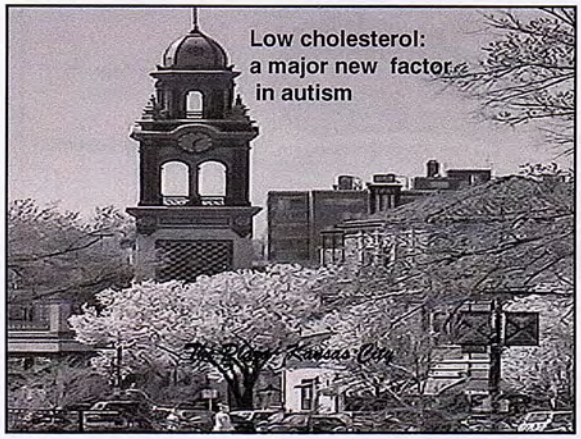



New nutritional therapies for autism/PDD

William Shaw, Ph.D.

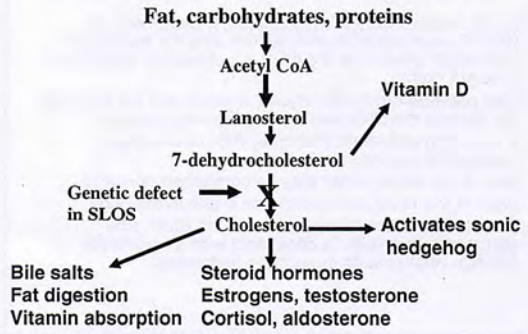
Symptoms of SLOS

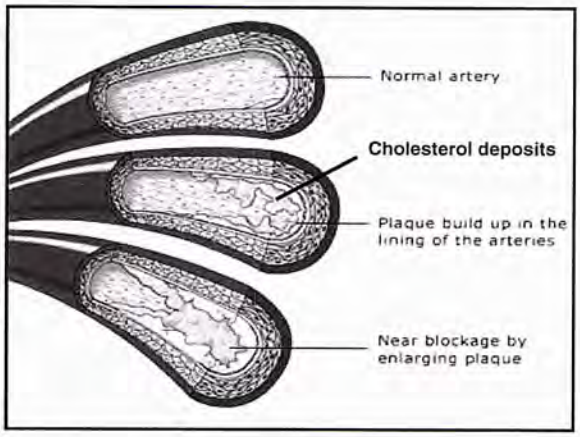
- Extremely low cholesterol- some even 0 mg/dL
- High 7-dehydrocholesterol
- 75% on autistic spectrum in one study
- Fused 2nd and 3rd toes
- Lack of speech
- Severe behavior abnormality: frequent temper tantrums, hyperactivity, violent outbursts, destruction of property, self-mutilation
- UV-light sensitivity

Fig. 3: Two brothers with facial features typical of SLOS: ptosis, epicanthal folds, small chin and short nose. The facial features are more pronounced in the younger brother (right).

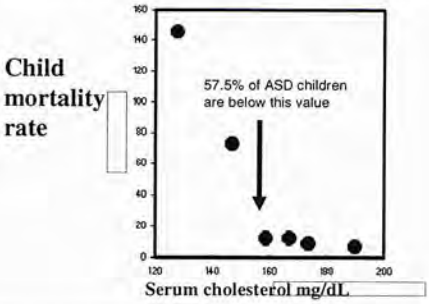
Y-shaped toe in SLOS

Formation of cholesterol

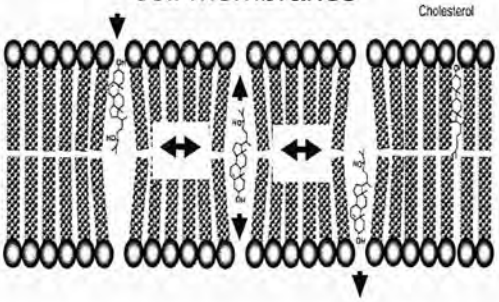




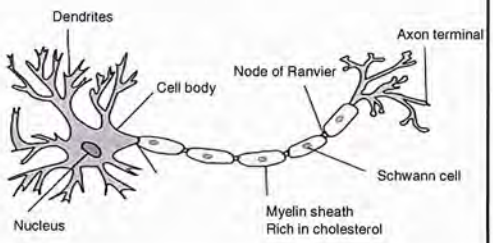
High cholesterol in children decreases mortality



