

In Autism, New Goal Is Finding It Soon Enough to Fight It

By ANAHAD O'CONNOR

SEATTLE — Sitting in a small evaluation room at the University of Washington, apprehension written on her face, Christa Zamora turned her eyes toward her son Connor and contemplated his future.

A talkative and animated 2-year-old, Connor appears normal, Ms. Zamora said, but it is too soon to be certain. Doctors diagnosed autism in her older son, Cameron, just before he turned 3. And with Connor, who is also at risk for developing the devastating neurological disorder, which runs in families, she has decided to be proactive, enrolling him in an early diagnosis study for children as young as 16 months.

"I'm very concerned," said Ms. Zamora, who is also worried about her third child, a boy due in February. "Connor seems to be past the danger zone. But Cameron repeats himself a lot, and sometimes I see Connor doing the very same things."

Across the country, thousands of toddlers like Connor are joining studies that could signal new hope for a baffling childhood disorder.

For years, autism was rarely noticed before the age of 2, its symptoms overlooked by busy parents or so subtle that pediatricians missed them. According to federal figures, only a third of the 6-year-olds who were receiving treatment for autism in 2002 had been identified by age 4.

But in the last two years much has changed. Propelled by an explosion of public awareness and growing evidence that early treatment with behavioral therapy can improve a child's chances, scientists have set out to diagnose the disorder as early as possible, and slowly, more children with autism

are being identified before they turn 2.

Doctors hope to be able to identify these kids at birth.'

Already, the average age of diagnosis in Britain has tumbled from roughly 43 months to 38 months or younger in only a few years, a pattern experts see emerging in the United States. And studies now under way could sharply alter the landscape of early detection by allowing physicians to routinely screen children before age 2, perhaps even in infancy.

"Part of it is that parents are more interested, and that pediatricians are getting a lot more sophisticated at detecting it," said Dr. Fred Volkmar, a professor of child psychiatry at Yale. "As these things have come together, there's no question we're seeing a lot more parents who are coming forward around the country with younger and younger children."

Autism isolates, robbing those afflicted of their ability to communicate or to grasp even basic social cues. Human faces, awash in meaning to most people, are inscrutable to people with autism; many cannot look another person in the eye. But behavioral therapy is one bridge to the outside world, and while experts say it can make a difference at any age, almost all agree that it has the largest effect on a child's language, social development and I.Q. when started before children turn 4.

"Intervention should start before the age of 3, and certainly by the age of 4," said Dr. Deborah Fein, a professor of psychology at the University of Connecticut. "After a certain point, you can still teach an autistic child certain things, ameliorate destructive behaviors, but you're not really going

to change the developmental path-way that they're on."

The goal now, experts say, is to augment screening techniques so cases no longer elude them as the window for intervention narrows.

At the University of Washington and elsewhere, researchers are experimenting with a routine test that can flag children by 18 months, the earliest point for reliably identifying the disorder, many experts contend. It is also early enough for therapists to intervene.

At the same time, other researchers see promise in more sophisticated diagnostic tools — devices that can measure brain and behavioral responses to the sound of a mother's voice, or genetic or biological markers that can be detected in infancy.

"The goal is to be able to identify these kids at birth," said Dr. Geraldine Dawson, director of the University of Washington's autism center. "Until fairly recently, we hadn't really defined the very early symptoms of autism. But in the last several years, research has identified the behaviors you can see in a child as young as 12 months."

Dr. Dawson and others hope to accelerate their progress by focusing on high-risk groups. About one person in 200 in the general population suffers from autism spectrum disorder, compared with roughly one person in 20 who has an autistic older brother or sister.

As a result, researchers are increasingly focusing on the families of autistic children, recruiting younger siblings who can be followed from birth to pinpoint when normal development veers off course.

Such studies could help scientists learn, among other things, why roughly a quarter of children with the disorder descend into autism seemingly overnight, quickly spiraling from talkative to mute, outgoing to aloof. In the past, when diagnoses were made after age 4 or 5, scientists were forced to rely on grainy home videos of first birthdays for early clues. Now, they are seeing autism unfold before their eyes.

"We're hoping that if we follow enough kids, we can watch that progression," said Dr. Catherine Lord, director of the autism and communication disorders program at the University of Michigan.

