale for Infants (AOSI) was developed to detect and monitor early signs of autism as soon as they emerge in high-risk infants. The instrument is currently being evaluated for use at 6, 12, and 18 months with early indications that inter-rater reliability and test-retest reliability are sufficient to make the instrument useful for early screenings.[65]

Another screening instrument designed for use in very young children is the Communication and Symbolic Behavior Scales Developmental Profile Infant-Toddler (CSBS DP IT checklist). The instrument consists of 24 items for the parents to answer about their child's emotions, eye gaze, communication, gestures, and other behaviors, and it takes about 5 minutes to complete. The checklist is available online for free download and is designed to be used in pediatricians' offices during well-child check-ups or routine visits, childcare centers, or other facilities serving infants and toddlers and their families. The checklist was not designed specifically for ASD but for a variety of developmental delays. Recent research found the instrument to be accurate 75% of the time when used for detecting ASD.[66,67]

To further evaluate familial patterns of ASD, and to gain a better understanding of genetic predisposition, the Broader Phenotype Autism Symptom Scale (BPASS) was developed for use with children who have a diagnosis along with their family members. The instrument has been able to differentiate scores by affected children from their unaffected parents, and it may be a useful tool in screening for ASD among siblings.[68]

It is also important to note that the different subcategories within the ASD spectrum may perform differently on screening tests. The Childhood Asperger Syndrome Test (CAST) uses parental responses to screen for high-functioning autism or Asperger Syndrome, which typically has milder and fewer symptoms as compared with autism disorder. The reliability was determined to be accurate for use among children enrolled in mainstream primary school, and test-retest reliability in the general population was found to be high (kappa test statistic for agreement 0.70; Spearman's rho correlation 0.83).[69] The test-retest reliability among a high-scoring group was determined to be of moderate level (kappa test statistic for agreement 0.41; Spearman's rho correlation 0.67).[70]

A number of screening instruments have also been translated into different languages and assessed for their accuracy. It can be particularly important to ensure that the screening process is linguistically and culturally appropriate because the evaluation of both language delays and intelligence can be affected when a child's primary language is a language other than English. The Modified Checklist for Autism in

Toddlers (M-CHAT) has been translated into several languages. Its Arabic translation demonstrated attainment of a sensitivity level of 0.86, a specificity level of 0.88, and a positive predictive value of 0.88.[71] The Autism Screening Questionnaire (ASQ) has been translated into Portuguese and adapted to Brazilian culture. Measurement properties of the translated instrument are deemed to be satisfactory with a sensitivity of 0.925 and specificity of 0.955.[72] The ASQ has been translated into Dutch with good reliability.[73] The Diagnostic Interview for Social and Communication Disorders (DISCO-10) has been translated into Swedish with good psychometric properties.[74]

Given the number of screening instruments available, and the apparent variation in accuracy based on the child's age, symptom severity, and ASD spectrum sub-type, selection of an appropriate screening instrument can be daunting. To gain better insight, researchers at the Ohio State University evaluated five different screening instruments. Each of the instruments was designed to be completed by a care-giver and to be administered to children over the age of three. The investigators reviewed the Social Communication Questionnaire (SCQ), the Gilliam Autism Rating Scale/Gilliam Autism Rating Scale-Second Edition (GARS/GARS-2), Social Responsiveness Scale (SRS), Autism Spectrum Screening Questionnaire (ASSQ), and the Asperger Syndrome Diagnostic Scale (ASDS). Results indicated that the SCQ performed well, with the SRS and ASSQ showing promise. The GARS/GARS-2 and ASDS demonstrated poor levels of sensitivity. The investigators emphasize that their review shows that ASD screening instruments are in need of much more scientific scrutiny.[75]

In 2007, the American Academy of Pediatrics and the National Center on Birth Defects and Developmental Disabilities at the Centers for Disease Control and Prevention collaborated to develop a communication piece called "Autism A.L.A.R.M."[76] This acronym stands for the phrases:
- Autism is prevalent
- Listen to parents
- Act early
- Refer
- Monitor

Additional information is provided in bullet-point format for each section as a short reminder for appropriate and recommended steps to improve awareness for appropriate screening, diagnosis, treatments, and referrals. The one-page flyer serves to highlight the prevalence of ASD, the value of screening, reminders to listen to care-givers' concerns, and the urgency of making referrals to both specialists who care for children with ASD and to early intervention programs with the ultimate goal of improved outcomes.[8]

The American Academy of Pediatrics has classified ASD-specific screening tools designed to be used for all children within the context of a primary care medical home as "Level 1" instruments.[77] Level 1 screening instruments are designed with the goal of differentiating children who are at risk for ASD from neuro-typically developing children. Level 1 screening instruments include the Checklist of Autism in Toddlers (CHAT), CHAT-Denver Modifications, Checklist for Autism in Toddlers-23 (CHAT-23), Modified Checklist for Autism in Toddlers (M-CHAT), and Pervasive Developmental Disorders Screening Test-II, Primary Care Screener (PDDST-II PCS).[8]

Several aspects of surveillance and screening underwent an evidence-based review for the development of a clinical practice guideline summarizing screening and diagnosis of autism.[78] Reviewers evaluated six specific aspects. The evidence-based process confirmed that screening specifically for autism should be performed on all children failing routine developmental surveillance procedures using either the Checklist for Autism in Toddlers (CHAT) or the Autism Screening Questionnaire (ASQ).

Modified Checklist for Autism in Toddlers: Usefulness in Optometric Practice

In review of the differing screening methods, the Modified Checklist for Autism in Toddlers (M-CHAT) is a tool designed to identify children between 16 and 30 months of age who are at risk for autism and who should be referred to the appropriate healthcare provider to provide an evaluation for autism spectrum disorder or a related developmental delay. According to the developers of the M-CHAT, the M-CHAT can be administered and scored during a well-child visit. They also advise that the instrument can be utilized by specialists or other professionals to screen for other developmental delay and autism. Doctors of Optometry are not specifically listed as one of the healthcare providers who can use this instrument. However, as primary care providers, optometrists can fill an important role in the process of screening for autism. The paper version of the M-CHAT can easily be administered, either when concerns arise or as part of a routine intake process. In addition, utilizing online resources makes it relatively simple to attain, administer, and score the test to assess for a child's risk of autism so they may be appropriately referred as needed.