Brain cholesterol in cell membranes



Nerve cell with myelin sheath



Importance of cholesterol in brain

- In the central nervous system (CNS), essentially all (99.5%) cholesterol is unesterified, and the majority of cholesterol present in the CNS is believed to reside in 2 different pools:
- One represented by the myelin sheaths and the other by the plasma membranes of astrocytes and neurons.
- It has been estimated that up to 70% of the brain cholesterol is associated with myelin.
- Half of the white matter may be composed of myelin
- Brain is the most cholesterol-rich organ in the body.
- The concentration of cholesterol in the brain, and particularly in myelin, is consistent with an essential function related to its membrane properties.

Risks from low total cholesterol

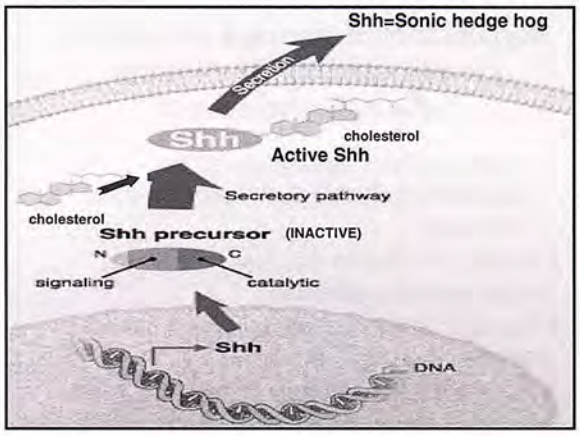
- Increased cancer
- Increased violent behavior, aggression
- Increased infection susceptibility such as tuberculosis and gastrointestinal infections
- Increased anxiety, suicide
- Increased depression, bipolar disorder
- Double the death rate in older adults
- Increased stroke rate
- Increased cataracts

Hedgehog protein

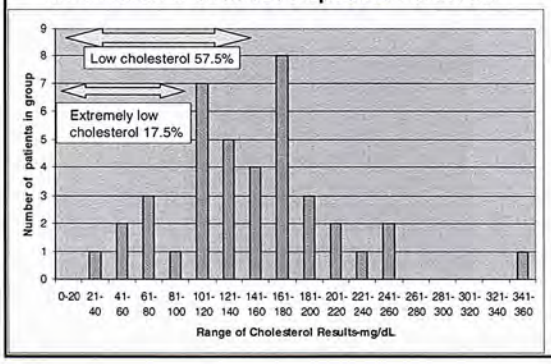
- Geneticists discovered a mutant fruit fly (Drosophila) whose larvae had bristles that resembled the animal called a hedgehog
- The entire development of the fly was altered by this mutation.

Hedgehog

Sonic hedgehog-new mutant associated with altered brain development named after video game character



The Great Plains Laboratory cholesterol study Of children with autistic spectrum disorder



Am J of Med Genetics Part B: Neuropsychiatric Genetics
Vol 141B, Issue 6, Pages 666 – 668,2006
Abnormalities of cholesterol metabolism in autism spectrum disorders. Elaine Tierney et al.

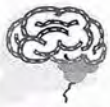
- Using gas chromatography/mass spectrometry, cholesterol was quantified in 100 samples from subjects with ASD obtained from the Autism Genetic Resource Exchange (AGRE) specimen repository.
- Although no sample had cholesterol levels consistent with SLOS, 19 samples (19%) had total cholesterol levels lower than 100 mg/dl, which is below the 5th centile for children over age 2 years.
- These findings suggest that, in addition to SLOS, there may be other disorders of sterol metabolism or homeostasis associated with ASD.

