ADD-ing it up: soy infant formula, ADD/ADHD and manganese toxicity

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Abstract

Manganese is an essential trace mineral, but high levels are neurotoxic to newborns. Infants fed soy infant formula ingest as much as 80 times more manganese per day than those who are breast fed. Although healthy toddlers, children and adults exposed to excess manganese can usually eliminate most of it, infants cannot because their immature livers are not fully functional. At the same time, their growing brains and other organs are highly susceptible to damage from neurotoxins. This article reviews research showing that neonates exposed to the high levels of manganese present in soy formula are at increased risk for neurodevelopmental abnormalities, including an impaired ability to make the neurotransmitter dopamine and damage to the substantia nigra, caudate, putamen and globus pallidus areas of the brain. These findings suggest that soy infant formula is a likely contributor to the epidemic of ADD/ADHD and other cognitive and behavioral disorders.

This paper is a slightly revised and updated version of Chapter 21 from my book *The Whole Soy Story: The Dark Side of America's Favorite Health Food* (**Publisher:** NewTrends Publishing, Inc. (March 10, 2005); **ISBN:** 0967089751).

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1. Introduction

Over the past few decades, soy has become America's favorite health food. Newspapers, magazines and best-selling health writers have proclaimed the "joy of soy" and promoted the belief that soy is the key to disease prevention and maximum longevity. Sales of soy foods grew 200% from 2000-2004, and represented a US$4 billion industry last year. Sales of soy infant formula are also escalating and now represent 25% of the bottle-fed market.

Soy has received so much favorable press that most people would be surprised to learn that soy has a dark side and that many respected scientists have stated that the possible benefits of eating soy should be weighed against proven risks. Although this warning applies to people of all ages, it particularly applies to infants and children whose bodies and brains are still developing.

At greatest risk are babies on soy formula because of their small size, critical developmental phase and the fact that formula is their main source of nutrient. The Swiss Federal Health Service, British Dietetic Association, and Israeli Health Ministry (Siegel-Itzkovich J. Health Ministry: Eat soya only in moderation. *The Jerusalem Post*, July 20, 2005. Available online at health.jpost.com) have warned parents and pediatricians that soy infant formula is so dangerous that it should be used only as a last resort [1,2]. These agencies are concerned because the plant estrogens (known as phytoestrogens, isoflavones or genistein and daidzein) in soy formula have been linked to premature puberty in girls, delayed or arrested puberty in boys, thyroid disease, ADD/ADHD and other problems. Indeed figures from the Swiss Federal Health Service and reviewed by leading toxicologists indicate that babies on soy formula receive the equivalent of three to five birth control pills every day [3].

Unfortunately, the plant estrogens are not all that is wrong with soy formula. Recently, another danger has come to light–manganese toxicity. Infants fed soy formula take in as much as 75 to 80 times more manganese per day than infants who are breast fed. Per liter, breast milk contains 3 to 10μg manganese, cow's milk formula 30 to 50 μg, and soy formula a whopping 200 to 300 μg. Although manganese is a vital trace mineral, high levels are toxic to newborns [4-7].

2. Mad scientists

At a conference held in September 2000 at the University of California at Irvine, leading nutritionists, pediatricians and toxicologists warned that newborns exposed to the levels of manganese present in soy formula could suffer brain damage in infancy that could lead to learning disabilities, attention deficit and other behavioral disorders, and even violent tendencies [8].

Although healthy toddlers, children and adults who ingest excess manganese can usually eliminate most of it, infants cannot because their immature livers are not fully functional. At the same time, their growing brains and other organs are more susceptible to manganese damage. Even tiny amounts of excess manganese are dangerous when stored long term in the body and brain where they do not belong [9]. Hair mineral analysis tests of children with learning and attention deficits have revealed elevated levels of manganese compared to normal youngsters. Youths convicted of felonies are also much more likely to show elevated hair levels. Although few infants are chronically exposed to high levels of manganese from industrial sources, many are exposed to toxic levels through soy infant formula. Indeed, hair mineral analysis tests on infants using soy formula reveal high levels of manganese in their scalp hair, a clear indicator of manganese toxicity [10-13].

