

The Unique Vulnerability of the Human Brain to Toxic Chemical Exposure and the Importance of Toxic Chemical Evaluation and Treatment in Orthomolecular Psychiatry

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Abstract *The human brain and the brains of whales and dolphins (cetaceans) are especially susceptible to a variety of toxic chemicals because of natural selection that favors brain structures promoting advanced brain functions such as long-term memory and rapid learning. The high fat content of these brains also makes them especially susceptible to long term storage of the same fat soluble toxic chemicals that accumulate in adipose tissue. The high rate of metabolism in these mammalian brains and high content of polyunsaturated fatty acids also makes them much more susceptible to free radical damage mediated by toxic chemicals, leading to increased damage to brain macromolecules like deoxyribonucleic acid, ribonucleic acid, proteins, cell organelles, and small molecules. The sulfur amino acids are also highest in these brains, making them exquisitely susceptible to exposure to heavy metals. All of these biochemical factors make human and cetacean brains extremely susceptible to neuropsychiatric diseases and criminal behaviors caused by exposures to a variety of toxic chemicals. Toxic chemicals are probably involved in the etiology of many different (possibly most) neuropsychiatric disorders and as a factor in criminal acts. Heavy metals and anti-bacterial cleaners are used as examples. Some simple orthomolecular methods useful for detoxification from a variety of toxic chemicals are briefly reviewed.*

The application of nutritional therapy for the treatment of mental illness has considerably advanced since the pioneering work of Abram Hoffer and his colleague Osmond on the nutritional treatment of schizophrenia using megadoses of vitamins, especially niacin. The clinical benefit of this work was given a significant boost in its theoretical underpinnings by the double Nobel Laureate, Linus Pauling, in the highly influential article¹ in the journal *Science* called "Orthomolecular Psychiatry." I can still remember the excitement that the article generated for me while in graduate school preparing for my Ph.D. in biochemistry at the Medical University of

South Carolina. The concept was as simple as the name (ortho=right + molecular or supplying the right molecules). The practice of orthomolecular psychiatry and orthomolecular medicine in general was a little more complicated than the concept because there were many molecules to measure to ascertain which molecules were not right. The development of cost effective screening tests (total price of about \$600-800 with many of the tests covered by insurance) for large numbers of fatty acids, amino acids, organic acids, and minerals allows the clinician to analyze 200-400 different molecules to find out which compounds deviate from the values in healthy people.

The overall principle as applied to the testing of small molecules can be summed up briefly as: find simple nutritional means to lower molecules that are too high and to increase molecules that are too low. In some cases, values of nutrients needed are much higher than usual in certain people to compensate for enzymes with poor catalytic activity, receptors with poor binding, or transport proteins with inefficient transport due to genetic polymorphisms or mutations. As physicians and/or scientists, we knew that the physiological processes of living beings had been honed by the sharpening stone of evolution to perform optimally within the limits of a somewhat defined internal milieu of intracellular and intercellular fluids. We also knew that vitamins and other nutritional factors had evolved together from the primordial organic molecular soup with almost all living things and that this coexistence over a billion years or more of evolution selected the existence of vitamins and other nutritional factors that, with few exceptions, were remarkably safe to the majority of living beings on this planet. A recent survey of poison control centers found no deaths associated with vitamin overdose.

Difficulties arose when the application of this therapy to a disease was compared to standard pharmacological therapy using a single drug. If the person had severe deficiencies of lithium, iron, magnesium, and iodine, omega-3 fatty acid deficiency, deficiencies of tryptophan and phenylalanine, abnormal elevated molecules from yeast and bacteria from the intestinal tract, deficiencies of vitamin B6 and vitamin C and was severely depressed it made no sense to the orthomolecular practitioner to treat a single biochemical imbalance by applying standard monodrug pharmacological treatments of depression. Individuals familiar with left and right brain functions know that overemphasis on double-blind studies is a left brain proclivity while dealing with all factors involved in an illness holistically requires the involvement of both left and right brain function. Many of the disagreements between mainstream and orthomolecular approaches to treatment

are based on a disregard for an integrative whole-brain approach by prescription-pad medicine proponents.

