Detoxification

Reducing Total Toxic Body Burden and Enhancement of Detoxification Pathways

One of The Foundation of Functional Medicine
David M. Brady, DC, CCN, DACBN, ND (Cand.)

PHYSICAL
• Injury
• Inflammation
• Excessive Exercise

NUTRITIONAL
• Excess Food
• Additives
• Alcohol
• Trans-fatty acids

INFECTION
Endotoxins & Exotoxins
• Bacterial
• Fungal
• Parasitic

CHEMICAL
• Xenobiotics
• Organics

TOTAL TOXIC EXPOSURE

How serious is the problem?

In 1988, scientists from all over the world met to discuss the effects of our environment on our health.

Maltoni C and Selikoff IJ. Living in a chemical world. New York: NYAS, 1988;534
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Our cities are becoming unfit to live in.

More and more cities are being added to the list of having dangerously polluted air.

―"Smoggy cities, 1991." Environmental quality: The twenty-second annual report of the Council on Environmental Quality together with the President's message to Congress.

Our polluted environment

We are continuously adding to the burden by producing more new chemicals. Currently over 100,000 and increasing by about 3 new chemicals per day.


Our polluted environment

The EPA tracks the release of toxic chemicals into our environment.

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Our polluted environment

In 1989, 5,705,670,380 pounds of chemicals were released. Some went into our air, some our rivers and streams, and some into our ground water supply.


Our polluted environment

This is enough to fill a line of semi-trucks stretching from Los Angeles to Des Moines, Iowa with cancer-causing toxins.

Even at home...

Even in the home, it is impossible to completely escape the effects of toxins: radon exposure has become of concern.

Even at home...

Outgassing from carpet, cleaning materials and common chemicals found in homes contributes to the overall burden.

Even at home...

As far back as 1964 it was known that charcoal-broiled meat contained polycyclic aromatic hydrocarbons, known carcinogens.


Even at home...

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Other sources of PAH include roasted coffee and leafy vegetables grown in urban areas.

Our polluted environment

Sperm counts declined by an average of 1.5% per year in the U.S. and 3.1% per year in Europe between 1938 and 1990, according to a report by epidemiologists at the California Department of Health Services.

*Chemical Week: December 10, 1997*

**LIVER DETOXIFICATION**

TOXINS (non-polar)
- Endotoxins
- Xenobiotics

INTERMEDIATE METABOLITES may be toxic

PHASE I
- Cytochrome P-450 enzymes
- Hydroxylation via redox reactions
- Critical Co-factors: NADH, NADPH, B6, Mg

PHASE II
- Conjugation reactions
- Glutathione Conjugation
- Amino Acid Conjugation
- Glucuronidation
- Sulfation
- Methylation
- Acetylation

EXCRETION (polar molecules)
- Kidney — Urine
- Bile — Feces

**Detoxification pathways in the liver**

- Benzene → Phase I
- Oxidation → Reduction → Hydrolysis
- Phenol

This modification sets the stage for Phase II, ultimately allowing the elimination of the toxin.

Detoxification pathways in the liver

Sometimes the intermediary metabolites of biotransformation are more damaging than the toxins themselves were.

Importance of antioxidants

These intermediary metabolites often generate free radicals, or are free radicals themselves. Thus higher levels of antioxidants may be required during detoxification to compensate.
Recently, molecular and cellular research approaches have demonstrated that ROS and antioxidants can directly affect the cellular signaling apparatus and, consequently, the control of gene expression.

**Know Your Color! Know Your Anti-Oxidant!**

<table>
<thead>
<tr>
<th>Color</th>
<th>Foods</th>
<th>Phytochemicals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Green</td>
<td>Broccoli, Cabbage, Okra, Greens, Beans, Spinach</td>
<td>Chlorophyll, Carotenoids, Thioyanates</td>
</tr>
<tr>
<td>Orange-Red</td>
<td>Apricots, Cantaloupe, Carrots, Mangos, Peppers, Pumpkins, Tomatoes, Squash, Yams, Watermelon</td>
<td>Carotenoids: Lycopene, Lutein, Zeaxanthin</td>
</tr>
<tr>
<td>Purple-Red</td>
<td>All Berries, Grapes, Red Wine</td>
<td>Anthocyanins, Ellagic Acid, Resveratrol, Quercetin</td>
</tr>
<tr>
<td>Black</td>
<td>(Organic) Kale, Spinach</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>Apples, Berries, Cherries, Cucumber</td>
<td>A-tocopherol, A-tocotrienol, Selenium</td>
</tr>
<tr>
<td>Cream</td>
<td>Cauliflower, Potatoes</td>
<td>Anthocyanins</td>
</tr>
<tr>
<td>Brown</td>
<td>Baked Beans, Peanuts, Soy</td>
<td>Isoflavones, Genistein, Diadestin, Sapogenins</td>
</tr>
</tbody>
</table>
Mitochondria

- Mitochondrial DNA is 20X more susceptible to oxidative damage than nuclear DNA
- Without adequate energy production, all functional systems are impaired
- Important nutrients: Coenzyme Q₁₀, carnitine, lipoic acid, and vitamins C & E
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Oxidative Stress and mDNA

Normal mitochondrial function generates the majority of ROS in the brain. An individual produces about 1 kg of oxygen radicals per year. The consequence of this is about 100,000 oxidative attacks on mDNA per cell per day.

