I. Introduction

Mercury is one of the most toxic substances commonly encountered, and according to Government agencies causes adverse health effects in large numbers of people in the U.S.[1,2]  The extreme toxicity of mercury can be seen from documented effects on wildlife by very low levels of mercury exposure. Because of the extreme toxicity of mercury, only ½ gram is required to contaminate the ecosystem and fish of a 10 acre lake to the extent that a health warning would be issued by the government to not eat the fish[3].  Over half the rivers and lakes in Florida have such health warnings[4] banning or limiting eating of fish, as do approximately 20% of all U.S. lakes, all Great Lakes, 7% of all U.S. river miles, and many bays.  Other countries including Canada have similar experience.

Mercury has been documented by studies on animals to be extremely cytotoxic, neurotoxic, immunotoxic, genotoxic, and to be an endocrine disrupter and cause of infertility and fertility problems(153). Humans have significant toxic exposures other than mercury but mercury and other toxic metals have been documented to have similar synergistic effects on children and adults (151,153). Toxic metals have been documented by the U.S. Department of Health and EPA to cause large numbers of adverse health effects each year, more than any other toxic exposures, with mercury, lead, and arsenic affecting the largest number of people(1).  A study by the National Academy of Sciences and other similar studies have documented that in the 1990s the majority of U.S. pregnancies resulted in birth defects, neurological, or other significant developmental conditions(150). Studies have documented that the majority of these were due to toxic exposures, with toxic metals being the major factor in most(151,152). Vaccines and other toxic exposures have been documented to be the main cause or a major factor in many chronic developmental children’s conditions including autism, ADHD, learning disabilities, eczema, epilepsy, asthma and chronic lung conditions, diabetes, SIDS, etc. (151,152).  Exposures to mercury along with other toxic metals together have been found by hundreds of thousands of medical tests to be very common, and synergistic toxic effects that are more than 10 fold more dangerous have been documented(155).

That mercury can affect fertility is well known since mercury has been commonly used as a spermicide in birth control products. Potential effects can again be seen from effects on wildlife. Some Florida panthers that eat birds and animals that eat fish, frogs, and turtles containing very low
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levels of mercury (about 1 part per million) have died from chronic mercury poisoning[5,6]. Since mercury is an estrogentic chemical and reproductive toxin, the majority of the rest cannot reproduce. The average male Florida panther has estrogen levels as high as females, due to the estrogentic properties of mercury. Similar is true of some other animals at the top of the food chain like alligators and wading birds[5,6,7], and marine mammals such as polar bears, seals, beluga and orca whales.

Under the Proposition 65 procedures, passed by the state of California in 1986, mercury has been determined to be a reproductive toxin, and to cause birth defects. Thus, products that use mercury and cause significant mercury exposure must provide warnings to the public of the known health risk(156). Use of dental amalgam by dentists in California requires such a warning. Several other states have passed similar laws requiring warnings by dentists of the known health risk related to use of dental amalgam. Dental amalgam has been documented by tests at medical labs to be the largest source of mercury exposure for most people who have several amalgam fillings (31), with exposure levels as much as 10 times the average for those without amalgam fillings. And as later shown mother’s dental amalgam is similarly the largest source of mercury to the fetus and young infants.

Historically most of the research and concern regarding mercury's toxic effects on humans and in particular on fetal development have focused on methyl mercury rather than mercury vapor or inorganic mercury or the type of mercury in vaccines, ethyl mercury. This has been due to a combination of factors, but basic misunderstandings of the differential nature and effect mechanisms of the different forms of mercury appears to have played a role in this. There have been highly publicized major acute poisonings affecting many people and infants of those exposed through fish in Japan and food in Iran. Methylmercury has also been shown to be extremely neurotoxic, much more so than inorganic forms that do not as readily cross cellular membranes such as the blood-brain barrier, even though they are also very neurotoxic.

