Guest Editorial: Jaquelyn McCandless, M.D.

Clinical use of methyl-B12 in autism

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One of the most important treatment modalities to come out of the strong focus on biomedical and metabolic aspects in autism in recent years is the use of injectable methylcobalamin, or methyl-B12. The evidence for transmethylation defects in autism disorders was already starting to accrue thanks to talented researchers helping us to understand the basic science behind our clinical observation that certain treatments help these children.

In May 2002 my DAN! colleague and friend Dr. James Neubrander made the "accidental" discovery that showed him methyl-B12's profound effect on autism. Experimenting with different members of the cobalamin family, Dr. Neubrander was able to ascertain that the benefits of methylcobalamin far surpassed the cyanocobalamin and hydroxycobalmin forms primarily used for autism prior to 2002. Since every cell in the body expresses the folate/methionine cycle, defects in transmethylation can affect vital biochemical reactions at many places in intermediary metabolism.

At the 2003 Fall DAN! conference we heard Jill James, Ph.D., discuss the impairment in transulfuration and the resulting oxidative stress that occurs in ASD from depletion of glutathione, the major intracellular antioxidant essential for detoxification in the body. Her studies using certain nutrients showed a highly significant increase in plasma methionine, cysteine, and glutathione after only three weeks.

Dr. Paul Cutler, another DAN! practitioner, had heard Dr. Neubrander's initial methyl-B12 DAN! presentation in the fall of 2003, and provided this nutrient to 8 of the 20 children in Dr. James' group. These 8 children continued on this dietary schedule for 3-4 months with the added injectable methyl-B12 and results were even more positive, suggesting that methylation capacity and antioxidant potential can be increased with obvious clinical benefits in ASD children. The dietary nutrients Dr. James showed as supportive of methionine synthesis were zinc; folinic acid; betaine (TMG)–later seen as part of an alternate pathway and helpful only for a small percentage of children; methyl-B12; and choline.

This exciting presentation at the DAN! was followed by that of Richard Deth, Ph.D., who described his research showing the effects of thimerosal on methionine synthase and emphasized the devastating role this neurotoxin can have in the disordered methylation in our afflicted children. We had been finding more every day about how sulfhydryl (SH) reactive metals such as mercury, lead, arsenic and cadmium appeared to be "triggers" for multiple disease symptoms in ASD. Dr. Deth's studies showed how thimerosal alters methionine synthesis activity with the potential to disrupt normal development via its neurotoxic effect on DNA methylation and gene expression. His studies lent tremendous credence to the importance of methylation disorders and their treatment in autism.

Prior to my DAN! presentation in Spring 2005 I queried three of the more popular compounding pharmacies about the number of autistic children for whom they were providing the methyl-B12 injectables, and the total was 4500 children being given injections two or three times per week at that time. By now it is being used all over the United States and in many other countries.

Methyl-B12 is estimated to be active and effective to some degree in 80-90% of ASD children. Dr. Neubrander has an elegant Parent Designed Report Form which helps parents assess whether their child is a responder, downloadable for free from his website www.drneubrander.com. He advises parents to make no changes in their child's nutrient program when adding the methyl-B12 for a period of five weeks to see how responses show its effect. Then he adds folinic acid and any other nutrients that testing has shown the child needs, as he agrees with the DAN! priniciple that these children need a multi-pronged treatment approach. Though the parent form looks for many possible responses, the primary ones for methyl-B12 are executive function, speech, language, socialization, and emotion. However, Dr. Neubrander fears that if parents only look for these signs, they may give up before adequately utilizing this treatment, and he feels that if methyl-B12 is given in the right dosage, timing, and form, up to 94% of children will show benefit.

Besides the myth that methyl-B12 only works in 30-40% of ASD children, other myths Dr. Neubrander would like to dispel are:

1) That this nutrient works better for younger children.

2) That oral, sublingual, transdermal, or intramuscular routes are just as effective as the subcutaneous injections. (At the present time, a nasal spray has been introduced which has become popular with parents who do not want to give their children injections; many of us are testing to compare this with the tried and true subcutaneous route, and the jury is still out at this time.)

3) That the concentration of the methyl-B12 solution does not matter as long as the total dose remains the same. (Many tests have shown that 25mg/ml injections at 64.5mcg/kg every three days is the optimal dose, volume, and frequency.)

4) That the fat in the arm, abdomen, or thigh produces the same results as from the fatty part of the buttocks.

Lowering the dose until side effects disappear is a mistake, because the children with the most side effects who stay with the course are the ones who make the most recovery. However, side effects must be dealt with. The most common are hyperactivity with or without increased stimming, changes in sleep patterns, and increased mouthing (not pica, or eating of non-food item) of objects. Dr. Neubrander agrees that certain side effects are an indication to stop this nutrient, such as an older child becoming uncontrollable and potentially dangerous to others or side effects that are so disruptive that a child can no longer function or learn. However, he encourages parents to continue as long as a child can learn, attend to tasks, and stay focused in a controlled situation no matter how much increased activity there may be at home when the child can just let loose. Mouthing objects is a sign that previously inactivated peripheral nerves are waking up and this represents a "positive negative" and a sign that the methyl-B12 is working. Within two to six months the majority of side effects diminish or disappear completely while the child continues to improve.

Other caveats: Use a good compounding pharmacy that can make the proper dose as recommended by Dr. Neubrander. Do not pinch the fat for the injection. Inject as narrow an angle as possible to avoid hitting any muscle; pink urine means you injected too deeply. The shots if given correctly are seldom painful. There is no way if proper needles (BD 3/10 cc insulin syringe with an 8 mm, 31-gauge needle, item #328438 only) and injection technique are used that the sciatic nerve could be injured, even in the smallest baby.

There is no way to test who will be a responder to methyl-B12. Blood B12 levels are high-normal in almost all children documented to be responders. Though there may be a high level in the blood, it is in an oxidized form that cannot be reduced and recycled. Genomic testing is not yet advanced enough to reliably predict response, as these tests may miss the majority of children who clinically respond and should be treated.

The only way to know if your child is one of the majority of autistic children who will benefit from methyl-B12 is to use it. This is one of the important DAN! biomedical interventions along with dietary restriction, nutrients, attaining gut health, detoxification, and immune enhancing strategies that are improving and even recovering more and more autistic children every day now.