Appendix E

Table Summary of Exposure and Effects from Articles Reviewed

(Separate file – please attach here to Report hard copy)

Appendix E: Literature Summary for Mercury Vapor and Dental Amalgam – 34 articles

Article	Exposure Scenario	Amalgam Exposure	Urinary Mercury[1] (ug/L; ug/g creat)	Reported Effects
Bjornberg et al., 2005. Environ. Hlth. Persp. 113:1381-1385. Transport of methylmercury and inorganic mercury to the fetus and breast-fed infant.	Maternal amalgam; maternal and infant blood and milk levels. N = 20.	Amalgam surfaces (mean = 5; range: 0 – 24)	All tissue inorganic Hg levels reported were mean <0.2 ug/L (cord blood, maternal blood and infant blood)	Total Hg exposure is greater in utero than after birth via breast milk; true for both MeHg and I-Hg. Breast milk levels of I-Hg are about 1/3 those of maternal blood. Infant blood levels decrease after birth even while breast feeding. Strengths: humans, maternal, infant, and cord blood and milk levels. Weakness: small n (20), low exposures (mean #surfaces=5; range = 0-24).
Dye et al., 2005. Occup. Environ. Med. 62: 368-375. Urinary mercury concentrations associated with dental restorations in adult women aged 16-49 years: United States, 1999-2000.	Amalgam. National Health And Nutrition Examination Survey (NHANES) data.	Amalgam surfaces: 12.3	Urine mercury levels increase 1.8 ug/g creatinine for every 10 dental amalgam surfaces. Arithmetic mean = 0.71 ug/g Cr. Geometric mean = 1.1 ug/g Cr.	Primarily serves as reference resource for exposure using association between # dental surfaces and urinary Hg levels. Urine levels (uncorrected for creatinine) correlate significantly with # amalgam surfaces (R ~0.26 to 0.34), but after correction for creatinine, the correlations are even better (R~0.37 to 0.46). Strengths: large n, well-defined population; reference data set.
Jonsson et al., 1999. Tox. App. Pharm. 155:161-168. A compartmental model for the kinetics of mercury vapor in humans.	Hg vapor (~400 ug/m^3) in 9 human subjects for 15 min followed by light exercise.	No amalgam fillings	Expired air; urine and plasma levels measured. Urine Hg – 0.2-5.6 nmol/day (~ 1-28 ug/day).	~70% inhaled Hg absorbed. Human subjects; half-life of respiratory depot ~1.8 days; $T_{1/2}$ for excretion depot ~63 days. Excretion in urine would not plateau for several months post-exposure for most subjects. Strengths: Human subjects; 24hr urine levels; followed for 30 days. Weaknesses; small n; reported values in nmole.

Article	Exposure Scenario	Amalgam Exposure	Urinary Mercury (ug/L; ug/g creat)	Reported Effects
Kingman et al., 1998. J. Dent. Res. 77:461-471. Mercury concentrations in urine and whole blood associated with amalgam exposure in a US military population.	Dental amalgam in subjects from the Air Force Health Study of Vietnam-era veterans. Approx 50% participants, "ranch hands", exposed to dioxins in Vietnam during 1960s and 1970s; controls - 50% served in Vietnam but not exposed to dioxins. For this study: males, age 40-79 yrs old (avg. 52.8 years), 95% Caucasian, n= 1127.	Amalgam surfaces: mean =19.9. No of teeth with amalgam: mean = 8.2.	Urine - total and inorganic Hg levels were 3.09 ug/L and 2.88 ug/L. 47% had U-Hg < 2 ug/L; 1.3% > 15 ug/L. 93% Hg was inorganic. Blood - total and inorganic Hg in whole blood were 2.55 ug/L and 0.54 ug/L.	Significant correlation found between amalgam exposure and total and inorganic Hg in urine, with or without corrections for creatinine. Weak but statistically significant correlation was found between whole blood and total and inorganic Hg. Results used to estimate that, on average, each ten-surface increase in amalgam exposure is associated with an increase in urine concentration of 1 ug/L Hg. Results clearly show that Hg concentrations in blood and urine increase with amalgam exposure; however, no significant changes in Hg levels were found when data divided into different age groups.
Luglie et al., 2005. Arch. Gynecol. Obstet. 271:138-142. Effect of amalgam fillings on the mercury concentration in human amniotic fluid.	Dental amalgam in pregnant women, n=72; other factors such as fish consumption; smoking; neurological disease history and liver problems considered.	Number of fillings: mean = 2.26 ± 3.19 in Hg-negative group and 5.32 ± 3.03 in Hg-positive group.	Hg levels in amniotic fluid for all subjects – mean = 0.37 ± 0.49 ug/L.	Total subjects: 72 pregnant women 19 consider as negative group b/c Hg level <0.08 ug/L. 53 consider as positive group b/c Hg level >0.08 ug/L. Number and surface areas of dental amalgam fillings influence Hg concentration in amniotic fluid but not at a significant level; no adverse outcomes were detected through pregnancies and in the newborns.