Additionally, doctors and researchers have traditionally tended to use blood tests to test for mercury exposure, without the understanding from more recent experience that has found blood tests mainly relevant to methylmercury, not mercury vapor or inorganic mercury body burden and only measure recent exposures. Mercury vapor has been found to have an extremely short half-life in the blood[8-10] since the vapor form rapidly crosses cellular membranes including the blood-brain barrier and placenta, where it is rapidly oxidized to inorganic forms. While the half life of vapor in the blood has been found to be about 8 seconds[8], the inorganic form does not readily cross cellular membranes resulting in accumulation in the body organs, especially the brain where the half life can be over 20 years[11,12]. The form of mercury found in the blood by blood tests is thus mostly organic[9,13], while most of the mercury in body organs and urine is mostly inorganic.

However, unfortunately there is no simple or commonly accepted test methodology for inorganic mercury body burden, other than post-mortem autopsies which have verified the accumulation of inorganic mercury in the brain and other organs [12,14,15,127]. In a large U.S.CDC survey more than 16 % of infants had blood levels of mercury above the upper level of mercury exposure recommended by the German Commission on Human Biomonitoring of 10 micrograms per liter in the blood(54), and over 10% of women of childbearing age had blood levels above the WHO standard of 40 ug/L at which infants born would be at significant risk of developmental disabilities(1). The upper level of mercury exposure recommended by the German Commission on Human Biomonitoring is 10 micrograms per liter in the blood(54), but adverse effects such as increases in blood pressure and cognitive effects have been documented as low as 1 ug/L, with impacts higher in low birthweight babies(54). Thus the European and U.S. National
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Academy of Sciences mercury limit was lowered to 5 ug/L(54b). A much higher percentage of child bearing women are thus seen to have mercury levels above the new safety limits. Studies have found that prenatal mercury exposure commonly results in metal retardation, lowered IQs, learning disabilities, and autism (138,148,149,118,119,132-137).

While urine mercury correlates with inorganic mercury exposure and is a better measure than blood, urine mercury is an unreliable measure for those chronically exposed since mercury excretion through the kidneys deteriorates with cumulative exposure. It apparently also is not widely understood that mercury commonly changes forms within the body, both from organic mercury to inorganic mercury and from inorganic mercury to organic mercury. It has been demonstrated that bacteria in the mouth and intestines as well as yeast methylate inorganic mercury to organic mercury, and methylation of mercury from amalgam is the largest source of methyl mercury in most people with amalgam[11,16,31,29]. Some patients who eat no fish but have high levels of inorganic mercury exposure have been tested to have high levels of organic mercury in the body.

Also while it has been known that the general public is commonly exposed to methylmercury which is the main form of mercury in fish, it has not been commonly understood that there was significant widespread exposure to inorganic mercury. Although it has now been well documented that the major exposure to mercury for most people is from amalgam fillings and that likewise maternal amalgam fillings are a major source of exposure for the fetus and infants, this information has not been widely publicized and appears to be unknown to the majority of doctors, dentists, and the public. This paper clarifies and documents some of these recent findings, and also reviews the fertility and fetal development effects of mercury vapor, which have been documented at even lower levels than for methylmercury in some cases.

II. Mechanisms of Mercury Leakage from Amalgam fillings & Levels of Exposure

The average amalgam filling weighs more than ½ gram and is 50% mercury. Mercury is known to have a low vapor pressure and to be continuously vaporized and absorbed by the body. Amalgam has also been shown to act like a battery, setting up galvanic currents in the mouth, resulting in high levels of mercury being deposited through this action in the oral tissues and mucosa, from which it also spreads to other parts of the body[17-23]. Levels commonly found in the oral tissues of those with amalgam fillings were 100 to 1200 times the FDA/EPA action level for health warnings in food, which is 1 part per million (ppm) mercury[4].

