

VITAMIN K DEFICIENCY AS A CAUSE OF AUTISTIC SYMPTOMS

Catherine Tamaro, B.S.M.E.
Mercer Island, Washington

Vitamin K overview

Vitamin K is a fat-soluble vitamin important in blood coagulation and bone metabolism. One of its functions is to keep calcium in the bones and out of soft tissues, blood vessels, and the nervous system. Vitamin K1, the predominant circulating form, is found in green leafy vegetables, some dietary oils including olive, hemp, canola, soybean & cottonseed oils, liver, and fish meal. Vitamin K2 can be found in chicken egg yolk, butter, cow liver, certain cheeses, and fermented soybean products such as natto, and it is also produced by intestinal bacteria. Vitamin K3 is a synthetic form.¹ Many of the recent studies on Vitamin K have found that the K2 form is the most effective in calcium and bone health.²

Vitamin K has a number of interesting functions, many of which relate specifically to autism:

- Vitamin K regulates calcium in the body through osteocalcin and the matrix G1A protein.³ Both bone proteins are active only after undergoing carboxylation, a process in which Vitamin K is a required cofactor. Carboxylated bone proteins have a strong affinity for calcium and control its movement, directing it to the bones and teeth and preventing its deposition in soft tissues.

Calcium management appears to be dysregulated in people with the E4 form of Apolipoprotein.^{4,5,6} Osteocalcin is found in the brain; in its absence, it appears that brain cells become more vulnerable to the effects of calcium.

Vitamin K deficiency appears to play a role in the development of osteoporosis and in the deposition of calcium into blood vessels.^{7,8} Calcification of the arteries, known as “arteriosclerosis,” contributes to heart attacks and strokes.

- Vitamin K, an anti-oxidant that is more powerful than Vitamin E or CoQ10, is able to potently inhibit glutathione depletion-mediated oxidative cell death.^{9,10}
- Vitamin K inhibits production of Interleukin-6, an inflammatory cytokine.¹¹
- Vitamin K is found in high concentration in the pancreas and appears to be involved in controlling blood sugar.¹²
- Vitamin K is involved in the development of the nervous system.¹³

- Vitamin K has a role in glutamate conversion.¹⁴

In this paper I am proposing that a deficiency in Vitamin K causes unregulated calcium movement and deposition in the body of the autistic child, and that unregulated calcium is a cause of many of the symptoms associated with autism. I am also proposing that a Vitamin K deficiency is the cause of the calcium oxalate crystals found in many autistic children.

Calcium, in tandem with the neurotransmitter glutamate, is essential to the functioning of the excitatory cells of the nervous system: once glutamate opens the neuronal cell's calcium channel, calcium pours into the channel and triggers the neuron to fire. The concentration of glutamate within the nervous system is therefore carefully regulated by the nervous system (specifically the astrocytes, which can be negatively affected by mercury and by neurotoxins produced by Lyme spirochetes) because excess glutamate will keep the calcium channels open, allowing calcium to continue to enter, and excite, the neurons. Dr. Russell Blaylock, among others, has written extensively about the neurotoxicity associated with an excess of glutamate.¹⁵ However, I believe that unregulated calcium may play an unappreciated role in triggering the incessant neuronal firing and resultant cell death that are a hallmark of excess glutamate in the nervous system. If a child is unable to regulate calcium due to a Vitamin K deficiency, that child may display signs of glutamate toxicity and uncontrolled neuronal firing that manifest as the cluster of behavioral disorders called autism.

Russell Blaylock, M.D., characterizes glutamate as

“one of the most common neurotransmitters in the brain. Its role is primarily that of an excitatory substance, that is it causes the brain to be stimulated, much the way cocaine does. Using biochemical mapping techniques, we now know that many areas of the brain (such as the cortex, striatum, hippocampus, hypothalamus, thalamus, cerebellum, and the visual and auditory system) all contain an extensive network of glutamate type neurons. This means that glutamate is involved in a wide variety of brain functions. It has also been demonstrated that activation of cortical glutamate neurons can in turn activate other neurons within the nuclei located deep within the brain, even those not using glutamate as a neurotransmitter...