Although many vitamins and minerals evolved with new life forms, initially in the organic soup of pre-biotic earth, and then in independent organisms over a billion years of co-evolution, a massive change took place in the last few thousand years and the rate of this change has massively accelerated in the last 100 years or so. The changes involved altering the entire biosphere in which life has evolved by mining heavy metals that were predominantly in the deeper layers of earth's crust because of their higher densities and the development of new synthetic organic chemicals on such a massive scale and speed that there has been inadequate time to step back and critically evaluate what was happening. Unfortunately, most living things did not evolve with high concentrations of such metals or in association with these new organic chemicals. Evolution is still occurring but the sheer volume of these chemicals means that natural selection will be on a merciless rampage unless humans intervene to develop better ways to assess and control the flood of toxic chemicals.

A recent two-day seminar sponsored by the Canadian Society for Orthomolecular Medicine on the treatment of depression and other psychiatric disorders using orthomolecular techniques was an intensive summary of the biochemical and/or clinical experience by the presenters, Dr. Greenblatt and myself, of the published studies and clinical experience of many of the practitioners who have attended this seminar and similar integrative medical conferences for many years.² A considerable portion of the seminar was also devoted to the role of toxic chemicals in mental health. With many toxic chemicals, the correct concentration for optimum health and especially for good mental health may be very close to zero. Thus, the person involved in the practice of orthomolecular psychiatry today must consider the influence of the sea of toxic chemicals in the treatment of their patients.

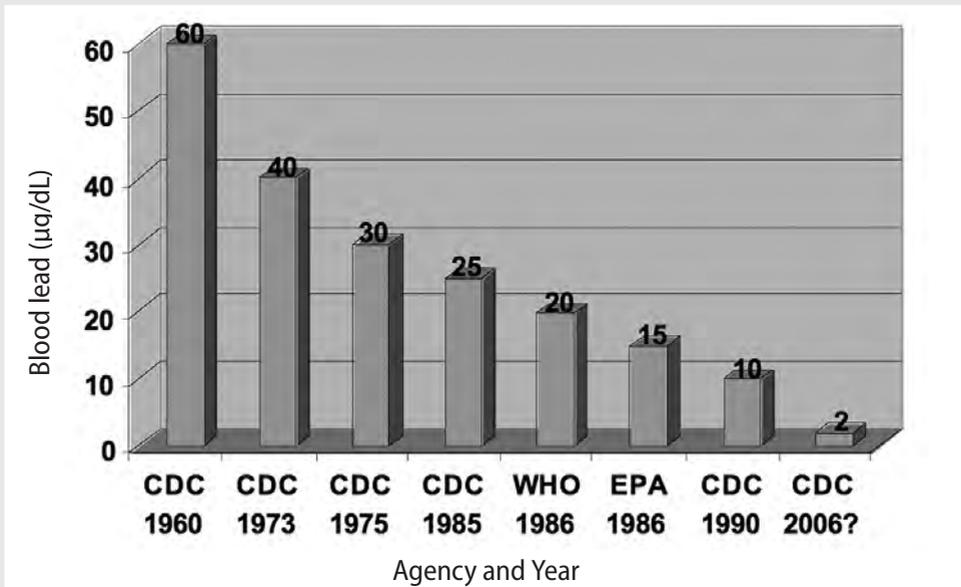
The case of lead is a great example of

government failure to protect the public. Lead has been studied perhaps more than any other toxic chemical in history. A Google search of lead toxicity revealed nearly 4 million citations and a PubMed search of lead exposure yielded more than 22,000 citations. A TOXNET search yielded 50,000 citations. Studies published in the past few months indicate that values of lead in the “normal” range that are 40-60% below the current upper limit of common laboratory normal ranges (5-10 mcg/dL) are associated with significantly increased incidence of kidney damage, depression, developmental delays, and panic attacks.³⁻⁵

Figure 1 (below) dramatically indicates the reason that confidence in government safety assessments are deeply flawed primarily because of industry pressures to reduce or eliminate safety measures that can protect the public.⁵ Thus, only blood lead values that are less than 1 mcg/dL have not been found to have significant negative impact on health at the present. Thus, in 50 years the safety

threshold for lead in blood promulgated by national and/or international safety experts has dropped approximately 59 mcg/dL, a decline of approximately 1.7% a year. It takes little imagination to conclude that there is likely no safe limit for lead, that even the smallest amounts of lead may cause a certain degree of human impairment. The mental developmental index (MDI) test of infants assesses habituation, problem solving, early number concepts, generalization, classification, memory, vocalization, language and social skills. In a study in Poland,⁵ infants with the lowest mean lead values had the highest performance on the MDI test while infants with cord blood lead values at only 1.6 mcg/dL (a value almost 70% below the upper limit of many laboratory normal ranges) had significantly lower test scores than children with only slightly lower lead concentrations. I have physician friends who routinely take metal chelating agents every couple of weeks to reduce their toxic metal burden from the environment at large.

