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Autism Spectrum Disorders: A Changing Landscape

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Disclosure:

Dr. Brazdziunas has no industry relationships to disclose and does not refer to products that are still investigational or not labeled for the use in discussion.

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Dr. Mary Nevin, Course Director; Vita Lerman, Editor; Dr. John X. Thomas, Senior Associate Dean for Medical Education; Genevieve Napier, CME Director, Tara Scavelli and Jennifer Banys, CME Project Specialist have nothing to disclose.

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Educational objectives

At the conclusion of this activity, participants will be able to:

- Describe the DSM-5 changes to the definition of autism spectrum disorders
- Discuss the current understanding of etiology of autism spectrum disorders
- Identify common comorbid conditions associated with autism spectrum disorders

Estimated time to complete: 0.5 hours

CME Credit: 0.5

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"On our own we simply don't know how to get things done the same way you do things. But, like

everyone else, we want to do the best we possibly can. When we sense you've given up on us, it makes us feel miserable. So please keep helping us, through to the end."

- Naoki Higashida, *The Reason I Jump: The Inner Voice of a Thirteen-Year-Old Boy with Autism*

Autism spectrum disorder is a neurodevelopmental disorder characterized by deficits in social communication, social interaction as well as restricted interests, rote or repetitive behaviors. The disorder typically presents during infancy and early childhood, though diagnosis may not occur until much later. Pediatricians and other primary care providers for children are at the front line of early identification and diagnosis, referral for treatment, advocacy and family support.

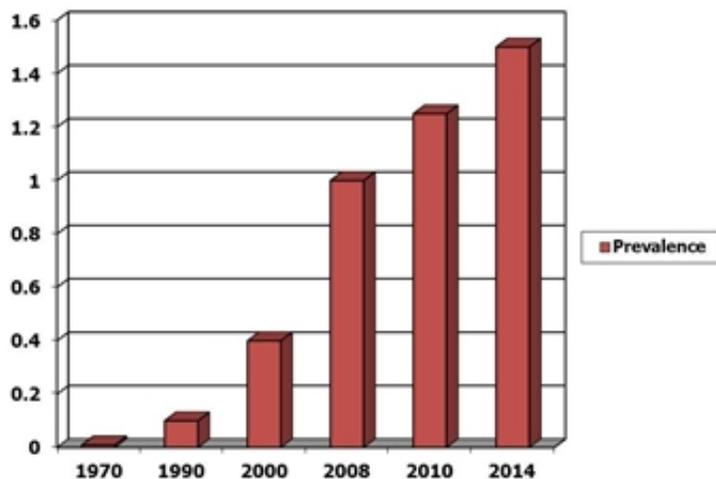
Early treatment has been linked to better language, cognitive and adaptive behavioral outcomes for children with autism spectrum disorders. It has been estimated that effective early treatment can reduce the lifetime cost of caring for the individual with the disorder by 2/3. Though autism spectrum disorders are generally not curable, they are treatable. Primary care pediatricians need to be aware of recent changes in the definition of the disorder, prevalence, and understanding of etiology, importance of comorbid conditions and treatment to be able to better care for children with autism spectrum disorder in the medical home.

Prevalence

Over the last 20 years in the United States, the prevalence of autism spectrum disorders has steadily increased (Table 1).

Table 1: Autism Spectrum Disorder Prevalence

(Prevalence shown in percentage among 8-year-olds in US by year of CDC reports)



The CDC reported in 2014 that among 8-year-olds, 1 in 68 children has an autism spectrum disorder. The prevalence in boys is 1 in 42, while for girls, the prevalence is 1 in 189. Much of the increase has been attributed to the understanding of autism as a spectrum disorder resulting in the diagnosis of children with milder symptoms and diagnostic substitution, although these changes do not fully explain the increase in prevalence. Despite increased screening for autism spectrum disorder, the average age of diagnosis remains about 4 ½ years.

Etiology and Genetics

Autism was originally conceptualized as a disorder caused by poor parenting, specifically “refrigerator” mothers. By the 1960s-1970s, it was conceptualized as disorder of neurodevelopment. It is now seen as a disorder of brain development and connectivity that likely starts prenatally. A recently published study of brain autopsy samples of children with autism spectrum disorder showed focal areas of disruption in the laminar architecture of the cortex, providing further evidence for the prenatal origins of this disorder.

Genetics play an important role in the etiology of the disorder, though recent studies suggest that environmental factors, especially prenatal environmental factors may be equally important. Environmental factors that may contribute to the development of autism spectrum disorder include advanced parental age at conception, prolonged fever during pregnancy, extreme prematurity and twins or multiples. A genetic syndrome can be identified in 10%-15% of children with autism spectrum disorder. The most common syndromes associated with autism spectrum disorder are tuberous sclerosis and fragile X syndrome. Additional syndromes to consider are Rett syndrome in young girls, Angelman syndrome, neurofibromatosis type 1, PTEN mutation associated with macrocephaly and others. Copy number variants (duplications and deletions found on microarray) can be identified in about 10%-15% of children with autism spectrum disorder. For families with 1 child with autism spectrum disorder, the recurrence risk is 5%-20% in a subsequent child.