Scientists have known about manganese toxicity for years. In 1980, the U.S. government set permissible manganese levels at 2.5 to 3.0 mg per day for adults; 1.0 to 1.5 mg per day for toddlers; and 0.5 to 1.0 mg per day for infants [8]. The calculations for the "safe" levels set for infants seem to have been based on their smaller size alone and did not take into account the fact that infants with immature livers cannot

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successfully metabolize excess manganese. As it happened, the soy industry put little or no effort into keeping manganese under the permissible—but still unacceptable—levels [8]. Soy formulas on the shelves in the early 1980s contained anywhere from 0.2 to 2.2 mg of manganese per quart; during that same period, scientists confirmed the likelihood of risk to newborns from manganese storage in the brain [10,14-16]. In 1983, Phillip J. Collipp, MD, a pediatrician at Nassau County Medical Center, confirmed a correlation of high manganese levels with childhood learning disabilities and speculated that soy based infant formula might determine a child's likelihood of developing ADD/ADHD later in life [13].

Despite the alarming and consistent results of these studies, few people have ever heard of the link between soy infant formula and manganese toxicity Now teams of scientists have moved from speculation about a probable connection to ADD/ADHD and other behavioral and learning problems to studies using rats, monkeys and human subjects designed to fully elucidate cause and effect [17].

3. Triple threat man'

Manganese toxicity is a problem for people and animals of all ages, but represents a triple threat for infants. Newborns absorb more manganese because of their immature and permeable intestines, fail to eliminate excess manganese because of their immature livers, and are extremely vulnerable to manganese damage because their brains and other organs are still growing. By eight months of age, an infant on soy formula absorbs 1.1 mg of manganese per day above its metabolic needs and deposits about eight percent of that in the basal ganglia cells of the brain. Years later, this manganese may impair the brain's ability to make the neurotransmitter dopamine and trigger behavioral problems ranging from Attention Deficit (ADD) and Attention Deficit Hyperactivity Disorders (ADHD) to violent and sociopathic behavior [8,17]. Bo Lonnerdal, Ph.D., of the University of California at Davis pulls no punches when he says, "Ingestion of soy-based formula in infancy could impair brain development [17]."

Animals fed even small excesses of manganese during the first weeks of life have shown biochemical abnormalities followed by lesions in the substantia nigra, caudate, putamen and globus pallidus areas of the brain. These areas all depend upon dopamine production for proper function and relate to our abilities to think clearly and flexibly, focus, complete tasks and perform well under stress [6,18].

Trinh Tran, Ph.D., while working with Dr. Lonnerdal at UC Davis, found that baby rats given manganese chloride supplements at levels comparable to the manganese in soy-formula-fed infants showed no adverse effects until reaching adolescence. At that point in their development, they displayed a range of behavioral and brain disorders, including poor performance on burrowing, detour and shock avoidance tests. Because rats cannot survive without maternal breast milk, investigators fed the animals manganese supplements, not soy formula [5]. Studies on Rhesus monkeys fed with soy formula resulted in higher tissue manganese absorption. Whether the higher tissue levels will result in lowered dopamine levels and behavioral deficits later in life is he subject of future research. This group of researchers plans two prospective studies with human newborns on soy formula that will chart manganese levels and behavior as they grow up [17].

In a separate study, rat pups fed manganese at levels found in breast milk grew up as healthy as controls. However, if given five times more manganese they showed a 48% decline in levels of basal ganglia dopamine. Given ten times the appropriate amount, they suffered a 63% decline [6]. These results are particularly sobering when we consider that levels of manganese in soy infant formula are 75 to 80 times higher than the levels found in breast milk.

Francis Crinella, Ph.D., of the University of California Irvine Child Development Center, notes that "Most behaviorists assume that cognitive benefits of breast feeding are associated with mother-child intimacy," then asks, "Could another advantage be that the child is also protected against over-absorption of manganese [17]?"

4. Mad bean disease

Whether manganese enters the body by the mouth, lungs or injection, the metal lodges in the basal ganglia. Neurology and toxicology textbooks have reported disorders known as "Manganese Madness" and "Manganism" since the turn of the century. Until soy formula entered the picture, most cases involved miners exposed to manganese dust or people who breathed in high amounts of tetraethyl lead in the emissions from tail pipes or methylcyclopentadienyl manganese tricarbonyl from gasoline. Symptoms of manganism include instability, impulsivity, irrationality and hallucinations, or, with chronic exposure, the *paralysis agitans* of Parkinson's Disease [8,19-21]. The area of the brain most affected in Parkinson's is the dopamine system, the very part of the brain now associated with ADD/ADHD [22].

