Effects of Toxic Metals on Learning Ability and Behavior

by Bernard Windham

I. Mechanisms of Developmental Damage by Toxic Metals.

The human brain forms and develops over a long period of time compared to other organs, with neuron proliferation and migration continuing in the postnatal period. The blood-brain barrier is not fully developed until the middle of the first year of life. Similarly there is postnatal activity in the development of neuronal receptors and transmitter systems, as well as in the production of myelin. The fetus has been found to get significant exposure to toxic substances through maternal blood and across the placenta, with fetal levels of toxic metals often being higher than that of maternal blood(30-32,41-43). Likewise infants have been found to get significant exposure to toxics, such as mercury that their mother is exposed to, through breast-feeding(26,43).

Studies have found that heavy metals such as mercury, cadmium, lead, and tin affect chemical synaptic transmission in the brain and the peripheral and central nervous system(24a,37-40,43,57). They also have been found to disrupt brain and cellular calcium levels that significantly affect many body functions: such as (a) calcium levels in the brain affecting cognitive development and degenerative CNS diseases(5,28,43,74) (b) calcium-dependent neurotransmitter release which results in depressed levels of serotonin, norepinephrine, and acetylcholine(5,28,44-47,43) - related to mood and motivation; (c)cellular calcium-sodium ATP pump processes affecting cellular nutrition and energy production processes(5,28,43); (d) calcium levels in bones causing skeletal osteodystery(5,74) . Toxic metals have also been found to affect cellular transfer and levels of other important minerals and nutrients that have significant neurological and health effects such as magnesium, lithium, zinc, iron, Vitamins B-6 & B1-12 (5,27,43,46,75). Based on thousands of hair tests, at least 20 % of Americans are deficient in magnesium and lithium(5,68,76), with zinc deficiencies also common. The resulting deficiency of such essential nutrients has been shown to increase toxic metal neurological damage(5,43,74,75).

Lithium protects brain cells against excess glutamate and calcium, and low levels cause abnormal brain cell balance and neurological disturbances (75). Lithium also is important in Vit-B12 transport and distribution, and studies have found low lithium levels common in learning disabled children, incarcerated violent criminals, and people with heart disease(76).

In one study a group including violent offenders and family abusers were divided into 2 groups. Half got lithium supplements and half a placebo. The group getting lithium had significantly increased scores for mood, happiness, friendliness, and energy, while the other group did not(77). In a large Texas study, incidence of suicide, homicide, rape, robbery, burglary, theft, and drug use were significantly higher in counties with low

lithium levels in drinking water(78). In a placebo controlled study on prisoners with a history of impulsive/aggressive behavior, the group taking lithium supplements had a significant reduction in aggressive behavior and infractions involving violence(79). The authors suggest that for those areas with low lithium levels in water, water systems should add lithium; and those with deficiencies in lithium or displaying aggressive or impulsive behavior would likely benefit from lithium supplements(78,79).

Studies have also found heavy metals to deplete glutathione and protein-bound sulfhydryl SH groups, resulting in inhibiting SH-containing enzymes and production of reactive oxygen species such as superoxide ion, hydrogen peroxide, and hydroxyl radical(39,43,45-47). This has been found to be a major factor in neurological and immune damage caused by the heavy metals, including damage to mitochondria and DNA(37-40,43) , as well as chronic autoimmune conditions and diseases(29) . High lead levels have been found to be associated with Attention deficit hyperactivity disorder(ADHD), impulsivity, and inability to inhibit inappropriate responding(20a). High aluminum levels have been found to be related to encephalopathies and dementia(49). Some individuals have been found to be more sensitive to toxic metals depending on genetic sensitivity and past exposure to toxic substances(28,29). Nickel exposure is common and nickel exposure has been found to be significantly related to perinatal unthriftiness and mortality in animal studies and large numbers of people affected by allergic conditions such as eczema and psoriasis vulgaris(59) and serious autoimmune conditions such as lupus and CFS(28).

