

Drugs Make Other Autism Interventions Easier

BY JANE SALODOF MACNEIL
Southwest Bureau

SANTA FE, N.M. — Pharmacotherapy does not cure autism, but it can make autistic children accessible to other modes of treatment, Bennett L. Leventhal, M.D., said at a psychiatric symposium sponsored by the University of Arizona.

"There are no pharmacological treatments for the cardinal symptoms of autism. Those things are not responsive to medication," advised Dr. Leventhal, director of child and adolescent psychiatry at the University of Chicago.

"But making kids available to other interventions may help them improve," he said.

When children are referred for pharmacotherapy, psychiatrists should begin with a complete work-up, he said. Though additional measures may be used, he said no child should be diagnosed without evaluation by two standard instruments: an Autism Diagnostic Interview (ADI) and the Autism Diagnostic Observation Schedule (ADOS).

Dr. Leventhal recommended doing a physical examination with neurologic studies even if the child has been referred by a family physician. Family physicians are not equipped to examine children with disruptive behavior in their offices, he said.

Moreover, these children may have other impairments that were missed because of challenges in communicating with them. For example, he said he has seen deaf children who were classified as autistic because no one recognized hearing loss.

Attention-deficit hyperactivity disorders used to be ruled out in autistic children, he said. While these youngsters can concentrate intensely on what interests them, specialists now recognize that many autistic children have difficulty paying attention.

Dr. Leventhal said he treats them with the same stimulants used for attention deficit in children who are not autistic. "There are no studies of stimulants in children with autism, but there is no reason to think these agents would not apply here," he said.

No one stimulant has proved better than another, he added. The biggest problem, he said, is getting autistic children to swallow pills. He suggested that that problem can be overcome by breaking up Ritalin or Adderall capsules and sprinkling the medication on food.

Dr. Leventhal recommended serotonin reuptake inhibitors (SSRIs) for control of stereotypic behaviors, such as repetitive behaviors, self-stimulatory behaviors ("stimming"), habits, and tics. He cited studies showing improvements with fluvoxamine (Arch. Gen. Psychiatry 1996;53:1001-8) and fluoxetine (Neuropsychopharmacology 2005;30:582-9).

An added benefit is SSRIs can reduce aggression, he added, describing aggression and irritability as another serious problem for people with autism. "It is one that limits access to community," he said.

Dr. Leventhal reported that he no longer uses traditional neuroleptics because of side effects. Atypicals are coming into use, he said, but there is not much evidence in this population, except for risperidone (Risperdal).

Johnson & Johnson, parent company of risperidone maker Janssen Pharmaceutica Inc., announced in May that the Food and Drug Administration had informed the company that risperidone was "not approvable" for autism. Dr. Leventhal expressed bafflement at the decision, as he quoted data from studies that found risperidone to be effective (J. Am. Acad. Child Adolesc. Psychi-

atry 2002;41:140-7; Arch. Gen. Psychiatry 1998;55:633-41; N. Engl. J. Med. 2002;347:314-21).

"There's more than ample evidence that at least risperidone as an agent leads to better overall function and reduces irritability. The FDA did not think of much of the application. It looks like ample data to me," said Dr. Leventhal, who listed a consulting relationship with Janssen in a disclosure of interests with several pharmaceutical companies.

The risperidone doses are "relatively modest": 1-3 mg per day, he added, reporting better outcomes and fewer side effects with lower doses. Lithium is another option that reduces aggression regardless of diagnosis or cause, according to Dr. Leventhal, who said he has also used propranolol in extreme cases.

Whatever the agent, attention to dosing is critical, Dr. Leventhal advised.

"In children with autism, side effects are very difficult to treat and very difficult to follow because these kids are not verbal," he said. "If there are side effects, you have to look for them."

He discouraged use of novel anticonvulsants for mood disorders, anxiolytics for anxiety disorders, and chelation to remove heavy metals when treating autistic patients. Secretin, a drug that failed several randomized trials in autism, "may actually be harmful," he said.

Pharmacotherapy will change with development of new medications, but treatment will remain multimodal, Dr. Leventhal predicted. The cognitive enhancers approved for Alzheimer's disease are a possibility for autism, he said. "Whether it works or not is an open question. Some of our data suggest this might have some utility."

Studies support the use of SSRIs for control of stereotypic behaviors, such as repetitive behaviors, self-stimulatory behaviors, habits, and tics.