Except for special populations such as occupationally exposed workers and populations with a high level of fish in the diet, the number one source of mercury in most people has been documented to be dental amalgam fillings[13,24-31]. Most of the thousands of people with several amalgam fillings who have been tested were found to have daily exposure levels of mercury vapor exceeding government safety guidelines. The U.S. ATSDR mercury vapor minimum risk level(MRL) is 0.2 micrograms per cubic meter(ug/M3)[32]. Most people with amalgam fillings who have been tested have been found to have much higher levels of mercury in their oral air than this, with some as high as 100 ug/M3[24,25,28-31].

For an adult breathing 0.2 ug/day of mercury and breathing approximately 20 cubic meters per day of air[27], the ATSDR MRL gives a guideline level of exposure of approx. 4 micrograms per day. Most of the many thousands tested who have 9 or more amalgam fillings were found to have exposure levels above this level and above U.S. government health guidelines for mercury[11,13,24-31]. While most studies such as Richardson’s analysis for Health Canada[27] that are primarily based on urine measurements use conservative estimates of daily mercury exposure from amalgam
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in the range 3 to 5 ug/day, studies which measure levels of mercury in feces or saliva found considerably higher daily exposure levels. Two studies found daily excretion in feces between 30 to 190 ug for subjects with between 18 and 82 amalgam surfaces, with an average of 60 ug/day[25,28]. Another study[29] found daily excretion through feces from 10 to 87 ug. A medical laboratory, BIOSPECTRON SWEDEN AB, that has performed thousands of fecal tests for mercury reports a similar range of daily excretion.

Large studies that measured mercury levels in saliva have found that over 90 % of mercury in saliva typically comes from amalgam fillings, and the level of mercury found in saliva has a similar range as the studies for level in feces previously quoted[24,29]. A large study of mercury levels in the U.S. military population found average daily excretion levels in urine for subjects with 20 amalgam surfaces to be approximately 6.2 ug, assuming 2 liters of urine excreted per day[13]. Significant levels of mercury have also been found in sweat and appear to often be more than 2 ug per day for subjects with approximately 1200 ml of sweat per day. Additionally autopsy studies[12] have found that for those with chronic exposure, daily exposure levels are higher than excretion levels so mercury accumulates in the major body organs including the brain, heart, kidneys, liver, etc. Thus altogether daily exposure levels for those with several fillings appear to often exceed 50 ug/day, with exposure levels of over 100 ug/day not uncommon[24,29]. Studies have also found the majority of such exposure to come from vapor rather than particles, with relatively high absorption rates in the body[25].

III. Effects of Mercury Exposure on Fertility and Fetal Development

Many studies have documented health effects occurring to the neurological, immune, hormonal, and reproductive systems due to the high levels of mercury accumulating from chronic occupational exposure. But many recent studies have found reproductive effects including infertility (153,154) and developmental effects in the fetus and infants at much lower levels than those having significant effects on adults. As compared to adults, the fetus and newborns have been found to be much more susceptible to the effects of low levels of mercury exposure due to low body weight with higher food consumption rate per kilogram of body weight, higher gastrointestinal absorption rate, less effective renal excretion, and a less effective blood-brain barrier[33].

Mercury has been found to be a significant cause of seizures and epilepsy(147). The effects of chronic, low-dose fetal and lactational organic (MeHgCl) and inorganic (HgCl2) mercury intoxication on epilepsy/seizures were investigated and compared in rats and were found to have significant correlations between seizure susceptibility and cortical mercury level(147a) Inorganic mercury exposure facilitated the duration of seizure discharges in younger animals and appeared to be more permanent than methyl mercury exposure. Another researcher had similar findings for infants(147b)