Non-autistic siblings of children with autism spectrum disorder are at higher risk of language and learning disorders and other behavioral disorders, such as anxiety. Some siblings will show signs of autism spectrum disorder, but not enough for a diagnosis. The term “broader autism phenotype” is used to describe this phenomenon.

Autism and Comorbid Conditions

Few children have autism spectrum disorder as their only developmental diagnosis. At least 80% of children with autism spectrum disorder have other significant comorbid conditions including:

- Developmental disorder such as intellectual disability, language disorder, apraxia/dyspraxia, fine and gross motor coordination deficits and learning disorder
- Behavioral problems such as anxiety disorder, obsessive compulsive disorder, attention deficit hyperactivity disorder, oppositional defiant disorder, tic disorders and aggression
- Neurological, genetic and medical conditions such as seizures, genetic disorders such as fragile X, sleep problems, feeding/eating disorder such as extreme food selectivity and gastrointestinal problems

The prevalence of intellectual disability in autism spectrum has decreased as more children have been diagnosed. Previously, it was believed that 70% of children with autism have intellectual disability, but the latest data shows that the rate has dropped to about 30%.

Identifying and treating comorbid conditions is as important as treating the autism spectrum disorder itself. For example, anxiety disorder in children with autism spectrum disorder may prevent a child from learning in school until it is treated.

DSM-5 Definition

DSM-5 has changed the classification of autism spectrum disorders because of evidence showing lack of reliability and consistency in the interpretation of the DSM-4 criteria among diagnosticians

in distinguishing autism, Asperger syndrome and pervasive developmental disorder- NOS, and the need to move to a more dimensional classification system that allows for a comprehensive description of comorbid and associated conditions. In efforts to better define symptomatology and update the criteria to reflect current scientific knowledge, the DSM-5 combined autistic disorder, Asperger syndrome, pervasive developmental disorder-NOS, and childhood disintegrative disorder into a single disorder. Rett syndrome is no longer classified as an autism spectrum disorder, as it is a distinctive genetic syndrome with a specific etiology.

Autism spectrum disorder in DSM-5 is defined by 2 symptom domains:

- Persistent deficits in social communication and interaction
- Restricted, repetitive patterns of behaviors, interests or activities

Symptoms must begin in the early developmental period and cause significant impairment in everyday functioning. Sensory symptoms (under- or over-reaction to sensory stimuli such as pain, sound, textures, touch, or smell) have been added to the definition under the “restricted, repetitive behaviors” domain. These symptoms were not part of DSM-4 criteria for any of the pervasive developmental disorders. DSM V also requires the clinician to indicate whether cognitive impairment, language impairment and/or catatonia are present and to identify comorbid medical, genetic and behavioral conditions. Criteria may also be met by history, recognizing that certain symptoms may improve or disappear over time. DSM-5 also added severity rating for both symptom domains.

A new disorder called “social communication disorder” was added to the DSM-5 in order to account for children who present with deficits in social and pragmatic communication without significant restricted or repetitive patterns of behaviors, interests or activities. The disorder is conceptualized as a disorder of pragmatic language, a persistent difficulty with the social use of verbal and nonverbal communication not explainable by the child’s cognitive level. Social communication disorder is considered a separate diagnosis from autism spectrum disorder. Children diagnosed with this disorder must have no history of restricted, repetitive patterns of behaviors, interests or activities. It is not a replacement diagnosis for PDD-NOS and an autism spectrum disorder should be ruled out prior to using this diagnosis.

Concern has been raised that the DSM-5 criteria may change, and particularly reduce, the number of individuals diagnosed with autism spectrum disorders. Initial studies suggest that children under 2 years of age may not fully meet criteria because of their young age. Research is ongoing to test the criteria in all populations, especially in young children and adults.

Some have questioned whether children previously diagnosed under DSM-4, need to be reevaluated using DSM-5 criteria to determine eligibility for continued services. The Federal Interagency Autism Coordinating Committee issued a statement in April 2014 stating that the individuals with a previous diagnosis of an autism spectrum disorder should retain their diagnosis and not be reevaluated.

The new DSM-5 criteria do not change the recommendations for screening young children in the medical home in any way.

