Understanding the Role of Oxalate Toxicity in Chronic Health Problems
Lecture Overview

• What is oxalic acid (aka. oxalate)?
• Tissue/organ damage examples
• The chemistry of oxalates
• Oxalate and heavy metals
• Treating high oxalate
• Supplement support for high oxalate
What are Oxalates?

- Oxalate, and its acid form, are organic acids found from 3 primary sources:
  - Diet
  - Fungus, such as mold and candida
  - Cell metabolism
- Oxalic acid is the most acidic organic acid in body fluids.
- Used to clean rust from radiators
- Ethylene glycol’s (antifreeze) primary toxicity is from oxalate crystal formation.
Oxalate Anion
Calcium Oxalate
Tissue Damage From High Oxalates
Normal Kidney
Staghorn Oxalate Crystal in Kidney
Oxalate Crystals in Bone
Oxalate Crystals in Brain

Fig. 3  Crystals in brain \( \times 350 \).

Oxalate crystal in meninges
Oxalate Crystal in Nerve Tissue
Thyroid Oxalate Accumulation
Oxalate Crystals in Aspergillus
Oxalate Metal Complexes from Aspergillus

Scanning electron micrographs of crystals of (a) cobalt oxalate and (b) zinc oxalate produced by the soil fungus Aspergillus niger during the solubilization of
Calcium oxalate crystal deposition in a patient with Aspergilloma due to *Aspergillus niger*

Thoracic CT 9 months (A, B, C) and 3 weeks (D, E, F) before arrival at our hospital and upon admission (G, H, I). Old inflammatory and cystic changes in right upper lobe (A and B); Fungal, ball-like lesion 2.5 cm in diameter with air space consolidation in right upper lobe (D and E) and mild consolidation in right lower lobe (F); Right lung (G) and left middle lobe (H) are replaced by massive consolidation with air and bilateral pleural effusion is evident (I).

Parasites and Oxalates

Possible link with oxalates and certain parasitic diseases (Dempsey, et. al, Urinary Oxalate Excretion, Metab. Clinic Exptl 9:52, 1960).

- Schistosomiasis, Giardiasis, Amebiasis, Ascariasis.

*Doing a parasite stool test on anyone with high oxalates could be worthwhile.*
The Chemistry of Oxalates

Solubility Factors
Solubility Problems with Oxalates

[Oxalate] -- + [Ca]++ $\rightleftharpoons$ CaOxalate

soluble soluble Insoluble

The higher the solubility product constant is, the more soluble the compound

Ksp is indicator of Strength of reaction

Its value indicates the degree to which a compound dissociates in water
Oxalate Interconversions

Oxalic Acid

Oxalate, monobasic

Conjugate bases

pK 1.27

pK 4.28

pH where oxalate becomes dibasic

Ca++

Zn++

Hg++

pH where there are equal amounts of oxalic acid and its monobasic form

At the pH of blood (7.4) most oxalates in the dibasic form

Integrative Medicine Academy
Oxalate Chelates Mercury

COOH

| COOH |
| Oxalic Acid |

COOH

Oxalate, monobasic

COOH

HOOC

Oxalate, dibasic

Deposits in bone, other tissues

+Hg+

Hg++

COO-

COO-

COO-

COO-
# Solubility is the Factor That Determines Oxalate and Heavy Metal Toxicity

## Salt Ksp (solubility product constant)

<table>
<thead>
<tr>
<th>Salt</th>
<th>Ksp</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mercury I</td>
<td>$1.75 \times 10^{-13}$</td>
</tr>
<tr>
<td>Lead</td>
<td>$8.6 \times 10^{-10}$</td>
</tr>
<tr>
<td>Copper II</td>
<td>$4.4 \times 10^{-10}$</td>
</tr>
<tr>
<td>Zinc</td>
<td>$1.4 \times 10^{-9}$</td>
</tr>
<tr>
<td>Cadmium</td>
<td>$1.42 \times 10^{-8}$</td>
</tr>
<tr>
<td><strong>Calcium</strong></td>
<td><strong>$1.5 \times 10^{-8}$</strong></td>
</tr>
<tr>
<td>Magnesium</td>
<td>$8.5 \times 10^{-5}$</td>
</tr>
</tbody>
</table>

The smaller the value of the Ksp, the greater insolubility of the salt. For example, the lower the Ksp value for Mercury versus Calcium means it is more insoluble - less likely to dissociate.