Figure 1. Acceptable childhood blood lead levels

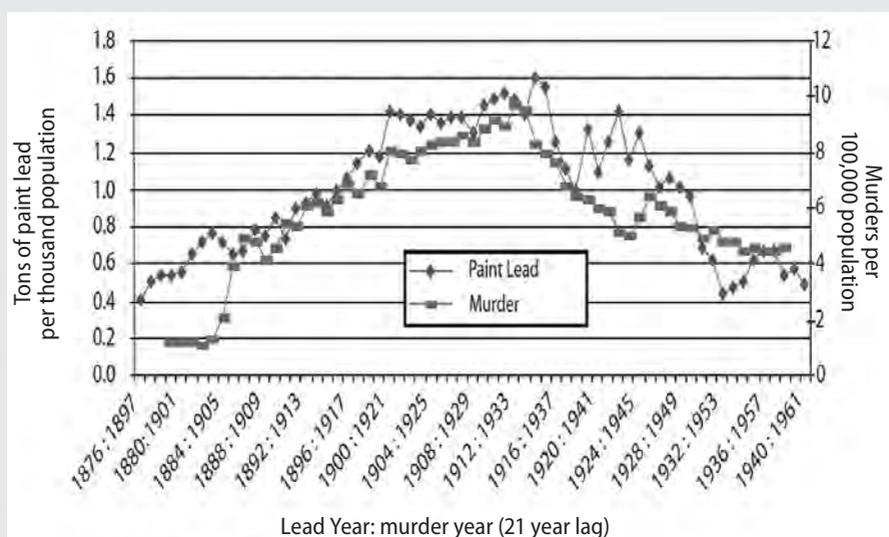


Reproduced with permission from: PowerPoint Presentation of Steven Gilbert. Lead and Child Development or Why the CDC Should Lower the Blood Lead Action Level from 10 to 2 mcg/dL. Harm's Way: Preventing Toxic Threats to our Children's Health. Sponsor WPSR. October 15, 2005. Spokane, WA.

Even more provocative are studies⁶ that look at historical records of lead exposure compared to crime rates in the United States (Figure 2, below). In the figure, lead exposure the population received during infancy is compared to murder rates 21 years later, the peak age for murder. The 21-year lag is consistent with the typical age of those arrested for murder and the impact of lead on a child's early cognitive development. Similar correlations were found when comparing crime rates associated with the use of gasoline containing tetraethyl lead. Thus, toxic chemicals to which humans are exposed in infancy and childhood may be time bombs that explode many years after exposure. Early lead exposure has been proposed as a significant risk factor for dementia.⁷ I consulted with a physician (personal communication) who obtained reversal of Alzheimer's disease symptoms following removal of mercury dental amalgams and subsequent massive excretion of mercury and lead. The source of the lead was a miniature army of toy British soldiers constructed from melted lead bullets by the patient as a child. Presumably inhalation of lead vapors and oral

contamination by handling the lead soldiers both contributed to causing lead toxicity. Another physician (personal communication) obtained significant reduction of Alzheimer's symptoms after chelation treatment of an elderly man with elevated aluminum and mercury in hair. Prior to treatment, the man was incontinent and could not remember friends and family members. After only two months of treatment, the man remembered his friends and family, was able to make his own appointments by phone, and take care of his bathroom functions. Blood tests of lead may not be a good indicator of lead deposited in the body fifty years previously;⁷ evaluation of bone lead by X-ray fluorescence is much more sensitive for past exposures to lead.⁷ Recently, the same delayed, late-life increase in Alzheimer's disease-related proteins was reported in aged monkeys exposed in infancy to low levels of environmental lead. In addition, these monkeys showed Alzheimer's (amyloid) plaques in the frontal association cortex, an Alzheimer's disease-related brain region, as well as biochemical evidence of epigenetic imprinting.⁸

Figure 2. Murder, 1900 –1959 versus paint lead



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Despite recent reductions in lead exposure, it can be argued that current baseline blood lead levels continue to constitute a global public health risk, as preindustrial humans are estimated to have had 100- to 1,000-fold lower blood lead levels than the population of today.⁹

