

Table 6. Effects on the metabolism and distribution of methyl mercury: foods and macronutrients.

Nutrient	MeHg exposure	Nutrient dose	Animal model	Duration of experiment	Effects	Ref.
Protective effects						
ADP	10 or 50 nmol MeHgCl/g bw (i.p. injection)	ADP, 250 μM, 1-hr incubation	Mouse, <i>in vitro</i> rabbit lysate translation system	12 hr	Decreased elevation of mitochondrial protein synthesis	(100)
Cysteine	1–100 μM MeHg, 24 hr	0.8 mg Cys/mL, 24 hr	<i>In vitro</i> mouse neuron culture	24 hr	Blocked neurotoxicity	(145)
Cysteine	5–50 μM MeHgCl	Cys, 12-min preincubation 0.2–2 mM	<i>In vitro</i> human placental syncytiotrophoblast	90 min	Partially blocked inhibition of carnitine acyltransferase	(108)
Cysteine	0.95 μg Hg/g shark muscle	Cys, 0.5%	<i>In vitro</i> shark muscle	1–24 hr	Decreased Hg concentration but efficiency was not high enough to make process efficient	(176)
Cystine	25 ppm MeHg in diet	0.4% cystine in diet	Rat	10 wk	Prevented increase in SGPT and SGOT levels	(177)
Cystine	15–25 ppm MeHgCl in diet <i>ad libitum</i>	0.4% L-cystine in diet <i>ad libitum</i>	Rat	6–10 wk	Increased weight gain; slightly decreased kidney Hg; no effect on survival	(70)
Cystine	10 ppm MeHgCl in diet	0.3% cystine in diet	Japanese quail	16 wk	Improved egg production; no effect on survival	(71)
Fish protein	15–25 ppm MeHgCl in diet	10–20% fish protein in diet, <i>ad libitum</i> vs casein diet	Rat	6–10 wk	Improved weight gain and survival	(70)
Fish protein	Organic Hg, oral and parenteral dose (dose NA)	High fish protein vs low fish protein or caseinate diet	Mouse	NA	Reduced whole-body retention of Hg; oral dose increased liver deposition; no effect on relative organ distribution	(174)
γ-Linolenic acid	MeHgCl, 10 ⁻⁵ to 10 ⁻⁷ M	10 ⁻⁹ M γ-linolenic acid	<i>In vitro</i> human lymphocytes	72 hr	Reduced sister chromatid exchange	(75)
Garlic	4 ppm MeHgCl in drinking water	1.7–6.7% raw garlic in diet, p.o.	Rat	12 wk	Decreased brain, kidney levels of Hg; high level of garlic decreased severity of histologic damage	(73)
Glucose	MeHg–GSH 1 mmol MeHg/L packed erythrocytes	2 mM D-Glucose	<i>In vitro</i> rat erythrocytes	30 min	Inhibited MeHg uptake; MeHg uptake might use the passive D-glucose transport system	(93)
Glutathione	4 μM MeHgCl	0.6 mM GSH	<i>In vitro</i> rat hepatocytes	240 min	Reduced cellular uptake of MeHg from medium	(74)
Glutathione	1 mg/kg/d or 10 mg MeHgCl (i.m. injection, 0–7 d)	100 or 150 mg GSH/kg bw/d (i.m. injection, 7–14 d)	Rat	15 d	Allowed recovery of cholesterol concentration and duration-dependent recovery of triglyceride concentrations in areas of the CNS (cerebral hemisphere, cerebellum, medulla oblongata, spinal cord)	(102)
Glutathione	4 μmol MeHgCl/kg bw (single i.v. injection)	8 μmol Cys/kg bw (single i.v. injection pre-mixed with Hg)	Rat	4 hr	Increased uptake of Hg in kidney and decreased liver and blood content	(74)
High-protein diet	40 μmol/kg bw (injection)	24.8% protein diet	Mouse	16 d	Mice survived	(89)
Isoleucine	10 μmol MeHgCl (injection, with 100 μmol Cys/rat)	20 μmol L-isoleucine, (i.v. injection)	Rat	2 hr	Isoleucine inhibited the effect of L-Cys on increased brain uptake of MeHg	(178)
Leucine	50 μmol MeHgCl/hr for 1 hr (at 24, 48, and 72 hr) (continuous infusion to external jugular vein)	0.1 mmol L-leucine/hr, (continuous infusion to external jugular vein) 4 d	Rat (pregnant)	92 hr	Inhibited brain uptake of Hg in nonpregnant rats; did not alter Hg distribution between pregnant or nonpregnant rats	(76)
Low molecular weight thiols	1–50 μmol MeHgCl (i.v. injection)	Low molecular weight thiols (i.v. injection, equimolar, simultaneous)	Rat	60 min	Increased short-term accumulation of MeHg in liver, kidneys, cerebrum; decreased Hg in plasma	(101)
Marine mammal meat; Se	17.5 ppm MeHgCl in diet, in either seabastes or sperm whale meat	Marine mammal meat Se, 0.3–0.6 ppm in diet (either seabastes or sperm whale meat or sodium selenite)	Rat	12 wk	Sebastes meat protected growth (to an extent similar to selenite) and delayed neurologic signs (tail rotation, paralysis of hind limbs) for 7 wk (more protection than selenite); sperm whale meat was less effective; Se in organs was positively correlated with neurologic protection	(179)
Monothiols (glutathione, N-acetyl-DL-homocysteine thiolactone)	1 mg MeHgCl/kg bw/d (s.c. injection)	Monothiols (50 mg GSH/kg bw and 40 mg N-acetyl-DL-homocysteine thiolactone/kg bw)	Mouse	15 d	α-gal and β-gal activities recovered toward normal in brain and spinal cord; GSH recovered α-gal in liver and testes and β-gal in kidney and testes	(180)