Benefits of cholesterol feeding in SLOS

Adv Pediatr 2000;47:1-53 Inborn errors of cholesterol biosynthesis. Kelley RI

- Beginning to walk
- Start to run
- Growth improvement
- Less infections
- Less UV light sensitivity
- Increased alertness
- Head banging stops
- Decreased tactile defensiveness
- Increased sociability
- Behavior improves
- Talking has started in adults who were not talking before
- Verbal people say they feel better
- Many improvements in only a few days after supplement
- Decreased irritability
- Increased muscle tone

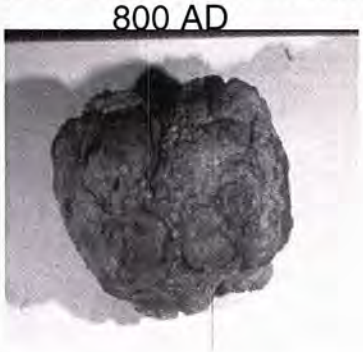
High cholesterol foods

- Eggs  2 egg yolks-500 mgs
- Brain  3 oz-1000 mg
- Liver  3oz-372 mg

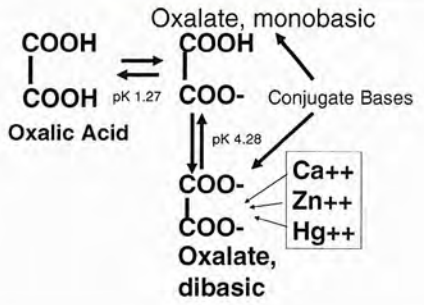
Supplement to increase cholesterol New Beginnings Nutritionals "*Sonic*® cholesterol"

- Highly purified cholesterol with no detectable toxic metals or environmental chemicals
- Useful for children with low cholesterol who have egg allergies
- Useful if children or parents don't eat brain or liver
- Available approximately October 15,2007

Oxalate stone from mummy 800 AD



Interconversion of oxalate



Improvements in Urinary functionaccording to Susan Owens:

1. Loss of excessive urination
2. Loss of urinary frequency
3. Obtaining nighttime continency
4. Obtaining daytime continency
5. Loss of vulvar or penis pain & inflammation

Improvements in motor skills according to Susan Owens :

1. Improved energy (mitochondrial?)
2. Vastly improved gross motor skills
3. Improved handwriting
4. Improved fine motor skills
5. Beginning to enjoy sporting activities with friends and siblings

Digestive improvements associated with low oxalate diet according to Susan Owens:

1. Improved gut function: digestion
2. Loss of chronic diarrhea
3. Loss of chronic constipation
4. First normal stools in lifetime despite previous
5. Loss of ravenous hunger
6. Needed increase in appetite
7. Loss of food allergies or sensitivities
8. Eating foods previously avoided
9. Losing tendency to stomach ache or migraine
10. Loss of distended belly
11. Ability to get off all GI medications
12. Big changes with introduction of VSL #3, an oxalate-degrading probiotic

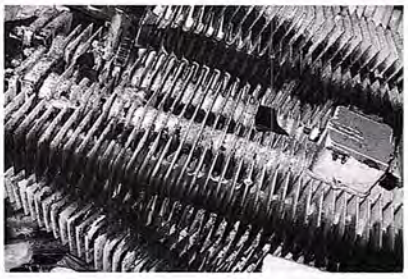
Cognitive improvements associated with low-oxalate diet according to Susan Owens:

1. Better counting
2. Better and more spontaneous coloring
3. Better sight word retention
4. Less rigidity
5. Better expressive language; losing apraxia
6. Better receptive language
7. Increased imitation skills
8. Asking more questions: who, what, where
9. Improved cognition: more complex thought
10. Speaking in much longer sentences
11. Understanding cause and effect
12. Increases in imaginary play
13. Sociability
14. Developing negotiating skills
15. Playfulness: enjoying life; jokes
16. Calming of temperament

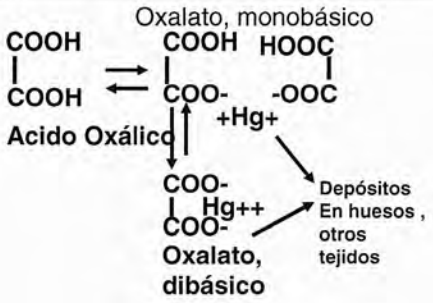
Areas improving in adult on Low oxalate diet according to Susan Owens

