Physiology and Biology of Detoxification

What is Detoxification?

A definition of Detoxification from Taber's Medical Dictionary:
“Detoxification is the reduction and chemical alteration of the toxic properties of a poisonous substance, which, when taken into the body by ingestion, inhalation, injection or absorption, causes damage to structure and interferes or disturbs normal physiological functions.”
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Toxicity Is Everywhere

Exogenous Toxicity
- Toxins in our food
- In our air and our breath
- In our homes
- In our water
- Drugs and Medications

We All Have Toxins In Our Bodies
- EPA biopsy studies showed:
  - 100% of human fat biopsies contain styrene
  - 100% of human fat biopsies contain dioxins
  - 100% of human fat biopsies contain xylene
  - 100% of human fat biopsies contain 1,4-dichlorobenzene

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**Exogenous Toxins**
- Pesticides
- Benzene
  - A known cause of leukemia
- PCBs
  - Contaminate soil and food, never go away
- Xenoestrogens
  - Styrene, pesticides, detergents, solvents, trichloroethylene, auto exhaust
- Phthalates

**Heavy Metals**
- Mercury
  - From coal fired power stations, dental applications, pesticides etc..
- Cadmium
  - Accumulates from seafood, car tyres, auto exhaust
- Arsenic
  - Cigarettes, treated wood, paints, dental work

**Endogenous toxicity**
- Waste and toxicity of normal physiology
- Gut toxicity – large amounts of toxins are produced in our gut from:
  - Maldigestion of our food
  - Metabolic waste products from parasitic, bacterial or fungal infections in the GI
- Toxic Teeth
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Toxic Teeth
- Amalgam filings – 50% mercury!
- Metallic mercury in mouth becomes methylmercury via sulphydryl enzymes
- Mercury denervates nerves and inhibits hormonal action
- Mercury and candida
- Other chemicals in the mouth

Effects of Toxicity on Our Body
- Functional changes that manifest as poor health with symptoms such as:
  - Fatigue
  - Headaches
  - Lethargy
  - Weight problems
  - Depression
- Pathological changes that manifest as actual diseases such as:
  - Cancer
  - Auto-immune disease
  - Neurological disease
  - Arthritis
  - Gastrointestinal disease
  - Cardiovascular disease

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The Nervous System

Symptoms
- Slow or fuzzy thinking
- Depression
- Poor memory
- Poor coordination
- Numbness in extremities

Diseases
- Parkinson’s disease
- Tourette’s syndrome
- Alzheimer's disease

The Liver

Symptoms
- Poor skin tone
- Yellowish color to skin
- Bitter taste in mouth
- Headaches
- Irritability
- Dark circles under eyes
- Sensitive to chemicals
- Difficulty digesting fat
- Yellow tongue coat

The Kidney

Symptoms
- Urine has strong odor
- Pruritus/skin eruptions
- Pain in mid-back region
- Urine is frothy
- Urinate infrequently
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### The Immune System

**Symptoms**
- Frequent colds
- Frequent infections (bladder, skin, ear, sinus)
- Night sweats

**Diseases**
- Chronic Fatigue Syndrome
- Multiple chemical Sensitivity Syndrome
- Fibromyalgia

### The Digestive System

**Symptoms**
- Bloating
- Diarrhea or constipation
- Belching or Gas
- Bad breath
- Stools loose or unformed
- Undigested food in stool

### How does the body get rid of toxins?

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The Organs of Detoxification

- The major organs of detoxification and elimination are:
  - The Liver/Gallbladder
  - The Lymphatic system
  - The Gastrointestinal tract
  - The Kidneys
  - The Skin

1. The Liver

Functions of the Liver

- Carbohydrate metabolism
- Fat metabolism
- Protein metabolism
- Storage of nutrients
- Immune
- Detoxification
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The Liver & Detoxification

- The liver plays a number of different roles in detoxification:
  - **Filtration of the blood**: Approximately 4 pints or 1.82 L of blood flows through the liver every minute.
  - **Production and secretion of bile**: The liver produces about 2 pints or 0.9 L of bile per day.
  - **The biotransformation of toxic substances**: by a complex system of inter-connected enzymes.