“After studying a number of brains specifically stained for these special receptors, scientists determined that the glutamate receptor is located on the cell body of the neuron and its dendrite – on the fibers emanating from the neuron cell body like the branches of a tree. Being excitatory transmitters, glutamate and aspartate both are involved in activating a number of brain systems concerned with sensory perception, memory, orientation in time and space, cognition, and motor skills.”^a

^a Russell L. Blaylock, M.D., *Excitotoxins: The Taste That Kills*, (Santa Fe, NM), 1997, pp. 31-32

Dr. Blaylock explains that glutamate causes neurons to fire by opening their calcium channels. He explains the process this way:

“It has been known for some time that many cells, especially neurons, contain special pores or channels that regulate the entry of calcium into the cell. These special pores are named calcium channels. These channels play an important role in the normal functioning of the neurons. In fact, it is thought that the calcium channels play a vital role in activation of neurons and transmission of their impulses. When a neurotransmitter (the chemical messenger or key) comes into contact with the receptor (the lock) on the neuron fiber’s membrane, the calcium channel opens and the in-flowing calcium triggers the neuron to fire or be activated.

“Normally this opening and closing of the calcium channel is carefully regulated. When stimulated this channel opens for only a fraction of a second, allowing minute amounts of calcium to enter the neuron. Like glutamate concentrations outside the cell, calcium concentrations inside the cell are carefully controlled by special protective mechanisms. Should too much calcium enter the cell, special calcium pumps drive the excess back out of the neuron. Some of the calcium is also captured and stored within the endoplasmic reticulum of the cell, a long wavy structure within the cytoplasm.

“It appears that several of the excitotoxins, including glutamate and aspartate, work by opening the calcium channels, at least on certain subtypes of receptors. When these neurotransmitters are allowed to come into contact with the receptor in too high a concentration or for too long a period of time, the calcium channel gets stuck in the open position, allowing calcium to pour into the cell in large amounts.

“When this happens the protective mechanisms are triggered. But, as with the glutamate pumps, the calcium pumps also require large amounts of energy as ATP. This energy must be supplied continuously, especially if the calcium continues to enter in large amounts and for a prolonged period of time.”^b

Dr. Blaylock’s book concerns the toxicity of glutamate, and he warns readers of the hazards of ingesting dietary glutamate. He describes the role of the calcium channels but does not address the questions of how much calcium is or should be present in the extracellular fluid, how it got there, how it is removed, or whether its presence is or should be controlled. He does, however, implicate calcium deposits in the brain in the etiology of age-related neurodegenerative diseases.

Given its potential toxicity to the nervous system if uncontrolled, it appears that one of the important functions of Vitamin K is to regulate the availability and concentration of calcium throughout the nervous system. Calcium that is regulated is essential to life. Calcium that is unregulated is hazardous to neuronal and organ functioning. If

^b Ibid, pp. 42-43

uncontrolled it will leave its proper storage places, which are the bones and teeth, because it has not been firmly cemented into place, and instead it will be deposited in the soft tissues and blood vessels of the body. If it enters the nervous system unaccompanied by its carboxylated “escort” proteins, it seems possible that it could enter the calcium channels in excessive amounts and trigger uncontrolled neuronal firing. I believe that once the autistic child’s body has an adequate intake of Vitamin K it will be able to carboxylate the bone proteins, which will then be able to control calcium and keep excess amounts out of the nervous system. This should lead to an amelioration of the child’s neurological symptoms.

Recent research into the etiology of autism has targeted mutations or polymorphisms of the genes controlling the glutamate receptors and the calcium channels as areas of interest. Studies looking at mutations of the glutamate receptor genes have produced mixed results.^{16,17,18} However, a paper published in September 2006 examined 116 autistic subjects and found a problem in a gene regulating the calcium channels.¹⁹ It seems possible that a mutation in a calcium channel-controlling gene, coupled with a Vitamin K deficiency and resultant lack of carboxylated proteins, could lead to uncontrolled neuronal firing that presents as neurological or “psychiatric” symptoms.^c It is also possible that mutations, deletions or substitutions exist in the gene(s) encoding the enzymes that require Vitamin K as a cofactor, making those enzymes less efficient and thereby increasing the need for Vitamin K.