The Mercury-Oxalate Salt is approximately 100,000K **less soluble** than Calcium-Oxalate.
Some Facts About Oxalate Chemistry

• At the pH of blood (fairly constant) most oxalates are in the dibasic form.

• In the urine, the pH fluctuates more widely and oxalates are mostly found in dibasic form, but a combination of monobasic and dibasic is found with more acidic urine.

• Oxalates have the ability to form salts with a wide variety of metals.

• Calcium levels in blood are fairly constant, but oxalates levels can vary widely.

• It is the oxalate level in the blood which tends to drive calcium oxalate crystal formation in tissues.
Magnesium and Oxalates


Oxalate Metabolism

Glycolate Oxidase (GO)

Glycine → Glyoxylate Glycerate

AGT, Alanine Glyoxylate Amino Transferase Type I Hyperoxaluria

LDH, Lactate dehydrogenase

Glyoxylate reductase (GRHPR)

Type II Hyperoxaluria

Oxalate

Ethylene glycol

Oxalates diet

Protein, Gelatin

Collagen, Candida collagenase

Hydroxyproline

Ascorbate Arabinose

Yeast Fungi

Gelatin

Protein, Collagen

Candida collagenase

Ethylene glycol

Protein, Gelatin

Collagen, Candida collagenase

Hydroxyproline

Ascorbate Arabinose

Yeast Fungi
Primary Hyperoxalurias
Ref: Metabolic Basis of Inherited Disease

- Can be fatal diseases. Often require combined liver and kidney transplants – *Type 1 more than Type 2.*
- Large number of transplant failures because oxalate deposits cause severe damage for many years after transplants.
- 10% cases diagnosed <1 year of age
- Most cases 5-40 years
- 80% of diagnosed patients die before age of 20 years
- May be misdiagnosed as gout or arthritis
Hyperoxaluria Types

**Primary:** Group of autosomal recessive disorders

- **Type I (PH1)** - *Primary Hyperoxaluria Type 1* is caused by the deficiency of the oxalate breakdown liver specific enzyme called *alanine:glyoxylate aminotransferase (AGT)*:
  - AGT is a Vitamin B6 dependent enzyme
  - Leads to high glyoxylic acid which is then converted to glycolate by the enzyme GRHPR or to oxalate by LDH (lactate dehydrogenase).
  - *Elevated Oxalate and Glycolate (glycolic on the OAT)*
Hyperoxaluria Types

• **Type 2 (PH2)** – *Primary Hyperoxaluria Type 2 is caused by the deficiency of Glyoxylate reductase/hydroxypyruvate reductase (GRHFR):*  
  • It is often less severe than Type 1 usually causing kidney stone damage versus end-stage kidney failure.  
  • *Tend to see elevated Oxalate and Glycerate (glyceric on OAT).*  
  • PH2 is also called L-glycero aciduria
Hyperoxaluria Types

Secondary – *dietary consumption, increased digestive absorption, and mold and yeast production.*

- Potential with vitamin C and oxalate formation (discussed shortly).
- Some foods have PEG (polyethylene glycol), a petroleum compound made from ethylene glycol, the main ingredient in antifreeze, i.e. sport drinks, laxatives, baked goods, creams.

Idiopathic – *unknown cause*

Oxalosis: *defined as oxalate crystals forming in extrarenal organs. Extrarenal accumulation most commonly affects bone, blood vessels, central nervous system, peripheral nervous system, retina, skin, and thyroid.*
Vulvodynia

• It is a syndrome of unexplained vulvar pain, frequently accompanied by physical disabilities, limitation of daily activities, sexual dysfunction and psychological distress.