1. Improvement in hypertension
2. Alleviation of carpal tunnel problems
3. Loss of fibromyalgia pain
4. Cysts healed
5. Improved cognition
6. Loss of back pain
7. Loss of joint stiffness
8. Loss of heel pain
9. Weight loss
10. Improvements in libido
11. Monthly periods are starting back in w
12. Improvement in balance (cerebellar--per physician)
13. Regaining daytime urinary continence
14. End of severe insomnia

Oxalic acid is used to clean rusty car radiators



Oxalate binds mercury



Problems of solubility with oxalates

$$[\text{Oxalate}]^{--} + [\text{Ca}]^{++} \rightleftarrows \text{CaOxalate}$$

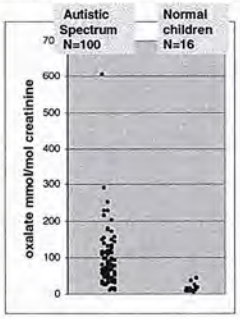
soluble soluble Insoluble

Ksp is an indicator of the reaction strength

The solubility is the principal factor that determines the toxicity of oxalates and heavy metals

Salt	Ksp (product of solubility constant)
Mercury I	1.75 X 10-13
Lead	8.6 X 10-10
Copper II	4.4 X 10-10
Zinc	1.4 X 10-9
Cadmium	1.42 X 10-8
Calcium	1.5 X 10-8
Magnesium	8.5 X 10-5

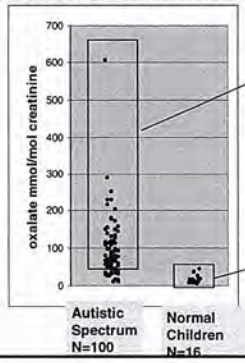
Comparison of oxalates in the autistic spectrum and normal children



t-test

$p < 10^{-16}$

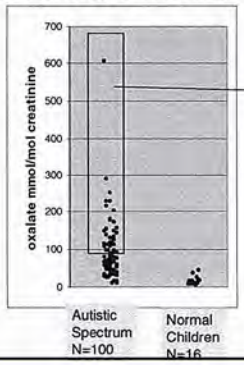
Comparison of urine oxalate in autistic spectrum and normal children



84% of individuals with autism are outside the normal range Mean ± 2 sd

Normal range 0-36 mmol/mol creatinine

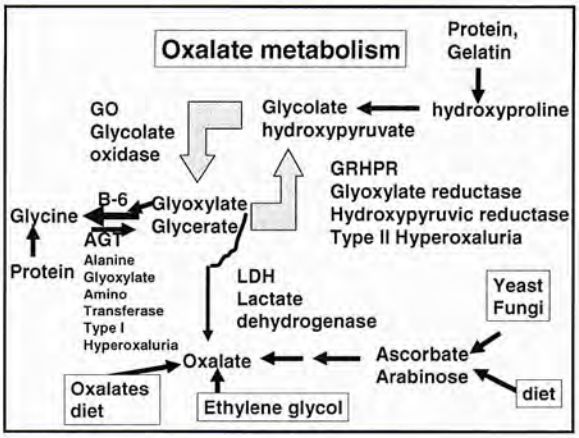
Comparison of urine oxalate in autistic spectrum and normal children



Range of oxalates in genetic diseases of oxalate- 36% of people with autism in this range

Mol Genet Metab. 2006 Aug;88(4):346-50.
High incidence of hyperoxaluria in generalized peroxisomal disorders. Van Woerden CS, et al

- The Zellweger syndrome is characterized by a generalized loss of peroxisomal functions caused by deficient peroxisomal assembly.
- Hyperoxaluria was present in 19/23 patients with Zellweger syndrome (83%).
- The presence of hyperoxaluria was statistically significant correlated with the severity of neurological dysfunction.