Vitamin K and Oxalic Acid Production

Calcium dysregulation appears to play an important role in the development of calcium oxalate deposits in humans, a topic whose relationship to autism is currently being explored by autism researchers. Oxalic acid is an organic acid produced by plants, sometimes in abundance, in order to manage and store calcium. Oxalic acid can be produced endogenously by humans in situations of deficiency of certain vitamins and it can be produced by various species of fungi including *Aspergillus niger*. Oxalic acid is highly corrosive, with a pH of approximately 1.4-1.6. Much but not all of the oxalic acid in plants is bound to calcium, thereby making it insoluble. When oxalate-containing plants are eaten by humans, the soluble and insoluble oxalates are normally degraded in the GI tract by the anaerobic bacterium *Oxalobacter formigenes*, which is easily destroyed by antibiotics^d. Insoluble oxalates that are not degraded in the GI tract tend to pass out in the stool. The soluble oxalate can also bind to calcium consumed in food, thereby becoming insoluble. However, if the soluble oxalate is not either degraded by bacteria or bound to calcium consumed in food, then it can be absorbed through the intestinal membrane. Soluble oxalate, whether absorbed by the digestive tract, produced by the human liver, or produced by infectious fungi, will either bind to calcium and other

^c It is worth remembering that most vaccines contain glutamate in various forms. Infants have not developed the enzyme system necessary to handle exogenous loads of glutamate, so the regular injection of glutamate from the many infant vaccines could either initiate or accelerate the process of neuronal hyperexcitation.

^d The vaccine preservative thimerosal, if excreted through the baby’s biliary system into the stool, would also have acted as an antibiotic on gastrointestinal flora.

minerals and become insoluble or will be carried into cells on the same transporters that carry sulfate, bicarbonate, and chloride. (Oxalic acid binds to cations, including calcium, zinc, sodium, potassium, and magnesium.)

Calcium oxalate (CaOx) salts are insoluble and are found in many different locations in the body, including areas that have already sustained injury, causing or increasing inflammation. CaOx salts can be found in organs, soft tissues, blood vessels, and joints. They will upregulate inflammation, they will cause mechanical damage, and they will interfere with the electrical signaling that is the means by which the nervous system communicates with the body.

Kidney stones, for example, are often composed of CaOx, and they cause both inflammatory and mechanical damage to the kidney tubules. Vitamin K deficiency appears to be a factor in the formation of kidney stones,²⁰ and Vitamin K-dependent carboxylase enzymes are found in the kidney tubules.²¹

The Low Oxalate Diet (LOD) was developed by the Vulvar Pain Foundation (VPF) to ameliorate the vulvar pain that was found by Dr. Clive Solomons to be linked to the presence of oxalates. Dr. Solomons discovered the role of oxalates in triggering pain, and the assumption was made that the major source of oxalates was dietary. Over time the VPF developed a diet low in oxalates that was designed to lower dietary oxalate intake, with the goal of reducing body stores of oxalates and therefore reducing pain. The VPF's diet has recently been presented as a solution to some of the behavioral and health problems plaguing children with autism.

The LOD as presented by the VPF and the listserv *Trying_Low_Oxalates* (TLO) does not contemplate or advise the use of Vitamin K. Since the purpose of LOD is to lower dietary oxalates, it discourages the consumption of leafy greens which are high in oxalates but which are a main food source of Vitamin K1. LOD does encourage the use of citrate minerals, namely calcium citrate and magnesium citrate, because citrate seems to be able to chelate calcium from the CaOx salts in the body.