(Continued)

Table 6. Continued.

Nutrient	MeHg exposure	Nutrient dose	Animal model	Duration of experiment	Effects	Ref.
Monothiol (glutathione)	1 mg MeHgCl/kg/d for 7 d (s.c. injection)	50 mg GSH/kg s.c. injection (for 7 d) after the 7 d MeHg treatment	Mouse	14 d	Showed recovery of α - and β -glucosidases activities enzymes in the CNS	(103)
Monothiol (glutathione, <i>N</i> -acetyl-DL-homocysteine)	1 mg MeHg/kg bw/d (7 d) s.c. injection	40 mg <i>N</i> -acetyl-DL-homocysteine thiolactone/kg bw, 50 mg GSH/kg bw for 7 d (8–14 d after Hg exposure)	Mouse	14 d	Mobilized Hg from all tissues except brain; decrease in Na, K, Mg, Mn, Cu, Zn, Cr, and Ni for most organs was restored toward normal, but recovery was not complete; decreased kidney Fe	(127)
<i>N</i> -acetyl-DL-homocysteine	1 or 10 mg MeHgCl mg/kg bw/d (i.m. injection, 0–7 d)	40 or 80 mg <i>N</i> -acetyl-DL-homocysteine/kg bw/d or 80 mg/kg bw, i.m. injection, 7–14 d	Rat	15 d	Allowed recovery of cholesterol and duration-dependent recovery of triglycerides in the CNS (cerebral hemisphere, cerebellum, medulla oblongata, spinal cord)	(102)
Ringed seal liver	About 3% of Hg was organic; equivalent to about 0.25 mg Hg/kg bw/d	Ringed seal liver vs MeHg-supplemented beef liver	Cat	90 d	Seal liver group had no neurologic symptoms; cats fed MeHg-supplemented beef liver developed neurologic symptoms of toxicity (convulsions, hind limb weakness); elevated brain levels of Hg in supplemented beef liver group	(181)
Shark flesh	0.02–2.0 ppm in diet from shark flesh	0.01–0.46 ppm Se in diet from shark flesh	Rat	56 d	Increased GSH–peroxidase in brain and liver with Se supplementation up to 0.3 ppm; no effect on ornithine transcarbamylase activity; fish diet yielded higher GSH-peroxidase activities than yeast diet with equivalent Se as selenite	(182)
Soy protein	Organic Hg, oral and parenteral dose	High-soy protein vs caseinate or low-soy protein	Mouse	NA	Reduction in whole-body retention of Hg; relative organ distribution not affected; oral dose increased liver deposition	(174)
Succinate	10 or 50 nmol MeHgCl/g bw (single i.p. injection)	150 μ M succinate, 1 hr incubation	Mouse	12 hr	Decreased elevated mitochondrial protein synthesis	(100)