Article	Exposure Scenario	Amalgam Exposure	Urinary Mercury (ug/L; ug/g creat)	Reported Effects
Tsuji et al., 2003. Environ. Hlth. Perspect. 111:623-630. Evaluation of mercury in urine as an indicator of exposure levels of mercury vapor.	Compiles ten studies using different exposure scenarios to see if urinary Hg can be used as reliable predictor of Hg exposure.	Includes two studies: Eti et al., 1995 Khordi-Mood et al., 2001 where exposure was via dental amalgam	Compared urinary Hg across different studies	Overall conclusion was that a correlation between air and urinary Hg does exist at airborne Hg levels <50 ug/m^3. However, the relationship between urinary mercury and air concentrations of elemental mercury is only reliable down to concentration of ~10 ug/m^3. For <10 ug/m^3, predicted urinary Hg levels are within background ranges. Urinary Hg is therefore not an accurate measure for understanding exposures of persons to most environmental air concentrations which are typically well below 10ug/m^3.
Vamnes et al., 2003. Sci. Total Environ. 308:63-71. Blood mercury following DMPS administration to subjects with and without dental amalgam.	Dental amalgam. 20 patients – self-reported symptoms attributed to dental amalgam; 21 healthy controls with amalgams; 19 controls – no amalgams placed; 20 patients – amalgams removed. DMPS chelator injected – blood collected after 15, 30, and 120 min, and 24 hrs; urine collected pre-chelator and at 30 min.	Median amalgam surfaces: alleged Hg symptoms: 37.5; healthy w/ amalgams: 43; no amalgams placed: 0; amalgams removed: 48.	Mean Hg excreted in urine 30 min after chelator: Pooled 2 grps w/o amalgam = 3.1 ug; pooled 2 grps w/ amalgam = 10.7 ug. Max loss of blood Hg after chelation: Pooled 2 grps w/o amalgam = 4.7 ug; pooled 2 grps w/ amalgam = 7.1 ug. This study evaluated the use of DMPS as a diagnostic tool in patients with symptoms allegedly caused by Hg from dental amalgam.	This study showed that blood Hg levels is lowest in group who never have any dental amalgam, where as the blood Hg level was similar in healthy subjects w/ amalgams, subjects w/ alleged symptoms from dental amalgam, and subjects w/ amalgam removed. This study showed that the blood Hg is almost same in all three groups of subjects who have/had amalgams. The DMPS exposure also reduced blood Hg levels within 15-30 minutes in all alleged versus non-alleged groups.