The Low Oxalate Diet developers do not appear to have examined the question of what happens to the calcium freed from the calcium oxalate salts. However, at least in the case of autistic children, it is probable that they have low levels of Vitamin K and therefore low levels of carboxylated bone proteins. Thus the children presumably have little ability to manage this freed calcium, which will circulate unimpeded into the nervous system and other organs and tissues. This influx of unmanaged calcium into circulation and then into the nervous system is, I believe, the reason that so many autistic children are exhibiting adverse responses to the LOD, including seizures, behavioral regression, hyperactivity, and depression. These symptoms do not indicate that oxalates have moved from storage into circulation for transport to the disposal sites (termed "oxalate dumping" on the TLO listserv), but rather reflect the deleterious effects of an influx of unmanaged calcium into the nervous system. Some of the autistic children on the LOD begin to experience heavy nosebleeds, which could reflect an exacerbation of an existing Vitamin K deficiency since on the LOD, Vitamin K-containing vegetables have been removed

from the diet. The body's first priority use of Vitamin K is manufacture, in the liver, coagulation factors that prevent bleeding and clotting disorders. If Vitamin K is withheld from the diet to the point where nosebleeds develop, then other, less apparent problems with clotting may be present also.

I believe that most if not all children with autism are producing oxalic acid endogenously and that they have large body stores of insoluble oxalates, primarily in the form of calcium oxalate crystals. Humans produce oxalic acid in the liver, which is the only organ in the human body that stores Vitamin K.²² Humans are known to produce oxalic acid in response to certain vitamin deficiencies; at this time it is known that a deficiency of Vitamin B6 will cause the human liver to manufacture oxalic acid. I believe it is probable that the liver is also producing oxalic acid in response to a Vitamin K deficiency.^e If this is true, then reducing dietary intake of oxalates will not solve the problem of endogenous production but could in fact increase oxalate production since a low-oxalate diet excludes dietary sources of Vitamin K1 such as leafy greens.

Vitamin K-dependent enzymes are found in the kidney tubules, a fact which seems to indicate that the kidneys have a mechanism for disposing of oxalic acid while preventing it from crystallizing with calcium. However, without Vitamin K these enzymes cannot work, which may lead to the formation of numerous CaOx crystals in the kidney tubules. Once the kidney tubules become "clogged" they will have difficulty in excreting many substances, including oxalic acid, metabolic waste products, toxins, and heavy metals.

Another means of disposal of oxalic acid is across the intestinal lumen into the GI tract, where intestinal bacteria degrade the acid into harmless substances. However, oxalate-degrading bacteria, which includes Oxalobacter formigenes and various form of lactic acid bacteria (and Vitamin K-producing bacteria too) are easily destroyed by antibiotics so the intestinal flora of most autistic children probably does not include these types of "good" bacteria. Therefore if kidney tubule efficiency is reduced due to the presence of CaOx crystals, and the intestines don't contain the types of bacteria that can degrade oxalates, the autistic child will have difficulty disposing of the oxalic acid via either urine or stool, so it will remain in the body to form mineral crystals.

However, once the Vitamin K deficiency is rectified, I believe that the child's body will slow or cease its endogenous production of oxalic acid. Consumption of lactic acid bacteria, especially those found in the commercial preparation VSL#3, will introduce bacterial species into the intestines that are capable of degrading oxalates.²³ Soluble oxalate secretion across the intestinal membranes will then increase, and once the soluble oxalate reaches the intestinal contents, the probiotics will degrade it. The probiotics should be able to degrade dietary oxalates (soluble and insoluble), allowing the child to consume the healthy vegetables containing both oxalates and Vitamin K. The probiotics

^e Dr. Clive Solomons found that, if the diet is very low in oxalates, the dieter would begin to produce oxalates endogenously. The very-low-oxalate dieter is by definition eating few or no leafy greens, the main dietary source of Vitamin K1, lending some credence to the hypothesis that a Vitamin K deficiency is one reason the liver would manufacture soluble oxalates.

should also begin to degrade any insoluble oxalate crystals attached to the intestinal lumen.