The M-CHAT is a checklist comprised of 23 yes or no questions which a parent answers based on observed behaviors of their child (Table 3). It was designed and validated based on parent responses for children aged 16 to 30 months. The parent completes the checklist as it pertains to how the child usually is. If a behavior is questioned, and the child only rarely (once or twice) has demonstrated the behavior, then the answer should reflect that the child does not do this behavior. After the parent has completed the form, the provider administers a set of specifically designed follow-up questions. Failure of two of the critical items, or failure of any 3 items, warrants referral to a specialist for a more thorough evaluation and possible diagnostic assessment.

An online version can also be found at www.mchatscreen.com or m-chat.org. It is intended to be administered by a trained healthcare professional. Parents may also complete this

Table 3: M-CHAT

Please fill out the following about your child's usual behavior, and try to answer every question. If the behavior is rare (you've only seen it once or twice), please answer as if your child does not do it.

ITEM

1. Does your child enjoy being swung, bounced on your knee, etc.?
2. Does your child take an interest in other children?
3. Does your child like climbing on things, such as up stairs?
4. Does your child enjoy playing peek-a-boo/hide-and-seek?
5. Does your child ever pretend, for example, to talk on the phone or take care of a doll or pretend other things?
6. Does your child ever use his/her index finger to point, to ask for something?
7. Does your child ever use his/her index finger to point, to indicate interest in something?
8. Can your child play properly with small toys (e.g. cars or blocks) without just mouthing, fiddling, or dropping them?
9. Does your child ever bring objects over to you (parent) to show you something?
10. Does your child look you in the eye for more than a second or two?
11. Does your child ever seem oversensitive to noise? (e.g., plugging ears)
12. Does your child smile in response to your face or your smile?
13. Does your child imitate you? (e.g., you make a face-will your child imitate it?)
14. Does your child respond to his/her name when you call?
15. If you point at a toy across the room, does your child look at it?
16. Does your child walk?
17. Does your child look at things you are looking at?
18. Does your child make unusual finger movements near his/her face?
19. Does your child try to attract your attention to his/her own activity?
20. Have you ever wondered if your child is deaf?
21. Does your child understand what people say?
22. Does your child sometimes stare at things or wander with purpose?
23. Does your child look at your face to check your reaction when faced with something unfamiliar?

© 1999 Diana Robins, Deborah Fein, & Marianne Barton

on their own. If parents complete the screening online, they will answer the same 23 questions. Based on their answers, they will automatically be asked the follow-up questions. When the parent has finished, they will be given a printout which tells them the risk that the child has for autism and which answers indicate this; however, results should be discussed with the patient's healthcare provider regardless of the score. It is also worthwhile to note that the M-CHAT has been translated into over 50 other languages, although it has not been validated in any language other than English.

The developers of the M-CHAT, Robins, Fein, and Barton, developed the test with the intent to detect as many children with autism as possible. This strategy tends to rely on high test sensitivity but low test specificity and can result in a high false positive rate. The M-CHAT screening strategy will result in over-referrals in an effort to avoid the potential of missing children who may benefit from an early intervention. As a result, the test developers introduced the structured follow-up interview. They state that even with the follow-up questions, a number of children who fail the M-CHAT will not be diagnosed with autism but can still be at risk for other delays. Most organizations recommend that a structured follow-up interview be provided every time the M-CHAT is administered due to the high false positive rate. As with any screening instrument, there are also cases when the M-CHAT may not detect autism when it is actually present. Nonetheless, it is a good tool to have in the toolbox.

Diagnostic Process

A review of the body of literature about ASD can produce varying results due to the diversity in the diagnostic process. Some publications rely on the standardized diagnostic criteria found in the DSM-IV, while others used the International Classification of Disease, 10th edition (ICD-10). Some reports rely on diagnosis by a clinical specialist, while others are based on parental communication or past history of a diagnosis.[79] Beginning in May 2013, some may be adopting the DSM-5 criteria.

Diagnosing ASD is not a definitive process, in particular when differentiating between the different types and subcategories and when establishing an estimate of the level of severity. Autism Spectrum Disorders are diagnosed purely from a behavioral standpoint by determining whether certain behaviors are present.[79] Typically, this involves a formal interview, administration of questionnaires, and observation of the child, and it frequently takes place in a setting that is unfamiliar to the child.

In the healthcare setting, the diagnostic process most commonly involves a multidisciplinary team. The professionals that should be involved include a psychologist, a psychiatrist, a speech and language pathologist, and a neurologist. It can also be helpful to include a physical therapist and/or an occupational therapist. Perhaps all too infrequently, a doctor of optometry may also be a participant in the diagnostic team. Genetic testing may be recommended, as well as screening for related medical issues such as sleep difficulties or gastrointestinal conditions. The diagnostic process can be done as a group, in situations when the health care delivery system allows, or may be conducted as a series of individual appointments with each type of health care professional in different settings or locations.[79,80]

The American Psychiatric Association's Diagnostic and Statistical Manual-IV, Text Revision (DSM-IV-TR) 1 provides standardized criteria to help diagnose ASD.[81] The criteria are summarized in Table 4.

As previously mentioned, the DSM-5 diagnostic criteria were published in May 2013. These new criteria are summarized in Table 5. This change has been somewhat controversial. Criticism regarding the conceptualization, collapsing of categories, and heterogeneity in the phenotype expression has been leveled.[82-85] Implications for over- and under-diagnosis must be considered.

School systems may also provide diagnostic assessments based on observations made in the educational setting. The school district's multidisciplinary team usually includes a school psychologist, a special education teacher, a speech and language pathologist, an occupational therapist, a

Table 4: DSM-IV Criteria

Diagnostic Criteria for 299.00 Autistic Disorder

A. Six or more items from (1), (2), and (3), with at least two from (1), and one each from (2) and (3):

  1. qualitative impairment in social interaction, as manifested by at least two of the following:

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

     b. failure to develop peer relationships appropriate to developmental level

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

     d. lack of social or emotional reciprocity

  2. qualitative impairments in communication as manifested by at least one of the following:

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

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

     c. stereotyped and repetitive use of language or idiosyncratic language

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

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

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

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

     c. stereotyped and repetitive motor manners (e.g., hand or finger flapping or twisting, or complex whole-body movements)

     d. persistent preoccupation with parts of objects

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

C. The disturbance is not better accounted for by Rett's Disorder or Childhood Disintegrative Disorder.

Diagnostic Criteria for 299.80 Asperger's Disorder

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

  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 to other people)

  4. lack of social or emotional reciprocity

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

  1. encompassing preoccupation with one or more stereotyped and restricted patterns of interest that is abnormal either in intensity of 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, or complex whole-body movements)

  4. persistent preoccupation with parts of objects

C. The disturbance causes clinically significant impairment in social, occupational, or other important areas of functioning.