Other agents including mercury are known to accumulate in endocrine system organs such as the pituitary gland, thyroid, and hypothallamous and to alter hormone levels and endocrine system development during crucial periods of development(33,37,43,27). Such effects are usually permanent and affect the individual throughout their life. Some of the documented effects of exposure to toxic metals include significant learning and behavioral disabilities, mental retardation, autism, etc. But even some of the relatively subtle effects that have been found to occur such as small decreases in IQ, attention span, and connections to delinquency and violence, if they occur in relatively large numbers over a lifetime can have potentially serious consequences for individuals as well as for society(26,37,41,42). The incidence of neurological conditions in children such as autism has increased over 200% in the last decade(80), and mercury has been found to be a factor in most of those tested(81).

II. Extent of Exposure of Children to Toxic Metals

The U.S. Center for Disease Control ranks toxic metals as the number one environmental health threat to children, adversely affecting large numbers of children in the U.S. each year and thousands in Florida(1-4). According to an EPA/ATSDR assessment, the toxic metals lead, mercury, and arsenic are the top 3 toxics having the most adverse health effects on the public based on toxicity and current exposure levels in the U.S.(1), with cadmium, chromium and nickel also highly listed. Large numbers of people have been found to have allergic conditions and immune reactive autoimmune conditions due to the toxic metals, especially inorganic mercury and nickel(28,29).

The heavy metals(lead,mercury,cadmium,nickel) tend to concentrate in the air and in the food chain along with other toxic metals like arsenic and aluminum, facilitating metal poisoning which is the most widespread environmental disorder in the U.S. Mercury and cadmium from combustion emissions are also accumulating in coastal estuaries and inland water body sediments, and are widespread in shellfish and other organisms (34-36). Mercury and cadmium are extremely toxic at very low levels and have serious impacts on the organisms in water bodies that accumulate them(34,2). These heavy metals have also been found to be endocrine system disrupting chemicals and have been found to be having effects on the endocrine and reproductive systems of fish, animals, and people similar to the organochlorine chemicals (33,43). Estrogenic chemicals like mercury have been found in Florida wildlife at levels that feminized males to the extent of not being able to reproduce, and also had adverse effects on the female reproductive systems(33,36). Similar effects have also been documented in humans (33,37,43).

III. Developmental Effects of Toxic Metals on Cognitive Ability and Behavior.

According to studies reviewed, over 20% of the children in the U.S. have had their health or learning significantly adversely affected by toxic metals such as mercury, lead, and cadmium; and over 50% of children in some urban areas have been adversely affected. Significant behavioral effects were also documented. Such effects similarly affect adults(43). Many epidemiologists believe the evidence demonstrates that over 50% of all U.S. children have had their learning ability or mental state significantly adversely affected by prenatal and/or postnatal exposure to toxics substances. The toxic metals have been documented to be reproductive and developmental toxins, causing birth defects and damaging fetal development, as well as neurological effects, developmental delays, learning disabilities, depression, and behavioral abnormalities in many otherwise normal-appearing children(5-33,37-43).

Prenatal exposure to 7 heavy metals was measured in a population of pregnant women at approximately 17 weeks gestation(9). Follow-up tests on the infants at 3 years of age found that the combined prenatal toxic exposure score was negatively related to performance on the McCarthy Scales of Children’s Abilities and positively related to the number of childhood illnesses reported. Many similar studies measuring child hair levels of the toxic metals aluminum, arsenic, cadmium, lead, and mercury have found that these toxic metals have significant effects on learning ability and cognitive performance, explaining as much as 20 % of cognitive differences among randomly tested children who have low levels of exposure not exceeding health guidelines for exposure to any of these metals(8,9,12,13,17). These toxic metals have been found to have synergistic negative effects on childhood development and cognitive ability(8,13-15,19.).

