DAN! think-tank: making strides toward treating autism, understanding its causes

More than 50 scientists and clinicians from around the world, representing a wide range of biomedical fields, attended the October 2006 Defeat Autism Now! (DAN!) think-tank and shared state-of-the-art information about the treatment and causes of autism spectrum disorders. Several attendees presented reports on work in progress, shared questions they encountered, or suggested topics for general discussion.

Among the key findings discussed at the think-tank:

• **Jim Adams, Ph.D**., reported that some autistic children have unusually low red blood cell levels of glutathione, a key antioxidant whose function appears to be impaired in autism, while others have unusually high levels. After three days of treatment with oral DMSA—a chelating agent that helps remove heavy metals from the body—glutathione levels normalized in all of 40 treated children; low levels went up to normal, and high levels went down to normal. This was an unexpected and dramatic effect. All subjects also showed improvements in behavior.

• **Vasken Aposhian, Ph.D**., reported new and encouraging findings about the effectiveness of D-penicillamine in removing mercury from the brains of mice. He also noted that urine of children with autism shows significantly less excretion of mercury than control children (unprovoked); this demonstrates a mercury efflux problem in children with autism spectrum disorders.

• **Jeff Bradstreet, M.D.,** reported that treatment with spironolactone, an anti-inflammatory and anti-androgen drug, causes a drop in markers of inflammation and oxidative stress (e.g. TNF-alpha, interferon gamma). Autistic children taking spironolactone for four weeks showed decreases in irritability, stereotypy, aggression, and inappropriate speech and behavior. These findings strongly support research implicating inflammation as a culprit in autism. Dr. Bradstreet has also been doing patient trials on Oxytocin, which appears to help some patients but not those with inflammatory bowel disease.

• **Norman Schwartz, M.D.,** described the possible application of network systems theory to the analysis of "biochemistry-gone-wrong" in autism. According to Schwartz, It might be possible to identify series of biomarkers that categorize autistic types, by looking at a matrix of nodes and connections that correspond to metabolism sequences that are affected or non-affected in various subgroups. This could vastly improve the speed and efficacy of treatment, by reducing the trial-and-error involved in identifying optimal interventions for a wide variety of children with differing problems.

• **Robert Hendren, D.O**., Director of the M.I.N.D. Institute at U.C. Davis in California, updated participants on a study by the Institute using Dr. James Neubrander's methylcobalamin (methyl-B12) protocol. To date, eight of 15 participants in a short-term intervention showed positive responses to methylcobalamin, as measured on the Stanford-Binet non-verbal test. Longer, open-label trials showed improvements on the Clinical Global Impressions scale for 3 of 8 participants (3-month trial) and 2 of 5 participants (6-month trial).

Dan Rossignol, M.D., reported data from a pilot study of 19 children undergoing 40 sessions of low-pressure hyperbaric oxygen therapy (HBOT). All children exhibited positive trends, ranging from mild to marked, on two measures of autism symptoms (CARS and ATEC). In addition, their motivation and communication improved, and levels of C-reactive protein dropped. No serious adverse events occurred. A double-blind, placebo-controlled multi-center trial is now underway.

• **Paul Shattock, OBE**, presented research showing a historical correlation between the use of organophosphate pesticides and the autism epidemic. His findings implicate pesticide- and herbicide-related molecules including phenylpyridinium, methylphenylpyridinium, and paraquat (all close cousins structurally) as possible autism-triggering chemicals.

• **Jon Pangborn, Ph.D.,** discussed his research into methinin, a natural peptide in cells that inhibits methylation. (Current research indicates that impairments in methylation are a key issue in autism.) In addition, he described how exposure to pyridinium compounds and phenylpyridinium might cause methinin to reduce methylation in dopamine cells.

• **Cindy Schneider, M.D.,** reviewed the recent clinical research findings about PON1 and autism. PON1 is a gene coding for a detoxifying enzyme that acts on organophosphate chemicals foreign to the body, one example being "paraoxon" (diethyl para-nitrophenyl phosphate). This is one of the chemicals shown to inhibit dipeptidyl-peptidase IV (DPP4), which is an integral part of the DAN! molecular model of autism. PON1 is associated with autism in the USA where such pesticide chemicals ("parathion," "diazinon") have been used widely.

Aristo Vojdani, Ph.D., reported on differences in metallothionein (MT) function in subgroups on the autism spectrum. These variations strongly affect the need for, and the response to, detoxification therapies that remove heavy metals from the body.

David Quig, Ph.D., reported that different challenge agents (e.g. EDTA, DMPS, DMSA) may need to be used at different times (NOT simultaneously) for effective detoxification of metals. He stated that transdermal applications were not effective because they don't deliver enough agent.

John Green, M.D., reported on his research regarding measuring and reducing oxidative stress. One possible marker is nitrotyrosine, which is increased by gut inflammation and in children with allergic responses. Other biomarkers for inflammation were also discussed. Dr. Green has used PPAR (Actos) to reduce nitrotyrosine production.

Martha Herbert, MD, Ph.D., is interested in the interaction of secondary (environmental) perturbation of development, versus inborn errors of metabolism. She stressed the importance of looking at each child's individual picture, not just one biomarker or one label. Multiple triggers (stresses) can lead to similar pathophysiologic responses (inflammation, toxicity, oxidative stress).

William Rea, M.D., the guest lecturer, provided a 90-minute "Grand Round" on chemical sensitivity, environmental illness and detoxification procedures. In this case, detoxification was focused on pesticides, herbicides, fungicides, petrochemicals and solvents. He noted that detoxication (the body cleansing itself) requires optimum nutrition; the process is very nutrient-dependent. B6, folate, B1, B2, B3, A, C, magnesium, and amino acids are all very necessary and can become depleted.

Michael Elice, M.D., spoke on the topic of Arnold-Chiari Malformations (ACM), which can be associated with autism. This is a condition in which brain structures become displaced and/or oversized, and cerebrospinal fluid flow can be impeded, leading to altered CO2/O2 levels. The condition can be surgically ameliorated, often with considerable improvement in autistic symptoms.

Sidney Baker, M.D., and Andrea Libutti reported on their studies on lead and mercury removal with DMSA rectal suppositories. They found a reciprocal dependency between lead and mercury. Their results indicate that removing lead first, then mercury, is most effective.

Dr. Robert Nataf and K. Espiard spoke on the Philippe Auguste Laboratory's porphyrin profile and its uses as an indicator for arsenic, lead, and mercury. They consistently find high porphyrins levels in children with autism, seizures, and Rett syndrome.

Dr. Rimland had an all-encompassing vision to heal every child with autism, and the knowledge and dedication to educate the whole autism community—medical staff, families, and educators. He stood tall as a shining example who proved that one dad's love and commitment for his son can change the world.

Cynthia Stark
Vancouver, B.C., Canada