Many studies have found that mercury (Hg) exposure is associated with selenium (Se) accumulation in vivo. However, human studies are limited. To study the interaction between Se and Hg, we investigated the total Se and Hg concentrations in body fluids and serum Se-containing proteins in individuals exposed to high concentrations of Hg. Our objective was to elucidate the possible roles of serum Se and selenoproteins in transporting and binding Hg in human populations. We collected data from 72 subjects: 35 had very low Hg exposure as evidenced by mean Hg concentrations of 0.91 and 1.25 ng/mL measured in serum and urine, respectively; 37 had high exposure (mean Hg concentrations of 38.5 and 86.8 ng/mL measured in serum and urine, respectively). An association between Se and Hg was found in urine (r = 0.625; p < 0.001) but not in serum. Hg exposure may affect Se concentrations and selenoprotein distribution in human serum. Expression of both selenoprotein P and glutathione peroxidase (GSH-Px) was greatly increased in Hg miners. These increases were accompanied by elevated Se concentrations in serum. In addition, selenoprotein P bound more Hg at higher Hg exposure concentrations. Biochemical observations revealed that both GSH-Px activity and malondialdehyde concentrations increased in serum of the Hg-exposed group. This study aids in the understanding of the interaction between Se and Hg, and selenoproteins play two important roles in protecting against Hg toxicity. First, they may bind more Hg through their highly reactive selenol group, and second, their antioxidative properties help eliminate the reactive oxygen species induced by Hg in vivo.

Key words: antagonism, Hg-exposed subjects, mercury, selenium, selenoproteins, serum. Environ Health Perspect 114:297–301 (2006). doi:10.1289/ehp.7861 available via http://dx.doi.org/ [Online 18 January 2006]

Mercury (Hg) is currently one of the most prevalent pollutants in the environment. It is highly bioconcentrated through the food chain and damages mainly nerves and immune systems. It is harmful both to humans and animals (Clarkson 1997).

Selenium (Se) is an essential micronutrient with important biological and biochemical functions in organisms because of its unique antioxidant properties and its ability to regulate thyroid gland metabolism. It is well known that Se is an antagonist that moderates the toxic effects of many heavy metals such as arsenic, cadmium, Hg, and lead in organisms. Although Se and Hg co-accumulate in humans and other mammals is well known (Fahnoga et al. 2000; Kosta et al. 1975), the mechanism of interaction between Se and Hg is still not understood. It is thought to be attributed to the formation of biologically inert Hg–Se compounds. Burk et al. (1974) suggested that the Hg–Se–protein complex plays a role in restraining the acute toxicity of inorganic Hg by binding Hg to prevent it from reaching the target tissues. Recent in vitro studies suggest that Se and Hg could form Hg–Se complexes in a reducing environment and that this 1:1 complex is then bound with plasma selenoprotein P (SeP) (Suzuki et al. 1998; Yoneda and Suzuki 1997).

In mammalian serum, Se is incorporated mainly into three proteins—SeP, extracellular glutathione peroxidase (GSH-Px), and albumin. The first two are well-known selenoproteins. Naturally occurring selenoproteins such as thioredoxin reductases, GSH-Px, SeP, iodothyronine deiodinase types I, II, and III, and others with specific functions have also been identified (Kryukov et al. 2003). Among them, SeP is a unique selenoprotein and contains several selenocysteine (Sec) and cysteine (Cys) residues, indicating that it is capable of transporting Se and binding heavy metals. The sequence of the cloned DNA shows that SeP contains 10 Sec groups encoded by UGA stop codons in the open reading frame of its mRNA (Burk et al. 2001; Ma et al. 2002). But purified SeP from humans and rats was recently characterized by immunofinity chromatography and was found to contain 7–8 Se atoms per Sec molecule as Se attached to a Cys base. On the basis of both in vitro studies (Suzuki et al. 1998), it has been suggested that Se exhibits protective effects against Hg toxicity in humans because of formation of an Hg–Se complex bound to SeP in blood; however, this has not been demonstrated in vivo in human populations.