Consider Genetic Disorder in Some Milder Autism Cases

BY LINDA LITTLE
Contributing Writer

GRAPEVINE, TEX. — Physicians need to be alert to a cause of autism that might not be immediately apparent in milder cases, a Colorado pediatrician warned.

Smith-Lemli-Opitz syndrome (SLOS), a disorder caused by a defect in the cholesterol metabolic pathway, should be in the differential diagnosis for children presenting with autism, said Ellen Elias, M.D., director of the special care clinic of the Children's Hospital, Denver.

Some SLOS children with autism never see a geneticist and may be followed by a developmental pediatrician or neurologist, she said. "Often, they are not diagnosed if they are a milder case without the usual facial features."

Yet a simple blood test can alert parents to the 25% recurrence rate as well as treatment that can alleviate some behavioral problems in this syndrome, she said.

SLOS is an autosomal recessive disorder caused by a metabolic error in the cholesterol pathway. Children with SLOS have distinct facial features: smaller heads, upturned noses, and small chins; growth retardation; mental retardation; and multiple birth defects. In milder forms of the syndrome, children might not have the distinctive facial features and may present with autism, Dr. Elias and her associates wrote in a poster presentation at the American College of Medical Genetics.

In a study of 15 patients with confirmed SLOS followed in the clinic, the researchers found that three males had the classic autism phenotype but didn't have the classic physical features of SLOS. Two of the boys had sisters with SLOS but without autism. Dr. Elias predicts that the syndrome is far more common than the estimated 20,000 children with the classic form. "People at the mild end of the syndrome don't get tested or identified," she said.

"The incidence of autism has increased dramatically over the past 10 years," she said. Although genetic etiologies are suspected, only 10% of autism patients are identified as having a genetic diagnosis.

The simple blood test for SLOS testing for elevated serum 7-dehydrocholesterol was developed in 1994 and can be used prenatally and in children suspected of having the syndrome. It also allows diagnosis of the children who fall into the milder end of the spectrum, particularly those who lack the typical facial features or birth defects associated with the classic SLOS.

In children presenting with autism without the typical features with SLOS, she advised physicians to test for SLOS in children with milder features. Physicians should look for growth retardation, a head that is on the small side, and webbing between the second and third toe.

If children aren't diagnosed correctly, they won't receive adequate treatment, and there is a chance of siblings being born with the syndrome, Dr. Elias said.

Children with SLOS can benefit from cholesterol treatment, which lessens some behavioral side effects of the syndrome, such as irritability and attention deficit, she said. In addition, children with SLOS should not be treated with Haldol (haloperidol) or BuSpar (buspirone), which can exacerbate the biochemical parameters of the syndrome.

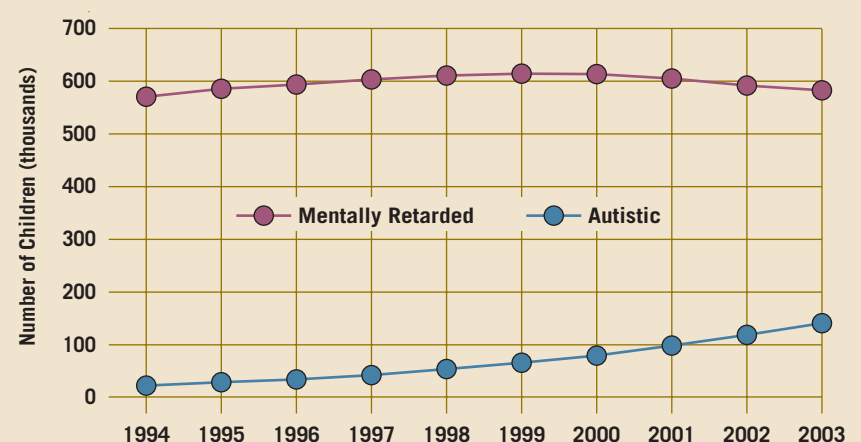
If SLOS is suspected, it is important that the blood sample be sent to a special laboratory, because many hospital-based lab-

oratories cannot distinguish between cholesterol and its precursor, 7-dehydrocholesterol, she said.

"There is a tendency to look at these children and think they are normal in appearance and simply have autism," Dr. Elias said. "It is important not to miss a diagnosis of a child with SLOS in a child presenting with autism, so that appropriate genetic counseling can be provided to the family and [cholesterol treatment] may ameliorate problematic behavior in the child."

DATA WATCH

Disabled Children Aged 6-21 Years Served Through Public Special Education Services



Source: U.S. Department of Education