Sulfur amino acids in low protein diet	20 μ mol MeHg/kg bw orally (24 hr before death)	7.5% protein diet vs 24.8% protein diet plus 0.03% cysteine in diet and 1.1% methionine in diet, 5 d	Mouse	5 d	Increased Hg uptake to brain and liver more than low-protein diet; increased urinary Hg over normal-protein diet; decreased Hg in kidney, blood, and plasma	(69)
Synthetic liquid diet (high protein, low fat)	0.6 mg MeHgCl/kg bw, single dose, p.o.	Synthetic diet (high protein, low fat) <i>ad libitum</i> vs milk or pellet diet	Mouse	2 wk	Lowered Hg concentration in blood, brain, liver, kidneys; increased percent Hg ²⁺ compared to mice on milk diet or pellet rodent diet; Hg ²⁺ body burden was higher than rodent pellet diet; Hg burden of the gut was highest in the cecum	(88)
Tuna fish	MeHg (from tuna fish, 17% of diet)	17% tuna diet vs corn soya diet	Japanese quail	6 wk	Decreased MeHg toxicity and prolonged survival; decreased incoordination, mortality, growth inhibition	(183)
Wheat bran	5.0 mg Hg/kg bw (single dose, p.o., as MeHgCl)	5, 15, 30% wheat bran in diet compared to fiber-free diet	Mouse	104 d	Decreased Hg in blood, brain, small intestine with 30% diet; Hg elimination affected by dietary bran may reduce neurotoxic effects	(78)
Enhanced toxicity						
Cellulose	5.0 mg MeHgCl/kg bw, single dose, p.o.	5% cellulose in diet compared to fiber-free diet	Mouse	104 d	Increased Hg retention; did not alter percentage inorganic Hg	(78)
Chemically defined liquid diet	0.46 mg MeHgCl/kg bw, single dose, p.o.	GIBCO 116 EC <i>ad libitum</i> vs pellet rodent diet	Mouse	14 d	Organ Hg levels were increased	(85)
Coconut oil	5 μ mol MeHgCl/kg bw (single oral dose after 3 wk)	Coconut oil, 5–50% of energy vs cod liver oil diet	Mice	5 wk	Increased whole-body, liver, and kidney retention of Hg; 50% diet decreased retention in liver and kidney	(111)
Cysteine	10 μ mol MeHgCl, injection	100 μ mol L-Cys, injection	Rat	1 hr	Increased brain uptake of MeHg	(178)
Cysteine	4 μ M MeHgCl	0.08–0.8 mmol Cys	<i>In vitro</i> rat hepatocytes	240 min	Increased cellular uptake of MeHg from medium	(74)
Cysteine	0.05 mM MeHgCl, intracarotid injection	0.1 mmol L-Cys (simultaneous intracarotid injection)	Rat	15 s	Increased brain Hg uptake	(82)
Cysteine	4 μ mol MeHgCl/kg bw (single i.v. injection)	Cys, 8 μ mol/kg bw (single i.v. injection premixed with Hg)	Rat	4 hr	Increased uptake of Hg in kidney but decreased liver and blood content	(74)

