Secretin: positive, negative reports in the "top of the first inning"

The media frenzy started about December 3, when the December 9 issue of the *New England Journal of Medicine* began arriving at most of the major newspapers and television networks throughout the U.S. For the next week, we were besieged by requests for telephone interviews and for informational faxes by ABC, CBS, CNN, *USA Today*, and a multitude of journalists from other segments of the media, large and small. The stimulus for all this activity was, as you are almost certainly aware, the publication in the NEJM of the first formal report of the results of a controlled study of the use of secretin with autistic children.

The study was conducted at the Olson Huff Center for Child Development at the Thoms Rehabilitation Hospital in Asheville, North Carolina. Data had been collected on 56 children, two thirds of whom had been diagnosed autistic and the remainder PDD. Half were given secretin, the other half received a placebo saline infusion. The title tells the story that had so excited the media: "Lack of benefit of a single dose of synthetic human secretin in the treatment of autism and pervasive developmental disorder."

The article was followed by an editorial titled "Lessons from secretin," by Fred R. Volkmar of Yale University, which many of the journalists and parents who have contacted us found particularly offensive and patronizing. "Pursuing unproven treatments risks depleting the financial and psychosocial resources of families," Volkmar informs us, adding, "It is important that physicians help families make informed decisions about treatment for autism."

Unlike the authors of the research article itself, Volkmar seemed quite willing, if not eager, to dismiss secretin on the basis of very preliminary results with a single dose of the hormone. Volkmar believes genetic research is a better bet, saying recent research has uncovered "several promising leads." (In fact, recent genetic research has *not* produced promising leads—see next issue of the ARRI.) Volkmar also tells the readers of the NEJM that autism still affects 1 in 2,000 children, apparently unaware that the current studies show figures in the range of 1 in 130 to 1 in 500.

The authors of the report (Sandler et al., 1999) are frank in discussing some of the shortcomings of the study: "Our study had several weaknesses. First, this was a short-term study, and it is unlikely that significant changes can occur in a brain-based disorder within days or weeks. Second, this was a single dose study and multiple doses may prove to be efficacious".... Third, (use of controversial diagnostic instruments) and fourth, use of synthetic rather than natural secretin.

A major problem, not mentioned by the authors, is the lack of instruments sensitive to change due to treatment. The Autism Research Institute has addressed this long-standing problem by developing the Autism Treatment Evaluation Checklist (ATEC), which is discussed on page 2 of this issue of the ARRI. The need for a tool capable of measuring change due to treatment is widely acknowledged.

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I responded to numerous questions about autism, about secretin, and about the Sandler study in my interviews with journalists. Janet McConnaughey of the Associated Press did a fine job of reporting her interview with me:

"Rimland, who has a 43-year-old autistic son, said a dozen more secretin studies are nearly complete. 'This is the top of the first inning. There is a tremendous backlog of very convincing, very hard-to-explain-away case history data showing, in many kids, a remarkable response that simply does not occur under normal circumstances,' Rimland said.

'Immediately after getting secretin, kids who never had a normal bowel movement have a normal bowel movement. Kids who never slept the night through sleep the night through. Kids who never said 'Daddy' are beginning to react to their parents.'"

One very interesting finding reported by Sandler et al. is that 69 percent of the parents, after being told that the single-dose study had not produced positive results, replied that they nevertheless continued to want secretin for their children. The NEJM did not permit the media to publish or broadcast news about the Sandler article until the evening of Wednesday, December 8. On Thursday, after the story was published, the ARI office was hit by a second wave of phone calls and faxes (we don't do e-mail). This time the calls were mostly from outraged parents who repudiated the study in view of their own, and their acquaintances', experiences with secretin. Two of the phone calls, both from Asheville, the site of the study, were particularly interesting.

One was from a mother, an accomplished professional, whose child was in the study. "I don't care what anyone says," she told me. "My son has made excellent progress with secretin. He has had two infusions since the study, and he continues to improve." She mentioned that a local Asheville television station had interviewed another mother whose child had also been in the study, and that mother was also very pleased and was also continuing the secretin.

The second phone call from Asheville was even more interesting. It was from Dr. Sandler himself. Despite the way in which the story had been told in the NEJM, and in the media, Dr. Sandler is impressed with the potential of secretin and wants to do a multi-dose trial. I promised to help him find the funds he needs.

A few hours before I sat down to write these words, I received a phone call from a Michigan physician who is the mother of a four-year-old autistic son. The boy's neurologist had given him six infusions, three with secretin and three with saline solution, in a single-blind study. The physician-mother said she could easily tell which three infusions were secretin: the boy slept the night through, was relieved of chronic diarrhea, and had a much better attention span each time.

The bottom line: secretin is here to stay. Don't let the naysayers discourage you!

Actually, the hullabaloo about the Sandler study has resulted in almost eclipsing a far more important, from a scientific standpoint, University of Maryland secretin study. Dr. Karoly Horvath et al., using standard gastroenterological tests to compare 36 autistic children to normal controls, found the autistic children to be strikingly different in many aspects of gastrointestinal function, including in particular their response to secretin (*Journal of Pediatrics*, November 1999).

The researchers report, "Histologic examination in these 36 children revealed grade I or II reflux esophagitis in 25, chronic gastritis in 15, and chronic duodenitis in 24." Additional abnormalities included partial villus atrophy, Paneth cell hyperplasia, and significantly elevated numbers of Paneth cells in the duodenal crypts. More than half of the children also exhibited decreased activity of two enzymes needed for the digestion of carbohydrates.

Horvath et al. administered secretin to autistic subjects and controls, and report that 75 percent of the autistic children showed a significantly stronger response to the secretin than did the controls. This strong response to secretin, the researchers say, may be due to an upregulation of secretin receptors in the pancreas due to a lack of normal secretin stimulation. They also report that children with chronic diarrhea who responded to secretin had improved stool consistency for at least two weeks.

In an editorial accompanying the article, physicians Pasquale Accardo and Howard Bostnick say that Horvath et al.'s study "demonstrates consistent physiologic abnormalities... in autism that are not known to occur in any other specific gastrointestinal disorder." They conclude, "The correlation of these findings with a clinical symptom... and its response to secretin... provide further support for a true physiologic abnormality."

—Bernard Rimland