Thus, our aim in this study was to evaluate the relationship between Se or selenoproteins and Hg exposure in humans. First, we compared Se and Hg concentrations in serum and urine from highly Hg-exposed and control subjects to determine whether Hg exposure affects the distribution and absorption of Se. Second, we investigated the role of plasma selenoproteins in transporting or accumulating Hg, and finally, oxidative stress as evidenced by malondialdehyde (MDA) concentration and GSH-Px activity in the Hg-exposed population. We also attempted to elucidate the antagonism between Hg and Se.

Materials and Methods

Collection of samples. We selected subjects from the town of Wanshan in the Guizhou Province in southwest China, which is representative of an Hg-contaminated region. Present global Hg emission into the atmosphere is estimated to be 5,000 tonnes per year (Chen et al. 2005). The environment polluted by Hg in Guizhou Province is typical of other areas in China, where Hg comes from several sources: Hg mining and ore processing, coal combustion for power production, and chloralkali industries. The main source of environmental Hg pollution in Wanshan is the emission of elemental Hg vapor from an Hg-mining plant that had produced large quantities of Hg for more than 50 years. The plant was closed in 2001.

In 2000 and 2003, serum and urine samples were collected from 37 individuals (including 25 miners and 12 local residents) from a heavily Hg-contaminated area. These individuals are the exposed group. Samples were also collected from 35 residents from a noncontaminated area. These individuals form the control group. Between the groups there were no differences in sex, age (28–66 years of age), body mass index, and physical activity. All participants volunteered and agreed to the test. This study was approved and supported by the local Committee of Human Subjects.

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and the local hospital. Detailed handling of samples was performed as described elsewhere (Chen et al. 2005).

**Chemicals and equipment.** Reagents and solvents were at least of analytical grade. The Milli-Q system (Millipore, Bedford, MA, USA) was used to prepare ultrapure water. We used a dual-channel hydride generation-atomic fluorescence spectrometer (HG-AFS) with a quartz furnace atomizer (model AFS-820; Beijing Little Swan Co., Beijing, China) to determine Hg and Se concentrations.

**Measurement of Hg exposure.** Total Hg concentrations in urine and serum samples were determined by HG-AFS. Detailed procedures have been described elsewhere using a sodium tetrahydridoborate (NaBH₄)-acid system to generate Hg vapor for AFS (Zhao et al. 2004). The detection limit was 0.05 μg/L Hg. Hg-certified NIST (National Institute of Standards and Technology, Gaithersburg, MD, USA) bovine liver 1577a, IAEA horse kidney H-8 (International Agency Atomic Energy Agency, Vienna, Austria), and Chinese bovine liver GBW 080193 (National Research Center for Certified Reference Materials, Beijing, China) were analyzed for Hg as quality control standards, with analytical errors less than ±10%.

**Determination of Se concentration.** We measured Se using HG-AFS according to detailed procedures described elsewhere (Chen et al. 1999). Briefly, samples were digested with a mixture of ultrapure nitric acid and perchloric acid (3:1) at 100°C for 2–3 hr. One milliliter of 5 mol/L HCl was added to the clear digested sample solution for an additional 10 min to reduce the existing selenate(VI) to selenite(IV). The solutions were then diluted to 15 mL, introduced into a NaBH₄-acid system to generate hydrogen selenide, and subjected to HG-AFS. Quality control standards were analyzed as described in “Measurement of Hg exposure.”

