

Unravelling the mystery of autism

by Lenny Rappaport, MD, MS

Autism, which is now seen as a group of related conditions called autism spectrum disorders (ASDs), appears to be the fastest growing serious developmental disability in the United States. In fact, recent estimates suggest that one in 165 children is diagnosed with an ASD, and these figures are consistent world-wide. The Harvard School of Public Health estimates that it costs \$3.2 million to take care of an autistic person over his lifetime; the majority of the cost is lost productivity and adult care.

The gold standard treatment for ASDs is intense, individualized, one-to-one behavioral intervention, and outcomes in children identified and treated before age 3 appear to be much better than those diagnosed later in life. There's currently no medical treatment for the core symptoms, although medications have been used successfully for related symptoms, such as hyperactivity, attention problems, anxiety and behavioral disorders.

The cause of the increasing prevalence of ASDs is unclear. Certainly, the diagnostic category has been widened and some of the children placed on the autism spectrum would not have been diagnosed with ASDs in the past. In addition, many children have been reclassified as having ASD with mental retardation rather than just mental retardation. There also may be an environmental cause of autism or perhaps an environment stimulus on top of a genetic vulnerability that's responsible for the increase in prevalence. Immunizations have been suggested as this stimulus, but all research to this point does not support them as a cause of ASDs.



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Center

Due to the seriousness of ASDs and their impact on individuals, families and society, Children's Hospital Boston has undertaken major initiatives to improve early identification and diagnosis, advance research into the causes of ASDs and develop novel diagnostic and treatment modalities, including the translational research being carried out by several of our scientists (see page 2). Our clinicians and scientists are beginning to unravel the mystery, and thanks to funding from Children's and philanthropy, as well as

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LATOYA GAYLE with her children, Summer and Troy. Troy has been diagnosed with Pervasive Developmental Disorder, Not Otherwise Specified (PDD-NOS), which is on the autism spectrum.

Early identification and continuity of care

There is much that isn't understood about autism spectrum disorders (ASDs), but experts agree on one thing: Behavioral intervention is the only treatment that has shown efficacy in multiple clinical trials, and the younger a child starts, the better her chances of improvement. But only about 30 percent of children with developmental and behavioral problems, including autism, are identified before kindergarten. This number doesn't impress Alison Schonwald, MD, an outreach director at Children's Hospital Boston's Developmental Medicine Center (DMC), who is leading a statewide effort to ensure that children across Massachusetts are screened as early as possible, and that services are available once a diagnosis is made. "We need to do a better job identifying kids earlier so they can quickly access services," she says.

Progress in early identification has been facilitated by the outcome of the *Rosie D. v. Romney* case, which required developmental and behavioral screening at all primary care visits for children and adolescents; this mandate has led to Medicaid coverage for screening and has been adopted by many private insurers throughout the state. While not fully instituted, this change has put the promise of early identification within reach, and Children's has led the statewide

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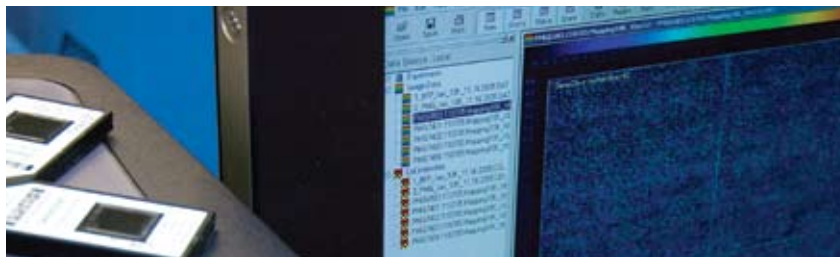
About this publication

Through this publication, Children's Hospital Boston's Office of Child Advocacy strives to serve as a resource on legislative issues that affect children's health and their pediatric providers. This issue of *Advisory* focuses on the ways Children's is breaking new ground to help autistic children and their families.

Can we detect autism in babies?