“Several hypotheses suggest that defective mitochondria contribute to, or are responsible for aging...with aging there is an increased production of reactive oxygen species, a decrease in certain antioxidants, a decreased transcription, translation, and cytochrome oxidase content, and an increase in the extent of DNA modifications.”

Detoxification

Acidic Metabolic Wastes of Anaerobic Metabolism

\[
\begin{align*}
\text{CH}_3 & \quad \text{NADH} & \quad \text{NAD}^+ \\
\text{C=O} & \quad \text{HC-OH} \\
\text{C=O} & \quad \text{C=O} \\
\text{OH} & \quad \text{OH}
\end{align*}
\]

pyruvic acid
(from glycolysis)

lactic acid

Energy Deficient Metabolic States Resulting from Toxicity

Mitochondrial Dysfunction

- Oxidative damage to mitochondrial DNA
- Oxidative phosphorylation disorders
- Shifting of aerobic to anaerobic metabolism
- Accumulation of metabolic toxins
- Can result in clinical disorders such as:
  - Chronic Fatigue Syndrome
  - Fibromyalgia
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Factors Contributing to Functional Impairment of Energy Producing Pathways

Poor Dietary Choices
Excess Calories
Nutrient Deficiencies
Vitamins B₁, B₂, B₃, B₅, B₆
Lipoic Acid, Co Q₁₀
Mg, Mn, Fe
Mitochondrial Damage
Oxidative stress

Direct evidence of metabolic blocks in energy metabolism

Direct evidence of increased toxicity

Direct evidence of bacterial and yeast growth and resulting toxic burden

Phase II

During Phase II, the toxin is further modified by the addition of a molecule making the substance polar and therefore water soluble.

Detoxification pathways in the liver

**Phase II**
- Conjugation
  - Sulfate
  - Glycine
  - Glutathione
  - Glucuronide


### Detoxification Chemistry

![Chemical reaction diagram]

**Clinical Detoxification**

**Treatment goals:**
- reduce toxin exposure
- increase antioxidant support
- supplement phase II conjugating substances (e.g. glutathione, sulfates, glycine, taurine)
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When things break down

Symptom Picture of General Toxicity

General Malaise
- fatigue, headache, joint & muscle pain
Chronic Mucous Production
Poor Exercise Tolerance
Skin Rashes, Peri-orbital edema
Immune Weakness
Environmental and Chemical Sensitivity
Mental Status Changes
- lack of concentration, depression, mood changes, confusion, memory loss, sleep disturbance, anxiety, PMS, etc.

“Doc, lately I’ve been feeling a bit sluggish…”
How does this affect our health?

“Thomas Latimer used to be a vigorous, athletic man, a successful petroleum engineer with a bright future.


How does this affect our health?

“Then he mowed the lawn.”

Latimer was “poisoned by an organophosphate pesticide used to treat his yard.”


How does this affect our health?

Latimer was taking *Tagamet*. This suppressed his normal liver detoxification pathways, leaving him open to the toxic effects of a common lawn pesticide.

Detoxification

Neurological disorders

Illnesses such as Alzheimer’s and Parkinson’s have been linked to “xenobiotics” (toxic chemicals).


Pesticides and Parkinson’s Disease

In a study comparing 496 people with newly diagnosed PD to 541 matched controls, “People who recalled using in-home pesticides on at least 160 days of their lives were 70% more likely to develop PD than those who never used pesticides... Using garden pesticides for same number of days conferred a 50% increase in risk.” (No relationship was seen with fungicides)

Lorene Nelson, PhD, Stanford University
American Academy of Neurology annual meeting, 2000

Food allergy

Some researchers have stated that what has been diagnosed as food allergy may in fact be an inability to process chemicals in the liver: poor detoxification pathways.

Hunter JO. Food allergy—or enterometabolic disorder? Lancet 1991;338:695-6
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The role of nutritional support

Significant evidence exists to support the contention that diet and nutritional supplementation plays an important role in helping maintain these detoxification pathways.


Macronutrients and detoxification

Total protein and energy requirements

- In animals, depression of detoxification pathways occurs in as little as 36 hours of fasting