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

Formation of cholesterol

Fat, carbohydrates, proteins → Acetyl CoA → Lanosterol → 7-dehydrocholesterol

Genetic defect in SLOS: Cholesterol not produced → Vitamin D activates sonic hedgehog

Bile salts, Fat digestion, Steroid hormones, Estrogens, Testosterone, Vitamin absorption → Cortisol, aldosterone
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.

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

- Extremely low cholesterol 17.5%
- Low cholesterol 57.0%

Am J of Med Genetics Part B: Neuropsychiatric Genetics

- 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

- 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 3 oz-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

Oxalates in autism

Oxalate stone from mummy
800 AD
**Interconversion of oxalate**

![Diagram of oxalate interconversion]

**Improvements in Urinary function according to Susan Owens:**
1. Loss of excessive urination
2. Loss of urinary frequency
3. Obtaining nighttime continence
4. Obtaining daytime continence
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
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**

![Image of oxalic acid cleaning a radiator]
Oxalate binds mercury

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

Comparison of oxalates in the autistic spectrum and normal children

Comparison of urine oxalate in autistic spectrum and normal children
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

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

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Clinical Symptom and Pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney and urinary tract</td>
<td>Urinary calculi, nephrocalcinosis, renal failure, hypertension, and hypertension</td>
</tr>
<tr>
<td>Bone</td>
<td>Bone pain, multiple fractures, and osteoporosis</td>
</tr>
<tr>
<td>Eye</td>
<td>Photophobia and optic atrophy</td>
</tr>
<tr>
<td>Teeth, mouth, and associated structures</td>
<td>Root resorption, pulp exposure, tooth mobility, and oral-pain</td>
</tr>
<tr>
<td>Nerves</td>
<td>Peripheral neuropathy, external degeneration, and segmental demyelination</td>
</tr>
<tr>
<td>Skin and membranes</td>
<td>Heart block, mycarditis, and cardiogenic shock</td>
</tr>
<tr>
<td>Heart</td>
<td>Vasoospasm</td>
</tr>
<tr>
<td>Periphera vascular</td>
<td>Leuko retinias, peripheral gangrene, and carotid cufus aneurysm</td>
</tr>
<tr>
<td>Brain</td>
<td>Epilepsy</td>
</tr>
<tr>
<td>Bone marrow</td>
<td>Fibrosis of bone marrow</td>
</tr>
<tr>
<td>Thyroid gland</td>
<td>Thyroiditis and hypothyroidism</td>
</tr>
<tr>
<td>Blood brain barrier</td>
<td>Anemia</td>
</tr>
</tbody>
</table>

Oxalate metabolism

Protein, Galatin

- GO Glycolate oxidase
- GRPR Glyoxylate reductase
- B-6 Glyoxylate
- AGT Glucose
- LDH Lactate dehydrogenase
- Yeast Fungi

Correlation between urine arabinose and oxalate

R=0.587

Arabinose mmol/mol creatinine

Oxalate mmol/mol creatinine
**Organic acid test-dysbiosis markers**

<table>
<thead>
<tr>
<th>Sample</th>
<th>Reference Range</th>
<th>Low</th>
<th>Normal</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citric</td>
<td>20 - 75 mg/L</td>
<td>*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malate/Malic</td>
<td>30 - 45 mg/L</td>
<td>*</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>Succinate</td>
<td>20 - 65 mg/L</td>
<td>*</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>Formate/Fumarate</td>
<td>30 - 45 mg/L</td>
<td>*</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>Oxalic</td>
<td>30 - 45 mg/L</td>
<td>*</td>
<td>*</td>
<td></td>
</tr>
</tbody>
</table>

**Organic acid test-oxalate related**

<table>
<thead>
<tr>
<th>High</th>
<th>Low</th>
<th>Medium</th>
</tr>
</thead>
<tbody>
<tr>
<td>*</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>

**Oxalate crystal formation in GI tract**

- Oxalate + Ca++ → Calcium Oxalate Crystals
- Eliminated in stool

**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
- roasted beets
- 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
- Caper
- 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

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), folic acid, and trimethylglycine—Dr. James Neubander

- 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

Supplements that increase defective methylation reactions due to mercury

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

Effect of supplementation of autistic children on plasma glutathione

<table>
<thead>
<tr>
<th></th>
<th>Autism baseline</th>
<th>Autism + folic</th>
<th>Autism + TMG</th>
<th>Autism + methyl B12</th>
<th>Normal</th>
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<tbody>
<tr>
<td>suicides</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>2</td>
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<td>P&lt;.01</td>
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</tbody>
</table>

Effect of method of administration on methyl B-12 absorption

Subcutaneous: 5000 mcg
Nasal: 1000 mcg
Nasal: 500 mcg
Oral: 5000 mcg
Oral: 2400 mcg
Lithium intake from water supplies was 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.

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

References for lithium in brain function
Toxic Metals and Essential Minerals in the Hair of Children with Autism and their Mothers
J.B. Adams¹; C.E. Holloway²; F. George³; D. Quig⁴

- 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.

Increase in bottled water related to autism epidemic?

<table>
<thead>
<tr>
<th>USA water consumption (gallons) per year</th>
<th>1975</th>
<th>1985</th>
<th>1995</th>
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<tbody>
<tr>
<td></td>
<td>0</td>
<td>4</td>
<td>8</td>
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<tr>
<td></td>
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<td>6</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>8</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>10</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>12</td>
<td>16</td>
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</table>

Hair elements test profile – autism

Lithium RDA

<table>
<thead>
<tr>
<th>Weight Kilograms</th>
<th>Micrograms per day</th>
</tr>
</thead>
<tbody>
<tr>
<td>70</td>
<td>1000</td>
</tr>
<tr>
<td>52.5</td>
<td>750</td>
</tr>
<tr>
<td>35</td>
<td>500</td>
</tr>
<tr>
<td>17.5</td>
<td>250</td>
</tr>
<tr>
<td>8.75</td>
<td>125</td>
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</table>
Lithium supplement available from New Beginnings Nutritionals