What Does The Research Say About Mercury Toxicity

General Concepts of Health and Toxicity

Overview

1. Chronic Exposure: a state of constant exposure to environmental toxins.
2. Biological Individuality and its effect on immune resistance and susceptibility
3. The body's "fail-safe" system to maintain health
4. The Immune System:
    - Normal function: self vs. non-self.
    - Inflammation: the normal response to toxins.
    - Overstimulation: chronic inflammation and allergies.
    - Abnormal response leading to immune disease: autoimmunity and hypersensitivity.
5. The Detoxification System:
    - Normal function: processing of toxins and excess hormones.
    - Phase I: activation of toxins (P450 enzymes).
    - Phase II: Processing excretion through the nutritionally-dependent glutathione, methylation, and sulfation pathways.
6. The Elimination System:
    - Kidney elimination process.
    - Kidney disturbances (autoimmune problems and nephrotoxicity) limiting kidney elimination.
    - Colon elimination by way of the bile.
    - Disturbance such as enterohepatic circulation

(reabsorption) preventing colon elimination.
    - Skin elimination as a result of poor excretion.
7. Difficulties in establishing a diagnosis of toxicity:
    - Identifying the culprit (the xenobiotics).
    - Difficulty in assessing the functions of the immune, detoxification and elimination systems.
    - Genetic variations among patients
    - False negatives: the limitations of biomarkers
    - Misdiagnosis and/or referral for psychiatric therapy.

DISCUSSION

We are constantly being exposed to various toxins from our environment, such as heavy metals, chemicals, radiation, and acids. When these toxins enter our body, they may exert adverse effects which can result in symptoms or disease. As a result of our unique identity, called “biological individuality,” each of us reacts differently to a toxic exposure. Those who remain unaffected are called resistant; those who are affected are termed susceptible.

In order to understand resistance and susceptibility, we need to be familiar with the system designed to protect us and prevent disease. This system is composed of three sequential parts:

1. Identification: The Immune System carries out this process.
2. Neutralization: The Detoxification System performs this task.
3. Elimination: The colon and kidneys work to remove toxins.

Since the health of the individual is crucial to his or her survival, the body uses these three systems. It also provides a back-up or “fail safe” plan in the event one part fails. The back-up not only assists the individual parts, but allows

these parts to assist other systems. We refer to this as “compensation.”

The **Immune System** is the part of the body designed to recognize those aspects which are not part of the body, called “non-self” by immunologists. Under normal conditions, the immune system neutralizes toxins, micro-organisms, biotoxins (toxins made by micro-organisms) and other invaders. The Human Genome Project, which studied our DNA, discovered that all individuals are surprisingly similar, with the notable exception of the immune system. This system differs widely in all people, partly because of our biological individuality. It is this striking difference which partly accounts for resistance and susceptibility.

When the immune system encounters invaders such as toxins, it can act in a variety of ways.

- Under ideal conditions, it identifies the toxins or micro-organisms which are then neutralized and excreted.
- If the toxic exposure is severe, the entire system may shut down and go into “flight” or survival mode.
- A less drastic response is chronic inflammation, which is the body’s attempt to contain or eliminate toxins without success. Chronic inflammation may progress into chronic degenerative diseases which include cardiovascular, pulmonary, periodontal and dental decay diseases, as well as cancer and other diseases.
- The immune system may also overreact, resulting in tissue or organ damage. These can be the result of allergies (caused by undigested food particles), autoimmune disease (caused primarily by mercury, chemicals and therapeutic agents), and hypersensitivity (caused mainly by mercury, metals, genetically modified foods and organisms, latex and other therapeutic agents).
- Finally, a shutdown of the immune system may occur as a result of toxic insult or therapeutic intervention. Once

the immune system is compromised in any way, it is more difficult for the body to identify and eliminate toxins.

The Detoxification System, commonly thought to comprise only the liver, actually exists in some capacity in every cell. Points of entry, such as the gut and lungs, as well as any organs susceptible to damage from toxins (kidney, bladder, prostate, breast), also carry out detoxification. The gut, which controls absorption through a semi-permeable barrier, can selectively absorb nutrients and allow most toxins to exit through the colon. Certain toxins called xenobiotics, however, can mimic the shape of natural molecules and pass through the barrier. In fact, many patients with small intestine disorders (such as leaky gut disorder, celiac disease, and food sensitivity or allergies) may allow toxins to pass through the damaged barrier into the blood stream where they are delivered to the liver.