D. There is no clinically significant general delay in language (e.g., single words used by age 2 years, communicative phrases used by age 3 years).

E. There is no clinically significant delay in cognitive development or in the development of age-appropriate self-help skills, adaptive behavior (other than in social interaction), and curiosity about the environment in childhood.

F. Criteria are not met for another specific Pervasive Developmental Disorder or Schizophrenia.

299.90 Pervasive Developmental Disorder Not Otherwise Specified (Including Atypical Autism)

This category should be used when there is a severe and pervasive impairment in the development of reciprocal social interaction associated with impairment in either verbal or nonverbal communication skills or with the presence of stereotyped behavior, interests, and activities, but the criteria are not met for a specific Pervasive Developmental Disorder, Schizophrenia, Schizotypal Personality Disorder, or Avoidant Personality Disorder. For example, this category includes "atypical autism" - presentations that do not meet the criteria for Autistic Disorder because of late age at onset, atypical symptomatology, subthreshold symptomatology, or all of these.

Diagnostic Criteria for 330.80 Rett's Disorder

A. All of the following:

  1. apparently normal prenatal and perinatal development

  2. apparently normal psychomotor development through the first 5 months after birth

  3. normal head circumference at birth

B. Onset of all of the following after the period of normal development:

  1. deceleration of head growth between ages 5 and 48 months

  2. loss of previously acquired purposeful hand skills between 5 and 30 months with the subsequent development of stereotyped hand movements (e.g., hand-wringing or hand washing)

  3. loss of social engagement early in the course (although often social interaction develops later)

  4. appearance of poorly coordinated gait or trunk movements

  5. severely impaired expressive and receptive language development with severe psychomotor retardation

Diagnostic Criteria for 299.10 Childhood Disintegrative Disorder

A. Apparently normal development for at least the first 2 years after birth as manifested by the presence of age-appropriate verbal and nonverbal communication, social relationships, play, and adaptive behavior.

B. Clinically significant loss of previously acquired skills (before age 10 years) in at least two of the following areas:

  1. expressive or receptive language

  2. social skills or adaptive behavior

  3. bowel or bladder control

  4. play

  5. motor skills

C. Abnormalities of functioning in at least two of the following areas:

  1. qualitative impairment in social interaction (e.g., impairment in nonverbal behaviors, failure to develop peer relationships, lack of social or emotional reciprocity)

  2. qualitative impairments in communication (e.g., delay or lack of spoken language, inability to initiate or sustain a conversation, stereotyped and repetitive use of language, lack of varied make-believe play)

  3. restricted, repetitive, and stereotyped patterns of behavior, interest, and activities, including motor stereotypes and mannerisms

D. The disturbance is not better accounted for by another specific Pervasive Developmental Disorder or by Schizophrenia

Table 5: DSM-V Criteria

Diagnostic Criteria for 299.00 Autism Spectrum Disorder

A. Persistent deficits in social communication and social interaction across multiple contexts, as manifested by the following, currently or by history (examples are illustrative, not exhaustive; see text):
  1. Deficits in social-emotional reciprocity, ranging, for example, from abnormal social approach and failure of normal back-and-forth conversation; to reduced sharing of interests, emotions, or affect; to failure to initiate or respond to social interactions.
  2. Deficits in nonverbal communicative behaviors used for social interaction, ranging, for example, from poorly integrated verbal and nonverbal communication; to abnormalities in eye contact and body language or deficits in understanding and use of gestures; to a total lack of facial expressions and nonverbal communication.
  3. Deficits in developing, maintaining, and understanding relationships, ranging, for example, from difficulties adjusting behavior to suit various social contexts; to difficulties in sharing imaginative play or in making friends; to absence of interest in peers.
  Specify current severity: **Severity is based on social communication impairments and restricted, repetitive patterns of behavior.** (see next section in table)

B. Restricted, repetitive patterns of behavior, interests, or activities, as manifested by at least two of the following, currently or by history (examples are illustrative, not exhaustive; see text):
  1. Stereotyped or repetitive motor movements, use of objects, or speech (e.g., simple motor stereotypes, lining up toys or flipping objects, echolalia, idiosyncratic phrases).
  2. Insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior (e.g., extreme distress at small changes, difficulties with transitions, rigid thinking patterns, greeting rituals, need to take same route or eat same food every day).
  3. Highly restricted, fixated interests that are abnormal in intensity or focus (e.g., strong attachment to or preoccupation with unusual objects, excessively circumscribed or perseverative interests).
  4. Hyper- or hyporeactivity to sensory input or unusual interest in sensory aspects of the environment (e.g., apparent indifference to pain/temperature, adverse response to specific sounds or textures, excessive smelling or touching of objects, visual fascination with lights or movement).
  Specify current severity: **Severity is based on social communication impairments and restricted, repetitive patterns of behavior.** (see next section in table)

C. Symptoms must be present in the early developmental period (but may not become fully manifest until social demands exceed limited capacities, or may be masked by learned strategies in later life).

D. Symptoms cause clinically significant impairment in social, occupational, or other important areas of current functioning.

E. These disturbances are not better explained by intellectual disability (intellectual developmental disorder) or global developmental delay. Intellectual disability and autism spectrum disorder frequently co-occur; to make comorbid diagnosis of autism spectrum disorder and intellectual disability, social communication should be below that expected for general developmental level.
  Note: Individuals with well-established DSM-IV diagnosis of autistic disorder, Asperger's disorder, or pervasive developmental disorder not otherwise specified should be given the diagnosis of autism spectrum disorder. Individuals who have marked deficits in social communication, but whose symptoms do not otherwise meet criteria for autism spectrum disorder, should be evaluated for social (pragmatic) communication disorder.
  Specify if: With or without accompanying intellectual impairment; With or without accompanying language impairment; Associated with a known medical or genetic condition or environmental factor; Associated with another neurodevelopmental, mental or behavioral disorder; With catatonia.

