SUMMARY OF EXPERIENCE WITH AUTISTIC SPECTRUM DISEASE

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Dr. Derrick Lonsdale was a pediatrician at Cleveland Clinic from 1962 to 1982. He was Head of the Section of Biochemical Genetics and became acquainted with the complex biochemistry associated with inborn errors of metabolism. In 1982 he entered private practice in the field of therapeutic nutrition. Before the 1980s autism was considered to be rare, but within the last few years it has become obvious that there is an increasing incidence of a disease, now known as Autistic Spectrum Disease (ASD) occurring in young children. The “spectrum” refers to the fact that the symptoms are extremely variable in severity and attempts to classify symptomatology into separate disease entities have been largely futile.

Records in California have shown a present incidence of 10 new cases a day in that State and this evidence alone strongly suggests that it is not a purely genetically determined phenomenon. Dr. Bernard Rimland, who established the Autism Research Institute in San Diego founded a group of alarmed physicians and researchers, now known as DAN! (Defeat Autism Now) to try to identify the cause of this new disease. The accumulated evidence has given rise to a consensus in this group, and other researchers, that one or more environmental factors impact on a relatively common genetically determined predisposition involving one or more enzymes that are basic to cellular machinery, particularly in the central nervous system. Mercury, arsenic, lead and cadmium, the so-called SH-reactive metals, as well as other industrial pollutants, appear to be the leading environmental factors, although the measles virus and antibiotic abuse are also implicated.

One of the first therapeutic discoveries was the value of the gluten and milk free diet, revealing the close association of the brain with the bowel in this disease. Later, an observation made by the mother of an autistic child led to the use of the hormone, Secretin. Dr. Lonsdale’s first study was a single intravenous injection of this hormone in 48 autistic spectrum children, showing some improvement in behavioral characteristics in 80%. Bowel function improved in some (1).

An important study was published by Waring and associate (2), showing that sulfur metabolism was extremely abnormal in ASD children. Their discussion of this pointed out that it could explain virtually all of the mysteries in the clinical changes observed in these children. Because of the abnormalities in urinary sulfur containing components that they found, one of their hypotheses presented in this paper was that there might be a
dysfunction in the enzyme Rhodanese. This enzyme converts toxic cyanide ions, formed during metabolic processes, to non-toxic thiocyanate.

We had known for many years that a disulfide derivative of vitamin B1 had been shown by Japanese investigators to stimulate this enzyme and this gave us the idea that this vitamer might be helpful in treatment. Allithiamine is an active principle found in garlic. The name was given to this because it is found in a number of *allium* plants. Thiamine (vitamin B1), found in the bulbs of these plants, is converted to a disulfide derivative by the action of an enzyme, also naturally occurring in the bulb. This happens when the bulb is cut or crushed. The Japanese investigators who discovered this then found that the disulfide derivative had a more powerful biologic effect that the original thiamine and many studies were performed in both animals and humans. It was eventually synthesized as thiamine tetrahydrofurfuryl disulfide (TTFD) and was found to have therapeutic properties in many different diseases.

Another important clue was that thiamine had been found by veterinary investigators to remove lead from the tissues of animals that had been experimentally poisoned with this metal (3). Mercury has been implicated as a “trigger factor” in ASD and, like lead, is a SH-reactive metal. It was reasoned that if it extracted lead, then it would have the same action on any one of the SH-reactive metals and a pilot study was then performed, using TTFD therapy in 10 ASD children (4).

This study was carried out using TTFD in the form of suppositories since its appalling taste made it impossible to administer to small children. The results showed that arsenic and mercury appeared to be the dominant metals that were excreted in the urine of these children after one month of treatment. There was concomitant clinical improvement in 8 or the 10 children. One of the observations was that three of them were found to be thiamine deficient at the beginning of the study and this deficiency was corrected at the end. One of the as yet unexplained phenomena was that one child was found to be thiamine deficient at the end of the study, in spite of the fact that he had received thiamine as the therapy. It may be that thiamine dependent metabolism is deeply disturbed by factors other than dietary deficiency. In this presentation, the results of the Secretin and TTFD studies will be discussed.

Further experimental therapy (Neubrander Unpublished observations) has shown that methyl cobalamin, one of the two metabolically active derivatives of vitamin B12, is beneficial in many of these children. There is now a consensus that it is the complex mechanism of the transmethylation and transsulfuration pathways in intermediary metabolism that is where the damage is being wrought. This would explain most of the behavioral symptomatology, as well as the bowel dysfunction where digestive enzymes are heavily dependent upon sulfur metabolism. It would explain the therapeutic benefit of methyl cobalamin since it is a vital cofactor to methionine synthase, the enzyme that enables production of methionine and its yield of sulfur metabolites that includes the formation of glutathione. It has been suggested that TTFD acts in much the same way as glutathione, thus sparing the overuse of this metabolite in removing SH-reactive metals from the body. It also may have an important action in increasing efficiency of the citric
acid cycle and the production of thiamine triphosphate (TTP), both of which play a vital integral part in energy metabolism.

The transmethylation cycle is heavily dependent on another cycle where dietary folate (a B vitamin) is activated. The two cycles can be envisioned analogically as like two cog-wheels that have to mesh together. Damage to the folate cycle is viewed as a major factor in ASD. Thus, it can be envisioned that there could be a failure of the two cycles to “mesh” together. Identification of the missing “cog” would be an important step in unraveling the metabolic block. It is now known that mercury will inhibit methionine synthase in vanishingly small concentrations of the metal and makes it a prime candidate for being a major “trigger” factor. A polymorphism in this methyl cobalamin dependent enzyme is the major site where the two “cog-wheels” must “mesh.” This metabolism will be discussed in the presentation.

Even recent history is easily forgotten and we should remember that there was a disease in infants in the first part of the 20th century called “pink disease.” These infants languished and died and the mysterious phenomenon that gave rise to its name was that the tips of the fingers and toes were a bright pink color. It was a long time before someone realized that it was mercury that was the causative factor. Infants were being treated with “teething powders” that contained mercuric chloride. When this practice ceased, the disease disappeared. There is good evidence that Thimerosal, a preservative that has been used in vaccines and gives rise to ethyl mercury, replaces the “teething powders,” repeating the stupid mistake of nearly a century ago.

REFERENCES