According to toxicologists, "manganese toxicity arising from excessive intakes of the elements in foods was never reported" and "virtually impossible except where industrial contamination has occurred [23]." In the past few decades, cases *have* begun to emerge, with the most frightening reports of manganese poisoning happening to very sick babies and other patients receiving parenteral nutrition [23].

Manganese toxicity rarely exists in isolation. Fluoride—found in most of the tap water used to mix soy formula—can increase manganese absorption [24-36]. Zinc, calcium and iron deficiencies can also push manganese absorption up to toxic levels [27-29]. Animal studies suggest that an infant born to a pregnant woman who is low in calcium or iron, may be more susceptible to this condition [30]. Sub-optimal liver function can also contribute to manganese toxicity. These and other indications of higher manganese consumption and accumulation in the brain have spurred some scientists to study more thoroughly the impact of low-level manganese-induced neurotoxicity on the rate of aging [31].

Manganese deficiency is commonly associated with hypothyroidism, but excess manganese may be a problem as well. To date, scientists have linked toxic levels of manganese to goiter in female and castrated male mice. Castrated male mice treated with ordinary levels of testosterone, however, did not form goiters [32] suggesting that testosterone confers some protection. But infants and others who eat soy tend to experience a lowering of testosterone levels because of the soybean estrogens [3]. Altered T4, T3 and TSH levels have also

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been linked to manganese accumulations in the pituitary gland [33]. Finally, manganese-related auto-antibodies have been found in patients with Graves disease [34]. These studies are particularly interesting in the light of the many reports of damage to the thyroid caused by soy infant formula and other soy foods over the past 60 years. Clearly manganese deserves to join the list of soy goitrogens, the best known of which are the isoflavones [3].

USDA researchers J.W. Finley and C.D. Davis at the Grand Forks Human Nutrition Research Center in North Dakota have expressed concern about the potential for manganese toxicity in the growing ranks of vegetarians. Vegetarians eat more manganese because plant foods contain far more than animal foods. Vegetarians are also more likely to absorb more manganese because of zinc, calcium and iron deficiencies. Low protein diets also contribute to manganese toxicity [28,35,36]. All of these risk factors, of course, are seen in people who eat a lot of soy.

5. Spin the bottle

The soy industry is mostly in denial about the manganese problem in soy formula. When interviewed by David Goodman, Ph.D., an expert on neurological disorders, John Lasekan of Abbott Laboratories shifted the focus from manganese toxicity to manganese's role as a trace metal essential for life and claimed that deficiencies are the problem—at least for premature and low birth weight babies [8]. Because babies are not able to store manganese until they are born, premies need manganese, but at the minuscule, appropriate levels found in breast milk, not high levels that put the neonatal brain and other organs at risk [37]. Mardi Mountford, a spokesperson for the International Formula Council, told Goodman that there are "no reports of manganese toxicity in healthy infants fed soy formula [8]." This may very well be the case. Healthy infants—by definition—don't manifest manganese toxicity early in life although they can fall prey to negative effects later.

Dr. Tran—who has done much to bring the consciousness of manganese toxicity to the forefront—is appalled that some hospitals feed premature babies soy formula, and asks, "Can you imagine the effects of the soy formulas on these underdeveloped organs [correspondence of Trinh Tran to Valerie and Richard James, June 11, 2001]?" One industry supporter has faced the facts: Greg Caton, as Vice President of Lumen Foods, decided that the evidence was sufficiently damning to post a manganese toxicity warning on his cartons of soy milk [38]. Other companies have chosen not to post warnings.

Robert Presley, former CA State Senator and former Secretary of the CA Adult and Juvenile Corrections Agency, the world's largest prison system, is also convinced. "Somewhere in the soy formula story may lie the answer to a lot of crime [8]."

Everett L. "Red" Hodges, founder of the Violence Research Foundation agrees. On November 17, 2004, Hodges set up an informational hearing in Sacramento before the CA Assembly Public Safety Committee. Scientists who have recently conducted animal research testified to the dangers of soy formula and the growing evidence that the high manganese content in soy formula is contributing to behavioral disorders and violent crime [39]. If Hodges succeeds, California in 2005 will become the first state to make it illegal for soy formula to be given to infants under six months of age.

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