Among those more significantly affected by neurological deficits or problems, the affects appear even more significant. Comparison of groups of children who are mentally retarded or significantly learning disabled to normal controls found significantly higher levels of toxic metals in the affected groups(7,11,17,18,21), with the level of the toxic metals and minerals known to be affected by them correctly identifying those with significant disabilities in from 90 to 98% of cases in the studies. A study of rural children

with subtoxic exposure levels found significantly higher levels of lead and cadmium in a group of mildly retarded/borderline intelligence(IQ 55-84) than controls(11). 76% of the study group had one of 5 toxic metals exceeding the lab's upper safety limit. A large study found that hair cadmium level is highly correlated with and predictive of very significant learning disability or mental retardation(18). Over 90 % of those with hair cadmium levels of 0.4 parts per million or more were found to have significant disabilities and over 95% of those with levels above 0.7 were mentally retarded. In a group of students with normal range IQS who failed one subject area on a standardized test (paradiagatic LD), the groups cadmium and lead hair levels were significantly higher than controls; and hair metal levels with lithium levels included correctly separated the groups with 95% accuracy(7). Average hair cadmium levels in the group with learning disabilities was 1.7 ppm. Similar findings regarding toxic metal exposure levels were found for dyslexic children(10) and autistic children(16). A study of dyslexic children with normal IQS found the dyslexic group had a cadmium hair level average of 2.6 ppm, 25 times that of the control group(10) and exceeding the maximum of the normal acceptable range. The dyslexic group also had somewhat higher aluminum and copper levels. Studies of groups with schizophrenia have found increased levels of copper and mercury and reduced levels of zinc, magnesium and calcium, which are known to be inhibited by heavy metals and affect neurotransmitter levels(48,49).

These toxic metals have also been found similarly to have significant behavioral and emotional effects on children and adults(6-8,11,14-16,43). One group of students were scored by their classroom teacher on the Walker Problem Behavior Identification Checklist(WPBIC). A combined hair level score for mercury, lead, arsenic, cadmium and aluminum was found to be significantly related to increased scores on the WPBIC subscales measuring acting-out, disturbed peer relations, immaturity, and the total score(6) among a population of students with no known acute exposures. The combined metals score explained 23 % of the difference of the total WPBIC score, and 16 to 29% of the differences on the subscales for withdrawal, acting out, disturbed peer relations, distractibility, and immaturity(6). Similar results were found in the other studies, and have been found to have implications not only in the classroom but on relations at home, on driving habits, and on job performance. Studies have found evidence that abnormal metal and trace elements affected by metal exposure appear to be a factor associated with aggressive or violent behavior(37,60-62), and that hair trace metal analyses may be a useful tool for identifying those prone to such behavior. Similar tests in the California juvenile justice system have found significant relations to classroom achievement, juvenile delinquency, and criminality. Three studies in the California prison system found those in prison for violent activity had significantly higher levels of hair manganese than controls(61,37). Like several other studies they found higher levels of such toxic metals in blacks than in Caucasian populations. Studies of an area in Australia with much higher levels of violence as well as autopsies of several mass murderers also found high levels of manganese to be a common factor(37). Such violent behavior has long been known in those with high manganese exposure.

Studies have previously found that low levels of lead exposure is significantly related to hyperactivity and attention deficit(20a), school cognitive performance(20a,23,50,60a),