(Continued)

Table 6. Continued.

Nutrient	MeHg exposure	Nutrient dose	Animal model	Duration of experiment	Effects	Ref.
Cysteine	50 μmol MeHgCl/hr for 1 hr (at 24, 48 and 72 hr), continuous infusion to external jugular vein	0.1 mmol L-Cys/hr (continuous infusion to external jugular vein), 4 d	Rat (pregnant, 17 d, vs non-pregnant)	92 hr	Increased brain Hg in both types of rat; did not alter Hg distribution between pregnant and nonpregnant states	(76)
Cysteine	MeHg-GSH, 1 mmol MeHg/L packed erythrocytes	Cysteine	Rat	30 min	Increased MeHg uptake; MeHg uptake might use the Cys-facilitated transport system	(93)
Ethanol	MeHg (dose NA)	Ethanol (dose NA)	Mouse	NA	Potentiated toxicity and mortality	(184)
Ethanol	MeHg (dose NA)	Ethanol (dose NA)	Human	NA	Associated with increased mortality from liver cancer, chronic liver disease, and cirrhosis among Minamata disease patients	(38)
Ethanol	1.5 mg MeHg/kg bw/d or 1.5 mg/d for 45 d (oral gavage)	2.0 g ethanol/kg bw/d, 45 d	Rat	NA	Increased renal weight; caused oliguria and increased blood urea nitrogen levels; impaired kidney function; decreased glucose in urine	(185)
Ethanol	5 mg MeHgCl/kg bw/d (10 consecutive days after d 7)	2.5–10% ethanol in drinking water	Rat	50 d	Increased mortality; potentiated neurologic manifestations; increased Hg in kidney and brain	(186)
Ethanol	2.5 mg MeHgCl/kg bw (s.c. injection)	50% ethanol (s.c. injection, 0.1 mL/200 g bw)	Rat	44 d	Decreased body weight; increased severity of hindlimb ataxia	(187)
Ethanol	0.5 mg MeHgCl/kg bw/d	8 g ethanol/kg bw/d, orally	Rat	14 wk	Decreased renal γ -glutamyltransferase; no effect on the distribution of MeHg and its inorganic metabolites or GSH in brain and kidney	(188)
Ethanol	1–2.5 mg MeHgCl/kg bw in water	5.0 mL/kg bw of 25% ethanol	Rat	7 wk	Increased Hg in kidney but not brain and blood levels; lowered activity of aspartate amino transferase and increased creatine phosphokinase; increased kidney pathology; no effect on percentage inorganic Hg; no effect on neurotoxicity (ataxia, tail rotation, convulsion)	(79)
Glutamate	0.5–10 μM MeHg	100 μM glutamate, 4 or 8 min	<i>In vitro</i> (mouse astrocytes)	60 min	Hg inhibited amino acid uptake in astrocytes	(189)
Glutamate	0–10 μM MeHgCl	100 mM glutamate	<i>In vitro</i> mouse neonate astrocytes	14 min	Uptake of glutamate is inhibited in the presence of Ca^{2+}	(83)
High-protein diet	80 μmol MeHgCl/kg, injection	24.8% protein diet	Mouse	16 d	Killed mice within 16 d despite lower brain Hg than mice with a low-protein diet fed at a higher mercury dose; susceptibility to Hg was higher in normal-protein fed rats than low-protein-fed rats	(89)
High-protein diet	120 μmol MeHgCl/kg bw, injection	24.8% protein diet	Mouse	7 d	Killed mice within 7 d; plasma aspartate amino transferase and alanine amino transferase were higher than in low-protein group	(89)
Linoleic acid	15 ppm MeHgCl, in diet	1–3% linoleic acid in diet (remainder of fat was lard)	Japanese quail	15 d	Increased mortality as percentage linoleic acid increased in birds not receiving linoleic acid diets from hatching	(84)
Low-protein diet	20 μmol MeHg/kg, bw, orally (on d 0)	7.5% protein diet vs 24.8% protein diet	Mouse	7d	Increased Hg in brain, kidney, blood, and plasma	(87)
Low-protein diet	80 μmol MeHg/kg bw, orally	7.5% protein diet	Mouse	16 d	All mice died within 16 d but died earlier than mice with low-protein diets	(89)
Low-protein diet	120 μmol MeHg/kg bw, orally	7.5% protein diet	Mouse	7 d	Killed mice within 7 d	(89)
Low-protein diet	20 μmol MeHg/kg bw, orally (24 hr before death)	7.5% protein diet vs 24.8% protein diet, 5 d	Mouse	5 d	Increased Hg uptake to brain compared to mice on normal protein diets	(69)
Methionine	MeHg-GSH, 1 mmol MeHg/L packed erythrocytes	DL-Met	Rat erythrocytes	30 min	Stimulated MeHg uptake	(93)
Methionine	4 μM MeHgCl	0.6 mM GSH	<i>In vitro</i> rat hepatocytes	240 min	Increased cellular uptake of MeHg from medium	(74)
Milk	0.6 mg MeHgCl/kg bw, single dose, p.o.)	Evaporated whole milk, <i>ad libitum</i> vs rodent pellet diet	Mouse	2 wk	Increased Hg body burden; decreased percentage Hg^{2+} ; burden in gut was small intestine > cecum > colon; Hg retention in blood, brain, liver, kidneys was increased	(88)

(Continued)

Table 6. Continued.