Article	Exposure Scenario	Amalgam Exposure	Urinary Mercury (ug/L; ug/g creat)	Reported Effects
Bast-Pettersen et al., 2005. Neurotoxicol. 26:427-437. A neurobehavioral study of chloralkali workers after the cessation of exposure to mercury vapor.	Occupational chloralkali workers previously exposed to Hg^0. Avg duration: 13.1 yrs, adult males, n=49, avg age: 46.4 yrs. Non-Hg-exposed controls from same plant, adult males, n=49, avg age: 46.4 yrs. Follow-up study: 41 exposed subjects and 40 controls had been previously evaluated 5 years earlier (Ellingsen et al., 2001).	NA	Current U-Hg at time of study Hg-exposed workers: mean = 2.9 ug/L (2.2 ug/g Cr) Non-exposed controls: mean = 2.0 ug/L (1.6 ug/g Cr). Calculated cumulative U-Hg levels (past exposure) Hg-exposed workers: 16.5 ug/L/yr (12.7 ug/g Cr/yr). Current blood Hg_{total} Hg workers: 4.6 ug/L; controls: 3.5 ug/L	Hg vapor exposure had ceased ~5 yrs prior to current evaluation. No associations for any neuropsychologic or neurobehavioral tests. Digit-symbol performance improved in past 5 years after exposure ceased.
Bittner et al., 1998. Neurotoxicol. Teratol. 20:429-439. Behavioral effects of low-level exposure to Hg^0 among dental professionals: A cross-study evaluation of psychomotor effects.	Exposure to amalgam Hg^0 used in dental occupation. Dentists n = 230 pooled from 6 previous studies; 80% male. No non-dental practitioner controls.	Not reported.	Range < 1 to > 50 µg/ L. A binomial distribution: 50% subjects - urine levels < 3 µg/L; 30% w/ levels >20 µg/ L. Dentists stratified into 3 urine Hg groups: <1 µg/L, 1-20 µg/L and >20 µg/L.	Retrospective cross-study of combined 5 psychomotor performance data from 6 previous studies conducted between 1991 and 1996. Relationship of Intentional Hand Steadiness Test deficits to urine Hg levels highly significant. Some effect on Finger Tap Test but not significant. Even less relationship between One Hole Placement, NES Simple Reaction Time and Tremor tests and urine Hg levels.

Article	Exposure Scenario	Amalgam Exposure	Urinary Mercury (ug/L; ug/g creat)	Reported Effects
Echeverria et al., 1998. FASEB J. 12:971-980. Neurobehavioral effects from exposure to dental amalgam Hg^0: New distinctions between recent exposure and Hg body burden.	Exposure to amalgam Hg^0 used in dental occupation. Dentists n = 34; Hygienists n = 15. Male and female subjects served as their own controls. No non-dental practitioner controls. Pre- (recent exposure) and post-(body burden) chelation (DMPS) evaluation of U-Hg and neurobehavioral tests.	Mean number of amalgams placed/week: 16.1. Mean number of amalgams in mouth: 1.6.	Prior to chelation: Mean U-Hg levels = 0.9±0.5 ug/L (0.7 ug/gCr) After chelation: Mean = 9.1±6.9 ug Hg/L (7 ug/g Cr).	Subtle but statistically significant associations were demonstrated for recent Hg exposure and measures of mood, motor function and cognition, whereas Hg body burden was associated with symptoms, mood, and motor function. Strengths: Pre-chelation urine Hg levels are a metric of recent exposures; post-chelation levels represent longer term exposures (body burdens). Weaknesses: Duration of exposure unknown. No non-dental subjects with similar urine Hg levels. Possible chelation of other essential and non-essential metals.

Article	Exposure Scenario	Amalgam Exposure	Urinary Mercury (ug/L; ug/g creat)	Reported Effects
Echeverria et al., 2005. Neurotox. Teratol. 27:781-796. Chronic low-level mercury exposure, BDNF polymorphism, and associations with cognitive and motor function.	Exposure to amalgams Hg^0 used in dental occupation. Dentists n = 194; avg 26 yr exposure. Hygienists n = 233; avg 15 yr exposure. Adult male and females. No non-dental practitioner controls.	Dentists = 16 surfaces; Hygienists = 12 surfaces.	Dentists: 3.32 ± 4.87 µg/g Cr Hygienists: 1.98 ± 2.29 µg/g Cr	No significant effects on verbal intelligence and reaction time. Significant effects/correlations were found on 9 measures in dentists and 8 measures in hygienists including visual discrimination, hand steadiness, finger tapping and trail making tests with U-Hg levels. BDNF polymorph mutants had affects not attributable to U-Hg on 4 measures in dentists and 3 measures in hygienists. BDNF polymorphs with 5% frequency may have had aggravated/additive effects with U-Hg with respects to finger tapping dentist and hand steadiness and trail making in dental hygienists. Dentists and hygienists appear to respond differently comparing BDNF allele and U-Hg.
Echeverria et al., 2006. Neurotox. Teratol. 28:39-48. The association between a genetic polymorphism of coproporphyrinogen oxidase, dental mercury exposure and neurobehavioral response in humans.	Exposure to amalgams Hg^0 used in dental occupation. Dentists n = 194; avg. 19 yr exposure (compared to 26 in 2005 study). Hygienists n = 233; avg. 10 yr exposure. Adult males and females. No non-dental practitioner controls.	Not reported.	Same as the 2005 Neurotox. Teratol. Dentists: 3.32 ± 4.87 ug/ g Cr Hygienists: 1.98 ± 2.29 ug/ g Cr	Significant effects/correlations were found on 9 measures in dentists and 8 measures in hygienists including visual discrimination, hand steadiness, finger tapping and trail making tests with U-Hg levels. CPOX4 polymorphs with heterozygous 26-39% and homozygous 1-2% frequency was associated with poorer performance in 4 measures in dentists and 5 measures in hygienists (but not related to mercury exposure). Study uses the same subjects as the Tox. Sci. 2004 and 2005 Neurotox. Teratol. articles.

