On alert for Aut spectrum disorders

By Kathleen Peterson, PhD, RN, PNP-BC, and Paula Barbel, PhD, RN, PNP

IN MARCH 2012, the CDC published new data estimating that in the United States, 1 child in 88 (about 1%) has been identified with an autism spectrum disorder (ASD). The CDC also reported a 23% increase in ASD diagnoses since a prior report in 2009 and a 78% increase since 2007.[1,2]

What does the evidence show about the startling increase in the diagnosis of ASD? This article will review theories associated with the increase in diagnosed cases, discuss what we do and don't know about the causes of ASD, and suggest implications for nurses who care for children with ASD and their families.

What is autism?

Autism and *ASD* are terms that represent a group of complex neurodevelopmental disorders characterized by difficulties in social interaction, including verbal and nonverbal communication, repetitive behaviors, and stereotyped interests and activities.[3,4] The term ASD signifies that autism is a spectrum disorder, meaning that the onset and nature of signs and symptoms vary among people and can range from mild to severe.

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ASD can be classified into three types:[3,5]

- autistic disorder (sometimes referred to as classic autism)
- Asperger syndrome (also known as Asperger disorder)
- pervasive developmental disorder–not otherwise specified (PDD-NOS), also referred to as atypical autism.

Children who meet some but not all of the criteria for autistic disorder or Asperger syndrome are usually diagnosed with PDD-NOS.[6,7]

Many people diagnosed with ASD have intellectual disabilities, difficulties in motor coordination, attention deficit hyperactivity disorder, and sleep disturbances; however, some are intellectually gifted and excel in certain areas of learning. See *Comparing autism spectrum disorders* for more about the three types of ASD.

Current definitions of ASD are based on the fourth edition of the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* (DSM-IV-TR). A fifth edition is scheduled for release in May 2013.[5,8] Definitions for ASD may be revised in accordance with new diagnostic criteria.

Why the increase in ASD prevalence?

Although more children than ever are being diagnosed with an ASD,

ASD is characterized by difficulties in social interaction, including verbal and nonverbal communication, repetitive behaviors, and stereotyped interests and activities.

it's unclear exactly how much of this is a true increase and how much is due to a broader definition of ASD, changing diagnostic criteria, and greater awareness. A true increase in the number of children with an ASD can't be ruled out, but some of the increase reflects changes in the way that autism is evaluated and diagnosed based on DSM-IV-TR criteria.[6]

As the incidence of autism has risen, the incidence of diagnosed learning and intellectual disabilities has decreased.[9] Coo and associates found that one third of the increase in the prevalence of autism could be attributed to a change in many school-age children's diagnoses from another special education classification to autism.[10]

Another factor that's contributed to the increased incidence of ASD diagnosis is the fact that autism was added as a federally protected disability under the Individuals with Disabilities Education Act of 1990. For the first time, specific services became available for patients with ASD.[9] This prompted many parents to have their child properly diagnosed with autism.

Looking for causes

Many theories about the causes of ASD have been proposed, but no full explanation has yet been found. A controversial theory linking autism with the measles, mumps, and rubella (MMR) vaccine has been proven false. Research that supposedly supported the theory, originally published in the British medical journal *The Lancet* in 1998, was found to be fraudulent. *The Lancet* retracted the article in 2010 and the lead researcher lost his license to practice medicine. For details, see *Behind the MMR controversy*.[11-16]

The American Academy of Pediatrics (AAP) has compiled a summary of 41 studies demonstrating that no association exists between the MMR

Comparing autism spectrum disorders

	Autistic disorder	Asperger syndrome	PDD-NOS
Language delays	Significant	No	Fewer and milder
Communication impairment	Significant	No	Fewer and milder
Social challenges	Significant	Mild	Mild
Unusual behaviors and interests, such as flapping hands, rocking, spinning, obsessive interests	Yes	Mild	Fewer and milder
Intellectual disability	Often	No	Milder

Source: Centers for Disease Control and Prevention. Facts about ASDs. http://www.cdc.gov/ncbddd/autism/facts.html.

vaccine and ASD.[15] Yet because of misperceptions generated by the MMR research controversy, many in the lay public still believe that the MMR vaccine is associated with ASD. A devastating consequence of this false belief is that many parents have refused to immunize their children. Serious outbreaks of measles in Britain, Switzerland, Israel, and Italy have been linked to parental fear of the MMR vaccine. The United States experienced more cases of measles in the first 7 months of 2008 than any year since 1996 as a result of parents refusing to have their children vaccinated with the MMR vaccine.[9]

Another unsupported theory is that thimerosal, a preservative used in some vaccines in the past, is related to the increasing incidence of autism. However, Price et al. found no increase in risk of autism when children received immunizations that contained this preservative.[17] The Institute of Medicine's Immunization Safety Review Committee 8th and final report regarding vaccines and autism stated that "the evidence favors rejection of a causal relationship between thimerosal-containing vaccine and autism."[18]

Thimerosal is no longer used in any childhood vaccine (although it's still used as a preservative in multidose vials of flu vaccine). Interestingly, the MMR vaccine never contained thimerosal.[19]

Other possible causes still under investigation

Some more promising theories are still being explored. In a recent study, Maimburg et al. concluded that "accumulating evidence suggests an association between exposure to neonatal jaundice and autistic disorders."[20] In an earlier study, Maimburg and associates found an almost fourfold risk for infantile autism (now called autistic disorder) in full-term infants who had hyperbilirubinemia after birth.[21] They also observed a strong association between autism and abnormal neurologic signs after birth, especially hypertonicity.