It's difficult to diagnose autism spectrum disorders (ASDs) in babies because many early signs, such as not responding to the sound of one's name, aren't reliable before the child is 12 to 18 months old. Charles Nelson, PhD, director of Laboratories of Cognitive Neuroscience and research director of the Division of Developmental Medicine at Children's Hospital Boston, aims to move this diagnostic window back to the first few months of life—before babies reach their first birthdays. The ultimate goal of this work is to identify infants at greatest risk for developing autism and then develop appropriate early interventions that might prevent the disorder from progressing, or perhaps even from developing.

As part of their efforts to identify such early risk markers, Nelson's group is studying brain and behavior development in both high- and low-risk infants. High-risk infants are those with at least one older sibling with autism, whereas low-risk infants are those with no family history of the disorder. The babies perform several tasks: They view images of their mother and a stranger while researchers measure their brain activity and track their eye movements, listen to familiar and unfamiliar language sounds while their brain activity is measured and complete an array of behavioral tests. Preliminary findings suggest that at 6 months, at-risk infants show less differentiation between native and non-native speech sounds compared with controls; at 6 and 12 months, the high-risk group responds more slowly to their mother's faces than low-risk infants. Overall, their brains also generate less of a particular type of brain activity that has been associated with integrating information. The team will follow the infants up to age 36 months and see which children will be diagnosed with autism.



Genetic discoveries and clinical trials

Studies show that autism spectrum disorders (ASDs) are highly genetic and have the highest likelihood of heritability of any mental health disorder, estimated at 90 percent. Thanks to the genetic leap forward facilitated by the Human Genome Project, a number of genetic disorders causing ASDs have been recognized, such as deletions or duplications on chromosomes. However, at this point, genetic diagnoses can only be determined in 15 to 20 percent of children diagnosed with ASDs.

A number of Children's researchers are trying to drive this number up. A study led by Christopher Walsh, MD, PhD, chief of Genetics, studied 88 large Middle Eastern families with a high incidence of autism due to marriages between cousins (increasing the likelihood of rare inherited mutations). It found a half-dozen new genes that could be related to autism.

Louis Kunkel, PhD, director of Children's program in Genomics, and Isaac Kohane, MD, PhD, director the

hospital's Informatics Program, are leading an ambitious study looking for irregular patterns in the way genes are expressed in the white blood cells of autistic children. In addition, they're studying the DNA samples of children age 2 and older, along with their parents and affected siblings, to look for genetic differences shared within families. They plan to draw on hundreds of thousands of samples to compare patterns.

As genetic discoveries reveal causes of autism, Children's researchers are launching clinics to treat patients with each sub-disorder in which autism is a common finding, such as Fragile X syndrome (which accounts for some 2 to 6 percent of autism cases), Rett syndrome (the leading single genetic cause of autism in females), tuberous sclerosis and Smith Magenis syndrome. The more doctors understand the diverse causes of autism, the more they can translate new genetic discoveries into better clinical care and tailor treatments to a child's condition.

MEET OUR SPECIALISTS AND SCIENTISTS

Extremely premature infants are known to have a high prevalence of learning disabilities and attention and behavioral problems. Babies born

weighing less than 1,500 grams also have an increased risk for showing early signs of autistic features, according to a study conducted by

Catherine Limperopoulos, PhD, a researcher in Children's

Department of Neurology. Her findings suggest that early screening for signs of autism may be warranted in preterm infants. Her discovery also underscores the importance of providing better pre-natal care to expectant mothers to decrease the likelihood that their babies will be born prematurely.



Neuroscientist **Frances Jensen, MD**, is studying the long-term effects of early seizures. She's showing that shortly after certain kinds of sei-

zures, changes in the brain networks begin to happen that in some cases can result in severe cognitive problems and learning deficits later in life. Jensen hopes to avoid the lifelong complications of severe newborn seizures, which can include mental retardation, cerebral palsy and autism, by halting them as early as possible—ideally in the first hours after birth.