Article	Exposure Scenario	Amalgam Exposure	Urinary Mercury (ug/L; ug/g creat)	Reported Effects
Elghany et al., 1997. Occup. Med. 47:333-336. Occupational exposure to inorganic mercury vapour and reproductive outcomes.	Occupational exposure; n = 65; 46 women exposed (19 controls in same factory). All 104 pregnancies as part of study occurred from 1948 to 1977. Hg vapor exposures = 25 to 600 ug/m^3. Median exposure = 90 ug/m^3.	NA	Not measured.	Possible association between Hg exposure and risk of adverse pregnancy outcome (congenital abnormality) but not statistically significant. Incidence was 4.2% (3/72 pregnancies) in the exposed group, 0% (0/32 pregnancies) in the controls and 3% (3/104 total pregnancies) overall. [A recent study (Anthony et al., 2002) reports a congenital malformation rate of 2.7% in a population of over 314,000 natural births.] Strengths: humans; relevant endpoints. Weaknesses: retrospective study from medical records; individual exposure data were incomplete; no urine Hg levels; relatively small n; significant differences in age between comparison groups; lack of dose-response relationship.

Article	Exposure Scenario	Amalgam Exposure	Urinary Mercury (ug/L; ug/g creat)	Reported Effects
Ellingsen et al., 2001. NeuroToxicol. 22:249-258. Neuropsychological effects of low mercury vapor exposure in chloralkali workers.	Occupational chloralkali workers exposed to Hg^0 – avg duration – 13.3 yrs, adult males, n=47, avg age – 42 yrs. Non-Hg-exposed controls from same plant, adult males, n=47, avg age – 41.9 yrs.	NA	Current U-Hg at time of study Hg-exposed workers: mean = 10.4 ug/L (8 ug/g Cr) Non-exposed controls: mean = 2.3 ug/L (1.8 ug/g Cr). Calculated cumulative U-Hg levels (past exposure) Hg-exposed workers: 15.9 ug/L/yr (12.2 ug/g Cr/yr). Current blood Hg_{inorg} Hg workers: 4 ug/L; controls: 1.1 ug/L	No associations for any neuropsychologic or neurobehavioral tests with current U-Hg. Past exposure (U-Hg/yr) associated with WAIS Digit Symbol test. Small, but significant association of blood Hg levels for WAIS Digit Symbol and Benton Visual Retention tests, but not for Static Steadiness (Tremor) test. Table 3 – appears to be no effects on any of the psychomotor parameter tests evaluated including the WAIS Digit Symbol and the Benton Visual Retention tests.
Heyer et al., 2004. Tox. Sci. 81:354-363. Chronic low-level mercury exposure, BDNF polymorphism and associations with self-reported symptoms and mood.	Exposure to amalgams Hg^0 used in dental occupation. Dentists n = 193; avg 26 yr exposure. Hygienists n = 230; avg 15 yr exposure. Adult male and females. No non-dental practitioner controls.		Dentists: Log_{ln} 1.1 ± 0.5 µg/g Cr Hygienists: Log_{ln} 0.88 ± 0.55 µg/g Cr	Self reporting data for mood and depression. 23 associations reported between chronic Hg^0U and BDNF mutant allele were found. Study uses the same subjects as the Tox. Sci. 2004 and 2005 Neurotox. Teratol. articles by these authors.