Early Signs and Screening

Early signs of autism spectrum disorder can be detected in children as young as 6 months of age, typically as decreased use of eye contact and limited interest in social engagement, though diagnosis at that very early age is not yet possible. Common signs seen in infants with autism

spectrum disorder by 12 months of age include lack of response to name, decreased eye contact, lack of showing objects and lack of gestures such as waving or nodding head. Lack of pointing for social interest and lack of functional play by 18 months of age are other important early signs. Regression of language skills (loss of several words) or of social interaction skills between 1-2 years of age occurs in about 30% of toddlers with autism spectrum disorder. A list of red flags for autism spectrum disorder in young children is in Table 2.

Category	Red Flags
Social Interaction	<ul style="list-style-type: none"> ▪ Lack of appropriate use of gaze ▪ Lack of or delayed response to name ▪ Lack of interest in social games such as peek a boo ▪ Lack of back and forth social engagement ▪ Limited to no interest in other children
Communication	<ul style="list-style-type: none"> ▪ Lack of joint attention (following point, showing objects, pointing for social interest) ▪ Delays in use of gestures for communication ▪ Loss of words that were functionally used ▪ Use of repetitive speech or echolalia ▪ Use of other's hand as tool ▪ Speech delay, especially lack of use of words for functional communication
Repetitive Behaviors	<ul style="list-style-type: none"> ▪ Spinning or tossing toys perseveratively ▪ Repetitive body movement or unusual posturing such as hand flapping, finger flicking ▪ Lack of appropriate play with toys ▪ Delay in the development of functional and symbolic play ▪ Unusual sensory exploration of objects- interest in watching wheels spin for example or prolonged visual inspection of objects ▪ Excessive interest in a particular object
Behavioral	<ul style="list-style-type: none"> ▪ Excessive temper tantrums ▪ Difficulties with transitions ▪ Sudden, abrupt mood shifts ▪ Difficulty calming ▪ Excessive insistence on routine ▪ Extreme food selectivity

The American Academy of Pediatrics recommended universal screening of all young children at ages 18 months and 24 or 30 months using a standardized autism screening tool. The most widely used autism screening tool for this age group is the Modified Checklist for Toddlers. An

improved version with better psychometrics and ease of use is available and is called the Modified Checklist for Toddlers, revised with follow up (M-CHAT-R/F). This is a 2-stage screener that is free to download for use in clinical settings (<http://www.mchatscreen.com/>). Children who screen positive on the M-CHAT-R/F are 114 times more likely to be diagnosed with an autism spectrum disorder than those who screen negative. The tool has been standardized and performs best with toddlers, 16 -30 months of age, though it has been used in children up to 4 years of age.

Not all children will be identified as toddlers, so it is important to screen older children when possible autism spectrum symptoms are noted by a parent, teacher or health care provider. Standardized screening tools such as the Childhood Autism Spectrum Test (CAST, available for free download at www.autismresearchcentre.com/arc_tests), Social Communication Questionnaire (available for purchase at <http://www.wpspublish.com/>) and the Social Responsiveness Scales can be helpful in determining whether to refer an older child for a comprehensive evaluation.

Diagnosis

The DSM-5 definition of autism spectrum disorder requires the clinician not only to evaluate the child for autism spectrum symptoms, but also to evaluate the child's language and cognitive capacity, as well as fully assess the child for other behavioral, medical and genetic conditions associated with the disorder. This is best accomplished through a comprehensive assessment of the child's development and behavior, the use of autism-specific measures, history including detailed family history, and physical/neurological examination of the child. Examples of autism-specific measures include the Autism Diagnostic Observation Schedule, Autism Diagnostic Interview-Revised and the Childhood Autism Rating Scale-2. The diagnosis, however, is not based on the result of a single test, but on expert clinical judgment using DSM-5 criteria.

Physical exam should include growth parameters including head circumference, height, weight, dysmorphism examination, neurological examination, and skin examinations looking for signs of neurocutaneous disorders such as café au lait or ash leaf spots. Hearing testing should be completed for every child, even if the child passed newborn hearing screening. First-line neurogenetic evaluation includes chromosomal microarray and fragile X testing. Chromosomal microarray has been shown to have the highest yield of determining an etiology in autism spectrum disorders. Brain MRI can be considered in children with global developmental delay and autism spectrum disorder, though overall yield is low. Genetic and/or neurological consultation should be considered in cases where children have seizures, significant developmental regression or global developmental delay, signs of a genetic syndrome, tonal abnormalities or symptom and signs of a metabolic disorder. Testing for PTEN gene mutation may be considered after microarray and fragile X testing when a child with autism spectrum disorder has macrocephaly. MECP-2 genetic testing should be considered in young girls with a history of regression in motor and language skills, global developmental delay, deceleration of head growth in infancy, and/or loss of hand skill.