Janice Ware, PhD, associate director of the Developmental Medicine Center, is a specialist in developmental psychopathology and pediatric

psychology at Children's. In December 2008, she was appointed to Governor Deval Patrick's Commission on Mental Retardation (soon to be called Developmental Services) and will participate in the development of public policy related to people with disabilities. She has an expertise in autism and will play an important role in advising the Department of Mental Retardation as it moves forward with its new Autism Division and the provision of services to children with ASDs.



Early identification

effort to train pediatricians how to efficiently and effectively screen for developmental disorders.

To assist primary care providers who want to begin using the newest tools in their practice, Schonwald created an easy-to-use Web site with information on the many tools, time requirements and associated costs. She's also spoken to 600 pediatricians across the state about how to screen and the importance of early identification.

After children are identified with an ASD, the next challenge is connecting them with services. Too often, children with autism get placed in catch-all "disability" classrooms that don't focus on autism-



ALANA GREEN,
resource specialist

specific therapies, like building social skills. The Autism Consortium, a collaborative effort between researchers and physician-scientists from 14 institutions in the Boston area (of which Children's is a member), has

trained autism resource specialists to work at five major hospitals in the state to help connect patients with proper services and free up doctors so they can focus on screening, evaluation and treatment.

When a child is diagnosed with an ASD at Children's, a resource specialist based in Neurology or the DMC connects with the family. "The initial goal is to be there for them," says the DMC's Resource Specialist, Alana Green. "As you can imagine, getting a diagnosis like that can be overwhelming." Green then connects the family to resources near their homes and helps them follow through with specific treatment recommendations. "It becomes an ongoing relation-

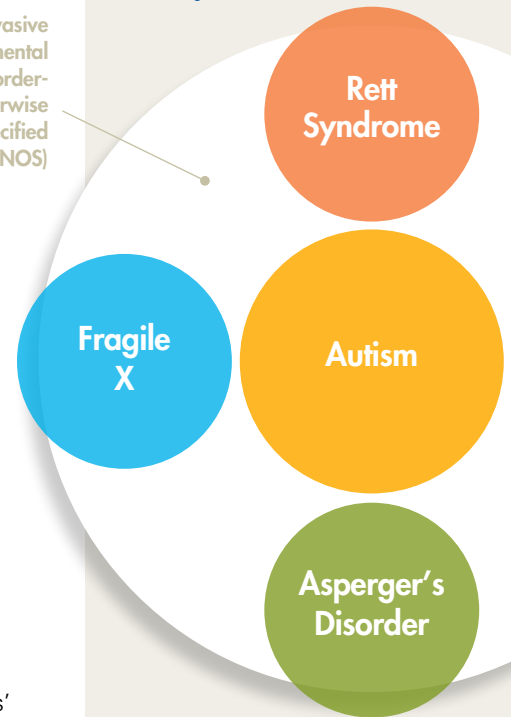
ship," she says. To further support patient families, Children's launched an email service to help manage their child's care. Following an autism diagnosis, families receive an email once a week for the first two months, and then every other week for the rest of the year. Green also sends blast emails when there are new breakthroughs in research, if autism is in the news or comes up in government affairs.

One challenge Children's and other diagnostic centers face is long waitlists, partly due to families wanting to be screened by more than one center. Some families may feel as though there are special services they'll only be told about at different institutions; Green tries to make it easier for families to feel satisfied with one contact. A greater challenge is the care delivery system: Despite parents', clinicians' and resource specialists' best efforts, there can be significant lag times from when children are diagnosed to the time they start therapy. Once they do start, schools often don't have the capacity to offer the necessary individualized, one-on-one therapy. Improved funding could go a long way toward getting kids into appropriate school-based treatment and the adequate management of kids once they're in the right program. Efforts are underway at the state and federal level to expand access to therapeutic services. Legislation to improve insurance coverage of the diagnosis and treatment of autism spectrum disorders has been introduced in many states and enacted in eight. Some states have successfully pursued Medicaid waivers to provide Medicaid eligible children with ASDs with intensive in-home services and have those costs partially reimbursed by the federal government.