The most common source of maternal exposure to mercury vapor, as previously shown, is amalgam fillings, while the most common sources of methyl mercury in people are amalgam(31) and fish. Both have been demonstrated to cause rapid transmittal through the placenta to the fetus [14,15,34-51/52-54]. The fetal mercury content after maternal inhalation of mercury vapor was found to be over 20 times that for maternal exposure to an equivalent dose of inorganic mercury[48-50], and levels of mercury in the brain, heart, and major organs have been found to be higher after equal exposure levels to mercury vapor than for the other mercury forms [8,55]. Some developmental and behavioral effects from mercury vapor have been found at levels considerably
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below that required for similar effects by methyl mercury [10,38,49,56-58]. The studies reviewed found that mercury vapor and organic mercury have independent and synergistic toxic and developmental effects along with those of other toxic metals such as nickel, palladium, gold, and cadmium, and that additionally conversions occur in the body between the various forms of mercury[16,59]. Extensive immune system tests for populations of patients with chronic autoimmune diseases such as Chronic Fatigue Syndrome or chronic neurological conditions have also demonstrated that a much higher percentage of the patients have autoimmune reactions to inorganic mercury than to organic mercury, and that immune reactivities and symptoms improve in the majority of cases when amalgam fillings are replaced[16,59]

Based on animal studies using rats, sheep, and monkeys as well as human studies, mercury from amalgam in the blood of pregnant women crosses the placenta and appears in amniotic fluid and fetal blood, liver, and pituitary gland within 2 days of placement [10,14,15, 34-36,43-47,60,54].

Studies have found a significant correlation between number of amalgam fillings of the mother and the level of mercury in the fetus, infants, and young children[10,14,15,34-40], and also with the level in mother's milk [10,38-42]. Breast milk has been found to increase the bioavailability of inorganic mercury, which was found to be excreted to milk from blood at a higher level than organic mercury(41,44,61). The main mechanism of transfer was found to be binding to albumin(45). For non-occupationally exposed populations and populations without high fish consumption, these studies found dental amalgams appear to be the main source of mercury in breast milk and the fetus, but significant levels of methyl mercury are also often found in breast milk [43,44,46,54,61]. U.S. ATSDR staff[62] indicate that under normal circumstances mercury in mother’s milk should be under 1.7 ug/L, and 3.5 ug/L appears to be an adequate screening level for health risk. They indicate that there is evidence that contaminated breast milk is a source of potential risk to infants. An Italian study indicates that a commonly used mercury tolerance level for human milk is 4 ppb(43).

Mercury is often stored in breast milk and the fetus at much higher levels than that in the mother [10,36,38-46,60,61/54]. Milk from mothers with 7 or more fillings was found to have levels of mercury approximately 10 times that of amalgam free mothers. The milk sampled ranged from 0.2 to 57 ug/L. In a population of German women, the concentration of mercury in early breast milk ranged from 0.2 to 20.3 ug/L. After 2 months lactation the level had declined and was 0.1 to 11.7 ug/L[64]. A Japanese study found that the average mercury level in samples tested increased 60% between 1980 and 1990[47b]. The study found that prenatal Hg exposure is correlated with lower scores in neurodevelopmental screening, but more so in the linguistic pathway(47b). The level of mercury in umbilical cord blood, meconium, and placenta is usually higher than that in mother's blood[43- 47].

Meconium(first stool) level appears to be the most reliable indicator of fetal mercury exposure and often has significant levels when there are low levels in mother’s blood and cord blood(46c). The level of maternal blood or hair mercury is significantly correlated with mercury level in meconium and in nursing infants, so maternal tests can be easily used as a screen for developmental dangers[43-47,127]. But fetal levels can be significant when there are low levels in maternal blood(46c).

The highest levels of mercury are usually found in the pituitary gland of the fetus which affects development of the endocrine, immune, and reproductive systems. Mercury has been well documented to be an endocrine system disrupting substance in animals and people, preferentially accumulating in and disrupting function of the pituitary gland[10,12,39,65], hypothalamus, and thyroid gland[12,65-67]; along with disrupting or blocking enzyme production processes[57,68-73], glucose transfer[57], and many hormonal functions[74-79] at very low levels of exposure. The
pituitary gland controls many of the body's endocrine system functions and secretes hormones that control most bodily processes, including the immune system and reproductive systems[79]. The hypothalamus regulates body temperature and many metabolic processes.