Nutrient	MeHg exposure	Nutrient dose	Animal model	Duration of experiment	Effects	Ref.
Milk	0.46 mg MeHgCl/kg bw, single dose p.o.	Evaporated whole milk diet <i>ad libitum</i> vs pellet rodent diet	Mouse	14 d	Increased Hg in whole body, brain, kidney, liver	(85)
Pectin	5.0 mg Hg/kg bw, single dose as MeHgCl	5% pectin in diet compared to fiber-free diet	Mouse	104 d	Increased percentage inorganic Hg in liver and brain	(78)
Soya oil	5 µM MeHgCl/kg bw, single oral dose after 3 wk	Soya oil, 20% of energy	Mouse	5 wk	Increased carcass Hg compared to cod liver oil diet; did not affect Hg in liver; decreased kidney Hg	(111)
Other effects						
Aspartate	0.05 mM MeHgCl (intracarotid injection)	0.1 mM L-Cysteine-L-aspartic acid (simultaneous intracarotid injection)	Rat	15 sec	No effect on Hg uptake across the blood-brain barrier	(82)
ATP	MeHg-GSH 1 mmol MeHg/L centrifuged erythrocytes	ATP	Rat	30 min	No effect on MeHg uptake (tests the active transport system)	(93)
Cholesterol	5 × 10 ⁻⁴ M MeHgCl, in buffer	NA	<i>In vitro</i>	NA	No effect on the flux of Hg across lipid membrane	(190)
Cod liver oil	5 µmol MeHgCl/kg bw (single oral dose after 3 wk)	Cod liver oil, 5-50% of energy	Mice	5 wk	No effect on whole-body retention of Hg; Hg retention was lower than with coconut oil diet	(111)
Cysteine	0.5 mg mercury cysteinide/kg bw (i.v. injection)	0.5 mg mercury cysteinide/kg bw (i.v. injection)	Mouse	14 d	No effect on distribution and excretion when compared to inorganic Hg	(191)
Cysteine	0.05 mM 0.5 mL MeHgCl (intracarotid injection)	0.1 mM D-Cys (simultaneous intracarotid injection, 0.5 mL)	Rat	15 sec	No effect on the rate of MeHg uptake in brain	(82)
Fiber	MeHgCl, oral, dose NA	Cellulose, pectin, oat, corn soy fiber, dose NA	Mouse	NA	No effect on whole-body Hg retention	(174)
Glutamate	10 µmol MeHgCl (i.v. injection, with 100 µmol Cys, 2 mL)	L-Glu 200 µmol (i.v. injection, 2 mL)	Rat	2 hr	No effect on brain Hg content	(178)
Glycine	4 µM MeHgCl	NA	<i>In vitro</i> rat hepatocytes	240 min	No effect	(74)
Glycine	MeHg-GSH 1 mmol MeHg/L centrifuged erythrocytes	Glycine	Rat erythrocytes	30 min	No effect on MeHg uptake; system glycine is not involved in MeHg uptake	(93)
Histidine	4 µM MeHgCl, i.v. injection	NA	<i>In vitro</i> rat hepatocytes	240 min	No effect	(74)
Kynurenine	MeHg 0.1-10 µM, 10 min	30 µM kynurenine, 2 min	<i>In vitro</i> mouse astrocytes	60 min	Hg inhibited amino acid uptake in astrocytes	(189)
Lysine	10 µmol MeHgCl (i.v. injection, with 100 µmol Cys 2 mL)	200 µmol L-Lysine, i.v. injection	Rat	2 hr	No effect on brain Hg content	(178)
Methionine	0.5-1.5 mg MeHgCl/kg bw/d oral gavage)	Met, 60, 100, 140% of sulfur amino acid requirement	Rat	5 wk	Serum thromboxane B ₂ was affected; Met deficiency caused increase in serum prostaglandin E ₁	(192)
Phenylalanine	10 µmol MeHgCl (i.v. injection, with 100 µmol Cys, 2 mL)	200 µmol L-Phenylalanine (i.v. injection)	Rat	2-12 hr	Phe inhibited the effect of L-Cys on increased brain uptake of MeHg	(178)
Seafood	121 nmol Hg/L in cord blood	Frequent whale meat dinners during pregnancy	Human	Birth cohort	Frequent ingestion of whale meat was associated with higher Hg in cord blood; blood Hg was correlated with blood Se	(32)
Soluble proteins	40 µM MeHgOH, aqueous	Soluble proteins 24 mg/mL protein, 1.4 mmol thiol groups, 1.5 mmol nonprotein thiol groups, in buffer	<i>In vitro</i> rat liver	1 hr	No effect on degradation of MeHg	(193)
Tannins	10-1,000 ppm Hg	Tree bark	<i>In vitro</i>		Tree barks were used in decontamination of industrial waste	(194)

Abbreviations: ADP, adenosine diphosphate; CNS, central nervous system; gal, galactosidase; i.m., intramuscular; i.p., intraperitoneal; i.v., intravenous; p.o., per os; s.c., subcutaneous, SGOT, serum glutamic-oxaloacetic transaminase; SGPT, serum glutamic-pyruvic transaminase.