Severity levels for autism spectrum disorder

A. Level 3 "Requiring very substantial support"
  1. Social communication: Severe deficits in verbal and nonverbal social communication skills cause severe impairments in functioning, very limited initiation of social interactions, and minimal response to social overtures from others. For example, a person with few words of intelligible speech who rarely initiates interaction and, when he or she does, makes unusual approaches to meet needs only and responds to only very direct social approaches.
  2. Restricted, repetitive behaviors: Inflexibility of behavior, extreme difficulty coping with change, or other restricted/repetitive behaviors markedly interfere with functioning in all spheres. Great distress/difficulty changing focus or action.

B. Level 2 "Requiring substantial support"
  1. Social communication: Marked deficits in verbal and nonverbal social communication skills; social impairments apparent even with supports in place; limited initiation of social interactions; and reduced or abnormal responses to social overtures from others. For example, a person who speaks simple sentences, whose interaction is limited to narrow special interests, and who has markedly odd nonverbal communication.
  2. Restricted, repetitive behaviors: Inflexibility of behavior, difficulty coping with change, or other restricted/repetitive behaviors appear frequently enough to be obvious to the casual observer and interfere with functioning in a variety of contexts. Distress and/or difficulty changing focus or action.

C. Level 1 "Requiring support"
  1. Social communication: Without supports in place, deficits in social communication cause noticeable impairments. Difficulty initiating social interactions, and clear examples of atypical or unsuccessful response to social overtures of others. May appear to have decreased interest in social interactions. For example, a person who is able to speak in full sentences and engages in communication but whose to-and-fro conversation with others fails, and whose attempts to make friends are odd and typically unsuccessful.
  2. Restricted, repetitive behaviors: Inflexibility of behavior causes significant interference with functioning in one or more contexts. Difficulty switching between activities. Problems of organization and planning hamper independence.

psychiatrist, and the child's classroom teacher. For young children, an early intervention specialist may also be included. The school's primary focus is to determine the child's educational needs, so recommendations for medical interventions and treatments are usually not included in this type of assessment. Though medical recommendations are not usually included, children may sometimes be referred for a medical evaluation if there are suspected seizures or if there are issues with medications. School systems tend to rely heavily on the results of standardized tests, with the goal of making the most objective determination possible.[79]

Currently, the Autism Diagnostic Observation Schedule (ADOS) and the Autism Diagnostic Interview-Revised (ADI-R) are considered to be the "gold standard" in the diagnostic evaluation for autism.[86] Researchers have also found that the inclusion of an assessment of an individual's adaptive functioning, as measured by the Vineland Adaptive Behavior Scales, can significantly improve diagnostic accuracy.[87]

One of the strategies that can be used in the diagnostic process is a structured or semi-structured interview system. One example is the Pervasive Developmental Disorders Assessment System (PDDAS) that was developed in Japan. The PDDAS consists of 91 items and takes approximately 90 minutes to

administer. Inter-rater reliability appears to be high, with good measures of discriminant validity.[88]

Questions remain about the earliest age at which diagnosis of ASD can be made. To help address this concern, investigators evaluated the reliability and stability of diagnoses made with very young children, around the age of 14 months. Results were promising, indicating that reliability and stability of diagnoses reviewed at 23 months and 42 months were consistent. At 23 months it was determined that the inter-rater reliability of a diagnosis of ASD was 87% with an overall stability for the whole category of ASD at 91%. Stability varied with different diagnoses within the autism spectrum. The lowest stability was found for PDD-NOS at 54% and for autistic disorder at 63%. At 42 months the majority of diagnostic changes were due to decreased symptom severity, which allowed some children to move from a diagnosis of autistic disorder to PDD-NOS. Those children who moved outside of the ASD diagnostic category at 42 months had demonstrated greater changes in cognitive and language skills as compared with children who had a stable diagnosis of ASD.[89]

The diagnostic process can be further complicated by the presence of other similar conditions, or when co-morbidities are present. For example, childhood onset schizophrenia may present with overlapping symptoms that could meet the ADOS and ADI-R criteria for an autism spectrum diagnosis.[86] Psychiatric co-morbidities of depression, anxiety disorders, and mood disorders are commonly present in half or more individuals with Asperger's syndrome.[90] A study of children diagnosed with PDD-NOS found that 80% had one or more psychiatric co-morbidities with disruptive behavior disorder and anxiety disorder being the most commonly occurring.[91] The likelihood of facing a complex interaction from a variety of interacting conditions has the potential to make the diagnostic process ambiguous and confusing for both the providers and the family members.

New Diagnostic Strategies

New strategies for the diagnosis of ASD rely on more objective and repeatable strategies using genetic profiles, phenotypic characteristics, and biological markers such as electrophysiological changes.[92] Recent advances are paving the way for diagnostic processes based on neuro-anatomical and neuro-physiological differences. Researchers began by noting that enlarged head circumference commonly occurs in children with ASD, and approximately 20-30% have macrocephaly, which is defined as a head circumference greater than 2 standard deviations above the mean value.[93,94] It was suggested that the large head size may result from increased brain volume, which has been found in MRI studies.[95,96]

Studies of brain tissue from people with autism have identified a variety of differences[97-99] that may become useful biomarkers, such as a reduction in the number of Purkinje cells in the cerebellum; abnormalities in the forebrain limbic system; abnormalities in the frontal and temporal lobe cortical microcolumns;[100] developmental changes in cell size and number in several identified regions such as the deep cerebellar nuclei, inferior olive, and diagonal band of Broca; and brainstem abnormalities and neocortical malformations.[101]

Researchers recently made headlines when preliminary data from magnetic resonance imaging (MRI) scans were used to diagnose ASD. An evaluation of the white matter microstructure in regions of the brain responsible for language, social functioning, and emotional behavior was able to differentiate a group of males with ASD from matched controls with 94% accuracy.