The liver has several systems and backup systems to insure toxins do not harm the body. It will even tag and detoxify toxins which won't harm the body but simply don't belong. During Phase I of detoxification, the P450 enzyme "family" activates or prepares toxins for the next stage. During Phase II, several important enzyme systems (glucuronidation, glutathione, methylation, sulfonation, N-Acetylation, TST) chemically and electro-statically attach to toxins. Toxins that are difficult to neutralize generally undergo a series of reactions until the body can safely contain them.

Because the liver processes these toxins, it may suffer damage to its own cells and tissues. In order to protect itself and the body, the organ has the unique ability to regenerate itself. This capacity for regeneration gives rise to the phenomenon called compensation. Compensation is the potential for the liver to assist other organs, such as the pancreas or spleen, to prevent an acute crisis in the body. The capacity for compensation, however, can be a double-edge sword. Although it helps other organs to function, it can provide a

false impression regarding the balance and health of the body. As a result, chronic degenerative diseases can progress without detection by laboratory biomarkers. Fortunately, techniques such as acupuncture, developed by the Chinese, can detect and correct these early imbalances. Acupuncture, augmented with cutting edge research, holds the promise of mapping out the early stages of disease (including dental disease). In this manner, a true early diagnostic and preventative model can be developed.

The final phase, the **Elimination System,** involves the coordination of various processes and systems. Everything entering the body, whether nutritive or toxic, is processed first in the liver. Nutrients enter the blood stream and lymph (fat-soluble molecules), allowing cells to absorb nutrients and release wastes. The blood and lymphatic systems route these wastes to the liver where they are absorbed and processed for elimination. The kidneys eliminate simple toxins by way of urine; the bile processes complicated and dangerous toxins, excreting them through the colon.

When patients suffer from intestinal dysbiosis disease, however, the process may be interrupted by gram-negative anaerobic bacteria. As a result, after the processed toxins enter the intestine, specific enzymes of these bacteria reverse the detoxification process. These toxins are then reabsorbed and again detoxified, only to be broken down and reabsorbed. This recycling of toxins is called enterohepatic circulation and may present an insurmountable obstacle for the body to rid itself of dangerous toxins.

The various types of toxins determine how smoothly the process of elimination occurs. The body’s own metabolic toxins include not only cellular wastes, but also old or excess molecules, such as vitamins and hormones. With some exceptions (hormones), these toxins are fairly efficient, particularly when nutrition is good. Microbial wastes, such as bacterial endotoxins and fungal mycotoxins, also must be processed.

Since the system is designed to process them, elimination can proceed efficiently, again with good nutrition. Exceptions would include acute (painful and localized) and chronic (silent and hidden foci) infections which can overwhelm the system.

Xenobiotics (foreign toxins such as heavy metals, chemicals and other agents) can place a great deal of stress on the entire system. Because of the complexity and toxicity of xenobiotics, the system may break down during the identification and processing stages. If the body successfully manages these stages, the elimination process can be equally as challenging. Excessive or unprocessed toxins in the liver may cause inflammation, autoimmune disease, and cell injury or death. In turn, they would limit the liver's ability to regenerate and compensate, rendering the body more susceptible to breakdown.

The kidneys, which also possess some regenerative and detoxification ability, would be subject to injury, too. Possible injuries include autoimmune glomerulonephritis (caused by mercury, heavy metals, pain killers and other agents) and nephrotoxicity (actual pathology of the structure and function due to the same agents listed above). Remarkably, when elimination is compromised and the body is burdened with excessive xenobiotics, the system will still attempt to compensate. For example, xenobiotics that cannot be processed can be stored in the lymph system and tissues of various organs. It's impossible, however, to determine by conventional means whether these storage sites are safe. Another example is that the body can excrete some toxins by extraordinary means, such as through the skin (as lesions and excessive sweating) and through the gut (as vomiting or diarrhea).