Vitamin K appears to be capable of chelating the calcium from calcium oxalate crystals, thus dissolving them and opening up the kidney tubules as another avenue for disposal of soluble oxalate. As CaOx crystals deposited around the body begin to dissolve, the autistic child's behavior should improve. Therefore once Vitamin K supplementation and VSL#3 consumption have been established the Low Oxalate Diet is probably unnecessary.

Baths or footbaths of Epsom salts, baking soda, and sea salt may accelerate the process of draining oxalic acid from the body. Oxalic acid shares the same cellular transporters as sulfur, bicarbonate, and chloride; when the circulatory levels of these three latter substances are increased, they are more available for transportation into cells to replace the oxalic acid. This will bring more oxalic acid into circulation. As the kidneys absorb the sulfate, bicarbonate, and chloride, they should be able to increase their rate of oxalic acid secretion into the urine.

Vitamin K, Calcium, and the Intestinal Membrane

A recent paper by Susan Owens, MAIS entitled "Mechanisms Behind The Leaky Gut"²⁴ points out the importance of calcium in regulating the opening and closing of the "tight junctions" of the intestinal membrane:

"I've put a study at the end of this article whose authors discovered that some of this process of opening and closing the tight junctions appeared to be mediated through an interaction with calcium. This did not involve the concentration of calcium that was inside the intestinal cells, but it only involved the calcium that was outside the cell. Removing the calcium from either side of that tight junction could really change things, but changing the level of calcium inside the rectangle (representing the inside of the cell) made no difference at all.

"Right next to where that gate is located on the basolateral (or blood side) are some molecules and a "sensor" that picks up calcium that is travelling in the fluid on this basolateral or blood side. I've represented that sensor as an asterisk. If there is adequate calcium at that sensor, then the leaky gut closes, just as if it had been zipped up. In fact, calcium is actually a key ingredient used to close the zipper. When there is not enough calcium present to close the gate, the gate stays open so that calcium from the food side can come in through the gap until there is enough calcium to close the gate again. In fact, at times, there are oscillations that occur as this gate opens and closes in response to calcium."^f

Owens' paper does not address the role of Vitamin K in regulating the extracellular calcium, but several interesting questions present themselves: Is the calcium needed to regulate the tight junctions either not present or not usable, due to lack of carboxylated

^f Susan Owens, MAIS, 'Mechanisms Behind The Leaky Gut', 2006, page 3

“escort” proteins? Would the addition of Vitamin K as a dietary supplement provide usable calcium to improve the GI tract’s functionality?

Vitamin K, Calcium, and the Specific Carbohydrate Diet

Some parents have noted that their children experience problems with the Specific Carbohydrate Diet (SCD), a diet designed to bring order and balance to the intestinal flora. It is quite possible that the regressions the parents are witnessing are actually due to the movement of uncontrolled calcium into circulation, regressions that would be more pronounced if the regressing children were consuming the yogurt recommended by the SCD designers. Yogurt made according to SCD directions would contain large amounts of both *Lactobacillus acidophilus* and *Streptococcus thermophilus*, both of which are known to degrade oxalates. If these two bacterial species begin degrading insoluble oxalates in the autistic child’s intestinal tract, thereby liberating calcium, the child will experience neurological problems if he/she is deficient in Vitamin K, which is probably the case. Therefore it seems that once the Specific Carbohydrate Diet incorporates Vitamin K, more children will be able to tolerate and benefit from it.

Recommended Dose of Vitamin K

There is considerable uncertainty about what constitutes an adequate intake of Vitamin K. The RDA is essentially the amount the liver needs for its clotting functions; the amount the bone proteins need is unknown.

The Japanese studies on osteoporosis in adults used 15 mg of Vitamin K2, three times daily. This dose was well-tolerated and without toxic effects. To adjust this dose for a child, divide the child’s weight by 150 and apply that fraction to the adult dose. Vitamin K2 is available in liquid, gelcap or capsule form. Because it is a fat-soluble vitamin it must be consumed with dietary fat.