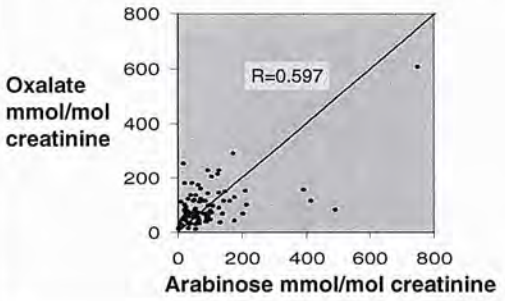


Primary Hyperoxalurias

Ref: Metabolic Basis of Inherited Disease

- Frequently fatal diseases that require combined liver and kidney transplants
- Considerable number of failures because oxalates deposits are considerable and cause severe damage for many years after transplants.
- 10% cases diagnosed <1 yr age
- Most cases 5-40 years
- 80% of diagnosed patients die before age of 20 yrs

Correlation between urine arabinose and oxalate



Where are oxalates deposited?

- bones
- joints
- blood vessels
- lungs
- eyes
- skin
- heart
- thymus
- skeletal muscle
- joints
- fat
- teeth
- mouth
- nerves
- brain
- bone marrow
- thyroid gland
- blood brain barrier

Multisystem effects of oxalates

Tissue	Clinical Symptom and Pathology
Kidney and urinary tract	Urolithiasis, nephrocalcinosis, renal failure, hematuria, pyelonephritis, and hydronephrosis
Bone	Bone pain, multiple fractures, and osteosclerosis
Eye	Retinopathy and optic atrophy
Teeth, mouth, and associated structures	Root resorption, pulp exposure, tooth mobility, and dental pain
Nerves	Peripheral neuropathy (axonal degeneration and segmental demyelination)
Brain and meninges	
Heart	Heart block, myocarditis, and cardioembolic stroke
Deep vasculature	Vasospasm
Peripheral vasculature and skin	Livedo reticularis, peripheral gangrene, and calcinosis cutis metastatica
Bone marrow	Pancytopenia and hepatosplenomegaly
Cartilage, ligaments, and synovial tissue	Arthropathy
Miscellaneous: thymus, adipose tissue, skeletal muscle, and liver blood vessels	

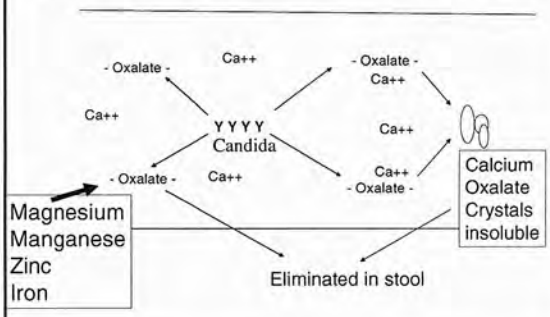
Organic acid test-dysbiosis markers

Compound	Reference Range mmol/mol creatinine	Patient Value		Reference Interval Low / Normal / High
Yeast/Fungal				
citramalic	0.0 - 2.0	17.82	H	
5-hydroxymethyl-2-furoic	0.0 - 80.0	8.56		
3-oxoglutaric	0.0 - 0.5	0.27		
furan-2,5-dicarboxylic	0.0 - 50.0	6.58		
furancarboxylglycine	0.0 - 60.0	1.18		
tartaric	0.0 - 16.0	4.48		
arabinose	0.0 - 47.0	695.97	H	
carboxycitric	0.0 - 46.0	10.50		

Organic acid test-oxalate related

Oxalate Related				
glycolic	0.0 - 10.0	8.41		
glyoxylic	0.0 - 100.0	10.58		
oxalic	0.0 - 37.0	359.93	H	

Oxalate crystal formation in GI tract



Supplements to reduce oxalates

- Probiotics-Help to control Candida and have enzymes that destroy oxalates
- Supplement with arginine, an amino acid that reduces oxalate crystal deposition in tissues and reduces oxidative damage to kidney cells
- Supplement with fish oil or cod liver oil
- Reduce arachidonic acid (omega-6)
- Supplement with B-6

High oxalate food list

- - kiwi
- - lemon peel*
- - lime peel*
- - orange peel
- - raspberries
- - rhubarb*
- - strawberries
- - tangerines
- - chocolate milk
- - almonds
- - baked beans in tomato sauce
- - cashews
- - tomato soup
- - vegetable soup
- - watercress
- - eggplant
- - escarole
- - kale
- - leeks*
- - mustard greens
- - okra*
- - parsley
- - parsnips
- - peppers, green
- - pokeweed*
- - rutabagas
- - sorrel
- - spinach*
- - summer squash
- - sweet potatoes*
- - Swiss chard*