In the face of such evidence, how can a **diagnosis of toxicity** be determined? First, the question of xenobiotics must be resolved. What specific toxins are there, where are they located, and to what extent are they affecting the body?

Second is the overwhelming question of breakdown in the three part system: Identification, Detoxification, Elimination. No biomarkers or laboratory tests exist to reveal the origin or extent of the system’s problem. Added to these challenges are the individual variations as a result of nutrition and genetics. Is diagnosis even possible? Frustrated physicians offer patients medications to numb the pain or numb the mind. Where, then, can the toxicity patient get diagnostic or therapeutic assistance?

The Mercury-Toxicity Algorithm (MTA)

Patient Responses to Heavy Metal Toxicity

RESISTANCE: Successful elimination of toxins. Resistance may change over time with age and in response to other stressors.
SUSCEPTIBILITY: The individual may manifest symptoms related to the body’s inability to eliminate the toxin. These cases can be classified as simple or complex:

- **SIMPLE:**A mono-factorial, dose-dependent (linear) relationship. As toxin levels increase, the patient feels symptoms. As they decrease, the patient feels healthy.

- **COMPLEX:** Multi-factorial. Diet, lifestyle, type and amount of toxins, as well as efficiency of the various systems designed to eliminate toxins all interact. If one or several of these factors breakdown, it is difficult to determine which part is not functioning. In addition, lab tests may show little or no toxins when, in fact, potentiation or exaggerated responses to small amounts of toxin may be occurring.

MTA Level I: Exposure

INORGANIC MERCURY
SOURCE
1. Amalgam (silver) Fillings
– Elemental Mercury is released as vapor which can be absorbed
– Vapor is released when fillings are agitated by brushing, chewing, tooth grinding and drinking hot fluids
– Mercury molecules may enter the saliva and be swallowed. These may enter the esophagus, stomach and intestine
– Increased vapor production occurs via galvanism (battery effect) when certain metals (such as gold, titanium, mercury and others) are placed together in the same mouth.
2. Amalgam Removal (Improper)
Elemental mercury released in large quantities can result in acute exposure to both the patient and dental staff. Specialized precautions must be taken to avoid this exposure.
ABSORPTION
Lungs
80% of mercury is absorbed and enters the bloodstream
METABOLISM
Elemental mercury, (found in the liquid and vapor) can cross the blood brain barrier. This conversion occurs in the bloodstream.
Inorganic mercury, the salt formed by oxidation in the blood, cannot cross the blood brain barrier

STORAGE
The mercury salts accumulate in and may impair these organs: brain, liver, kidney, stomach

ORGANIC MERCURY
SOURCE
Methyl mercury
– Fish swimming in contaminated waters are exposed to mercury in the food chain.
– Grains are exposed when treated with mercury containing antifungal agents.
Ethyl mercury
Synthetic form of mercury utilized in vaccines as an antimicrobial**ABSORPTION**

Gut/intestines
-95% Absorption of Methylmercury**METABOLISM**
Methyl mercury
Conversion to salts in gut and tissue
Ethyl mercury
Conversion to salts in blood and tissues
Inorganic Mercury (Salts)
STORAGE
Accumulation occurs in the following organs: brain, liver, and placenta (causing fetal exposure).

MTA Level II: Gastro-Intestinal (Gut) Disturbances

ABSTRACT: Elemental mercury(discharged from fillings) and methyl mercury (from fish and seafood) are ingested and enter the gut. The body responds according to its health status; the result is either resistance or susceptibility to the toxic threat.

RESISTANCE: TOXIN IS ELIMINATED FROM THE GUT
THE “FIRST PASS” PHENOMENON
“First Pass” occurs when the stomach and intestines maintain cellular integrity of the enterocytes (gut cells) and act as an impermeable seal or barrier to ingested toxins. This allows them to pass safely out by way of the colon. Toxins which the colon is susceptible to may be allowed to enter the enterocyte. Inside, detoxification enzymes (CYP 3A4) render the toxin less harmful to the colon. The MDRI and Multi-Drug Resistance “pumps” may propel the toxins back into the colon or allow passage into the portal vein to the liver for further detoxification.
SUSCEPTIBILITY: INABILITY TO ELIMINATE TOXINS FROM THE GUT AND POTENTIAL SCENARIOS.