• The patient's vulvar pain usually has an acute onset and, in most cases, becomes a chronic problem lasting months to years.

• The pain is often described as burning or stinging, or a feeling of rawness or irritation.
• Cyclic vulvovaginitis is believed to be a reaction to yeast, which may be detected at times, and not detected at other times with KOH preparation or fungal cultures.

• Because of the link with Candida, treatment for cyclic vulvovaginitis may include anti-candidal medication even if cultures are not positive.

• Other treatments that have been helpful in patients with vulvodynia are a low-oxalate diet and, in some cases, the addition of oral calcium citrate (Citracal), two tablets (200 mg/950 mg each) orally two to three times a day to neutralize oxalates in the urine.
Susan Owens, Ph.D

- Founder of [www.lowoxalate.info](http://www.lowoxalate.info)
- Independent biomedical autism researcher found that some children with Pervasive Developmental Disorder (PDD) and Autism improved with a Low Oxalate Diet (LOD).

- Urine oxalate levels in children on the autism-spectrum:
  - In a 116 children (100 autism, 16 neurotypical), 36% of the autistic children had oxalate levels greater than 90 mmol/mol creatinine - the value consistent with a genetic hyperoxaluria.
  - None of the neurotypical children had values this high
  - None of the ASD kids had either glyceric or glycolic elevated on their OATs.
Common Patient Complaints/Observations

- Sandy and grainy stools
- Bladder irritability
- Pain on urination (but no confirmation of infection)
- Urethral irritation, vulvar pain
- Eye pain (eye poking in children)
- Body aches, burning feeling in muscles
- Fibromyalgia-like discomfort
- Moodiness, irritability, and aggressive behavior – *often seen in autism.*
- Tendon pain, increased tension in muscles with movement
- Trigger point tenderness
Comparison of Urine Oxalate in Autistic-Spectrum and Neurotypical Children

Oxalate above 90 is consistent with genetic hyperoxaluria

\[ t\text{-test} \quad p < 10^{-16} \]

Autistic Spectrum N=100

Normal Children N=16
Mean value for autism at 90.1 is at the lower cut-off for genetic hyperoxaluria

<table>
<thead>
<tr>
<th>Statistic</th>
<th>Normal urine oxalate</th>
<th>Autistic Spectrum urine oxalate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>15.7</td>
<td>90.1</td>
</tr>
<tr>
<td>Median</td>
<td>11.5</td>
<td>70.5</td>
</tr>
<tr>
<td>Std dev</td>
<td>10.8</td>
<td>75.8</td>
</tr>
</tbody>
</table>
Correlation Between Urine Arabinose and Oxalate

R = 0.597
Some Oxalate Levels Can Be Extremely High

<table>
<thead>
<tr>
<th>No.</th>
<th>Substance</th>
<th>Range</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>Glycerol</td>
<td>0.74 - 13</td>
<td>3.5</td>
</tr>
<tr>
<td>21</td>
<td>Ethanol</td>
<td>27 - 221</td>
<td>105</td>
</tr>
<tr>
<td>22</td>
<td>Oxalic Acid</td>
<td>35 - 185</td>
<td>Highest 2016</td>
</tr>
</tbody>
</table>

Likely soy consumption
5. Glycolic

6. Alcohol

7. Arabinose

8. Lactic acid

Urinary metabolic markers

<table>
<thead>
<tr>
<th>Substance</th>
<th>Reference Value</th>
<th>Patient Value</th>
<th>Reference Population - 13 years and younger</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycolic</td>
<td>≤ 3.6</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>≤ 3.9</td>
<td>0.44</td>
<td></td>
</tr>
<tr>
<td>Arabinose</td>
<td>≤ 56</td>
<td>H 95</td>
<td></td>
</tr>
<tr>
<td>Lactic acid</td>
<td>≤ 34</td>
<td>19</td>
<td></td>
</tr>
</tbody>
</table>