High oxalate food list

- - Fig Newtons
- - fruit cake
- - graham crackers
- - grits, white corn
- - kamut
- - marmalade
- - soybean crackers*
- - wheat germ*
- - blackberries
- - blueberries
- - red currants
- - dewberries
- - figs, dried
- - grapes, purple
- - gooseberries
- - ginger
- - green beans
- - peanut butter*
- - peanuts*
- - pecans*
- - sesame seeds
- - sunflower seeds
- - soy protein
- - tofu (soybean curd)*
- - walnuts
- beans (green, wax, dried)
- - beets (tops, roots, greens)
- - celery
- - chives
- - collards

That's Impossible!

Super high oxalate food list

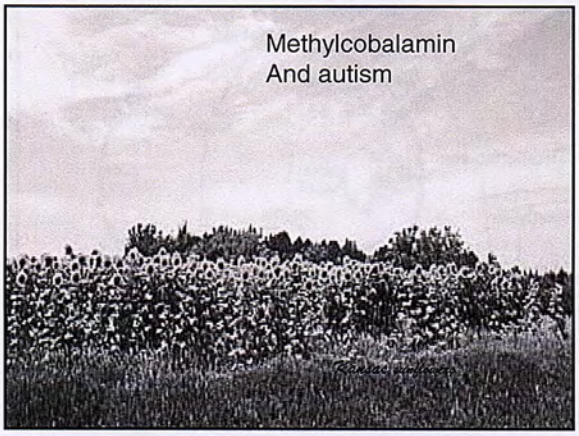
- Spinach
- Soy protein
- Tofu
- Peanuts
- Peanut butter
- Pecans
- Lemon, lime peel
- Rhubarb
- Swiss chard
- Parsley, raw
- Sweet potatoes
- Pokeweed
- Black pepper
- Chocolate
- Instant coffee
- Leeks
- Tea
- Okra
- Wheat germ

Summary

- Oxalates cause severe symptoms due to crystal deposition in virtually all tissues of the body including brain and blood brain barrier
- Oxalates in the GI tract bind essential elements like calcium, magnesium, zinc, and others, preventing their absorption
- Oxalates are powerful chelating agents that bind heavy metals but trap them in the tissues, preventing their release from the body
- Oxalates can cause significant damage by their sharp edges and are oxidizing agents as well

Summary

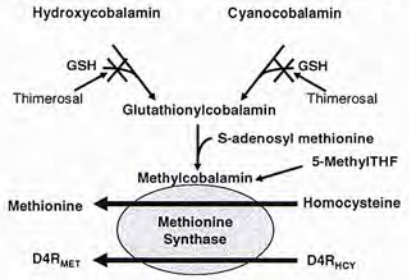
- Use calcium and magnesium citrate to prevent oxalate absorption
- Keep Candida under control all of the time
- Use low oxalate diet or at least eliminate foods highest in oxalates
- Vitamin C is not significant problem in producing oxalates unless free copper or iron is elevated
- Test for free copper and iron as soon as possible



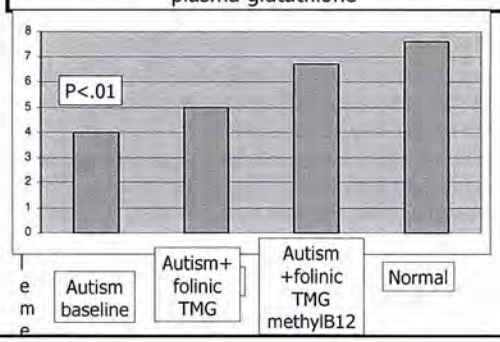
Percentage of children with autism improving after methylvitamin B12 (methylcobalamin),folinic acid,and trimethylglycine-Dr. James Neubrander

- Language 71%
- Awareness 65%
- Cognition 52%
- Engagement 43%
- Eye contact 37%
- Better behavior 35%
- More focus 35%
- Understanding 35%
- Vocalization 35%
- Trying new things 33%
- Increased words 35%
- More calm 33%
- Socialization 30%