The most important point to be made here is not that lead is an especially toxic chemical (although it is) but that it has taken more than perhaps 50,000 published articles, well over 50 years, as well as the efforts of countless government, academic, and industry conferences, regulatory interventions, and bureaucratic reorganizations to determine at the end of the day that miniscule amounts of lead may lead to impaired mental development. What about all the other toxic chemicals in the environment? Unfortunately, the focus of tremendous government bureaucracies at international, national, regional, and local levels on lead testing, research, and regulation to a large extent drained resources away from interest in the tens of thousands of other toxic chemicals present in the environment. If each one of these commonly-used chemicals were subjected to the same scrutiny as lead there might be 65,000 chemicals times 50,000 scientific research papers per chemical or more than three and a half billion papers would have been written over the same time period. Another less bureaucratic, less costly, and much more rapid method of determining what substances are harming our minds is to see what chemicals are present in the body fluids of people with neurological and psychiatric disorders and to find out what happens to their mental health when those chemicals are removed by stopping or reducing exposure and accelerating the removal of these toxic substances.

Although many living creatures and many different organs in the human body are subject to environmental toxic chemicals, the human brain and the brains of marine mammals such as whales and dolphins are especially vulnerable. The brain is a very vulnerable target in humans and large marine mammals because of its large size compared to total body weight among animal species

and its high concentrations of fats including cholesterol and unsaturated essential fatty acids present in myelin and neuron cell membranes. Many fat-soluble environmental chemicals deposit readily in this fatty tissue. The brain is also extremely metabolically active, generating high quantities of free radicals, making it a target for a large number of toxic chemicals that further increase the production of free radicals beyond baseline levels present even in the toxic chemical-free brain. The excessive free radicals easily damage the unsaturated fatty acids so important to brain function.

Another evolutionary change greatly increased the susceptibility of the human brain to toxic chemicals, especially toxic metals. There is a direct relationship between the amount of sulfur-containing amino acids in the brain and phylogenetic brain development. Birds' brains possess the lowest percentages; then next those of rodents and cows, those of primates are higher, while those of humans and cetacean (whale-like) mammals have the highest percentage.¹⁰ Hair has a very high percentage of sulfur amino acids. (Think of the strong sulfur odor when hair burns.) It is tempting to hypothesize that the dramatic loss of human body hair (compared to our ape ancestors) with its high stores of sulfur was an evolutionary sacrifice in order to put more sulfur-containing amino acids into the brain. It is interesting that the whales and dolphins are also largely free of hair as well. Sulfur-containing amino acids react readily with toxic metals like mercury and lead, making the brain an extremely vulnerable target for these chemicals. Much of the sulfur amino acids not used for protein synthesis are used for the production of glutathione, which serves as a potent antioxidant and a potent detoxification agent for perhaps thousands of environmental chemicals like dichlorodiphenyltrichloroethane and polychlorinated biphenyls. The threat posed by such compounds has increased greatly in the last century but has probably existed as long as life itself due to the presence of toxic substances in animals, plants, fungi, and bacteria. Exposure of the brain to

these toxic chemicals results in the depletion of glutathione as glutathione-toxic chemical adducts, diminishing the amount of glutathione available for antioxidant duty. Glutathione used as an antioxidant can be recycled, but every molecule of glutathione used to remove a toxic chemical is gone forever.

Because of its unique evolutionary position, human and cetacean brain function may be the most vulnerable living biological process on earth to the effects of toxic chemicals. Because of this unique vulnerability in the entire biological world, all cosmetics, genetically altered foods, food additives, and pharmaceuticals should be tested for the effects they may have on human mental health after they have passed all standard toxicity and mutagenicity testing.

An excellent recent paper by Genuis¹¹ summarized a case study involving disturbing thoughts of a teacher involving harming his grammar school students. Conventional therapy with a variety of psychiatric drugs was completely ineffective, leading to increased suicidal ideation and continuation of disturbed homicidal ideation. Referral to an expert on environmental exposures, lead to a more thorough case history that revealed increased tuna fish consumption. All psychiatric symptoms cleared after elimination of fish diet and use of chelation agents to remove elevated blood mercury due to excessive mercury-laden tuna consumption.