In an effort to improve early detection, researchers have begun to note that children who develop autism show signs of different brain responses as early as the first year of life. A recent study conducted in Great Britain found that babies who were first evaluated at six to ten months of age, then followed at the age of three years, showed unusual patterns of brain activity associated with the development of ASD. Babies who were typically developing had a significant difference in brain activity in response to a face looking towards them compared to a face looking away. Babies who later developed symptoms of ASD showed much less difference in brain activity in response to eye contact or a face that was looking away. The investigators hypothesize that direct brain measures might help predict the future risk of autism in babies as young as six months old.[103]

Conclusion

As the expanding specter of the autism "epidemic" continues to unfold, and as clinicians learn more about the condition, its causes, and its manifestations, doctors of optometry must continue to develop their knowledge of the condition and to embrace further their roles and responsibilities in the care for individuals with ASD. The Quality Standards Subcommittee of the American Academy of Neurology and the Child Neurology Society recently published an evidence-based practice guideline entitled "Practice parameter: screening and diagnosis of autism."[78] The guideline names 20 different participating organizations and authors and lists representatives from 8 different associations. The authors and representatives include pediatricians, neurologists, psychiatrists, psychologists, occupational therapists, audiologists, speech-language-hearing specialists, and researchers. The guidelines have been endorsed by eight different professional associations and professional societies. Despite the role that vision plays in the identification of autism symptoms, the diagnostic process, and potential therapies, doctors of optometry, ophthalmologists, and vision professionals were not included at any point in the development or endorsement process. Furthermore, while the guideline includes recommendations for assessment of gait and cranial nerves (along with other assessments) there is no mention of vision, visual function, visual perception, or visual processing noted anywhere in the document.

The authors of the guideline note that:

"The immediate and long-term evaluation and monitoring of autistic individuals requires a comprehensive multi-disciplinary approach and can include one or more of the following professionals: psychologists, neurologists, speech-language pathologists and audiologists, pediatricians, child psychiatrists, occupational therapists, and physical therapists, as well as educators and special educators."[78]

Doctors of optometry can, and should, play an important role in the care for individuals with ASD. It is time that optometrists assume their role as primary care providers to care for vulnerable populations such as individuals on the autism spectrum. By providing needed services, by increasing awareness about the importance of vision, and by assuming an inter-professional role in the collaborative care for complex needs, doctors of optometry will serve the public to help fill in the missing presence in care coordination for patients with ASD.

Acknowledgements

References

1. Morbidity and Mortality Weekly Report (MMWR) Prevalence of Autism Spectrum Disorders — Autism and Developmental Disabilities Monitoring Network, 14 Sites, United States, 2008 Surveillance Summaries. March 30, 2012 / 61(SS03);1-19. http://1.usa.gov/1njIo17

2. Kasari C, Freeman S, Paparella T. Joint attention and symbolic play in young children with autism: A randomized controlled intervention study. J Child Psychol Psychiatry 2006;47:611-20. http://bit.ly/1u41bhv

3. Kelley E, Paul JJ, Fein D, Naigles LR. Residual language deficits in optimal outcome children with a history of autism. J Autism Dev Disord 2006; 36:807-28. http://bit.ly/1vozQWS

4. Sallows GO, Graupner TD. Intensive behavioral treatment for children with autism: Four-year outcome and predictors. Am J Ment Retard 2005;110:417-32. http://bit.ly/1uQqrFZ

5. National Research Council, Committee on Interventions for Children with Autism: Educating Children with Autism. Educating Children with Autism. Washington, DC: National Academies Press, 2001. http://bit.ly/1BlP8wb

6. Myhr G. Autism and other pervasive developmental disorders: exploring the dimensional view. Can J Psychiatry 1998;43:589-95. http://bit.ly/1uQraqH

7. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision. Washington, DC, American Psychiatric Association, 2000:70. http://amzn.to/1rAqxmF

8. Johnson CP, Myers SM. The Council on Children with Disabilities. Identification and evaluation of children with autism spectrum disorders. Pediatrics 2007;120:1183-215. http://amzn.to/1rAqxmF

9. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Washington, DC: American Psychiatric Association, 2013. http://bit.ly/1uv0OOr

10. Ganz ML. The lifetime distribution of the incremental societal costs of autism. Arch Pediatr Adolesc Med 2007;161:343-9. http://bit.ly/1uQs7zg

11. Knapp M, Rome, R, Beechum J. Economic cost of autism in the UK. Autism 2009;13:317-36. http://bit.ly/1omDmfh

12. Montes G, Halterman JS. Association of childhood autism spectrum disorders and loss of family income. Pediatrics 2008;121:821-6. http://bit.ly/1qGy4eb

13. Autism Society. http://www.autism-society.org/about-autism/. Last Accessed September 23, 2011.

14. Datz T. Autism has high costs to U.S. society. Harvard School of Public Health Press Releases 2006. http://bit.ly/1sCr7lS Last Accessed September 23, 2011.

15. Prevalence of autism spectrum disorders--autism and developmental disabilities monitoring network, six sites, United States, 2000. MMWR Surveillance summaries : Morbidity and mortality weekly report Surveillance summaries / CDC. 2007;56(1):1-11. Epub 2007/02/09. http://bit.ly/1qGymBI

16. Autism and Developmental Disabilities Monitoring Network Surveillance Year 2002 Principal Investigators; Centers for Disease Control and Prevention. Prevalence of autism spectrum disorders – autism and developmental disabilities monitoring network, 14 sites, United States, 2002. MMWR Surveill Summ 2007;56(1):12-28. http://1.usa.gov/1rlcVMJ

17. Centers for Disease Control and Prevention. Mental health in the United States: parental report of diagnosed autism in children age 4-17 years – United States, 2003-2004. MMWR Morb Wkly Rep 2006; 55(17):481-6. http://1.usa.gov/ZhHfwb

18. Manning SE, Davin CA, Barfield WD, Kotelchuck M, et al. Early diagnoses of autism spectrum disorders in Massachusetts birth cohorts, 2001-2005. Pediatrics 2011;127(6):1043-51. Epub 2011/05/18. http://bit.ly/1vnSKvR

19. Blumberg SJ, Bramlett MD, Kogan MD, Schieve LA, et al. Changes in prevalence of parent-reported autism spectrum disorder in school-aged US children: 2007 to 2011-2012. National Health Statistics Reports 2013;65:1-11. http://bit.ly/ZhHvLO

20. Mulvihill B, Wingate M, Kirby RS, Pettygrove S, et al. Prevalence of autism spectrum disorders – Autism and Developmental Disabilities Monitoring Network, United States, 2006. MMWR Surveill Summ. 2009;58(10):1-20. http://bit.ly/1vfloRQ