Article	Exposure Scenario	Amalgam Exposure	Urinary Mercury (ug/L; ug/g creat)	Reported Effects
Letz et al., 2000. Neurotoxicol. 21:459-474. Residual neurologic deficits 30 years after occupational exposure to elemental mercury.	Former industrial workers exposed to elemental Hg – exposed to Hg, n=104; unexposed to Hg, n=101. Mean age – 71 yrs.	No.	Mean peak U-Hg concentration >600 ug/L.	A battery of tests which includes both peripheral and central nervous system function were evaluated 30 years after heavy Hg exposure. Results showed that exposure to high levels of Hg can have adverse effects (mostly on peripheral nerves) long after the exposure occurred.
Urban et al., 2003. Neurotoxicol. 24:711-716. Color discrimination impairment in workers exposed to mercury vapor.	Chloralkali worker (n=24 males, mean age 42 yrs) contact with Hg^0 (8-hr TWA = 59 ug/m^3. Mean exposure duration ~14.7 yrs. Age and gender-matched controls (n=24)	NA	Hg-exposed workers: mean = 20.5 ± 19.3 µg/g Cr; controls: no values assessed in this group, but background levels from author previous studies – 1 ug/L.	Subclinical visual impairment assoc with Hg^0 exposure. Appears to be same subjects as used in the other Urban et al. 2003.
Urban et al., 2003. Neurotoxicol. 24:23-33. EEG photic driving in workers exposed to mercury vapors.	Chloralkali worker (n=24 males, mean age 42 yrs) contact with Hg^0 (8-hr TWA = 59 ug/m^3. Mean exposure duration ~15 yrs. Controls (n=24, mean age 36 yrs)	NA	Exposed workers: mean = 64 ug/24 hr. Controls: not measured or reported.	Photic driving is a physiologic response of EEG activity to intermittent photic stimulation. No significant associations between 5 parameters of photic driving and urinary Hg (24 hr and cumulative index [duration x U-Hg-24 hr]).

Article	Exposure Scenario	Amalgam Exposure	Urinary Mercury (ug/L; ug/g creat)	Reported Effects
Ventura et al., 2004. Visual Neurosci. 21:421-429. Multifocal and full-field electroretinogram changes associated with color-vision loss in mercury vapor exposure.	Former fluorescent lamp workers exposed to Hg^0 used in manufacturing (n=43). Evaluated 5.3 $\pm$ 3.2 yrs after a 9.8$\pm$ 3.6 yr exposure. Age-matched controls (n=21)	NA	Not measured.	Retinal function deficits as assessed via full-field electroretinograms and the Cambridge Color Test associated with Hg. Nothing else tested. All subjects evaluated for CCT; 34 evaluated for EEGs.
Yoshizawa et al., 2002. N Engl J Med 347:1755-1760. Mercury and the risk of coronary heart disease in men.	Subjects from Health Professionals Follow-up Study. Patient group – n=470 men with history of coronary heart disease. Controls – n=464 men. Majority of the subjects (63% of controls) were dentists and therefore can be assumed to have had occupational mercury vapor exposures.	NA	Toenail Hg levels: Dentists = 0.91 ug/g; non-dentists = 0.45 ug/g. Significant correlation between toenail Hg levels and fish (i.e., methylmercury) intake.	Nested case-control design. Findings do not support association between total Hg exposure and risk of coronary heart disease. Weak relationship cannot be ruled out.