Thimerosal blocks GSH-dependent synthesis of MethylB12

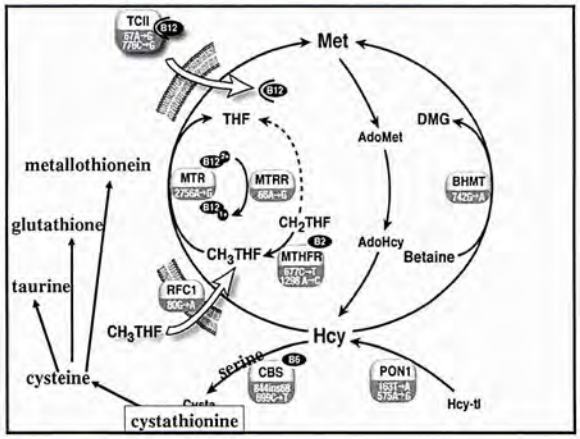


Effect of supplementation of autistic children on plasma glutathione

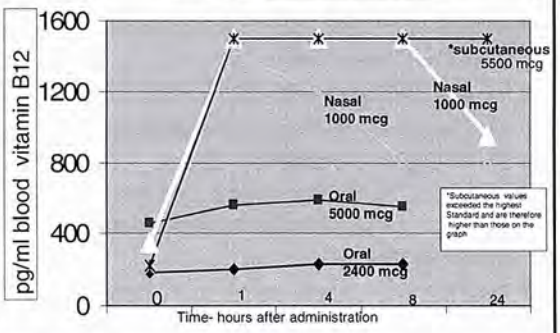


Supplements that increase defective methylation reactions due to mercury

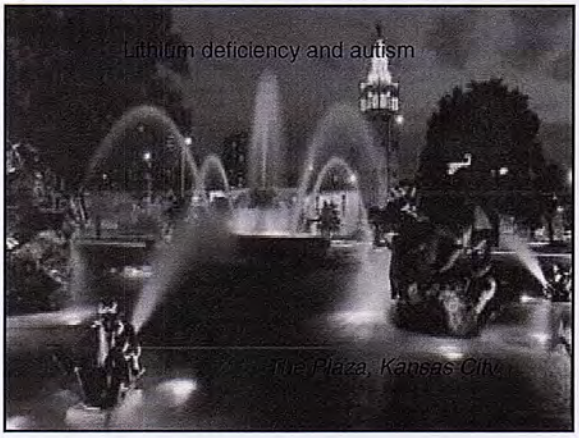
- Methylcobalin (methyl B12) injectionsublingual
- Trimethylglycine (TMG)
- S-adenosylmethionine (SAM)e
- Folinic acid
- Glutathione-oral if Candida under control
- DMSA to remove mercury



Effect of method of administration on methyl B-12 absorption



Methylcobalamin liquid- high potency New Beginnings



J Am Coll Nutr. 2002 Feb;21(1):14-21.
Lithium: occurrence, dietary intakes, nutritional essentiality.
Schrauzer GN.

- Low lithium intakes from water supplies were associated with increased rates of suicides, rape, homicides and the arrest rates for drug use and other crimes.
- The available experimental evidence now appears to be sufficient to accept lithium as essential; a provisional RDA for a 70 kg adult of 1,000 micrograms/day is suggested.

Food Addit Contam. 2003 Jan;20(1):44-56.
Determination of several elements with ICP-MS detection: estimation of daily dietary intake.
Noel L, Leblanc JC, Guerin T.

- The estimated mean daily intakes were 11 microgram for lithium in typical foods ingested-1% of RDA
- 9 microgram for mercury and 34 microgram for lead in the same foods
- If water is deficient, then lithium deficiency is likely

Lithium stimulates brain stem cells to reproduce in culture

- Research of De-Maw Chuang of the Mood and Anxiety Disorder Program at the USA National Institutes of Health in Bethesda, Maryland
- May also help to restore function of damaged brain cells
- Helps to restore protect against toxic effects of glutamate, a neurotransmitter that is also an excitotoxin, kills neurons
- Excess glutamic acid is common abnormality in autism and Asperger's syndrome
- Giving rats lithium after they have had a stroke helps them to regain balance and mobility.