Faint Signs Often Missed

In some cases, researchers are already reporting breakthroughs. Last month, Dr. Ami Klin, an associate professor of child psychology and psychiatry at Yale, published one of the most comprehensive case re-ports of a toddler with autism. The child, called Helen by Dr. Klin in the article to protect her identity, was 15 months old when autism was diagnosed. At 12 months, her language skills deteriorated and she began withdrawing. By the time she reached the clinic, she had almost no interest in other people. Her brother, two years older, is also autistic.

"Historically, children wouldn't reach a specialized center like ours until a much later stage," Dr. Klin said.

Experts say that while more and more children like Helen are coming to their attention, for now, they are the exception. It is too soon, many agree, for most children that young to be spotted by anyone other than a specialist or an alert parent who has already raised an autistic child.

At that age, the range of social behaviors is limited, and most tests were developed for older children, intended to see if a child was engaging in age-appropriate activities like playing peek-a-boo or showing interest in other children.

Detecting Autism Soon Enough to Fight It



Gary Settle for The New York Times

Christa Zamora reads to her sons, 2-year-old Connor and 4-year-old Cameron. Autism was diagnosed in Cameron just before he turned 3, and Connor is also at risk for developing the neurological disorder.

The signs of autism may be too faint to show up in such tests, or simply not yet present.

"One big problem is that some kids just don't have all the features by 2 or 3," Dr. Volkmar said.

Chances Slip Away

Another problem, even with older children, is that pediatricians rarely use the tests, which can take time to administer, to screen their young patients. Instead, one study by the American Academy of Pediatrics found, most physicians prefer to "eyeball" children, a notoriously unreliable method that probably allows many cases to go unnoticed.

Other doctors sidestep the issue altogether. Parents who express concerns about their toddlers are often told to wait a few months, "to see if the child grows out of it." Rather than make the fateful decision to refer a child to a specialist for a diagnosis, some experts say, pediatricians sometimes suggest instead that the children are late talkers, or only slightly behind.

"I think a lot of doctors, if they aren't completely sure about what they are seeing, are afraid to say so," said Dr. Isabelle Rapin, a professor of child neurology at the Children's Hospital at Montefiore in the Bronx. "So they tell the parent 'you're over-worried,' or they come up with all sorts of excuses because they don't want to give a parent the news that their child might be autistic."

But delaying a diagnosis, and as a result early treatment, can have life-long consequences. A child referred to a specialist can end up on a waiting list for months in some

parts of the United States. When the diagnosis finally comes, another year could go by while the child waits on a second list for treatment.

"The journey is easily over two years from the first step to getting treatment," Dr. Dawson said.

All the while, chances to slow the progression of the disorder slip away. To encourage parents and physicians to act quickly when a child's development is stagnating, experts at the Centers for Disease Control and Prevention, working with other groups, have begun a public awareness campaign, called "Learn the Signs. Act Early."

It is designed to educate parents and health care professionals about the major milestones, from imitating facial expressions to finger-pointing and telling stories, that a child needs to achieve at various developmental points between 3 months and 5 years.

Casting a Wide Net

And who better to spot autism than parents? Subtle changes in behavior may be more obvious to a mother or father who sees a child daily than to a pediatrician who has 50 other patients.

So experts want parents to play a larger role. They have taken a widely used screening tool, the Checklist for Autism in Toddlers, or the CHAT, and replaced a section that pediatricians complete with a series of yes-or-no questions for parents. It can be filled out in just a few minutes, ideally at home or in a waiting room before a child's checkup. It is available online at firstsigns.org.

Unlike its earlier version, which is extremely precise, the new M-CHAT casts a wide net. In England, studies of thousands of children showed that the CHAT, although it accurately identified many cases of autism, was so specific that it failed to detect a majority of cases. The M-CHAT, with looser boundaries and greater sensitivity, is intended to flag even subtle cases. Experts say that it will probably produce more false positives — flagging children who are not actually autistic — but that they prefer to err on the side of caution.

Dr. Fein, of Connecticut, is leading a large study to help validate the M-CHAT's usefulness. In the last five years, about 4,000 New England toddlers, ages 18 months to 24 months, have been screened with the test during normal visits to their pediatricians. At the age of 4, they are evaluated once more to determine whether the M-CHAT is accurate. So far, Dr. Fein said, autism has been diagnosed in about 200 cases, and the test is holding up.

"Most of the kids stay with their diagnosis," she said. "If we didn't think they were autistic at 2, then they aren't autistic at 4."

