Editor's Notebook: Bernard Rimland, Ph.D.

Secretin Update, December 1999: The safety issue

Secretin is widely regarded as being remarkably safe. In the several decades that the hormone secretin has been used clinically worldwide, there have been no published reports of significant adverse effects.

During the past two years, according to our best estimates, about 10,000 doses of secretin have been administered to several thousand autistic children, by several hundred physicians, with few noteworthy side effects. Until recently, the side effects reported have been primarily increased hyperactivity (16%), stimming (5%), and aggressiveness (4%). These problems have usually subsided in less than one week (77%) or less than two weeks (90%). (Percentages are based on 1,089 responses.)

In our March, 1999 newsletter, we mentioned a two-year-old boy who experienced a seizure while secretin was being administered intravenously. This was the child's first and only seizure, and lasted less than a minute. He recovered quickly and there were no apparent after-effects. Since this was an isolated incident, and since one-quarter to one-third of all autistic children are reported to experience at least one seizure in any case, it was difficult to evaluate its significance.

In the meantime, we have learned of two additional cases of potentially serious reactions to secretin infusions which we feel should be called to the attention of parents and physicians. In one of these cases, a seven-year-old boy experienced a 30-minute grand mal seizure immediately after his fourth infusion of secretin. Paramedics were called to help restore the boy's breathing. The child had responded well to the three prior infusions, each of which had consisted of an entire vial of Ferring secretin at 4- to 6-week intervals. The mother was especially dismayed to have the seizure occur, inasmuch as she had been so pleased with the outcome of the initial infusions. The physician and mother both reported still further behavioral improvement, and no further seizures, after this fourth infusion. Fortunately, the infusion took place in a well-equipped medical setting, so appropriate help and equipment were available. The father has a serious immune deficiency, which may have been a factor.

The third case was a five-and-a-half-year-old boy who did not suffer a seizure, but stopped breathing and had to be resuscitated after being given a third whole vial of Ferring secretin within a 20-day period—only 10 days apart. The child's behavior and language had shown such remarkable improvement after each infusion that, after thorough testing by an allergist, he has since been given two more infusions. The more recent infusions were given about five weeks apart. He continues to make excellent progress, which the mother attributes largely to the secretin: "His school reports two-and-a-half years of progress in receptive and expressive speech, and in fine motor skills, in only eight months. There is no question that it has made all the difference in the world to him."

The occurrence of these incidents is distressing and certainly raises a cautionary flag to all those involved in the use of secretin, particularly when given intravenously. Secretin, given IV, is generally infused at a dosage level of about 2 clinical units (CU) per kilogram of body weight, which is reported to bring about improvement for four to six weeks, on average, in those autistic individuals it helps.

I am confident that the changeover from the use of porcine secretin to the much purer human synthetic secretin, as well as improved administration of secretin, will improve secretin's already excellent safety record.

Secretin may be given in small daily increments by topical (through the skin), sublingual, or intramuscular means. Presumably, the risk of side effects is much lower in those cases where the secretin is given on a daily basis, using dosages perhaps only 3% as high. The Repligen Company plans to develop a system for administering secretin painlessly in small daily doses.

Although the number of cases at this point with adverse effects is quite small, we feel it is important to call attention to them to alert physicians to proceed cautiously and to be well-prepared for emergency conditions should another such event occur.

It is possible that the problems described above may not be caused by secretin but instead by the panic and stress experienced by a child who is held down by adults while an IV needle is inserted.

It is also quite possible that the children who experienced seizures or apnea were affected not by the quantity of secretin given, but rather by impurities in the product. The porcine (derived from pigs) secretin contains a significant percentage of impurities which have not been identified. That is a major reason for the heavy emphasis upon the much purer synthetic human secretin which is being used in some ongoing research.

At our Defeat Autism Now (DAN!) conference in October, Repligen's president, Walter Herlihy, presented convincing data on secretin safety which had been compiled for the purpose of obtaining FDA approval for secretin use in autism. Among the secretin studies discussed was a clinical trial in which 37 adult ulcer patients were given a 7CU/kg dose of secretin each day for seven days (as compared with a single 2CU/kg dose at 35-day intervals, as typically given in autism). No toxicity was found. In another study, eight adult ulcer patients were given 18CU/kg six times per day for 10 days with no adverse effects.

While caution is certainly indicated in the use of secretin, there are almost no biomedical treatments which do not entail some level of risk. Fatalities from prescription drugs are a leading cause of death in the United States. Some 140,000 people die annually as a result of prescription drug use. The drugs that are routinely prescribed for autistic children are certainly not devoid of risk. No drugs have been approved by the FDA for use with autistic children, and all drugs present the risk of serious side effects including seizures, apnea, coma, cardiac arrest, and other life-threatening symptoms. These drugs trade the symptoms of autism for the symptoms of drug toxicity. Not a satisfactory solution!

In my view, secretin, although commonly referred to as a drug, is not truly a drug in the sense that Ritalin, Prozac, and the like are drugs. Unlike Ritalin and Prozac, secretin is an integral part of the body's normal everyday physiology, just as are vitamins, minerals, and other nutrients. Like a nutrient, secretin is given to *facilitate* the body's normal functioning. Drugs, on the other hand, are *blocking* agents, foreign to the body, given to *interfere* with normal processes. That is why drugs are so much more toxic than vitamins, minerals, and hormones.

Two child psychiatrists, both mothers of autistic sons—mothers who did not know each other—have told me, in virtually identical words, "It is one thing to be reading the *Physician's Desk Reference* when you are looking for a drug to give another mother's child; when it is your own child, those words take on a totally different meaning."

I am confident that the changeover from the use of porcine secretin to the much purer human synthetic secretin, as well as improved administration of secretin (perhaps in small daily doses by other than intravenous means) will improve even further secretin's already excellent safety record. In the meantime, until these new forms of secretin, and better forms of administration, become readily available, great care should be exercised in the administration of secretin to help guard against the kinds of events that have been reported in a few cases thus far. Physicians should be prepared for the kinds of rare but possible events described.