Mercury has also been documented to be a reproductive and developmental toxin in humans. Some of mercury’s documented hormonal effects at very low levels of exposure include effects on the reproductive system resulting in lowered sperm counts, defective sperm cells, and lowered testosterone levels in males; along with menstrual disturbances, infertility, spontaneous abortions in women, and birth defects. Studies found that very low levels of exposure to mercury cause genetic/DNA damage[34,81-88] and inhibits DNA & RNA synthesis[81,85/86]; damages sperm, lowers sperm counts and reduces motility [34,81,88-92,5,6/88,93,95]; causes menstrual disturbances [96,97]; reduces blood’s ability to transport oxygen to fetus, and transport of essential amino acids and nutrients including magnesium, zinc and Vit B12 [40,57,71,72,98,99]; depresses enzyme function and isocitric dehydrogenase (ICD) in fetus[92-95,99]; causes reduced iodine uptake, inhibited ATP activity, & hypothyroidism[66]; causes infertility[74-78,89-93,95,100-104,146,106], and causes spontaneous abortions and birth defects[36,40,51,66,75,78,79,100,101,104,107-113/106,113,114]. Pregnant women who suffer from hypothyroidism (under active thyroid) have a four-times greater risk for miscarriage during the second trimester than those who don’t, and women with untreated thyroid deficiency were four-times more likely to have a child with a developmental disabilities and lower I.Q.(66)

Reviews of recent studies have found that the incidence of abnormalities of genitourinary abnormalities in human males has increased during the past 50 years, including cryptorchidism and hypospadias[79,81,115]. The incidence of testicular cancer was found to have increased 3 to 4 fold since the 1940s. The reviews also found that studies indicate that sperm quality and quantity have decreased significantly during this period, with an average decrease in sperm density of approximately 40% since 1940 along with increased sperm abnormalities. Mercury and other toxic metals are among the toxics that have been found in animal studies to have such effects [5-7,40,79,88,95].

A large cohort study of occupationally exposed women found an increased risk of spontaneous abortion and other pregnancy complications[101]. Women with hormonal problems seeking help at a gynecological clinic in Germany were found to have higher body burdens of heavy metals, including mercury[74,75,78], and women with idiopathic menstrual problems had higher levels of mercury[75,77,96,100]. Women with hormonal related alopecia(hair loss) also had higher mercury levels than controls[78,116,117] and the condition was alleviated by amalgam removal. Most women with very high levels of mercury were infertile, and after clearance of metals many were fertile again[74-78].

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 receptors and transmitter systems as well as in the production of myelin. Many of the toxic substances such as mercury are known to damage the developing brain by interfering with one of these developmental processes, interfering with structural development depending on what is developing at the time of exposure[118-126]. Mercury and other toxic substances are known to accumulate in endocrine system organs such as the pituitary gland, thyroid, and hypothalamus and to alter hormone levels and endocrine system development during crucial periods of development(10,12,33,41,47-49,79,132). Such effects are usually permanent and affect the individual throughout their life. 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[118,119]. Infant head circumference was found to be negatively correlated to infant meconium mercury levels(46c).

Animal studies of developmental effects of mercury on the brain have found significant effects at extremely low exposure levels, levels commonly seen in those with amalgam fillings or in dental staff working with amalgam. One study[120] found mercury vapor affected NGF concentration, RNA, and choline acetyltransferase in rat’s forebrain at between 4 and 11 parts per billion(ppb) tissue concentration. Another study[123] found general toxicity effects at 1 micromole(uM) levels in immature cell cultures, increased immunoreactivity for glial fibrillary protein at 1 nanomole (0.2 ppb) concentration, and microglial response at even lower levels. Other animal studies on rodents and monkeys have found brain cellular migration disturbances, behavioral changes, along with reduced learning and adaption capacity after low levels of mercury vapor or methylmercury exposure [49-53,58,128-130,92,124-126]. The exposure levels in some of these studies are seen in the fetus and newborn babies of mother’s with amalgam fillings or who had work involving amalgam during pregnancy[14,15].

