

## A Spectrum of Behaviors

Autism, or more specifically autism spectrum disorders (ASDs), range from a severe form, called autistic disorder, to a milder form, Asperger syndrome. In between is pervasive developmental disorder not otherwise specified (PDD-NOS). Other rare, very severe disorders included in (ASDs) are Rett syndrome and childhood disintegrative disorder (CDD). Rett syndrome occurs almost exclusively in girls and involves deteriorating behavior between 6 and 18 months. The child no longer responds to parents, loses the ability to speak, cannot control her feet, and wrings her hands.

The very rare condition called CDD occurs relatively late, between age 3 or 4, with a major decline in speech, social skills, and movement. CDD is also accompanied by loss of bowel and bladder control and often-times seizures and a very low IQ.

## Vaccines under Scrutiny

Many studies have examined whether there is a relationship between vaccines and autism. According to the Centers for Disease Control and Prevention (CDC), the weight of evidence indicates that vaccines are not associated with autism. However, the CDC is committed to protecting the health of children and identifying the biological and environmental causes of autism and other developmental disabilities, and will continue to study the role of vaccines.

## Autism: Unraveling the Mystery

Autism, a complex brain disorder, begins in the first three years of life and can persist into adulthood. Individuals with autism have problems communicating verbally and nonverbally, have limited or no social skills, and often engage in repetitive behaviors, such as rocking or twirling, which can lead to isolation.

Autism is a common name for a group of conditions, referred to collectively as autism spectrum disorders (ASDs). Symptoms vary from mild conditions, such as Asperger syndrome, to childhood disintegrative disorder, which is severely disabling.

An estimated 1 in 150 eight-year old children in the United States has an ASD, according to the Centers for Disease Control and Prevention. The risk is three to four times higher in boys than in girls. Currently, there is no cure and treatments are limited. However, with support from the National Institutes of Health (NIH), scientists at U.S. medical schools and teaching hospitals have made some remarkable research progress that has provided clues about how brain development goes awry in individuals with the disease, and how genes may play a role.

The NIH, principally through the National Institute of Mental Health (NIMH) and four other institutes (Neurological Disorders and Stroke, Deafness and Other Communication Disorders, Child Health and Human Development, and Environmental Health Sciences), supports research by medical schools and teaching hospitals on autism's causes, as well as detection and treatment strategies.

Some important findings from this NIH-supported research follow.

## What Causes Autism?

Both genetics and environment likely play a role in autism development. Recent studies suggest that several genes are involved. Many of the implicated genes control the communications pathways of the brain.

- In 2008, the Autism Consortium, a group of 14 Boston-area institutions, including **Harvard Medical School, Boston University Medical School, Beth Israel Deaconess Medical Center, and Children's Hospital Boston**, found a rare genetic variation on chromosome 16 that dramatically raises the risk of developing autism, opening new research targets for treating the disorder. The defect was inherited in some cases, but was more often the result of a random genetic accident.
- Scientists at **Johns Hopkins School of Medicine** have found a gene variation that may raise the risk of developing autism, especially when the variation is inherited from

### Autism Centers of Excellence

Thanks to crucial funding from the National Institutes of Health (NIH), the nation's medical schools and teaching hospitals are on the frontlines of autism research. On April 1, the NIH announced the latest awardees in the Autism Centers of Excellence program, designed to support studies covering a broad range of autism research areas. Three of the four award recipients are based at U.S. medical schools:

**Daniel Geschwind, M.D., Ph.D., David Geffen School of Medicine at UCLA:** Genetic risk factors among African Americans and whites.

**Diana Chugani, Ph.D., Wayne State University School of Medicine:** Can buspirone, a drug that stimulates serotonin production, promote normal brain growth and development in autistic children?

**Ami Klin, Ph.D., Yale University School of Medicine:** Eye-tracking technology for early detection of autism spectrum disorders, perhaps before symptoms emerge.

mothers rather than fathers. The gene, *CNTNAP2*, makes a protein that enables brain cells to communicate with each other through chemical signals and appears to play a role in brain cell development. In this 2008 study, researchers were able to link a specific variation in the protein's structure to autism.

- Two 2005 studies at **Vanderbilt University Medical Center** suggest that mutations in the gene regulating brain serotonin, a chemical necessary for communication between nerve cells, may be an autism risk factor. In 2008, these researchers determined how the mutation may block serotonin's activity.
- By age 2, children with autism show a generalized enlargement of their brains, according to a 2005 study of MRI scans by researchers at **University of North Carolina at Chapel Hill** and **Duke University medical schools**. In autistic children, the temporal lobe, where language is controlled, was enlarged, along with other parts of the brain. It is unclear whether the brain enlargement is a primary cause of autism or a downstream effect of another process occurring in the brain.
- In 2005, researchers at the **University of California (UC), Davis, School of Medicine** demonstrated that children with autism have different immune system responses than other children. The results provided important evidence that scientists may one day be able to diagnose autism through early biological changes, rather than the behavior-based diagnoses used today.

### Improving Diagnosis and Treatment

Researchers are looking for neurological or other biomarkers to enable earlier diagnosis and treatment. Most professionals agree on the importance of early intervention with highly structured, specialized programs. For serious behavioral disturbances, such as self-injury, aggression, hyperactivity, and tantrums, behavioral therapy (teaching children how to overcome anxiety and develop better social skills) and medications are the two main forms of treatment. Many people with autism continue to require a high level of support throughout their adult years.

- Risperidone, an antipsychotic medication, was effective and well tolerated in a 2002 placebo-controlled study for the treatment of serious behavioral disturbances associated with autistic disorder in children ages 5 to 17, according to research at **Yale University School of Medicine**. In 2006, the drug became the first medication approved by the Food and Drug Administration for the treatment of autism symptoms.
- Children with autism are often placed on restrictive diets in hopes of improving some symptoms. Researchers at **Cincinnati Children's Hospital Medical Center** collaborating with NIH investigators found in 2008 that dairy-free diets and unconventional food preferences could place boys with autism at a higher-than-normal risk for thinner, less dense bones when compared to a group of same-aged boys who did not have autism.

Several NIH-supported studies have been launched in the past year to improve treatments by taking advantage of new knowledge. For example, researchers are currently examining the use of an antibiotic minocycline in treating regressive autism. Children affected by this condition develop normally until about 18 months, when they lose speech and social skills. Research studies like the one at UC Davis School of Medicine referenced earlier, suggest that autism may be linked to changes in the immune system that cause inflammation in the brain. Minocycline has known anti-inflammatory effects. Others are determining the impact of chelation therapy, an unproven, though popular, treatment to remove heavy metals from the bloodstream. As scientists learn more about the origins of the disorder, more treatment options will be explored.

For more information about how medical schools and teaching hospitals are fulfilling the promise of medical research, go to [www.aamc.org/ftp](http://www.aamc.org/ftp).