behavioral problems(21,22), mental disorders(24), allergies(60), growth(54), gestational age(54), and spontaneous abortions(60). In one study children's umbilical cord blood at birth was recorded and a teacher assessment of learning/behavioral characteristics completed at the end of the school year at age 8 (20a). Girls with higher than average(> 10 ug/dL) chord blood level were found to be more likely to be dependent, inpersistant, and have an inflexible approach to tasks. (10 ug/dL blood approx. 8 ppm hair, #52) Boys with higher than average chord blood level were found to be more likely to have problems following simple directions or sequences of directions. A follow up study to the Cincinnati lead study measured blood lead levels and compared to standardized IQ test scores at approximately 6.5 years of age(50). The study found blood lead levels were significantly inversely related to both full-scale and performance IQ, and that blood lead levels over 20 ug/dL were related to an average deficit in IQ of 7 points on performance IQ as compared to those with below 10 ug/dL blood lead levels. Another study in Australia measured IQ at approximately 12 years of age and compared to blood lead levels measured from 1 to 7 years of age(51). Total , verbal, and performance IQ were all significantly inversely related with blood lead levels measured during the first 7 years of life. Two studies found average hair lead levels in groups of learning disabled children over 20 ppm(7,12), compared to 4 ppm in controls.

However other studies have pointed out that these studies generally did not investigate or consider the effects and synergistic interactions of the other toxic metals(6,11,20,28), and the fact that lead and cadmium levels tend to have positive correlations with each other. A study of rural school children without acute exposures and with IQS in the normal range found highly significant relations between lead and cadmium with intelligence scores and school achievement [tests(12)]. Lead and cadmium explained 29 % of the variance in IQ. These two metals have been found to have different mechanisms of CNS damage, with cadmium affecting verbal ability more and lead affecting performance measures more. The author of another study(28) of 9 year olds living in an area near an incinerator in Ohio concluded that part of the developmental effects attributed to lead in many past studies was mostly due to cadmium effects, with lead serving as a marker for cadmium effects due to their common origins and cadmium's effect of increasing lead accumulation. The findings of this study were generally consistent with a previous study(12) regarding higher levels of cadmium and lower levels of zinc in children with cognitive deficits.

However this study found zinc level, though significantly affected, can be increased in some depending on other factors. Cadmium as previously noted as well as mercury have anti metabolite effects that significantly affect calcium, zinc, and phosphate levels in the body(74,28,43). The reduction in zinc levels causes increased absorption of lead, and cadmium's affect on the pyrimdine-5-nucleotidase enzyme inhibits phosphorylation in the energy/respiratory ATP function(28). This study found the level of hair phosphorous, as affected by cadmium exposure, was the best indicator of cognitive function and disfunction. Lead was found to have a lesser effect on phosphorous level and ATP function. The entire group of learning disabled boys had low hair phosphorous levels compared to those without learning disabilities. The main factors appearing to affect those with high cadmium levels and low phosphorous hair levels were living within 2

miles of the incinerator, exposure to passive cigarette smoke, and living in a rural area that may have had high cadmium levels in wells. Another study found heavy smokers have cadmium levels in body tissues about 2 times that of non smokers, and hair cadmium levels in newborns of smokers were twice as great as in newborns of non smokers(53).

Other studies have found that cadmium causes significant decreases in birth weight through its antimetabolite actions(53,54) and significant increases in blood pressure(55). Newborn hair cadmium levels have been found to be significantly correlated to maternal hair levels and mothers exposed occupationally to heavy metals to have hair levels twice as high as controls(54). Likewise adults with higher than average cadmium levels performed less well on measures of attention, Psychomotor speed, and memory(56).

These toxic metals have also been found to have significant effects on motor-visual ability and performance(6a,8,20,43), as measured by the Bender Visual-Motor Gestalt Test score. Arsenic, lead, and cadmium levels had the highest correlation with cognitive scores, while aluminum had a significant relation mostly with motor-visual performance and mercury had lesser but highly significant correlations to both.