Conclusions

It is possible that the unregulated movement of calcium in the autistic child is responsible for some of the neurological symptoms of the disease: calcium triggers the neurons to fire; excess calcium, or uncontrolled calcium, may cause the neurons to fire until they die. Vitamin K is an essential cofactor in the development of bone proteins that can control calcium and most if not all autistic children are probably severely deficient. The dietary addition of Vitamin K would activate the bone proteins that manage calcium, thereby controlling that calcium and bringing some order to the metabolic chaos that is autism. It is possible that children with autism have problems with the gene(s) controlling glutamate management, calcium channel function, and/or Vitamin K-dependent enzyme production.

A Vitamin K deficiency may be a contributing factor in the autistic child’s endogenous production of oxalic acid, which can bind to and immobilize calcium. If the renegade calcium is bound to oxalates it cannot make its way into the nervous system and cause

damage. The human body seems to have a reason for producing oxalic acid: to control and manage calcium. It also has the means to dispose of it once the diet contains adequate Vitamin K again: the Vitamin K triggers carboxylation of bone proteins, which can then chelate the calcium from the crystals and put the calcium where it belongs. Meanwhile the oxalic acid will be disposed of, via secretion either through the kidney tubules or across the intestinal membrane. However, if the kidney tubules are not filtering well due to the presence of CaOx crystals, or if the intestines do not contain oxalate-degrading bacteria, then the oxalic acid will remain in the body and re-crystallize. Disposal of any other waste product or toxin will be compromised also.

The Low Oxalate Diet is a poor method of addressing the problem of CaOx crystals. LOD uses dietary manipulation and citrate minerals to dissolve CaOx stones, but as the child has low Vitamin K the calcium influx is unmanaged and causes additional damage to the nervous system. The avoidance of Vitamin K1-containing vegetables means that the child's stores of Vitamin K will be depleted and yet the liver will continue to produce oxalates.

There exists the distinct possibility that the heavy metal chelators (e.g. DMPS, DMSA, EDTA) cause dissolution of CaOx stones. The regressions and problems that children experience when undergoing heavy metal chelation are consistent with the effects from the release of uncontrolled calcium into circulation. Therefore perhaps heavy metal chelation should be halted while Vitamin K deficiencies are addressed and calcium, including the calcium bound to oxalates, is brought under control.

It is possible that the leaky gut cannot be closed until *controlled* calcium is brought to the tight junctions.

In conclusion, Vitamin K has a number of essential roles in the human body and it would appear its importance has been overlooked thus far. Vitamin K deficiency may be a cause of chronic neuronal hyperexcitement, which could manifest as autistic symptoms; it may also be a cause of the development of calcium oxalate crystals and stones, which may well be found in abundance in all autistic children. The administration of pharmacological doses of Vitamin K to children with autism disorders would appear to hold great promise in turning around some of the symptoms of the disease.

APPENDIX A

SOURCES

1. www.pdrhealth.com/drug_ingo/nmdrugprofiles/nutsupdrugs/vit_0267.shtml accessed 09/01/2006.
2. Zitterman A, Effects of Vitamin K on calcium and bone metabolism, *Curr Opin Clin Nutr Metab Care*, 2001 Nov;4(6):483-7.
3. www.pdrhealth.com/drug_ingo/nmdrugprofiles/nutsupdrugs/vit_0267.shtml accessed 09/01/2006.
4. Veinbergs I, et al, Neurotoxic effects of apolipoprotein E4 are mediated via dysregulation of calcium homeostasis, *J Neurosci Res.*, 2002 Feb 1;67(3)379-87.
5. Wang XS, et al, Rapid elevation of neuronal cytoplasmic calcium by apolipoprotein E peptide, *J Cell Physiol*, (1997) 173:73-83.
6. Tolar M, et al, Truncated Apolipoprotein E (ApoE) Causes Increased Intracellular Calcium and May Mediate Apo Neurotoxicity, *The Journal of Neuroscience*, August 15, 1999, 19(16):7100-7110.
7. www.pdrhealth.com/drug_ingo/nmdrugprofiles/nutsupdrugs/vit_0267.shtml accessed 09/01/2006.
8. Seyama Y, et al, Comparative effects of vitamin K2 and vitamin E on experimental arteriosclerosis, *Int J Vitamin Nutr Res.*, 1999 Jan;69(1):23-6.
9. Vervoort LM, et al, The potent antioxidant activity of the vitamin K cycle in microsomal lipid peroxidation, *Biochem Pharmacol*, 1997 Oct 15;54(8):871-6.
10. Jianrong L, et al, Novel Role of Vitamin K in Preventing Oxidative Injury to Developing Oligodendrocytes and Neurons, *The Journal of Neuroscience*, July 2, 2003, 23(13):5816-5826.
11. Reddi K, et al, Interleukin 6 production by lipopolysaccharide-stimulated human fibroblasts is potently inhibited by naphthoquinone (vitamin K) compounds, *Cytokine*, 1995 Apr;7(3):287-90.
12. Sakamoto N, et al, Low vitamin K intake effects on glucose tolerance in rats, *Int J Vitam Nutr Res*, 1999 Jan;69(1):27-31.
13. Tsaion KI, Vitamin K-dependent proteins in the developing and aging nervous system, *Nutr Rev.*, 1999 Aug;57(8)231-40.