GUT INFLAMMATION
The gut is lined with patches of immune cells (GALT). These cells may be stimulated to release inflammatory cytokines (interleukins 1 and 6 and TNF) which cause gut inflammation.

1. Liver cells may also be activated which may cause a wider (systemic) inflammatory response.
2. Chronic Inflammation, a state of constant inflammation, may result if exposure to mercury is not halted.**GUT DYSFUNCTION**
Mercury disturbs the cells (enterocytes) lining the gut which regulate absorption. Under normal conditions, the cells allow nutrients and prevent organisms, toxins and undigested food particles (which cause allergies) to pass between the cells to enter the blood stream. Mercury may disturb the cell structure, resulting in loss of regulation. At this point, organisms, toxins and food particles enter the bloodstream where they will encounter the immune system.
BIOFILM DYSBIOSIS
The microorganisms which comprise the gut biofilm may change from a normal (eubiotic) to a pathogenic (dysbiotic) form. The following changes may be seen:**1. Bacterial (gram-negative) Over growth** These bacteria are necessary in small numbers but in excessive numbers produce a toxic substance called endotoxin. Endotoxin can increase the effects of toxins, such as mercury and lead, over a thousand fold.**2. Antibiotic Resistance**
Mercury may counter the ability for biofilm to resist treatment. This helps to create a state of chronic infections.
3. Fungal and Opportunistic Infections
Candida overgrowth may occur as the organism itself absorbs mercury. (Note: An attempt to control candida can result in mercury exposure). Candida and other infections, such as viruses and parasites, may not come under control until exposure is controlled.

MTA Level III: The Immune System

RESISTANCE: THE IMMUNE SYSTEM IDENTIFIES AND ELIMINATES ALL TOXINS ENTERING THE BODY. This complex and seemingly impossible task is performed thousands of times a day without malfunction.

SUSCEPTIBILITY: IMMUNE SYSTEM BREAKS DOWN OR MALFUNCTIONS. An excellent immune system may present with one or several

‘Achille’s heels’ which may cause it to be temporarily overwhelmed (as in a cold or flu) or to malfunction (manifested as under- or overactivity).

UNDERACTIVE

TH IMBALANCE (aka Th2 Dominance) The Immune System has two regulatory components, the Th1 and Th2 systems. The Th1 system activates the Immune system to identify and eliminate components, such as organisms and toxins which do not belong. Mercury can cause an imbalance to occur resulting in Th2 Dominance. Once the system is in this mode, chronic infections will result.

Viral Infections:

Epstein-Barr
Cytomegalovirus
Varicella-zoster
Herpes type 1 (Oral)

Bacterial Infections

Lyme (Borrelia)
Mycoplasma
Bartonella
Babesia
Ehrlichia
Rickettsia

Fungal Infections

Candida
Aspergillus**LABORATORY TESTS**

Many rely on blood tests to determine the presence of an infection. If the immune system is underactive, the test may give a false negative. Specific tests have been developed to determine infections by using other biomarkers, although many of these have not been recognized)

OVERACTIVE

IMMUNE-MEDIATED DISEASE Toxins, such as heavy metals or xenobiotics, may get inside cells which are unable to remove them. In this case, the immune system may attack cells resulting in cell death. On a large scale, this may manifest as autoimmunity or hypersensitivity.

1. **Autoimmunity**

This may involve complicated reactions and not simple susceptibility or one trigger. Mercury is injected into test

subjects to study autoimmune disease. The kidneys (Glumerulonephritis) are a principal site of elimination and are particularly susceptible to autoimmune disease. The following are implicated:
Mercury
Silica
Halothane (Inhalation sedative)
Various Therapeutic Agents2. **Hypersensitivity**
These are also complicated reactions resulting in exaggerated reactions. The following are implicated:
Mercury
Metals (platinum, cobalt, chromium, nickel, beryllium)
Latex
Genetically modified foods and organisms
Formaldehyde (formalin)

MTA Level IV: Phase I – Bioactivation

NORMAL FUNCTIONP450 ENZYME SYSTEM
Most common enzymes and percentage of function:**1A2 (10% of metabolism)**
Caffeine, Tylenol®, theophylline metabolism.
2C (25% of metabolism)
Ibuprofen, Coumadin, D-Limone, Valium, naproxen, etc.