21. Wiggins LD, Baio J, Rice C. Examination of the time between first evaluation and first autism spectrum diagnosis in a population-based sample. J Dev Behav Pediatr 2006;27:S79-S87. http://bit.ly/1omEbVp

22. Gernsbacher MA, Dissanayake C, Goldsmith HH, Mundy PC, et al. Autism and deficits in attachment behavior. Science 2005;159:37-44. http://bit.ly/1omEbVp

23. Barbaresi WJ, Katusic SK, Colligan RC, Weaver AL, Jacobsen SJ. The incidence of autism in Olmsted County, Minnesota, 1976-1997: results from a population-based study. Arch Pediatr Adolesc Med 2005;159:37-44. http://bit.ly/1DIumLf

24. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 3rd Edition (DSM-III). Washington, DC: American Psychiatric Association, 1980. http://amzn.to/1py5OKg

25. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 3rd Edition, Revised (DSM-III-R). Washington, DC: American Psychiatric Association 1987. http://amzn.to/YqoaHh

26. Factor DC, Freeman NL, Kardash A. Brief report: A comparison of DSM-III and DSM-III-R criteria for autism. J Autism Dev Disord 1989;19:637-40. http://bit.ly/1sCtu85

27. King M, Bearman P. Diagnostic change and the increased prevalence of autism. Int J Epidemiol 2009;38:1224-34. http://amzn.to/YqoaHh

28. Individuals with Disabilities Education Act Amendments. Pub L No. 101-476 (1990). http://1.usa.gov/1yuYsSo

29. Eagle RS. Commentary: Further commentary on the debate regarding increase in autism in California. J Autism Dev Disord 2004;34:87-8. http://bit.ly/1u421ed

30. Laidler JR. US Department of education data on "autism" are not reliable for tracking autism prevalence. Pediatrics 2005;116(1):e120-4. http://bit.ly/1mBhTUf

31. Maenner MJ, Durkin MS. Trends in the prevalence of autism on the basis of special education data. Pediatrics 2010;126(5):e1018-25. http://bit.ly/1DIvqin

32. Kim YS, Leventhal BL, Koh YJ, Fombonne E, et al. Prevalence of autism spectrum disorders in a total population sample. Am J Psychiat 2011;168:904-12. http://bit.ly/1qGAMAd

33. Senecky Y, Chodick G, Diamond G, Lobel D, et al. Time trends in reported autistic spectrum disorders in Israel, 1972-2004. Isr Med Assoc J 2009;11:30-3. http://bit.ly/Yqpz0p

34. Wong VC, Hui SL. Epidemiological study of autism spectrum disorder in China. J Child Neurol 2008;23:67-72. http://bit.ly/YqpEBm

35. Chen CY, Liu CY, Su WC, Huang SL, et al. Factors associated with the diagnosis of neurodevelopmental disorders: a population-based longitudinal study. Pediatrics 2007;119(2):e435-43. http://bit.ly/1vfnFfS

36. Baird G, Simonoff E, Pickles A, Chandler S, et al. Prevalence of disorders of the autism spectrum in a population cohort of children in South Thames: The Special Needs and Autism Project (SNAP). Lancet 2006;368(9531):210-5. http://bit.ly/1wOg4E0

37. Oliveira G, Ataide A, Marques C, Miguel TS, et al. Epidemiology of autism spectrum disorders in Portugal: Prevalence, clinical characterization, and medical conditions. Dev Med Child Neurol 2007;49:726-33. http://bit.ly/1yuYKIN

38. Gillberg C, Cederlund M, Lamberg K, Zeijlon L. Brief report: "The autism epidemic." The registered prevalence of autism in a Swedish urban area. J Autism Dev Disord 2006;36:429-35. http://bit.ly/1vnSLQG

39. Fombonne E, Zakarian R, Bennett A, Meng L, McLean-Heywood D. Pervasive developmental disorders in Montreal, Quebec, Canada: Prevalence and links with immunizations. Pediatrics 2006:118(1):e139-50. http://bit.ly/1BlXnZa

40. Fombonne E, Quirke S, Hagen A. Prevalence and interpretation of recent trends in rates of pervasive developmental disorders. Mcgill J Med 2009;12(2):73. http://1.usa.gov/UXroQM Last Accessed June 9, 2014.

41. Reichenberg A, Gross R, Weiser M, Bresnahan M, et al. Advancing paternal age and autism. Arch Gen Psychiatry 2006;63:1026-32. http://bit.ly/1uv2g3r

42. Croen LA, Majjar DV, Fireman B, Grether JK. Maternal and paternal age and risk of autism spectrum disorders. Arch Pediatr Adoles Med 2007;161:326-33. http://bit.ly/1njWKyB

43. Lyall K, Pauls D, Santangelo S, Spiegelman D, Ascherio A. Association between ovulation inducing drug use, infertility, and autism spectrum disorders in the Nurses' Health Study II. International Meeting for Autism Research; May 20, 2010; Philadelphia, PA: International Society for Autism Research; 2010. http://bit.ly/YqrjGZ

44. Atladottir HO, Pedersen MG, Thorsen P, Mortensen PB, et al. Association of family history of autoimmune diseases and autism spectrum disorders. Pediatrics 2009;124:687-94. http://bit.ly/1mBjauB

45. Juul-Dam N, Townsend J, Courchesne E. Prenatal, perinatal, and neonatal factors in autism, pervasive developmental disorder – not otherwise specified, and the general population. Pediatrics 2001;107(4):E63. http://bit.ly/1pjE25b

46. Glasson EJ, Bower C, Petterson B, de Klerk N, et al. Perinatal factors and the development of autism: A population study. Arch Gen Psychiatry 2004;61:618-27. http://bit.ly/1voBPKL

47. Kolevzon A, Weiser M, Gross R, Lubin G, et al. Effects of season birth on autism spectrum disorders: fact or fiction? Am J Psychiatry 2006;163:1288-90. http://bit.ly/1rr6Zze

48. Hebert KJ, Miller LL, Joinson CJ. Association of autistic spectrum disorder with season of birth and conception in a UK cohort. Autism Res 2010;3:185-90. http://bit.ly/1rr7j12

49. Lee LC, Newschaffer CJ, Lessler JT, Lee BK, et al. Variation in season of birth in singleton and multiple births concordant for autism spectrum disorders. Paediatr Perinat Epidmiol 2008;22:172-9. http://bit.ly/1mBjPw2