14. Sugiura I, et al, Propeptide and glutamate-containing substrates bound to the vitamin K-dependent carboxylase convert its vitamin K epoxidase function from an inactive to an active site, *Proc. Natl, Acad Sci. USA*, Vol. 94, pp. 9069-9074, August 1997.
15. Russell L. Blaylock, M.D., *Excitotoxins: The Taste That Kills* (Santa Fe, NM), 1997
16. Ramoz N, et al, Linkage and association of the mitochondrial aspartate/glutamate carrier SLC25A12 gene with autism, *Am J Psychiatry*, 2004 Apr;161(4):662-9.
17. Segurado R, et al, Confirmation of association between autism and the mitochondrial aspartate/glutamate carrier SLC25A12 gene on chromosome 2Q31, *Am J Psychiatry*, 2005 Nov;162(11):2182-4.
18. Rabionet R, et al, Lack of association between autism and SLC25A12, *Am J Psychiatry*, 2006 May;163(5):929-31.
19. Laumonier F, et al, Association of a Functional Deficit of the BKCa Channel, a Synaptic Regulator of Neuronal Excitability, With Autism and Mental Retardation, *Am J Psychiatry*, 2006 Sep;163(9):1622-1629.
20. Chen J, et al, Decreased renal vitamin K-dependent gamma-glutamyl carboxylase activity in calcium oxalate calculi patients, *Chin Med J (Engl)*, 2003 Apr, 116(4):569-72.
21. Friedman PA, et al, Localization of renal vitamin-K dependent gamma-glutamyl carboxylase to tubule cells, *J Biol Chem.*, 1982 Sep 25;257(18):11037-40.
22. Guyton & Hall, *Textbook of Medical Physiology*, Tenth Edition, 2000
23. Campieri C, et al, Reduction of oxaluria after an oral course of lactic acid bacteria at high concentration, *Kidney Int.*, 2001 Sep;60(3):1097-105.
24. Susan Owens, MAIS, 'Mechanisms Behind The Leaky Gut,' 2006

APPENDIX B

CALCIUM OXALATES

In the urinary sediment, one can find two forms of calcium oxalate crystals. The most frequent form is the di-hydrated calcium oxalate. The mineralogical name of the calcium oxalate $2(H_2O)$ is Weddellite. The second form is the mono-hydrated calcium oxalate whose mineralogical name is Whewellite. The two forms have different crystallographic characteristics. It seems that the calcium/magnesium ratio plays an important role in the formation of the calcium oxalate crystals. Crystals of calcium oxalate are found mainly in an acidic urine, but these can also be seen in slightly alkaline specimens.

Weddelites: Calcium oxalates $2(H_2O)$



The weddellite or calcium oxalate di-hydrate crystallizes in the tetragonal system. The classic crystal shape is the eight-face bi-pyramid. In bright field microscopy, the weddellite crystals are recognized easily by their shape that reminds a mail envelope. More complex shapes of weddellite are possible. The dumbbell shape is not rare. The former has no precise angles or sides. This form is, in reality, an microcrystalline agglomerate that takes the shape of a biconcave disc.