Lundstrom and associates found a strong association between paternal age and risk for ASD in a study of two nationally representative twin studies from Sweden and the United Kingdom. Children whose fathers were over age 50 or under age 25 at the time of the children's birth had significantly higher autistic-like trait scores when compared with children whose fathers were ages 25 to 34.[22]

Nurses need to remind parents that studies such as these may suggest associations, but that much more research is needed before true causation can be established.

Behind the MMR controversy

In 1998, an article published in *The Lancet* described a small cohort study of 12 children with a history of normal development followed by regression coexisting with gastrointestinal (GI) complaints. The onset of regression occurred after administration of the measles-mumps-rubella (MMR) vaccine in 8 of the 12 children. The authors speculated "that persistent measles virus infection in the GI tract could have resulted in changes that allowed absorption of toxic neuropeptides, which then caused central nervous system damage and developmental regression."[11] The article didn't claim a cause-and-effect relationship between the vaccine and autism, but lead author Dr. Andrew Wakefield actively promoted this interpretation in the media.[12]

A closer review revealed that regression began before the GI symptoms in some of these children. In 2004, 10 of the original 13 authors issued a retraction and stated, "We wish to make it clear that in this paper no causal link was established between MMR vaccine and autism as the data were insufficient."[13]

In 2010, following a lengthy investigation, the British General Medical Council (GMC) concluded that Wakefield had engaged in "serious professional misconduct," including improperly conducting research on children without institutional review board approval, filing a patent for a vaccine that would compete with the MMR vaccine, and taking payment from attorneys involved in litigation against the MMR vaccine. Five days later, *The Lancet* issued a full retraction of the article.[14] Several months later, the GMC struck Wakefield from the medical register, banning him from practicing medicine in the United Kingdom.[12]

Despite the fact that many studies have shown no link between the MMR vaccine and autism,[15] the Wakefield article's sensational implications led to dramatic drops in childhood immunization rates for measles and have been directly linked to measles outbreaks in the United Kingdom, United States, and elsewhere. Discussing the effects of the Wakefield fraud in 2011, editors of the *British Medical Journal* wrote that "In 2008, for the first time in 14 years, measles was declared endemic in England and Wales. Hundreds of thousands of children in the U.K. are currently unprotected as a result of the scare, and the battle to restore parents' trust is ongoing."[16]

Is it in the genes?

According to the AAP, "ASDs are biologically based neurodevelopmental disorders that are highly heritable."[6] Scientists are studying how environmental changes over the past two decades may interact with genes to increase a person's risk of developing autism. An example is The Childhood Autism Risks from Genetics and the Environment (CHARGE) Study, a population-based case-controlled study of preschool children with autism initiated at the University of California-Davis Center for Children's Environmental Health in 2003.[23] Findings from the CHARGE study reinforce the importance of taking a prenatal vitamin not only during pregnancy but

before conception.[24] The CHARGE study has also revealed that children with ASD are far more likely to have deficits in their ability to produce cellular energy and are more likely to have mitochondrial dysfunction than children without ASD.[25] Nurses should monitor this ongoing study to stay well informed about new discoveries and associations, which may have assessment implications for children with or at risk for ASD.

Important progress is being made toward identifying genes associated with ASD, but evidence suggests that any genetic link results from complex multigenic interactions of susceptible genes rather than any single gene.[26,27]

Some studies show an increased risk in subsequent siblings when one child is diagnosed with ASD, supporting a hereditary component to the disorder. The incidence is higher in male children than in female children.[28]

Conducting a systematic review, Grafodatskaya and associates summarized knowledge about epigenetic modifications to genes possibly involved in the etiology of ASD. They found that several genetic syndromes also cause autistic-like symptoms, including Rett, Fragile X, and Prader-Willi. These authors point out that it's not clear whether these syndromes are comorbid with ASD or whether the intellectual disability often associated with them simply mimics aspects of ASD.[29]

A recent study of over 85,000 children found that use of prenatal folic acid supplements around the time of conception was associated with a lower risk of autistic disorder.[30] Previous research has suggested that excessive folic acid supplementation may have a role in the increased incidence of autism. Junaid and associates demonstrated that additional folic acid prescribed for pregnant women may be associated with widespread changes in the expression of genes in the developing fetus, possibly increasing the risk of neurodevelopmental problems including autism.[31] More research is needed to examine the possible relationship between folic acid supplementation and ASD.

Educating parents about immunization

Teach parents that no link has been found between the MMR vaccine (or any vaccine) and autism. Emphasize that children must receive the MMR vaccine to prevent potentially devastating consequences, including blindness, deafness, and death. Nurses need to be immunization advocates for infants and children.