Studies have also found evidence of a connection between low levels of zinc and two other common childhood diseases, childhood-onset diabetes(72) and epilepsy(73). Zinc is an antagonist to toxic metals like cadmium and mercury, and adequate levels are required to balance the adverse effects of these toxic metals on cellular calcium and other enzymatic processes(28,74)

It should be noted that both blood and hair mercury level have been found to not be highly correlated to exposure from mercury vapor, which is the most common exposure from mercury, because of special properties of mercury(43). Mercury vapor has an extremely short half life in blood, and rapidly crosses cell membranes in body organs where it is oxidized to inorganic mercury, accumulating in the brain, heart, kidneys, and other locations. Thus although elemental mercury exposures are typically greater than organic exposures, most mercury in the blood is organic. Likewise hair mercury has been shown to be more highly correlated with organic mercury exposure than with inorganic(43). Hair test are affected by external mercury exposure in occupational exposures such as dental offices which typically have fairly high levels of mercury. Other measures of mercury such as stool, saliva, and urine have been found to be better measures of mercury for such cases. Urine contains mostly inorganic mercury, but becomes less reliable with long term chronic exposure due to cumulative damage to the urinary detox system. Urinary fractionated porphyrin test is a good test of metabolic damage that has occurred due to mercury of other toxics. The level and distribution of the 6 porphyrins measured indicates extent of damage as well as likely source of damage(43).

Hair levels have been found to be generally reliable indicators of recent environmental metal exposures other than mercury(28,52,54,58). Similarly, blood levels have been found to not reflect chronic or historic cadmium exposure(52,53,58) since metals such as cadmium and mercury have extremely short half life in the blood but long half life in the

body.. Air measurements of cadmium or mercury tend to be very unreliable due to the small particle size, dispersion variation, and other factors. Measure of accumulation in area plants is one reasonably reliable method; areas with cadmium levels over 0.5 ppm indicate significant air pollution.

IV. Sources of exposure to Toxic Metals

The studies reviewed suggest that exposure to toxic metals may account for as many as 20% of learning disabilities, 20% of all strokes and heart attacks, and in some areas be a factor in over 40% of all birth defects(43). The U.S. Center for Disease Control has found that primary exposure to lead is from paint chips, drinking water, fertilizer, food, auto and industrial emissions, and dust. High levels of cadmium are found in regions with high emissions from incinerators, coal plants, or cars(28), as well as in shellfish(36) and cigarette smoke(28). Other common sources include rural drinking water wells(28), processed food, fertilizer, and old paint. Common exposures to aluminum include aluminum cookware, antiperspirants, cheese and other processed food. Nickel, which is highly toxic and commonly causes immune reactions, is commonly seen in dental crowns and braces, along with jewelry, etc.(nickel and inorganic mercury commonly produce allergic type autoimmune problems,29). Manganese and other metal exposure can come through welding or metal work. Cadmium, mercury, arsenic, chromium, silver, copper, and are other metals to which Floridians and others are commonly exposed in drinking water, food, or dental materials (34-36).

The most common significant exposure for most people is to mercury vapor from amalgam fillings(43). Most people with several amalgam fillings have daily exposure exceeding the U.S. government health guideline for mercury(4,43). Likewise a major exposure source of infants and young children is from placental transfer from their mother’s amalgam fillings and breast feeding(43). Another major exposure source to infants is from thimerosal used in vaccinations as a preservative. The majority of infants get exposure above Government health guidelines for mercury and large numbers of infants with related neurological problems such as autism and ADD have been documented(81). A major source of phenyl mercury is from mercury in paint, where many have been exposed to dangerous levels(82). The major source of exposure to organic(methyl) mercury is from fish and shellfish, but inorganic mercury has also been found to be methylated in the body by bacteria, yeast, etc.(43). Significant levels of various forms of organic mercury have also been documented from dental work such as root canals and gold crowns over amalgam base(43,29). Mercury vapor is the form that most readily crosses cellular membranes including the blood-brain barrier and placenta of pregnant women, and results in the highest levels in the major organs such as the brain, heart, and kidneys for a given level of exposure. But the average half-life of vapor in the blood is only 3 seconds so blood tests are not a good measure of such exposure. For similar reasons hair mercury is a less accurate measure of body inorganic mercury burden than for the other metals. Both mercury vapor and organic mercury have been found to be highly toxic and to have independent and synergistic effects at very low levels(43). However developmental effects have been found at comparable or lower levels from mercury vapor than from organic or inorganic exposure(43), and it has been well

established that the primary exposure for most people and children is from mercury vapor.