On the other hand, about 15 to 20 percent of the children labeled autistic at 2 no longer meet the definition by the time they turn 4. That could mean that they were false positives, Dr. Fein said, or simply that catching them early made a difference.

"One possibility is that they got good, effective intervention and recovered, which I think is what's really going on," she said. "I see a

lot of kids at 2 who are clearly autistic and then at 4 they are doing terrific. These are kids who have recovered enough so that no one would ever know that they were on the autistic



Kevin P. Casey for The New York Times

Dr. Geraldine Dawson of the University of Washington's autism center says, "In the last several years, research has identified the behaviors you can see in a child as young as 12 months."

spectrum."

Such outcomes, Dr. Fein said, are rare but not impossible. Many more children who begin behavioral therapies will make more modest gains, improving just enough to grasp a few rules of social interaction, or building a small vocabulary. Still others will remain severely disabled, beyond the reach of any therapy. Dr. Eric Fombonne at McGill University in Montreal, for one, says that some children cannot completely overcome autism.

He points to studies suggesting that children who show marked improvement after behavioral intervention are those labeled P.D.D.-N.O.S., or pervasive developmental disorder not otherwise specified, because they exhibit only some autistic symptoms. Those who meet the stricter definition of autism often show less impressive results.

"Some children, at base line, have more severe difficulties and won't always make the expected gains," said Dr. Fombonne, a professor of child and adolescent psychiatry.

The extent of behavioral therapy's potential remains an open question, and evidence suggests that it varies enormously from one child to the next. Yet even those who believe it has only limited effect on some children seem to agree, nonetheless, that it is most helpful when started early.

"What we do know is if you start it after a certain age, the outcome is going to be more negative," said Dr. Fombonne. "It makes sense that that would be the case."

In the coming years, some advocates hope, every child will be screened for autism by his or her second birthday, with the M-CHAT or a similar checklist. But casually observing a small child's behavior only reveals so much, and researchers say they will need more diagnostic tools if they are to detect faint glimmers of the disorder in infants.

A Mother's Melody

Dr. Patricia Kuhl and colleagues at the University of Washington think they have one answer. They have found that small children are naturally lured by the melody of a mother's speech — the stretched pronunciation of vowels that produces sounds like "ah" and "oo."

When exposed to this baby talk, or "motherese," normally developing children display a distinct pattern of brain activity that can be measured with electrodes, while autistic children show little interest and fail to produce the expected neural response. Autistic subjects, on average, prefer to listen to a computer generated warble instead.

The findings suggest that autistic brains may be wired differently from birth, leading to delays in language and other hallmarks of the disorder.

"The beauty from a practical aspect is that these simple measures can be used extremely early in life," Dr. Kuhl said.

Perhaps the simplest autism screening tool, one that many consider the holy grail of early detection research, is a genetic test. It is not clear to what extent environmental influences — infections and childhood vaccines, for example — play a role in the onset of the disorder, but experts are certain that heredity is a major factor. Studies of identical twins, for example, suggest

that if one twin has autism then the other has more than a 60 percent chance of being autistic as well.

After years of searching, they have homed in on several regions of different chromosomes that may lie behind autism, and earlier this year a team at the Mount Sinai School of Medicine in New York pinpointed at least one gene that contributes to the disorder. A simple genetic test, however, is more elusive than it seems. Experts suspect that more than 20 genes could be involved, each under-lying a different aspect of autism. Dr. Dawson, in her studies of high-risk siblings, is finding that even children who

inherit just a few of these genes, like Connor Zamora in Seattle, may periodically display repetitive movements or other quirky behaviors without actually crossing the threshold into full-blown autism. About 10 to 15 percent of siblings may have this milder variant, Dr. Dawson said.

"It's a new concept for parents to understand," she said. "They could have a young child who doesn't have enough symptoms to have autism, but has some mild aspects like language delay or social awkwardness that they might need help with."

Experts say that for all the promise it might hold, a screening technique that can consistently detect children

younger than 18 months, not to mention in infancy, is probably years away. To the extent that that is even possible, scientists say they would then have to grapple with a much larger problem: providing treatment to an explosion of small children when services are already stretched thin.

"We're going to have more and more children under 3 getting diagnosed," said Dr. Volkmar. "But sadly, it looks like we're going to have fewer and fewer services for them."