Article	Exposure Scenario	Amalgam Exposure	Urinary Mercury (ug/L; ug/g creat)	Reported Effects
Bates et al., 2004. Int. J. Epidem. 33: 894-902. Health effects of dental amalgam exposure: A retrospective cohort study.	Amalgam; New Zealand Defense. Force; n = 20,000; 85% male. Retrospective epidemiology study.	Amalgam surface years.	Not reported	No association of exposures with Chronic Fatigue Syndrome; slight increase (Hazard Ratio = 1.24) in Multiple Sclerosis but # cases small (7 or 0.035% vs. 0.14% for U.S. population). Significant protective effect: (HR 0.8 to 0.83) for several kidney disorders; for inflammatory responses and toxic neuropathy (HR 0.79); adjustment reaction (H 0.9). Strengths: detailed exposure data; large # of health outcomes. Weaknesses; lack important covariates: smoking, drug and alcohol history; diet, disease, Pb exposure, no urinary Hg levels.
Bellinger et al., 2006. JAMA 295:1775-1783. Neuropsychological and renal effects of dental amalgam in children: a randomized clinical trial.	Hg amalgam (n=267) vs. composite (n=267); 4-5 years of exposure.	Mean - 15 surfaces restored over 5 years (range 0-55).	Total Hg - 0.9 vs. 0.6 ug/g creatinine (amalgam vs. composite). Urinary albumin 7.4-7.5 mg/g creatinine.	No significant changes in IQ, memory, visuomotor function; urinary albumin (renal effects); if anything an increase in IQ favoring those kids with amalgam. Strengths: humans, prospective randomized clinical trial; 534 children age 6-10 at first exposure; relevant and well-standardized endpoints (IQ evaluated 3 times; neuropsych assessments, 4 times). Weaknesses: only 5 years of exposure; earliest exposure to amalgam at 6 years.
DeRouen et al., 2006. JAMA 295:1784-1792. Neurobehavioral effects of dental amalgam in children: a randomized clinical trial.	Hg amalgam (n=253) vs. resin composite (n=254).	Mean - 18.7 vs. 21.3 surfaces restored, amalgam vs. resin. Follow-up was 7 years.	U -Hg ~1.8ug/g creatinine at baseline; increased to max of 3.2 in cohort with amalgams; no change in composite group	No changes between amalgam vs resin groups for functional domains: memory; attention; visuomotor; nerve conduction velocity. Assessments conducted ~ annually; IQ at beginning and end. Those receiving composite were 50% more likely to need treatment than amalgam group. Strengths: 507 children (age 8-10 at start); randomized clinical trial; relevant measures; repeated assessments; longitudinal; follow up was high. Weaknesses: only 7 years of follow up.

Article	Exposure Scenario	Amalgam Exposure	Urinary Mercury (ug/L; ug/g creat)	Reported Effects
Factor-Litvak et al., 2003. Env. Hlth. Persp. 111: 719-723. Mercury derived from dental amalgams and neuropsychologic function.	Hg amalgam in 550 adults at 30-49 years of age. Exposure level correlations were done.	Groups stratified: 0; 1-5; 6-10; 11-15; 16-46 total amalgams.	Dose-response -Total U-Hg (in ug/g creatinine) increased with # of amalgams; means ranged from means of ~0.75 to ~2.9 (total range was 0.09 – 17.9 ug/g Cr).	No correlation between U-Hg and verbal/nonverbal memory, attention, psychomotor speed, fine motor coordination. Strengths: humans; long-term exposures; relevant endpoints; attempt to correlate exposure with effect (dose-response: no association). Weaknesses: cross-sectional study; absence of data on date of amalgam placements, removed or replaced, but suspect exposures of 10-20 years.
Hujoel et al., 2005. Am. J. Epi. 161:734-740. Mercury exposure from dental filling placement during pregnancy and low birth weight risk.	Amalgam. n=1117 with low birth weight infants (<2500g) vs. 4468 with bw >2500g.	Amalgam fillings (note that this is not # surfaces). Stratified into 0, 1-4 or 5-11 fillings for dose-response: correlation with low birth weight.	Not reported	Population-based, case-control study. No significant association with number of amalgam fillings) placed during pregnancy and low birth weight.