Glycolic
# Very Low Vitamin B6

<table>
<thead>
<tr>
<th>補充物</th>
<th>标记</th>
<th>范围</th>
<th>数值</th>
</tr>
</thead>
<tbody>
<tr>
<td>烟酸 (B6)</td>
<td>≤ 59</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>泛酸 (B5)</td>
<td>≤ 26</td>
<td>4.9</td>
<td></td>
</tr>
<tr>
<td>核黄素</td>
<td>≤ 1.1</td>
<td>0.48</td>
<td></td>
</tr>
<tr>
<td>抗坏血酸</td>
<td>10 - 200</td>
<td>0.92</td>
<td></td>
</tr>
</tbody>
</table>
High Oxalate + Low Glycolic

<table>
<thead>
<tr>
<th>Metabolic Markers in Urine</th>
<th>Reference Range (mmol/mol creatinine)</th>
<th>Patient</th>
<th>Reference Population - Females Under Age 13</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oxalate Metabolites</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20 Glyceric</td>
<td>0.71 - 9.5</td>
<td>3.4</td>
<td></td>
</tr>
<tr>
<td>21 Glycolic</td>
<td>20 - 202</td>
<td>L 6.9</td>
<td></td>
</tr>
<tr>
<td>22 Oxalic</td>
<td>15 - 174</td>
<td>H 359</td>
<td></td>
</tr>
</tbody>
</table>
www.lowoxalate.info

- General diet recommendations:
  - Adults following a low oxalate diet should be between 40mg to 60mg of oxalate consumption (maximum) a day on a 2000 calorie diet.

- Great resource for information about Low Oxalate Diet (LOD).

- Yahoo support group for people implementing LOD.

- Food list and recipes

- FAQ and Research section
Foods High in Oxalate

Good Place To Start

• Spinach
• Soy Products
• Nuts (including nut milk and butters).
• Berries (including berry juice and jams).
Soy protein is probably not a good food for humans - *Linda Massey, Ph.D., at Washington St U.*

- During their testing, the researchers found the highest oxalate levels in textured soy protein, which contains up to **638 milligrams of oxalate per 85-gram serving**.
- *Soy cheese had the lowest oxalate content, at 16 milligrams per serving.*
- *Spinach, measured during previous research, has approximately 543 milligrams per one-cup (2 oz. fresh) serving.*
Green Smoothie
Treating High Oxalates

*Beyond Dietary Intervention*
Other Support
Vitamin B6
Probiotics
Calcium + Magnesium
Treat Yeast
Diet
Oxalate Dumping

- Sandy or grainy stools
- Pain with urination
- Urinary urgency
- Irritability, moodiness, etc.
- ‘Potty’ accidents
- Painful bowel movements
- Possible rash – *red bumps on skin, hives, may be itchy.*
- Yeast flare
Supplement Support For High Oxalate
Oxalate Crystal Formation in GI tract

Ca++ - Oxalate - Candida

Y Y Y Y Y

Ca++

- Oxalate - Ca++

- Oxalate - Ca++

- Oxalate - Ca++

- Oxalate -

Calcium Oxalate Crystals insoluble

Eliminated in stool
Calcium/Magnesium Citrate

- 1 to 2 capsules before meals to help prevent oxalate absorption.
- Capsules can be swallowed or opened up and mixed into food or drink.

Cal/Mag Citrate – 600mg each of Calcium and Magnesium Citrate

Binding Oxalates in Gut
Calcium Chewable w/Magnesium

- 1 tablet with meals containing low to medium oxalates.
- 2 tablets with meals containing high oxalates.