2D6 (16% of metabolism)
Codeine, amphetamine, antiarrhythmics, (Metoprolol, Propranolol, etc.), antidepressants (amitriptyline, nortriptyline, etc.)

34A (34% of metabolism)
Local anaesthetics (lidocaine), erythromycin, cyclosporine, estradiol, testosterone, cortisone.

2E1 (4% of metabolism)
Acetaminophen (Tylenol®), caffeine, alcohol, etc.

MECHANISM OF ACTION
The P450 oxidase enzymes add an oxygen molecule to a toxin in order to ‘activate’ it, creating a free radical molecule.

BIOACTIVATION
The system is in balance regarding Phase I-generated free radicals, which are bioinactivated in Phase II. As a result no free radical damage occurs to the body.

ABNORMAL FUNCTIONPHASE I MALFUNCTION:

INDUCTION: Toxins, foods or drugs may cause the system to function too fast. This can result in free radical (oxidative) damage which the body balances with vitamins (antioxidants).
Inducers are: alcohol, exhaust and paint fumes, organophosphate pesticides, steroids, and sulfur amides.
Food inducers are: flavonoids (fruits and vegetables), cruciferous vegetables (cabbage, broccoli, bok choy, brussels sprouts), garlic, rosemary, soy, oranges, a high protein diet, and charcoal-broiled meats.

INHIBITION: Substances which may slow or shut down bioactivation. Doses of inhibitors need to be increased to obtain the same therapeutic effect.
Inhibitors (xenobiotics) are:
H-2 Receptor Blockers (Cimetidine) – All enzymes inhibited
Antibiotics – 1A2 fluoroquinone and 3A4 erythromycin.
Antiarrythmics – 2D6
Antidepressants – 2D6 (and all others)
Antifungals – 3A4
Food inhibitors are: grapefruit juice (powerful) and mineral depletion.

PHASE II OR III MALFUNCTION
Inflammation, poor nutrition, or acute toxic exposure may slow or shut down Phases II and III, resulting in a relatively ‘fast’ Phase I.

FAST (EXCESS) BIOACTIVATION
Since Phase I is faster, an excess of free radicals are generated, resulting in cell injury. Constant excess free radical production may result in cell death, causing symptoms

to arise.

MTA Level IV: Phase II – Bioinactivation

Phase II is a series of detoxification pathways caused by a specific set of enzymes. It follows successful Phase I bioactivation. When highly reactive molecules, such as heavy metals and certain chemicals, are activated, they may directly enter Phase II by their nature.

PHASE II DETOXIFICATION PATHWAYS

BILE (Glucuronidation)
ENZYME: UDP glucuronyl transferase
COFACTORS (NUTRIENTS): Taurine, choline
PURPOSE: Lipid soluble molecules, the most difficult toxins for the body to process and excrete, enter this pathway. After a series of reactions, these toxins are stored in the gall bladder.
When the individual eats a meal containing fats, the gall bladder releases bile into the small intestine. The bile assists the body in processing fats and allows the toxins to exit through the colon. In the colon, however, gram negative bacteria (intestinal dysbiosis) may reverse detoxification, allowing the toxins to be reabsorbed. This process is called enterohepatic circulation. It eventually causes nutritional depletion and results in toxin accumulation in the body.**GENETIC DEFECTS**

- Crigler-Nejjar syndrome
- Gilbert's disease
- Bladder cancer

GLUTATHIONE (GSH)
ENZYME: Glutathione S-transferase (GST)
COFACTOR (NUTRIENTS): Glutamine
PURPOSE: GSH utilizes GST to attach itself to free radicals. These metabolites (changed molecules) may need to undergo further detoxification to render them less toxic, more soluble and therefore easier to excrete.**TOXINS BROKEN DOWN BY GSH:**

- Heavy metals (mercury, arsenic, lead, etc.)
- Radiation (ionizing and nuclear)
- Biotoxins (bacteria and mold toxins)
- Chemicals (some medications, DDT and other pesticides, chloroform, bromides, etc.)