Article	Exposure Scenario	Amalgam Exposure	Urinary Mercury (ug/L; ug/g creat)	Reported Effects
Kingman et al., 2005. Neurotoxicology 26:241-255. Amalgam exposure and neurological function.	Hg amalgam; Clinical Air Force Hlth Study (AFHS; n=1663 and 986 Controls) versus 677 Ranch Hand vets (Vietnam dioxin exposure); all males.	Total # amalgam surfaces: stratified 0-7 (n=615); 8-14 (n=466); 15-23 (n=502); 24-61 (n=445); no '0' group.	None reported	No effects/associations with tremor, coordination, station or gait, strength, sensation, muscle stretch reflexes or peripheral neuropathy at any level. Significant effects on continuous vibrotactile response, but only in select groups (i.e., in combined non-diabetics and non-diabetic AFHS controls but not in diabetic Ranch Hand or among combined diabetics). Lack of dose-response. Strengths: Humans; amalgam. Weaknesses: lack of continuous variables (i.e., nerve conduction; since urinary Hg levels are unknown, it is difficult to interpret findings. No females; <5% African-Americans.
Saxe et al., 1999. J. Am. Dent. Assoc. 130: 191-199. Alzheimer's disease, dental amalgam and mercury.	N = 68 Alzheimer's Disease subjects; n = 33 controls (no AD).	Number of amalgams; number of amalgam surfaces; amalgam location and duration	U-Hg NA. Brain region Hg levels determined at autopsy.	Regional Hg levels in brain did not correlate with the number of amalgams or surfaces. No differences between AD and control groups with respect to number of amalgams or surfaces.

Article	Exposure Scenario	Amalgam Exposure	Urinary Mercury (ug/L; ug/g creat)	Reported Effects
Heyer et al., 2006. Toxicol. Lett. 161:159-166. A cascade analysis of the interaction of mercury and coproporphyrinogen oxidase (CPOX) polymorphism on the heme biosynthetic pathway and porphyrin production.	Exposure to amalgams Hg^0 used in dental occupation. Dentists n = 80; Hygienists n = 98. Adult males and females. No non-dental practitioner controls.		Dentists: 1.9 ± 1.8 µg/L Hygienists: 1.4 ± 1.6 µg/L Appears that individual U-Hg levels > 10 µg/g Cr have not been used.	Similar article to Woods et al., 2005 but has a better explanation of how Hg^0 interacts with CPOX4 to alter heme metabolism. Plausibility of hypothesis not evident, i.e., why CPOX gene interaction with Hg^0 should affect sensation and motor control.
Woods et al., 2005. Tox. Appl. Pharm. 206:113-120. The association between genetic polymorphisms of coproporphyrinogen oxidase and an atypical porphyrinogenic response to mercury exposure in humans.	Exposure to amalgams Hg^0 used in dental occupation. Dentists n = 252; Hygienists n = 230 Male and females. No non-dental practitioner controls.		Dentists and Hygienists: 2.32 ± 1.5 µg/ g Cr	Differences in heme pathway intermediates/products and the CPOX isoform in 15% of all people that may dispose these people to reduced heme synthesis capacity. Weak support for the possibility that isoforms of CPOX or BDNF may predispose humans to Hg^0 toxicity. Association observed in a subpopulation of dentists with very high mercury levels (>20 µg/g Cr. No neurotoxicity test information listed for the subjects in this manuscript.

Article	Exposure Scenario	Amalgam Exposure	Urinary Mercury (ug/L; ug/g creat)	Reported Effects
Davis et al., 2001. Tox. Sci. 59:291-296. Mercury vapor and female reproductive toxicity.	Nose-only Hg vapor in rats (0; 1, 2 or 4 mg/m^3) - 2hr/day for 11 days; cycling rats ~Gestation Day 80-90; dose Response and time course.	N/A	Total U-Hg reported as ng/g over 11 days of exposure: @ $1mg/m^3$, range = 3.2 to 19.1; @ 2 mg/m^3, range = 12.1 – 52.7; @4 mg/m^3 = 41-841.6; controls were 0.44 ng/g Urine.	No significant effect on pregnancy rate, implantation sites, estrous cycles slightly prolonged in the 2 higher dose groups. Kidney levels were 20-60X brain levels with no histological evidence of toxicity in kidney. Strengths: some dose-response with effects; inhalation of elemental mercury; nose-only exposures; relevant endpoints. Weaknesses: rodent model; acute, urines collected immediately after exposures so real 24-hr levels are not known; high doses (maternal toxicity at high doses).
Morgan et al., 2002. Tox. Sci. 66:261-273. Disposition of inhaled mercury vapor in pregnant rats: Maternal toxicity and effects on developmental outcome.	Elemental Hg vapor in pregnant rats; Doses were 0, 1, 2, 4 or 8 mg Hg/m^3 for 2 hr/day from gestation days 6-15.	NA	Hg levels in tissues such as brain, liver, kidney increased in proportion to exposure concentration a and number of days in both maternal animals and offspring. When were assessments made? At what PND? For Maternal and fetuses/offspring. Also, please list actual values.	Adverse effects on developmental outcome (increased resorptions; decreased litter size and pup body weights) occurred only at exposure levels of 8 mg/m^3, which also caused maternal toxicity. Maternal body weight decreased and maternal kidney weight increased at 4 and 8 mg/m^3. Urinary biomarkers elevated. Hg crossed the placenta and rate of elimination was higher in maternal tissue compare to fetal and especially when compared in the brain. Exposures are much higher than dental amalgam exposures.