Epidemiological studies have found that human embryos are also highly susceptible to brain damage from prenatal exposure to mercury[120,121,124-126,148,149]. Prenatal/early postnatal exposure to mercury affects level of nerve growth factor(NGF) in the brain and causes imbalances in development of the brain [40,120-123,130, /94,124-126]. Exposure of developing neuroblastoma cells to sub-cytotoxic doses of mercuric oxide resulted in lower levels of neurofilament proteins than unexposed cells[126]. Mercury vapor exposure causes impaired cell proliferation in the brain and organs, resulting in reduced volume for cerebellum and organs and subtle deficiencies[40,120-23]. Neurotoxicity as a result of mercury exposure has also been found to be due to the inducing of reactive oxygen species such as superoxide ion, hydrogen peroxide, and hydroxyl radical causing enhanced lipid peroxidation, DNA damage, and altered calcium and sulfhydryl homeostasis[120,121,131].

Recent studies found that prenatal mercury exposures from mother’s amalgams and other sources along with susceptibility factors such as ability to excrete mercury appear to be major factors in those with chronic neurological conditions like autism[148,149]. Infants whose mothers received prenatal Rho D immunoglobulin injections containing mercury thimerosal for RH factor or whose mother’s had high levels of amalgam fillings had a much higher incidence of autism. While the hair test levels of mercury of infants without chronic health conditions like autism were positively correlated with the number of the mother’s amalgam fillings, vaccination thimerosal exposure, and mercury from fish, the hair test levels of those with chronic neurological conditions such as autism were much lower than the levels of controls and those with the most severe effects had the lowest hair test levels, even though they had high body mercury levels. This is consistent with past experience of those treating children with autism and other chronic neurological conditions.

Several studies found that mercury along with other toxic metals cause learning disabilities and impairment, and reduction in IQ[40,58,129,132-139]. Mercury has an effect on the fetal nervous system at levels far below that considered toxic in adults, and background levels of mercury in mothers correlate significantly with incidence of birth defects and still births [36,40,100-102]. Prenatal exposure to 7 heavy metals was measured in a population of pregnant women at approximately 17 weeks gestation[134]. 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.
Exposure to mercury and 4 other heavy metals measured by hair tests in a study of school children accounted for 23% of the variation in test scores for reading, spelling and visual motor skills[135]. A Canadian study found that blood levels of a similar group of metals were able to predict with a 98% accuracy which children were learning disabled[136]. Another 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[133]. Similar tests in the California juvenile justice system have found significant relations to classroom achievement, juvenile delinquent temperaments, and criminality.

The saliva and feces of children with amalgams have approximately 10 times the level of mercury as children without[140,141], and much higher levels in saliva after chewing. A group of German children with amalgam fillings had urine mercury level 4 times that of a control group without amalgams[142], and in a Norwegian group with average age 12 there was a significant correlation between urine mercury level and number of amalgam fillings[143]. Since mercury vapor is known to rapidly cross cellular membranes and to bioaccumulate over time with chronic exposure, these relationships get stronger with age, with the most serious health effects occurring more commonly in middle-aged individuals.

Studies have found much higher levels of mercury and copper in infants whose mothers were treated with amalgam during pregnancy[37], as well as children with congenital hearing deficiencies[63]. Most researchers in this field advise that fertile women should not be exposed to vapor levels above government health guidelines or have amalgams placed or removed during pregnancy [10-12,15,16,24,27,39,40,65,74,103,144,145]; the U.S. ATSDR mercury health MRL is 0.2 ug/M3 [32]. Many governments of developed countries have bans or guidelines restricting use of amalgam by women of child-bearing age. These include Canada, Sweden, Germany, Norway, Austria, Great Britain, France, Australia, New Zealand, and Japan.

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