Large beaching of whales and dolphins might also be linked to psychiatric disturbances due to the high fish intake of these animals with resultant high mercury tissue loads.^{12,13} Mercury in whale meat has been reported to be as high 200 times the level of acceptable mercury contamination permitted by the Japanese government.¹³ The whales involved in attacks of trainers should be extensively tested to determine toxic metals and other chemicals to which they have been exposed.

Other chemicals used on a daily basis by a majority of the population may also be very toxic. I clearly remember a letter addressed to the chairman of the biochemistry department in which I was studying for my Ph.D. in

which a medical student from another university complained about the serious side effects that he experienced from exposure to a common chemical in consumer products called hexachlorophene and requesting that a formal investigation be done. Hexachlorophene was the active ingredient in an over-the-counter "skin cleanser" called pHisoHex that was supposed to be effective in the treatment of common acne, the bane of teenagers. The company produced another over-the-counter product called pHisoDerm that had even higher amounts of hexachlorophene; it was even more dangerous because it was spread all over the body (hexachlorophene is rapidly absorbed through the skin). The medical student wrote a long letter which included detailed graphs of symptoms like depression, anxiety, tremors, memory problems, and bizarre thoughts. He included graphs that showed that the intensity of his symptoms coincided with the dermal use of hexachlorophene and diminished when the use of the product was discontinued. His letter was read aloud by the chairman of the biochemistry department in a large laboratory bull session in which a good laugh was had by all.

I didn't laugh so much. I had noticed a correlation of hexachlorophene use with my own symptoms of depression a few years earlier and noticed how much better I had felt after throwing my large bottles of hexachlorophene-containing skin cleaners into the trashcan for good. As a student, however, I did not want to rock the boat and kept my mouth shut. Hexachlorophene at the time was added to virtually every consumer product available at the time from toothpaste, to mouthwash, to soap, to deodorants, and to feminine hygiene sprays. Hexachlorophene was also sprayed on crops as an antifungal agent and used as plant antibacterial agent and acaricide.

Shortly after I graduated with my Ph.D., by a strange coincidence, I started to work at the USA Center for Disease Control (CDC) in Atlanta, Georgia. Just down the hall from me, a pathologist, Dr. Renate Kimbrough was completing a study of the effects of hexachlorophene exposure on causing degenerative spongy vacuoles in the brains of rodents.¹⁴

Typical for government bureaucracy, she was in a heated battle with the administrators of government agencies over the release of her findings due to concern for the welfare of the manufacturers of the products and due to the fact that the chemical was widely used as an antibacterial handsoap in hospitals, doctors' offices, and at the CDC itself. Spongiform myelinopathy was found in babies with detectable amounts of hexachlorophene in their brains.¹⁵ In France in 1972, 36 children died after being exposed to talc contaminated with hexachlorophene.¹⁶ A veterinarian reported that, after only two small dermal exposures of topical hexachlorophene to puppies, all of the puppies developed uncontrollable muscle tremors, ataxia, apparent muscle weakness, and constipation.¹⁷ In another animal study in which beagle dogs were fed hexachlorophene in the diet for 13 weeks, the dogs developed swollen salivary glands, dry mouth, and status spongiosis in the brain, optic nerve, spinal cord and sciatic nerve at very small doses.¹⁸ Despite protests from the companies marketing these products, these chemicals were removed by regulatory agencies from over the counter use in many countries but could still be obtained by prescription. These chemicals are still available for over-the-counter use in Australia.

Organic chemists are highly creative, however. When new recreational drugs are banned, the addition of a methyl group here or the deletion of a chlorine atom there to the structure of the banned molecule may produce a new chemical that skirts the exact chemical structure ban by drug regulatory agencies for a few years. The same creative aspects appear to be active in producing skin cleaners as well.