Summary of the Liver's Detoxification Pathways

![Diagram of the liver and its detoxification pathways](image)


**LIVER DETOXIFICATION**

**TOXINS (non-polar)**

- Endotoxins
- Xenobiotics

**PHASE I**

- Cytochrome P-450 enzyme system
- Hydroxylation via redox reactions
- Critical Co-factors: NADH, NADPH, B6, Mg

**INTERMEDIATE METABOLITES may be toxic**

**PHASE II**

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

**EXCRETION**

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

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Phase 1 detoxification

Cytochrome P450

- Cytochrome P450 has 3 different methods of detoxification:
  - Chemically transforms a toxic compound into a less toxic form, which is then detoxified in phase 2.
  - Makes a toxic compound water-soluble, which is more easily excreted by the kidney.
  - Transforms chemicals into forms that are more easily detoxified by phase 2.

Phase 1 & Cytochrome P450

Phase 1- Potential Problems

- A number of potential problems can occur with phase 1 detoxification, leading to toxic build-up in the blood:
  - Phase 1 can slow down.
  - Phase 1 can work faster than phase 2.
  - Phase 1 generates superoxide and ROS
Phase 1 Inhibitors

- Many factors can cause phase 1 to slow down:
  - Medications
  - Heavy metals
  - Diet
  - Foods and spices
  - Toxic compounds from the gut

Phase 1 inducers

- The following substances activate phase 1 detoxification:
  - Drugs
  - Foods
  - Vitamins
  - Environmental toxins
  - Herbs and spices

Phase 1 - Free Radicals & Antioxidant Deficiency

- Phase 1 detoxification produces free radicals

- The main antioxidant defense in phase 1 is Glutathione

- Glutathione and other antioxidant deficiencies can cause oxidative stress
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Phase 1 & Toxic Intermediates

- High levels of toxin exposure in phase 1 can deplete nutrients that are also used in phase 2
- The key nutrients needed for phase 1 detoxification are:
  - B vitamins: B2, B3, B6, B12 and folic acid
  - Glutathione
  - BCAA
  - Flavanoids
  - Minerals: Copper, Zinc, and magnesium
  - Vitamin C

Symptoms of Phase 1 Dysfunction

- Symptoms of under active Phase 1
  - Caffeine intolerance
  - Perfumes and other environmental chemicals make you sick
  - Liver disease

- Symptoms of overactive Phase 1
  - Rapid caffeine metabolism

Phase 2 Detoxification
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Six Enzyme Pathways of Phase 2
- Glutathione conjugation
- Amino acid conjugation
- Sulfation and sulfoxidation
- Methylation
- Acetylation
- Glucoronidation

1. Glutathione Conjugation
- Glutathione detoxifies fat-soluble toxins and carcinogens making them water-soluble
- About 60% of the toxins excreted in the bile are detoxified via glutathione conjugation
- Circulates in the blood acting as a free radical quencher
- Glutathione reserves can be run-down quickly causing deficiency.

Glutathione- Sources
- Glutathione is available via synthesis or diet
- Synthesis:
  - Glutathione is synthesized from glutamic acid, glycine and cysteine
- Diet:
  - Glutathione rich foods include asparagus, avocado, walnuts, cabbage, broccoli, Brussels sprouts
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2. Sulfation & Sulfoxidation
- Sulfation uses sulfur containing compounds to detoxify toxins and make them water-soluble
- It is one of the weakest phase 2 pathway due to inadequate supply of sulfur from diet
- Sulfation is responsible for the transformation of the following:
  - Hormones (steroid and thyroid)
  - Drugs
  - Industrial chemicals
  - Phenol containing compounds (plastic, disinfectants)
  - Toxins from the intestines
  - Neurotransmitters

- Sulfoxidation is closely linked to sulfation
- Detoxifies sulfur-containing molecules and sulfites in drugs and foods
- Abnormal sulfoxidation makes it hard for the body to detoxify sulfites
- Sulfoxidation problems can be helped with supplemental molybdenum

3. Amino Acid Conjugation
- The body uses five amino acids for detoxification:
  - Glycine
  - Taurine
  - Glutamine
  - Arginine
  - Ornithine)
- All 5 amino acids can be synthesized by the body
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4. Methylation
- Methylation involves conjugating methyl groups to toxins.
- Used to inactivate estrogens both endogenous and xenoestrogens
- Most of the methyl groups used for detoxification come from S-adenosylmethionine (SAM-e).