Article	Exposure Scenario	Amalgam Exposure	Urinary Mercury (ug/L; ug/g creat)	Reported Effects
Herr et al., 2004. Tox. Sci. 82:193-206. Evaluation of sensory evoked potentials in Long Evans rats gestationally exposed to mercury (Hg^0) vapor.	Prenatal in utero exposure study in rats. Pregnant dams exposed to 0 or 4 mg/m^3 Hg^0 2hr/day from gestational days 6-15. Offspring evaluated at postnatal days 140 - 168.	NA	Brain Hg levels - No data reported but exposure identical to similar study where authors reported reported 0.02 ug/g brain at postnatal day 1. (Morgan et al., 2002).	Maternal weight decreased 7% during Hg vapor exposure but offspring weight not affected at 6 months. No changes in peripheral nerve action potentials, nerver conduction velocity, and evoked responses from somatosensory (cortical, cerebellar), brainstem auditory and visual flash modalities.
Yoshida et al., 2004. Tox. Sci. 80:69-73. Susceptibility of metallothionein-null mice to the behavioral alterations caused by exposure to mercury vapor at human-relevant concentration.	Adult mice exposed to 0.06 mg/m^3 of Hg^0 for 8 hr/day for 12 or 23 weeks. Metallothionein gene knock-out mice vs wild type.	NA	Brain Hg levels: Metallothionein KO- 0.66 ± 0.08 µg Hg/g brain Wild type- 0.97 ± 0.07 µg Hg/g brain	Brain Hg levels in the KO mice are <u>less</u> than the wild type. Authors report that KO mice had a higher open field activity and poorer performance in the passive avoidance test, but appears like there may not have been any effect at all.

Article	Exposure Scenario	Amalgam Exposure	Urinary Mercury (ug/L; ug/g creat)	Reported Effects
Yoshida et al., 2006. Toxicol. Lett. 161:210-218. Behavioral changes in metallothionein-null mice after the cessation of long-term, low-level exposure to mercury vapor.	Adult mice exposed to 0.055 mg/m^3 Hg^0 for 24 hr/day for 29 weeks. Evaluations occurred 12 weeks cessation of exposure.	NA	Brain Hg levels At 29 weeks: Metallothionein KO- 0.84 ± 0.04 µg Hg/g brain Wild type- 1.75 ± 0.34 µg Hg/g brain 37 wks (12 wks after exposure ceased): Metallothionein KO- 0.04 ± 0.01 µg Hg/g brain Wild type- 0.10 ± 0.01 µg Hg/g brain	Brain Hg levels in the KO mice are <u>less</u> than the wild type. For both times. At 12 weeks after the end of Hg exposure, no effect on Morris Water Maze performance, passive avoidance and locomotor activity. Authors report KO mice had a higher open field activity at 12 weeks but not apparent in analyses. Very weak effects at best.

[1]Conversion calculations for urinary mercury concentrations:

To convert from **nmol Hg/mmol creatinine** to **ug Hg/g creatinine**, multiply by 1.77.
(Based on 200.6 ug Hg/umol Hg and 113 ug creatinine/umol creatinine.)
To convert from **ug Hg/g creatinine** to **ug Hg/L urine**, multiply by 1.3.
(Based on mid-range of normal human urinary creatinine ~1.3 g creatinine/L urine.)