V. Measures to Reduce or Alleviate Toxic Metal Toxicity

The most important measure to alleviate effects of toxic metals is avoidance of exposure or reducing current exposures. Current exposure levels of most common metals can be tested by a stool test kit from a lab such as Doctors Data, and recent exposures can be tested somewhat easier and cheaper by hair tests(see 66).

As noted previously, the majority of those with amalgam fillings have significant daily exposures often exceeding government health standards for mercury. Daily inorganic mercury exposure can be assessed by stool or saliva test or mouth oral air measurement, but since many have been tested, several studies have developed analytical equations to estimate daily exposure based on number of amalgam surfaces in the mouth, which give reasonable estimates. The main way to reduce mercury exposure to elemental mercury is to avoid amalgam fillings and/or replace amalgam fillings by other materials. Other materials are available that perform as well as amalgam. .

Seafood and fish have often been found to have high levels of organic mercury, cadmium, and arsenic. For those eating significant amounts of such, the levels in the diet can be monitored by direct food testing or stool test for current exposure levels, or by hair or blood test.. Fish and seafood from areas known to contain high levels of toxic metals should be eaten only occasionally if at all, depending on levels. Those who eat a lot of freshwater fish or seafood often have levels of mercury or some other metal exceeding government guidelines. Hair tests offer a reasonable reliable low cost method of assessing the level of many toxic metals in one test. Aluminum exposures can be reduced by avoiding aluminum antiperspirants, food cooked in aluminum cookware, and foods such as processed cheese that have high levels of aluminum.

As previously noted one of the main mechanisms of toxic effects is generation of free radicals and oxidative damage(66). This can be partially alleviated by eating foods high in antioxidants or supplementation of Vit A, C, E, along with such as grapeseed extract, pinebark extract, bilberry, etc. Bioflavinoids like bilberry and other fruits have been found to improve the function of the blood brain barrier. Vit C provides prtection against toxicity of inorganic mercury by reducing the more toxic Hg^{2+} form to the less toxic Hg^{+} form of mercury. Vit B complex is also important to alleviate neurological effects. Most toxic metals also have mineral antagonist known to counteract toxic effects.

For example selenium and zinc are antagonists of mercury, while zinc and iron are antagonists of cadmium.(5,64,65,74). Iron and zinc deficiencies, which can be caused by exposure to toxic metals, increase metal toxicities and supplementation can reduce toxicities, but they can also be toxic if levels are too high. Likewise calcium and magnesium deficiencies and imbalances have been seen to be caused by toxic metals, and proper supplementation can reduce toxicities and reverse conditions caused by these deficiencies or imbalances. Several studies have found that most children with ADHD

have deficiencies of certain minerals that are commonly depleted by exposure to toxic metals, such as magnesium and zinc, and most show significant improvement after supplementation with these minerals(67-71). Magnesium is the most common significant mineral deficiency among ADHD children(67-69), but zinc is commonly deficient among children with ADHD and disruptive behavior disorder(68). One study found the level of free fatty acids also significantly lower in children with ADHD(70), and some practitioners recommend supplementation of essential fatty acids as well in treatment of ADHD.

Whey protein and N-acetylcysteine(NAC) can increase levels of glutathione which is necessary for detoxification and is depleted by toxic metals as previously noted(66). However care must also be exercised regarding proper level if these are supplemented, starting with low levels. Chelation with chemical chelators such as DMSA and EDTA can also greatly reduce metal body burden, but should only be considered for those with serious toxicities and with advice of a knowledgeable physician. DMSA and EDTA are mainly used for lead detoxification, but DMSA is also effective for mercury and other toxic metals. Studies have found that use of EDTA by patients with high levels of mercury can cause serious side effects, so EDTA should be used only when mercury levels have been found to be low(43).

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