NOTE: GSH deficiency can be induced if there are competing toxins (several toxins utilizing the same detox pathway).

GENETIC DEFECTS IN GST (enzyme)
GST genetic mutations result in increased susceptibility to the following conditions:

- Liver toxicity and cirrhosis (GST-A)
- Type II diabetes
- Leukemia and hemolytic anemia
- Schizophrenia
- Bladder cancer (GST-M1 and T1)
- Head, neck and lung cancers (GST-T1)
- Gut and lung cancers (GST-T1)
- Arsenic poisoning (GST-P1)
- Kidney problems (GST-A)

OVERVIEW OF PHASE II PATHWAYS

PATHWAY

Glucuronidation (Bile)

Glutathione

Sulfonation

Methylation

Acetylation

Amino Acid Conjugation

COFACTOR

Taurine, choline

Glutamine

Glycine

SAMe/methionine

N-acetyl cysteine (NAC)

Taurine, glycine, ornithine, arginine, acetyl co-A (acetic acid)

TOXINS/XENOBIOTICS
Aspirin (nsaids), acetaminophen, naptroxen, steroids, morphine, lorazepam (valium), vitamins A, D, E, KAcetaminophen (Tylenol), penicillin, tetracycline, heavy metals, petroleum, endotoxxin, mycotoxinsAcetaminophen, aniline (coal tar derivatives), phenols, thyroid hormones, sex hormones, exotoxins
Mercury, lead, arsenic tin, thallium, morphine, L-Dopa, neurotransmitters (dopamine, epinephrine, histamine)

Nitrogen-containing compounds, anilines, caffeine, choline, serotonin PABA, histamine, mescaline, sulfuramides

Nsaids, nicotine, bile acids, plant acids PABA, amines, organic acids

GENETIC FACTORS AFFECTING DETOXIFICATION

Each detoxification pathway consists of an enzyme or set of enzymes which are all encoded by a specific gene. Each gene may be a ‘perfect’ or ‘imperfect’ (mutation) copy. Perfect copies allow each enzyme to function at full capacity (100%). Mutations function somewhere between 50% and 90%. Mutations, however, may not be an issue if the individual is never exposed to that which he or she is susceptible to (biological individuality).

Each individual has two copies of genes, one from each parent. This allows for the (phenotypic) expression of three different functional qualities:

GENETIC VARIATIONS
Two perfect copies (one from each parent)
One perfect copy and one mutation
Two mutations
PHENOTYPIC EXPRESSIONFull function
Patient has perfect detox function.**Partial function**
Patient has good function if not stressed; vague symptoms may exist.
Poor function (up to 12% of the population)
Patient may have vague or specific symptoms. In a severe case, patient may express a disease.

SYMPTOMS OF POOR DETOXIFICATION

- Multiple chemical sensitivity
- Musculo-skeletal symptoms (Fibromyalgia-like symptoms)
- Neurological disturbances
- Cognitive disturbances (brain fog, memory loss)
- Digestive disturbances (diarrhea, constipation, irritable bowel syndrome, inflammatory bowel disease)

TOXIC LOAD PHENOMENON (Rea 1997, 2003)
Toxins must e assessed in terms of their complete range of exposure. The following is a short list of potential types of exposure:

- Xenobiotics
- Infection
- Microbial toxins
- Radiation (including EMFs)
- Lifestyle (smoking, alcohol, caffeine, etc.)
- Hormonal (DHEA, cortisol, estrogen, progesterone, testosterone)
- Inhalants (molds, pollen, algae, etc.)
- Psychosocial (belief systems stress, coping skills,

trauma, injury)

TOXIN POTENTIATION EFFECT

Scientists (Schubert Riley and Taylor, 1978) found a combination of toxins can exert a lethal effect in animals. Animals were given a small dose of mercury and lead (LD1 is the lethal dose which kills one percent of a population). This combined LD1 dosage exerted a synergistic effect resulting in 100% mortality (LD100) within five days. The study demonstrates the potential for low levels of toxins to exert a pathological effect. This phenomenon can have a profound effect. If laboratory tests show low levels of toxins (a false negative), this condition may never be diagnosed and, therefore, treated.