5. Acetylation
- Acetylation is the conjugation of toxins with acetyl-CoA
- The primary method to eliminate sulfa drugs.
- This system is sensitive to genetic variation
- This is the least understood phase II detox pathway.

6. Glucuronidation
- Glucuronidation is catalyzed by glucuronosyltransferase enzymes
- Detoxifies the following:
  - Bilirubin
  - Steroid and thyroid hormones
  - Retinoids
  - Bile acids
  - Lipophilic xenobiotics
- Glucuronidation and dysbiosis
**Phase 2 Conjugation Requirements**

- Phase 2 detoxification requires key nutrients for the activation of the enzymes
- It also requires energy to function and synthesize conjugating molecules
- Without nutrients and energy phase 2 detoxification can slow down, leading to increased toxin build-up
- There are also substances that inhibit phase 2 (phase 2 inhibitors), and substances that induce phase 2

**Phase 2 Nutrients**

<table>
<thead>
<tr>
<th>Required Nutrients</th>
<th>Glutathione, B6, C, precursors (Cysteine, Glycine, Glutamic Acid, and co-factors), EFAs (GLA, Flax Seed Oil, EPA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amino acids</td>
<td>Glycine</td>
</tr>
<tr>
<td>Methylation</td>
<td>S-adenosyl-methionine (SAM-e), Mg, Folic Acid, B-12, Methyl Donors</td>
</tr>
<tr>
<td>Sulfation/</td>
<td>Cysteine, methionine, molybdenum, MSM, Co-factors (B-12, Folic Acid, Methyl Donors, Magnesium, B-6/P-5-P)</td>
</tr>
<tr>
<td>Sulfoxidation</td>
<td></td>
</tr>
<tr>
<td>Acetylation</td>
<td>Acetyl-CoA, Molybdenum, Iron, Niacinamide, B2</td>
</tr>
<tr>
<td>Glucuronidation</td>
<td>Calcium d-glucarate, glucaric acid, Mg</td>
</tr>
</tbody>
</table>

**Phase 2 Inhibitors**

<table>
<thead>
<tr>
<th>Phase 2 system</th>
<th>Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glutathione</td>
<td>Deficiencies of: Selenium, B2, zinc, glutathione</td>
</tr>
<tr>
<td>Amino acids</td>
<td>Low protein diet</td>
</tr>
<tr>
<td>Methylation</td>
<td>Deficiencies: folic acid and vitamin B12</td>
</tr>
<tr>
<td>Sulfation/ Sulfoxidation</td>
<td>NSAIDS (aspirin), tartrazine (yellow food coloring), molybdenum deficiency</td>
</tr>
<tr>
<td>Acetylation</td>
<td>Deficiencies of: vitamin B2, B5 or C</td>
</tr>
<tr>
<td>Glucuronidation</td>
<td>Aspirin, probenecid</td>
</tr>
</tbody>
</table>
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### Phase 2 Inducers

<table>
<thead>
<tr>
<th>Phase 2 system</th>
<th>Inducers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glutathione</td>
<td>Brassica-family foods (cabbage, broccoli, Brussels sprouts), limonene (citrus peel, dill and caraway)</td>
</tr>
<tr>
<td>Amino acids</td>
<td>Glycine</td>
</tr>
<tr>
<td>Methylation</td>
<td>Lipotrophic nutrients (choline, betaine, methionine, folic acid, vitamin B12)</td>
</tr>
<tr>
<td>Sulfation</td>
<td>Cysteine, taurine and methionine</td>
</tr>
<tr>
<td>Acetylation</td>
<td>None known</td>
</tr>
<tr>
<td>Glucororidation</td>
<td>Fish oils, cigarettes, Phenobarbital, limonene (citrus peel, dill and caraway), oral contraceptives</td>
</tr>
</tbody>
</table>