Treatment

Treatment of autism spectrum disorder should be comprehensive, evidence-based and geared toward the individual needs of the child. One program does not fit all and there is great variation as to what is available for children depending on where they live. Children with autism rely on early intervention and then on their local public school system for the majority of the intervention that they receive. Until recently, most private insurance plans did not cover therapy for autism spectrum disorder. Laws have now been passed in over 30 states requiring private health

insurance plans to cover autism spectrum disorder treatment. In Illinois, the Affordable Care Act health plans must cover autism spectrum treatment. A future article in the *Child's Doctor Online CME Rounds* will address treatment of autism spectrum disorder in further detail. Table 3 lists useful resources for healthcare providers and families.

Table 3: Resources

Autism Speaks- www.autismspeaks.com 1-888-AUTISM2

- Supports research, increasing public awareness and providing support/information services for affected individuals and their families
- 100 day kit for new diagnosed children, available both in English and Spanish
www.autismspeaks.org/community/family_services/100_day_kit.php
- School and community resource kit www.autismspeaks.org/community/family_services/school_kit.php
- Other resource kits for going to the dentist, haircuts, use of visual support, medication management, applied behavioral analysis etc.
- On line resource directory covering all 50 states including resources in Spanish at www.autismspeaks.org/community/resources/index.php
- Video glossary- brief videos showing early signs of autism spectrum disorder vs normal
- Autism Response Team- email/phone access for families who would like assistance finding help for their child, have Spanish speaking line as well.

Autism Society of America www.autism-society.org

- Oldest support organization for autism
- Strong community and education emphasis
- National resource data base at <http://www.autismsource.org/>
- Has several chapters in Illinois- see above website for chapter list and local support groups
- Information and referral for families in Illinois 630-691-1276, <http://www.autismillinois.org/>
- Resources for Illinois at <http://www.autismillinois.org/resources/>
- Resources for Wisconsin at <http://www.asw4autism.org/>
- Resources for Indiana at <http://www.autismsocietyofindiana.org/>

The Autism Program- Illinois www.theautismprogram.org

- Statewide system network for autism spectrum disorders
- Center across state providing diagnosis, treatment, training , resources for autism spectrum disorders
- Services unique to each region
- Include family support
- State resource directory- available in print and online at <http://theautismprogram.org/resources/>

**Center for Disease Control and Prevention (CDC) Learn the Signs. Act Early Project
www.cdc.gov/ncbddd/actearly/index.html**

- CDC effort in promoting early recognition of autism spectrum disorder
- Has online curriculum for health care providers on early signs, diagnosis and treatment of autism spectrum disorder

- Has information on normal development and when to be worried for parents

First Signs www.firstsigns.org

- Organization that promotes early detection, screening and referral for parents and professionals
- Has online screening tools and video glossary for families

Birth to 5: Watch Me Thrive! www.acf.hhs.gov/programs/ecd/watch-me-thrive

- Federal initiative launched in March 2014 with many resources for families and providers to encourage healthy child development, universal developmental and behavioral screening for children
- Provides a [list of research-based developmental screening tools](#) appropriate for use across a wide range of settings
- Includes screening information for primary care providers:  www.acf.hhs.gov/sites/default/files/ecd/pcp_screening_guide_march2014.pdf

Outcome

Autism spectrum disorder is a treatable but typically not curable disorder. Many children with autism spectrum disorders will improve with treatment and with maturation. Children with better adaptive and cognitive skills and milder autism spectrum symptoms at presentation have a better prognosis. The diagnosis is generally stable; about 90% of children diagnosed at age 2 years will continue to retain their diagnosis at age 4 years and above.

Most children with autism spectrum disorder go on to be verbal. Previously it was considered that if a child is not talking by age 5 years, development of verbal skills is not likely. Recent research shows that verbal skills may emerge at any point during childhood.

Optimal outcome in autism spectrum disorder has been defined as a child who no longer meets criteria for the disorder based on current functioning. This may occur in as many as 5%-10% of children who are diagnosed at 2 years of age. Many of the children showing this pattern will transition to a different diagnosis, such as attention deficit hyperactivity disorder, anxiety disorder, speech/language disorder, obsessive compulsive disorder, or learning disorder.

Conclusion

Autism spectrum disorders have greatly increased in prevalence and every primary care pediatrician is likely to be identifying and following a number of children with this disorder in their practice. As the diagnosis has changed and expanded, the pediatrician's role has grown. What is unchanged though is our most important role to listen and "keep helping ... through to the end."

For Further Reading

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[6.] Volkmar F, Siegel M, Woodbury-Smith M, King B, McCracken J, State M, and the American Academy of Child and Adolescent Psychiatry Committee on Quality Issues. Practice Parameter for the Assessment and Treatment of Children and Adolescents with Autism Spectrum Disorder. *Journal of the Academy of Child and Adolescent Psychiatry* 2014 Feb; 53(2):237-257.

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