The autism spectrum

WE KNOW MORE ABOUT THE "CORE" of autism than its edges.

Pervasive
Developmental
Disorder-
Not Otherwise
Specified
(PDD-NOS)



Mystery of autism

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local, state and federal support, our progress has been astounding.

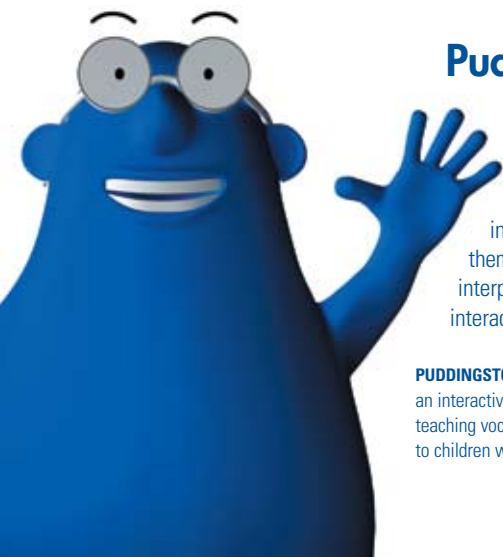
However, major obstacles stand in the way of definitive answers. First, developmental services are poorly reimbursed in primary care and specialty settings, limiting the availability of expert diagnostic services. Once identified, a child with an ASD requires the only treatment available—behavioral therapy—up to 30 hours per week—but there aren't enough certified specialists to meet the demand, and severe funding issues surround school-based therapy. Finally, research support for high-risk/high-impact diagnostic and therapeutic interventions for ASDs has been increasingly restricted due to National Institutes of Health and, recently, foundation budgets. But given that ASDs have reached epidemic proportions and a social and economic system to manage them isn't in place, we need to invest strongly in autism research.

Despite these challenges, great progress has been made to improve the lives of children with ASDs and their families. In the coming year, we anticipate at least three clinical trials in Rett syndrome, Fragile X and tuberous sclerosis—all major causes of autism symptoms whose therapies, if successful, may guide us to breakthrough treatments.

Puddingstone Place

Howard Shane, PhD, director of Children's Center for Communication Enhancement, creates tools to improve the language and communication skills of children with ASDs. Because autistic children usually have strong visual skills and an interest in computers, he's created interactive software systems to teach them how to perform tasks, interpret sounds and socially interact more appropriately.

PUDDINGSTONE COMMUNITY offers an interactive virtual environment for teaching vocabulary and language skills to children with autism.



From screening to diagnosis to treatment

Screening

The **Advocating Success for Kids program** screens children being treated at **Children's Primary Care Center** and other local health centers who are at risk for developmental issues due to medical, mental health, emotional and/or learning problems. The team identifies barriers to the child's care and makes personalized recommendations.

Diagnosis

The **Department of Neurology's** autism clinic provides complete neurological evaluation and diagnosis. Clinicians monitor children's medications and follow up on services. Clinicians share patients' full genetic work-ups with the families and with Children's researchers.

The **Developmental Medicine Center** provides developmental evaluation, short-term individual and group treatment services and behavioral and learning consultations. It treats children from birth to adolescence with a range of developmental, behavioral and learning difficulties, including autism.

Treatment

Children's Community Early Intervention (EI) program, based at Children's **Martha Eliot Health Center**, offers developmental screening and evaluation, home visits and play groups to support the developmental progress of children from birth to age 3. The EI team includes developmental specialists, social workers, physical therapists, speech-language pathologists, occupational therapists and other specialty providers.

The **Center for Communication Enhancement's Autism Language Program** helps children with autism spectrum disorders communicate more effectively. Children are evaluated and given a communication plan, including suggestions for both school and home. The center's **Language Therapy Program** focuses on social communication and play and uses music as one of its therapeutic options.



Advisory

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