**Assay of GSH-Px activity and MDA.** GSH-Px activity was measured according to the method of Hafeman et al. (1974). One unit was defined as a decrease of the reduced GSH (GSH-Px) activity was measured according to Bradford method using bovine serum albumin as a standard protein (Bradford 1976). We used the MDA-thiobarbituric acid (TBA) assay, which is used widely in studies of lipid peroxidation (Dahle et al. 1962). Serum (0.5 mL) from each subject was mixed with 1 mL of 10% (wt/vol) trichloroacetic acid, 0.8 mL distilled water, and 1 mL of 0.5% (wt/vol) TBA. After vigorous stirring, mixtures were incubated for 60 min in boiling water. After centrifugation at 6,000g for 15 min, absorbance of the supernatant at 532 nm was measured and corrected for unspecified turbidity by subtracting the absorbance at 580 nm. The blank was corrected by addition of 0.5% TBA solution in 10% trichloroacetic acid. We estimated the MDA concentration of each sample using a five-point standard curve with 1,1,3,3-tetraethoxypropane as an MDA standard.

**Separation of Se-containing proteins.** We separated Se-containing proteins using conventional chromatographic purification methods as described elsewhere (Deagen et al. 1993; Harrison et al. 1996; Mostert et al. 1998) with slight modification. Briefly, Se-containing proteins were purified using a tandem column system of two affinity chromatographic procedures. Serum (4 mL) was diluted with 4 mL equilibrium buffer of 0.02 mol/L ammonium acetate (pH 6.8), which was applied to a heparin-Sepharose column (1.0 × 10 cm²; Pharmacia, Uppsala, Sweden). The eluate was continuously passed through a blue-Sepharose column (1.0 × 10 cm²; Pharmacia). The eluate from the blue-Sepharose column contained the GSH-Px and was labeled fraction C. The fraction containing SeP (fraction A) was eluted from the heparin-Sepharose column with 500 U/mL heparin in equilibrium buffer. The fraction containing albumin (fraction B) was eluted from the blue-Sepharose column with 1.4 mol/L NaCl in equilibrium buffer at a flow rate of 0.5 mL/min. Protein profiles were monitored at 280 nm. Se and Hg concentrations in these three fractions and control buffer were determined by HG-AFS. Each fraction was then separated using sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) as described elsewhere (Gao et al. 2003; Laemmli 1970).

**Results and Discussion**

**Se and Hg in blood and urine.** Se and Hg concentrations in serum and urine samples analyzed by HG-AFS are shown in Table 1. The mean Hg concentration in serum of the exposed group was almost 40 times that of the control group, which was in agreement with the average background concentration of Hg. In urine of the exposed group, the mean Hg concentration was almost 75 times that of the control group. Among the exposed group, Hg concentrations in 12 subjects were extremely high, ranging from 67.5 to 210.3 ng/mL in serum and from 87.2 to 205.2 ng/mL in urine. The miners suffered typical symptoms: digestion dysfunction, hypomnesia, sleeping problems, tremor, and weight loss.

Although serum Se concentrations were significantly higher in the Hg-exposed group, the Se concentration in urine was only slightly higher and without statistical significance (Table 1). The molar ratio of Se to Hg was close to 1. The difference in the molar ratio between serum and urine concentrations of the Hg-exposed subjects was much greater than that in the control group. These results suggest that retention of Se increased in Hg-exposed individuals.

Total Hg concentrations in blood and hair are indicators of inhalation exposure to inorganic and methyl Hg vapor. In this study, we determined that exposure of local people and miners to Hg is due to not only inhalation of elemental Hg vapor but also to consumption of Hg-contaminated foodstuffs, which contained different Hg species. Even though the major source of Hg is elemental Hg, active transformation of inorganic Hg to organic Hg species (methyl Hg) was observed in water, sediment, and soil (Horvat et al. 2003). The average background concentration of Hg in urine has often been reported to be about 4 ng/mL in the general population, with an upper limit of about 20 μg/L (Agency for Toxic Substances and Disease Registry 1999; Iyengar and Woittiez 1988; Tsuji et al. 2003; World Health Organization 1990, 1991), whereas the normal range in serum is 1–8 ng/mL (Brune et al. 1991). The geometric mean concentrations of total blood Hg for women 16–49 years of age and children
1–5 years of age are 1.2 and 0.3 µg/L, respectively (U.S. Environmental Protection Agency 2001), which could be considered normal low levels for the general population. Thus, in the present study, the healthy control group from unknown contaminated areas also showed a normal Hg burden. However, the exposed group had high Hg concentrations, which was comparable with the data of the Mt. Diwata study in the Philippines (Drasch et al. 2001) and cases of Hg accidental poisoning (Hoeta and Lison 1997).