### Symptoms of Phase 2 Dysfunction

- **Sulfoxidation**
  - Adverse reaction to sulfite food additives
  - Asthma reactions after eating in restaurant
  - Eating asparagus causes strong odor of urine
  - Garlic makes you sick
- **Amino acid conjugation**
  - Toxemia of pregnancy
- **Glucororidation**
  - Gilbert’s disease
  - Yellow color to eyes and skin with no hepatitis
- **Glutathione**
  - Chronic exposure to toxins
- **Sulfation and amino acid conjugation**
  - Intestinal toxicity

### Toxins and Liver Detoxification Pathways

- **Endotoxins**
  - End products of metabolism
  - Bacterial endotoxins
- **Exotoxins**
  - Drugs otc recidential
  - Chemicals
  - Agricultural
  - Food additives
  - Household
  - Pollutants/contaminants
- **Microbial**
  - Superoxide

- **Reactive Oxygen Intermediates**
  - Free Radicals
  - Lipid soluble (non polar)
  - Toxins stored in adipose tissue
  - Contribute to increased/mobilised Toxic load with weight loss

- **Liver Detoxification Pathways and Supportive Nutrients**
  - Phase I
    - Cytochrome P450 enzymes
  - Phase II
    - Conjugation pathways
    - Glutathione conjugation
    - Glucororidation
    - Sulfation conjugation
    - Amino acid conjugation
    - Acetylation
    - Bile
    - Feces
    - Urine
  - **Antioxidants**
    - Plant derivatives
    - Bile
    - Feces
    - Urine
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Antioxidants/protective Nutrients plant derivatives

• Carotenes Vit A
• Ascorbic Acid Vit C
• Tocopherols Vit E
• Selenium
• Copper
• Zinc
• Manganese
• CoEnzyme Q10
• Thiols ( Cruciferous vegetables)
• Bioflavanoids
• Silymarin
• Oligomeric proanthocyanadins (OPCs)
and pycnogenols

What can be done to keep these phases healthy?

▪ Diet

▪ Eat foods that support healthy liver function

▪ Specific foods and nutrients have a beneficial effect on the body’s ability to detoxify

Foods That Support Liver Detoxification

▪ Brassica-family foods (cabbage, broccoli, Brussels sprouts)
▪ Cold water fish
▪ Flaxseed-oil
▪ Fresh fruit
▪ Garlic
▪ Nuts and seeds
▪ Onions
▪ Spices: turmeric, cinnamon, licorice

▪ Oils: Safflower, sesame & sunflower
▪ Fresh vegetables (artichokes, beets, carrots, dandelion greens)
▪ Walnut oil
▪ Wheat germ and oil
▪ Eggs
▪ Water-soluble fiber: pears, oat bran, apples, legumes
### Nutrients that support liver detoxification

- Bioflavonoids
- EFAs: black currant oil, evening primrose oil, borage oil
- CoQ-10
- Minerals: magnesium, manganese, iron, zinc, selenium
- Carotenes
- Choline
- Reduced glutathione
- Betaine
- N-acetylcysteine
- Methionine
- Vitamins: A, B2, B3, B6, B12, C, D, E, K, folic acid
- Trace minerals and electrolytes
- Milk thistle (Silymarin)

### 2. The Gallbladder & Bile Flow

![Diagram of the gallbladder and bile flow]

### 3. The Lymphatic System

![Diagram of the lymphatic system]

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4. The Gastrointestinal System

- A large portion of lymphatic tissue resides in the intestines.
- These nodes, known as Peyer’s patches, are imbedded in the intestinal wall.
- This tissue is known as the Gut Associated Lymphoid Tissue (GALT) and comprises about 60% of all lymph tissue.
- The Peyer’s patches act as a per-filter for all of the blood flowing from the intestines to the liver.

5. The Skin
6. The Kidneys

SUMMARY