1 tablet = 247 mg of calcium citrate & 50 mg of magnesium citrate
High Dose Probiotics

1 to 2 capsules daily (two capsules = 225 billion organisms)

½ to 1 packet (one packet = 225 billion organisms)
Vitamin B6

- Pyridoxine HCL
- Helps in oxalate metabolism enzyme function.
- Dosing suggestion is 100mg daily for adults.
- 25mg to 100mg daily for children.
Additional Supplement Options

• **Epsom Salt Baths** – 1/2 to 2 cups in bathwater - 3 to 7 times weekly.

• **Epsom Salt Cream** – *apply 1 gram to skin* - 2 to 3 times daily.

• **L-Arginine** – *500mg to 1000mg daily.* Need to watch for underlying herpes viral problems, i.e. blisters.
Additional Supplementation Options

- **Digestive enzymes:**
  - Zyme-Prime *(capsules or chewable)* - Houston Enzymes
  - DiZorb *(Betaine HCL), Support Digestion* - capsules

- **Biotin** – 5mg to 15mg daily. Can modify for children, i.e. 1mg or more daily.

- **Special Considerations:**
  - Chondroitin Sulfate – *to aide against calcium oxalate crystal formation.*
  - N-acetyl-glucosamine – *to stimulate hyaluronic acid production.*
Hydrate

• Consume ½ body weight in ounces of pure water daily.

• For example, a 40lbs. (18kg) child should drink approx. 20 ounces of fluids daily, or 0.59 liters.

• 1 fluid ounce = 0.0295 liters

• Adjust consumption with increased activity.
What About Vitamin C Supplementation?

• A number of studies show little to no correlation with moderate amounts of ascorbic acid and oxalate problems:
  
  • *85K women had no relation to kidney stones and ascorbic acid.*
  
  • *Great Plains Laboratory (GPL) found zero correlation between urinary oxalate and vitamin C.*

• The vast majority of ascorbic acids on the Organic Acids Test from GPL show low to low normal Vitamin C.
Additional Factors Regarding Vitamin C and Oxalate

- Free copper accelerates vitamin C breakdown to oxalates.
- High percentage of kids on the autism-spectrum tend to have high free copper.
- Low Oxalate Diet advocates recommend small amounts of ascorbic acid, i.e. 200mg to 400mg daily.
  - Some websites for kidney stone patients recommend no more than 2000mg daily.
Things to Do (and Not Do) with High Oxalate Patients

By Julie Matthews
Certified Nutrition Consultant
High Oxalate Foods

• Nuts, especially almonds & peanuts
• Beans, most
• Beets
• Figs
• Rhubarb
• Swiss chard
• Field greens
• Spinach
• Amaranth and buckwheat
• Soy

• Sweet potatoes
• Some berries - Gooseberries, raspberries and blackberries
• Chocolate
• Citrus peel
• Kiwi and starfruit
• Tea

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Remove Oxalates VERY SLOWLY From The Diet

• 5-10% per week

• For high oxalate patients, this could take a couple months or more.

• Removing them quickly can cause “dumping” symptoms, pain and can overwhelm the system.
Cooking to Reduce Oxalates

• While cooking can reduce oxalates:
  • Reduction from boiling and soaking – *it reduces soluble oxalate by 50% or so from boiling and discarding the water.*
  • Roasting at high heat for 30 minutes can reduce oxalates in tubers
  • However, this is not enough to make extremely high oxalate foods low enough to consume for a “low oxalate diet”
    • *For example, extremely high oxalates: Beets, sweet potato, spinach, Swiss Chard, and amaranth reduced by 50% will still be very high.*
    • *Although, cooking can help get medium/high vegetables (12-20 mg) into an acceptable range.*
Low Oxalate Diet
Experience and Length of Diet

• Typically, people that need a low oxalate diet because of endogenous production and those who have had high oxalates for years, will likely benefit from a long term diet strategy of low oxalate.

• The body can still be dumping oxalate a year or more after the source of high oxalate is gone.

• Unlike other diets, where when you remove a food you see a positive result - *with low oxalate, when you remove foods, you might see a negative result at first (from dumping).* If you go slowly enough, you may see relief and benefit right from the start.

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Autism Nutrition and Special Diets

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