Weddellite crystals are poorly birefringent and do not show any interference pattern under polarized light.

Weddellite crystals are usually of little clinical value. Many specimens develop weddellite crystals on standing.

Whewellites: calcium oxalates (H₂O)



The whewellite crystal is a rare form of crystallization of calcium oxalate. In theory, the whewellite, or calcium oxalate mono-hydrate crystallizes in a monoclinic leaf shape, but in the majority of cases, the former precipitates as an oval egg shape. The dumbbell structure is often erroneously associated to this form of oxalate. X-ray analysis have shown that the dumbbell structure can also represent weddelite crystals. Contrarily to the weddelite, the whewellite is found in situations of massive calcium oxalate precipitation. According to Berg, the abundance of oxalates formed of ovoid structures strongly agglutinated, twin structures, and microliths, is an indication of a pathological massive precipitation. Urines of patients with a calcium oxalate urolithiase have a tendency to have a sediment with some of the preceding characteristics.

Source: http://www.agora.crosemont.qc.ca/urinesediments/doceng/doc_025.htm, accessed 09/01/2006

Note: My 9-year-old son, diagnosed with Autism Spectrum Disorder, is urinating large amounts of crystals that appear to be whewellite CaOx crystals.

APPENDIX C

Suggested Approach to Oxalate Degradation and Disposal

1. Vitamin K2, adjusted for the child's body weight by dividing the child's weight by 150 and applying that fraction to the adult dose of 15 mg TID. (I am using the liquid from Thorne Research.)
2. Magnesium, which closes the calcium channel.
3. The commercial probiotic preparation VSL#3 (www.vsl3.com), which contains strains of lactic acid shown to be able to degrade oxalates in the GI tract. I have found that consuming yogurt cultured with VSL#3 is more effective in controlling the diarrhea induced by oxalates leaving the body than the probiotic alone. I use two envelopes of VSL#3 and two quarts of goat milk and culture it for 24 hours. I believe that, once established on Vitamin K, children who were previously dairy-intolerant may be able to tolerate dairy products, because their bodies can now control the absorbed calcium.
4. Baths or footbaths of Epsom salts, baking soda, and sea salt to exchange with soluble oxalates and encourage their release from cells.
5. Other supplements as required by the individual child.
6. The Specific Carbohydrate Diet. This diet is absolutely essential to re-establishing healthy GI flora.
7. When *Oxalobacter formigenes* becomes available as a prescription product it will be a useful addition to the child's arsenal of "good" GI bacteria. But its presence is not essential to the removal of oxalates from the body.

Vitamin K appears to be able to chelate the calcium from the CaOx salts, leaving behind oxalic acid that can be either filtered through the kidneys or secreted across the intestinal membrane for disposal. If the child's GI tract contains oxalate-degrading bacteria, the concentration of oxalates inside the GI tract will remain less than the concentration in the body, signaling the body to continue secreting oxalates across the intestinal membrane. Magnesium closes the calcium channels and will assist in controlling neuronal firing. The sulfate, bicarbonate, and chloride can all exchange with the oxalic acid inside cells, allowing the oxalic acid to leave the cell and be disposed of. The Specific Carbohydrate Diet will address the obvious imbalances in GI flora that have led to this situation, which include the absences of both *O. formigenes* and Vitamin K-producing bacteria. Children experiencing setbacks on the Specific Carbohydrate Diet, especially those consuming yogurt, may actually be manifesting the effects of a release of uncontrolled calcium from calcium oxalate crystals. The lactic acid bacteria *L. acidophilus* and *S. thermophilus*,

which are the classic yogurt-making bacteria, have been found to degrade oxalates effectively. Again, as I have stated elsewhere in this paper, degradation of calcium oxalate crystals results in the release of calcium, and if the child is Vitamin K-deficient, the released calcium will be uncontrollable and therefore potentially harmful to the nervous system.