Parents also need to understand that research doesn't prove associations and causes, but it may suggest cause and effect depending on the level (quality) of research completed. Nurses may want to discuss the levels of research findings when discussing the possible causes of ASD and explain to parents what constitutes the best evidence to help them objectively evaluate research findings related to ASD.

Parents must also be educated about normal and abnormal infant and childhood development so they recognize early signs of ASD. Signs and symptoms of ASD begin before age 3 (in some cases, in the first few months of life) and last a lifetime. Some children with ASD develop normally until around 18 to 24 months, then stop gaining skills or regress.[3,6] See *Signs and symptoms of ASD in young children*.

The American Academy of Neurology and The Child Neurology Society identify these "red flags" that signal the need for immediate evaluation:

- no babbling, pointing, or other gestures by age 12 months
- no single words by 16 months
- no two-word, spontaneous (not echolalic) phrases by 24 months
- loss of language or social skills at any age.[6]

Signs and symptoms of ASD in young children[3,6,35,36]

Signs and symptoms of ASD are highly individualized. A child who displays any of these warning signs should be referred to an ASD specialist for evaluation and treatment.

- doesn't babble or respond to his or her name by age 12 months
- doesn't wave bye-bye or point at objects to show interest by 14 months
- doesn't speak words by 16 months or meaningful phrases by 24 months
- doesn't imitate a parent's facial expressions or smile when smiled at
- doesn't make eye contact
- doesn't play "pretend" games (such as pretending to feed a doll) by 18 months
- flaps hands, rocks body, or spins in circles
- doesn't interact with others
- doesn't initiate or respond to cuddling
- doesn't reach out to be picked up
- automatically repeats words spoken by others (echolalia)
- repeats words or phrases obsessively
- lines up toys or other objects
- plays with toys the same way every time
- is easily upset by minor changes
- shows particular interest in a part of an object, such as a wheel on a toy car
- has unusual reactions to the way things sound, smell, taste, look, or feel
- loses previously learned social or communication skills.

Teach parents that early recognition and intervention is critical for their child's development. Although ASD isn't curable, patients can improve significantly with early intervention. Some may improve so much that they no longer meet diagnostic criteria for ASD.[32]

Screening guidelines

The AAP recommends ongoing surveillance for autism for all children. Besides administering a standardized validated autism screening tool as needed for all children at risk for ASD, primary care practitioners (PCPs) are urged to administer routine screening for all children at the 9- and 18-month well-child visit and again at the 24- and 30-month visits to assess for regression.[6]

Two well-validated screening tools can easily be incorporated into well-child care. Recommended by the AAP, the Modified Checklist for Autism in Toddlers (M-CHAT) screening test is a free, online screening tool for children ages 16 to 30 months.[6,33] PCPs can use it at well-child visits to identify early signs of ASD or developmental delay. The Ages and Stages Questionnaire is designed to screen children from ages 1 month to 5½ years.[34]

If screening reveals any red flags for ASD, the child should be referred immediately to an early intervention program for further evaluation, diagnosis, and treatment.

Referrals and resources

Federal law mandates that states provide publically funded early intervention programs. Having a child evaluated as soon as possible helps confirm the diagnosis and ensures that services for the child will begin as soon as possible.

Recommend the AAP website http://www.Healthychildren.org. Parents can insert "autism" in the search box to pull up the latest research and evidence-based practices.

See *Resources for families affected by ASD* for a list of national resources available on the Internet. Tell parents that many national organizations have local chapters that offer families the support of other families and healthcare providers who specialize in ASD.

Nurses who work with families affected by ASD may also want to become familiar with the local resources available. Inserting "area resources for families with autism" into a computer search engine will provide information about such resources. The child's primary care office is another source of support and information for families caring for children with ASD.

Offer education, resources, and support

Early diagnosis and treatment are the keys to effective care for children with ASD. By educating parents, directing them to the resources they need, and providing support, nurses can have a significant impact on the development of children with ASD. ■

Resources for families affected by ASD

- Healthychildren.org through the American Academy of Pediatrics
  http://www.healthychildren.org/English/Pages/default.aspx
- National Autism Association
  http://nationalautismassociation.org
- Autism Society
  www.autism-society.org
- American Autism Organization
  www.myautism.org
- Autism Science Foundation
  www.autismsciencefoundation.org
- National Autism Resources
  http://www.nationalautismresources.com
- Autism Speaks
  www.autismspeaks.org
- Autism Resources Through Easter Seals
  www.easterseals.com/site/PageServer?pagename=ntlc8_homepage

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Kathleen Peterson is professor and chair, Department of Nursing at The College at Brockport, State University of New York, Brockport, N.Y., and a pediatric nurse practitioner at the University of Rochester, Strong Memorial Hospital, Pediatric Clinic, Rochester, N.Y. Paula Barbel is an assistant professor at The College at Brockport and a pediatric nurse practitioner at Starlight Pediatrics in Rochester, N.Y.

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