References for lithium in brain function

- Hashimoto, R., Senatorov, V., Kanai, H., Leeds, P. & Chuang, D.-M. Lithium stimulates progenitor proliferation in cultured brain neurons. Neuroscience, 117, 55 - 61, (2003).
- Hashimoto, R. et al. Lithium induces brain-derived neurotrophic factor and activates TrkB in rodent cortical neurons: An essential step for neuroprotection against glutamate excitotoxicity. Neuropharmacology, 43, 1173 - 1179, (2002).
- Moore, G. J., Bebchuk, J. M., Wilds, I. B., Chen, G. & Manji, H. K. Lithium-induced increase in human grey brain matter. Lancet, 356, 1241 - 1242, (2000).

Toxic Metals and Essential Minerals in the Hair of Children with Autism and their Mothers

J.B. Adams[1]; C.E. Holloway[1]; F. George[2]; D. Quig[3]

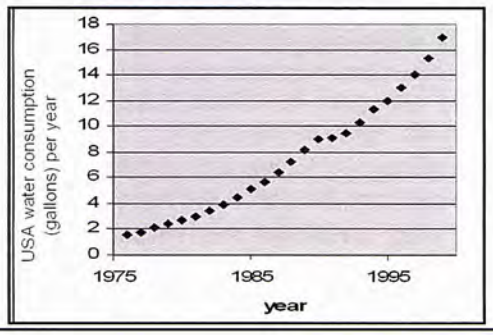
- The levels of 39 toxic metals and essential minerals in hair samples were determined for children with autism spectrum disorders and a subset of their mothers compared to controls.

- Iodine levels were 45% lower in the children with autism (p=0.005).

Lithium levels were 30% lower (p=0.04) in the younger children with autism . The mothers of young children with autism had especially low levels of lithium.

What if water is **too** pure?

Increase in bottled water related to autism epidemic?

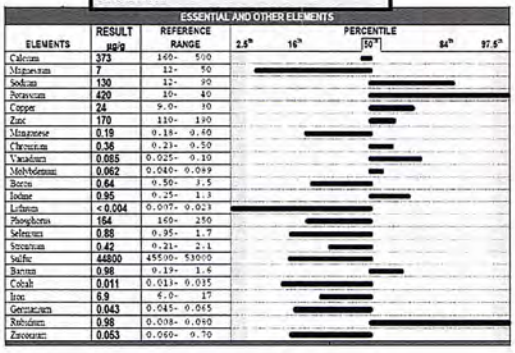


Is lithium deficiency due to purified water cause of autism epidemic?

Contains lithium

Does not contain lithium

Hair elements test profile – autism-



ESSENTIAL AND OTHER ELEMENTS			
ELEMENTS	RESULT µg/g	REFERENCE RANGE	PERCENTILE 2.5th 16th 50th 84th 97.5th
Calcium	373	160- 500	
Magnesium	7	12- 50	
Sodium	130	12- 90	
Potassium	420	10- 40	
Copper	24	9.0- 30	
Zinc	170	110- 190	
Manganese	0.19	0.18- 0.40	
Chromium	0.36	0.21- 0.50	
Vanadium	0.085	0.025- 0.10	
Molybdenum	0.062	0.040- 0.089	
Boron	0.64	0.50- 3.5	
Iodine	0.95	0.25- 1.3	
Lithium	< 0.004	0.007- 0.023	
Phosphorus	154	160- 250	
Selenium	0.88	0.95- 1.7	
Strontium	0.42	0.21- 2.1	
Sulfur	44800	45500- 53000	
Barium	0.98	0.19- 1.6	
Cobalt	0.011	0.013- 0.035	
Iron	6.9	6.0- 17	
Germanium	0.043	0.045- 0.065	
Rubidium	0.98	0.008- 0.060	
Zirconium	0.053	0.060- 0.70	

Lithium RDA

Weight Kilograms	Micrograms per day
70	1000
52.5	750
35	500
17.5	250
8.75	125

Lithium supplement available from New Beginnings Nutritionals