Free of depression for many years after my hexachlorophene elimination, I experienced multiple episodes of severe chest pains and severe depression lasting up to eight hours within 30 minutes of eating at McDonald's restaurants. Perhaps it was those high cholesterol cheeseburgers, I thought. Similar symptoms were reported in the movie "Supersize Me," a documentary movie in which the film's director and subject eats

all his meals at McDonald's for an extended time period. One night he has chest pains so severe he goes to the hospital. No heart disease was diagnosed. I remembered similar symptoms with hexachlorophene and had noticed that the hand soap in McDonald's had a strange odor. Maybe my symptoms and those of the "Supersize Me" subject were due to the soap instead of the hamburgers. On my next trip to McDonald's, I washed my hands at the lab restroom where I kept my own anti-microbial-free soap and did not wash my hands at McDonald's and found that I was symptom free after eating the hamburger. The next step was to ask the manager of the McDonald's to show me the label with the contents of the hand soap used in the restaurant. It is called Mac D with the D standing for detergent and contains an antibacterial chemical called parachlorometaxyleneol or PCMX, a chemical closely related to hexachlorophene and triclosan. Apparently, this PCMX hand soap is used throughout the chain. Burger King now also uses PCMX containing hand soap as well. The structures of PCMX and hexachlorophene are very similar. The PCMX was also used in some of the washrooms of the laboratory where I worked at the time and I found that approximately 50% of lab employees had symptoms similar to mine approximately 30 minutes after their coffee breaks which were preceded by PCMX hand washing. A letter to the USA Food and Drug Administration recommending an extensive evaluation of PCMX safety was unanswered. In a report in 1966 from Hill Top Research for the Ottawa Chemical Co.,¹⁹ oral administration to rats of PCMX with corn oil as the vehicle was used to determine that the oral LD50 of PCMX was 3.83g/kg. In this study toxic effects described for PCMX included depression, depressed righting, other reflex depressions, and central nervous system toxicity in some who had died. Gross autopsies on all dead rats showed congested lungs, gastrointestinal irritation, dark livers, congested adrenals, and hemorrhagic kidneys.

A chemically similar antibacterial agent, triclosan, is now also becoming very common

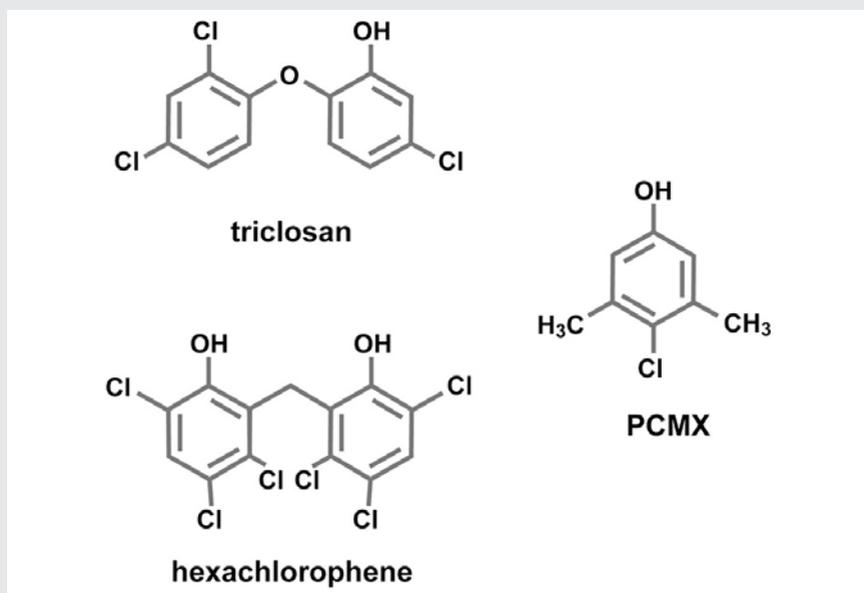
in antibacterial hand soaps and other consumer products such as deodorants, shaving creams, mouthwash, dishwashing liquids, toys, socks, and trash bags. Studies show²⁰ that triclosan is linked to bacterial resistance and impairment of thyroid function in animals. Mixing triclosan in tap water can lead to the production of the gas chloroform, a carcinogen and nervous system depressant. Other triclosan breakdown products include extremely toxic dioxins. As the final revisions of this article were being prepared, a lawsuit was filed by The National Resources Defense Council, a nonprofit environmental group, against the U.S. Food and Drug Administration, claiming the agency failed to regulate toxic chemicals found in "antimicrobial" soap and other personal care products, and alleging that two common ingredients, triclosan and triclocarban, can damage reproductive organs, sperm quality and the production of thyroid and sex hormones.

The structures of three common antibacterial agents in hand soaps and/or body washes are indicated in **Figure 3**, (below). Hexachlorophene, PCMX, and triclosan are all chlorinated phenol derivatives. All

of these compounds will be detoxified by reactions with glutathione, which will leave less glutathione available for its antioxidant function and other detoxification reactions.