50. Grant WB, Soles CM. Epidemiologic evidence supporting the role of maternal vitamin D deficiency as a risk factor for the development of infantile autism. Dermatoendocrinol 2009 Jul;1(4):223-8. PMID 2059279 http://bit.ly/1mBjUjo

51. DeSoto MC. Ockham's Razor and autism: The case for developmental neurotoxins contributing to a disease of neurodevelopment. Neurotoxicology 2009;30:331-7. http://bit.ly/1u437GX

52. Rutter M. Incidence of autism spectrum disorders: Changes over time and their meaning. Act Paediatr 2005;94:2-15. http://bit.ly/1rr7GsC

53. Liptak GS, Benzoni LB, Mruzek DW, Nolan KW, et al. Disparities in diagnosis and access to health services for children with autism: Data from the National Survey of Children's Health. J Dev Behav Pediatr 2008;29:152-60. http://bit.ly/1t4VH1K

54. Dosreis S, Weiner CL, Johnson L, Newschaffer CJ. Autism spectrum disorder screening and management practices among general pediatric providers. J Dev Behav Pediatr 2006;27:S88-S94. http://bit.ly/1BlZTyt

55. American Academy of Pediatrics, Council on Children With Disabilities, Section on Developmental and Behavioral Pediatrics, Bright Futures Steering Committee, Medical Home Initiatives for Children with Special Needs Project Advisory Committee. Identifying infants and young children with developmental disorders in the medical home: an algorithm for developmental surveillance and screening. Pediatrics 2006;118:405-20. http://bit.ly/1xqoyV9

56. American Academy of Pediatrics, Identification and Evaluation of Children with Autism Spectrum Disorders. Pediatrics 2007;120:1183-215. http://bit.ly/103myUQ

57. Gupta VB, Hyman SL, Johnson CP, Bryant J, et al. Identifying children with autism early. Pediatrics 2007;119:152-3. http://bit.ly/ZhJeAM

58. Nadel S, Poss JE. Early detection of autism spectrum disorders: Screening between 12 and 24 months of age. J Am Acad Nurse Pract 2007;19:408-17. http://bit.ly/YrtmdC

59. Auyeung B, Baron-Cohen S, Wheelwright S, Allison C. The autism spectrum quotient: Children's version (AQ-Child). J Autism Dev Disord 2008;38:1230-40. http://bit.ly/YrtCtd

60. Constantino JN, Davis SA, Todd RD, Schindler MK, et al. Validation of a brief quantitative measure of autistic traits: Comparison of the social responsiveness Scale with the autism diagnostic interview-revised. J Autism Dev Disord 2003;33:427-33. http://bit.ly/1rlejix

61. Fernandopulle N. Measurement of Autism: A Review of Four Screening Measures. Indian J Psychol Med 2011 Jan-Jun;33(1):5-10. http://1.usa.gov/1CvCxco

62. Pine E, Luby J, Abbacchi A, Constantino JN. Quantitative assessment of autistic symptomatology in preschoolers. Autism 2006;10:344-52. http://bit.ly/1py8wiY

63. Oosterling I, Rommelse N, DeJonge M, Van Der Gaag RJ, et al. How useful is the social communication questionnaire in toddlers at risk of autism spectrum disorder? J Child Psychol Psyc 2010;51:1260-8. http://bit.ly/1rsIVgJ

64. Johnson S, Hollis C, Hennessy E, Kochlar P, et al. Screening for autism in preterm children: Diagnostic utility of the social communication questionnaire. Arch Dis Child 2011;96:73-7. http://bit.ly/Yqw2bN

65. Bryson SE, Zwaigenbaum L, McDermott C, Rombough V, Brian J. The autism observation scale for infants: Scale development and reliability data. J Autism Dev Disord 2008;38:731-8. http://bit.ly/1rAxX9s

66. Pierce K, Carter C, Weinfeld M, Desmond J, et al. Detecting, studying, and treating autism early: The one-year well-baby check-up approach. J Pediatr 2011;159:458-65.e1-6. http://bit.ly/1pjG4Cp

67. Shattuck PT, Durkin M, Maenner M, Newschaffer C, et al. Timing of identification among children with an autism spectrum disorder: Findings from a population-based surveillance study. J Am Acad Child Adolesc Psychiatry 2009;48:474-83. http://bit.ly/1CvCZY2

68. Dawson G, Estes A, Munson J, Schellenberg G, et al. Quantitative assessment of autism symptom-related traits in probands and parents: Broader phenotype autism symptom scale. J Autism Dev Disord 2007;37:523-36. http://bit.ly/1DIB7Ne

69. Williams J, Allison C, Scott F, Stott C, et al. The childhood asperger syndrome test (CAST): Test-retest reliability. Autism 2006;10:415-27. http://bit.ly/1mBlDVJ

70. Allison C, Williams J, Scott F, Stott C, et al. The childhood asperger syndrome test (CAST): Test-retest reliability in a high scoring sample. Autism 2007;11:173-85. http://bit.ly/1rsJIOW

71. Seif Eldin A, Habib D, Noufal A, Farrag S, et al. Use of M-CHAT for a multinational screening of young children with autism in the Arab countries. Int Rev Psychiatry 2008;20:281-9. http://bit.ly/1vfuHky

72. Sato FP, Paula CS, Lowenthal R, Nakano EY, et al. Instrument to screen cases of pervasive developmental disorder: A preliminary indication of validity. Rev Bras Psiquiatr 2009;31:30-3. http://bit.ly/1py988f

73. Hoekstra RA, Bartels M, Cath DC, Boomsma DI. Factor structure, reliability and criterion validity of the autism-spectrum quotient (AQ): A study in Dutch population and patient groups. J Autism Dev Disord 2008;38:1555-66. http://bit.ly/1omH48A

74. Nygren G, Hagberg B, Billstedt E, Skoglund A, et al. The Swedish version of the diagnostic interview for social and communication disorders (DISCO-10). Psychometric properties. J Autism Dev Disord 2009;39:730-41. http://bit.ly/103qDs8

75. Norris M, Lecavalier L. Screening accuracy of Level 2 autism spectrum disorder rating scales. A review of selected instruments. Autism 2010;14:263-84. http://bit.ly/1vfv5j1

76. Johnson CP, Myers SM, American Academy of Pediatrics Council on Children With Disabilities. Identification and evaluation of children with autism spectrum disorders. Pediatrics 2007;120:1183-215. http://bit.ly/1rr34Ti

77. Coonrod EE, Stone WL. Screening for autism in young children. In: Volkmar FR, Paul R, Klin A, Cohen D, eds. Handbook of Autism and Pervasive Developmental Disorders, 3rd ed. Vol 2. Hoboken, NJ: John Wiley & Sons, 2005:707-29. http://bit.ly/103riKd

78. National Guideline Clearinghouse. Practice parameter: Screening and diagnosis of autism. Report of the Quality Standards Subcommittee of the American Academy of Neurology and the Child Neurology Society Rockville MD: Agency for Healthcare Research and Quality (AHRQ); [7/2/2013]. http://1.usa.gov/X28PfW. Last Accessed June 7, 2014.