How can toxic chemicals be removed? The most important step is to remove the exposed person from further contamination. If a child is eating paint chips from lead paint, treatment with detoxification agents will not work if the child continues to eat lead paint chips. Detoxification methods may be more effective when the exact toxic chemical exposure is known. However, the use of general detoxification methods may be useful when a person has been exposed to multiple chemicals or in an emergency when large numbers of people are exposed. For example, large numbers of emergency workers and the general public were exposed to a variety of chemicals following the terrorist attack on the World Trade Center including asbestos, radionuclides, benzene, dioxins, polychlorinated biphenyls, fiberglass, mercury, lead, silicon, and sulfuric acid.²¹ A large percentage of these people were detoxified with the Hub-

Figure 3. Chemical structures of common antibacterial agents in hand soaps



bard protocol performed under the supervision of a physician which includes the following:²¹

- Daily physical exercise, immediately followed by forced sweating in a sauna at 140-180°F for two-and-a-half to five hours with short breaks for hydration to offset the loss of body fluids and to cool down.

- Nutritional supplementation centered on gradually increasing doses of crystalline niacin to promote lipid mobilization of stored toxicants and stimulate circulation. Time-release niacin or nicotinamide are not recommended. It is unclear if flush-free niacin like inositol hexaniacinate is effective for this protocol. The mechanism of flush type niacin involves suppression of fatty acid release from adipose tissue followed by a rebound effect in which generation of fatty acids by lipolysis of triglycerides in adipose tissue is increased with concomitant release of toxic chemicals.

- Administration of additional vitamins, minerals, electrolytes, and oils includes vitamins A, D, C, E, B complex, B₁; multi-minerals including calcium, magnesium, iron, zinc, manganese, copper, and iodine; sodium and potassium; and a blend of polyunsaturated oils including soy, walnut, peanut, and safflower. Oils are administered in high quantities to prevent enterohepatic circulation of toxic chemicals excreted in the bile.

In addition, intravenous administration of glutathione has been shown to be highly effective for a wide range of organic toxic chemicals containing halogens such as chlorine, fluorine, bromine, and iodine and many other chemicals.²² Specific antidotes such as atropine and others are available for organophosphate pesticides. Chelation agents such as dimercaptosuccinic acid, ethylenediaminetetraacetate (EDTA), and 2,3-dimercapto-1-propane sulfonic acid have a good safety record in the removal of many toxic metals when used as oral or rectal agents. Intravenous use may be more risky especially when using the sodium salt of EDTA, which can chelate calcium and cause a sudden decrease in serum calcium

that can be fatal unless careful precautions are taken to monitor and make adjustments to maintain serum calcium. Other non-pharmaceutical agents such as cilantro and clays and many others have been used to remove toxic metals, but their use has not been documented to the extent of the three pharmaceutical agents mentioned above.

These few examples in this article indicate the urgency of screening methods similar to the Ames mutagenicity testing to determine which chemicals affect brain function and mental health that would be used on all current and future chemicals introduced into the environment. Until then, clinicians treating neurological or psychiatric disorders will need to increase their knowledge of the entire chemical universe that affects brain function, to perform thorough history of all occupational as well as home use of chemicals, and to become familiar with all common detoxification protocols available for different chemical entities. The brain is especially susceptible to chemical damage because of its high metabolic rate with resultant high free radical production, high amounts of sulfur containing amino acids that react with toxic metals, and very high amounts of polyunsaturated fatty acids that are vulnerable to oxidation and have a tendency to retain fat soluble toxic chemicals. Until proven otherwise, it should be assumed that any chemical compound may have an adverse impact on mental health. Furthermore, because of many studies connecting toxic exposures of metals like lead to murder, crime, delinquency, and attention deficit, any person who enters the criminal justice system should be tested and receive mandatory treatment for toxic chemical toxicity before receiving punishment. Such treatment will be considerably cheaper than incarceration and make the offender a much more productive member of society. Furthermore, regulatory agencies should regulate chemicals by chemical classes instead of banning just a single unique chemical to prevent similar toxic chemicals being produced by creative organic chemists.

Conflicts of interest

The author has no financial interest in any fast food restaurants or any other restaurants, disinfectants, or soap companies. The author is, however, the director of a lab that markets tests to identify different molecules to find out which compounds deviate from the values in healthy people.

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