79. Bruey CT. Demystifying Autism Spectrum Disorders: A Guide to Diagnosis for Parents and Professionals. Bethesda, MD: Woodbine House, 2004.

80. Autism Speaks. How is Autism Diagnosed? http://bit.ly/1wOgPNo Last Accessed June 18, 2013.

81. American Psychiatric Association. Pervasive developmental disorders. In: Diagnostic and statistical manual of mental disorders (Fourth edition---text revision (DSM-IV-TR). Washington, DC: American Psychiatric Association, 2000:69-70. http://amzn.to/1rAqxmF

82. Weitlauf AS, Gotham KO, Vehorn AC, Warren ZE. Brief Report: DSM-5 "Levels of Support:" A Comment on Discrepant Conceptualizations of Severity in ASD. J Autism Dev Disord 2014;44:471-6. http://bit.ly/1voFatl

83. Tsai LY, Ghaziuddin M. DSM-5 ASD Moves Forward into the Past. J Autism Dev Disord 2014;44:321-30. http://bit.ly/1uQGymV

84. Volkmar FR, Reichow B. Autism in DSM-5: Progress and challenges. Mol Autism 2013;4:13. http://bit.ly/1rsPKiu

85. Grzadzinski R, Huerta M, Lord C. DSM-5 and autism spectrum disorders (ASDs): An opportunity for identifying ASD subtypes. Mol Autism 2013;4:12. http://bit.ly/YqL9C7

86. Reaven JA, Hepburn SL, Ross RG. Use of the ADOS and ADI-R in children with psychosis: Importance of clinical judgment. Clin Child Psychol Psychiatry 2008;13:81-94. http://bit.ly/1CvHJwU

87. Tomanik SS, Pearson DA, Loveland KA, Lane DM, Bryant Shaw J. Improving the reliability of autism diagnoses: Examining the utility of adaptive behavior. J Autism Dev Disord 2007;37:921-8. http://bit.ly/1xqr51D

88. Kurita H, Koyama T, Inoue K. Reliability and validity of the pervasive developmental disorders assessment system. Psychiatry Clin Neurosci 2008;62:226-33. http://bit.ly/103DV7Y

89. van Daalen E, Kemner C, Dietz C, Swinkels SH, et al. Inter-rater reliability and stability of diagnoses of autism spectrum disorder in children identified through screening at a very young age. Eur Child Adolesc Psychiatry 2009;18:663-74. http://bit.ly/YrSEYW

90. Lugnegard T, Hallerback MU, Gillberg C. Psychiatric comorbidity in young adults with a clinical diagnosis of Asperger syndrome. Res Dev Disabil 2011;32:1910-7. http://bit.ly/1DINYyI

91. de Bruin EI, Ferdinand RF, Meester S, de Nijs PFA, Verheij F. Higher rates of psychiatric co-morbidity in PDD-NOS. J Autism Dev Disord 2007;37:877-86. http://bit.ly/1mBskr1

92. Levy SE, Mandell DS, Schultz RT. Autism. Lancet 2009;374:1627-38.

93. McCaffery P, Deutsch CK. Macrocephaly and the control of brain growth in autistic disorders. Prog Neurobiol 2005;77:38-56. http://bit.ly/1nkuMCP

94. Nelson KB, Nelson PG. Size of the Head and Brain in Autism: Clue to Underlying Biologic Mechanisms: The Neurobiology of Autism. 2nd ed. Baltimore, MD: Johns Hopkins University Press, 2005. http://bit.ly/1omMdxB

95. Courchesne E, Karns CM, Davis HR, Ziccardi R, et al. Unusual brain growth patterns in early life in patients with autistic disorder: An MRI study. Neurology 2001;57:245-54. http://bit.ly/1DIPFMQ

96. Sparks BF, Friedman SD, Shaw DW, Aylward EH, et al. Brain structural abnormalities in young children with autism spectrum disorder. Neurology 2002;59:184-92. http://bit.ly/1mBt5QI

97. Bauman ML, Kemper TL, eds. The Neurobiology of Autism. 2nd ed. Baltimore, MD: Johns Hopkins University Press; 2005:23-33. http://amzn.to/1BmjkaD

98. Pickett J, London E. The neuropathology of autism: A review. J Neuropathol Exp Neurol 2005;64:925-35. http://bit.ly/1rAHeOP

99. DiCicco-Bloom E, Lord C, Zwaigenbaum L, Courchesne E, et al. The developmental and neurobiology of autism spectrum disorder. J Neurosci 2006;26:6897-906. http://bit.ly/1pjQ5Q7

100. Casanova MF, Buxhoeveden DP, Switala AE, Roy E. Minicolumnar pathology in autism. Neurology 2002;58:428-32. http://bit.ly/1wOinHr

101. Rodier PM, Arndt TL. The Brainstem in Autism. In: Bauman ML, Kemper TL, eds. The Neurobiology of Autism. 2nd ed. Baltimore, MD: Johns Hopkins University Press, 2005:136-49. http://amzn.to/1BmjkaD

102. Lange N, Dubray MB, Lee JE, Froimowitz MP, et al. Atypical diffusion tensor hemispheric asymmetry in autism. Autism Res 2010;3:350-8. http://bit.ly/1rrmHdY

103. Elsabbagh M, Mercure E, Hudry K, Chandler S, et al. Infant neural sensitivity to dynamic eye gaze Is associated with later emerging autism. Curr Biol 2012;22:338-42. http://bit.ly/1omMU9V

> *The online version of this article contains digital enhancements.*