**Correlation analysis of Se and Hg.** There is a strong correlation (r = 0.746, p < 0.001) between Hg concentrations in serum and in urine of the Hg-exposed subjects, but there is no correlation for Se (Figure 1). A strong positive correlation is observed between Se and Hg concentrations in urine (r = 0.625, p < 0.001) but not in serum (Figure 2). It is reasonable that Hg excretion in urine is positively correlated with serum Hg concentrations. If serum Se and Hg concentrations are affected by short-term exposure, urinary Se and Hg concentrations may more accurately reflect their metabolism and excretion. Their correlation supports the interaction of Se with Hg in vivo. The results of our present study also suggest that Hg could interfere with the metabolic process of Se.

An earlier study by Hol et al. (2001) showed that the median concentration of Se in blood (119.2 ng/mL) was statistically significantly lower in subjects claiming to have symptoms of Hg amalgam illness than in healthy subjects with Hg amalgam but who had no symptoms of illness (130.3 ng/mL). Many studies indicated that retention and redistribution of Hg in experimental animal and fish were induced by administration of Se compounds (Bierregaard et al. 1999; Seppanen et al. 1998). It appears that the co-accumulated Se could alleviate the harmful effects of Hg exposure.

To our knowledge, the Se concentrations in individuals from the Wanshan area are not significantly higher than those in other areas (He 1996). Se concentrations in soil in the entire Guizhou Province range from 0.064 to 0.326 mg/kg, with an average of 0.369 mg/kg. In the Tongren District (including the Wanshan area), the Se content in soil of 0.15–0.20 mg/kg is considered relatively low (He 1996). The Se concentration in grain is 0.15–0.20 mg/kg is considered relatively low (He 1996). Se concentrations in soil in the entire Guizhou Province range from 0.064 to 0.326 mg/kg, with an average of 0.369 mg/kg. In the Tongren District (including the Wanshan area), the Se content in soil of 0.15–0.20 mg/kg is considered relatively low (He 1996).

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| Table 2. Se and Hg concentrations (ng/mL serum ± SD, n = 12) in SeP (fraction A) after affinity chromatographic separation of serum from Hg-exposed and control groups. |
|------------------|------------------|------------------|------------------|------------------|
| Subjects         | Se in SeP (%)    | Percent Se (%)   | Hg in SeP (%)    | Percent Hg (%)   |
| Hg exposed       | 59.7 ± 11.2      | 55.2 ± 8.4       | 19.4 ± 9.2       | 33.4 ± 15.9      |
| Control          | 31.5 ± 10.2      | 52.5 ± 7.9       | 0.15 ± 0.12      | 15.4 ± 8.2       |
| t-Test           | p < 0.05         | p > 0.05         | p < 0.05         | p < 0.05         |
| Molar ratio (Se:Hg) in SeP |                |                 |                 |                 |

| Table 3. Se and Hg concentrations (ng/mL serum ± SD, n = 12) in Se-containing proteins after affinity chromatographic separation of serum from Hg-exposed and control groups. |
|------------------|------------------|------------------|------------------|------------------|
| Fractions        | Se in total serum | Hg in total serum | Molar ratio (Se:Hg) | |
| Hg-exposed group  | 12.7 ± 5.8       | 2.2 ± 1.2        | 0.24 ± 0.18      |
| Control group     | 17.2 ± 7.8       | 1.2 ± 1.5        | 0.28 ± 0.25      |
| Fraction B (mainly albumin) | 11.7          | 6.6              | 24.7             |
| Fraction C (containing GSH-Px) | 33.1          | 60.5             | 59.8             |
SeP and GSH-Px was highly up-regulated in Hg miners and was accompanied by increased serum Se concentration. As shown in Figure 3, proteins of fractions A (SeP) and C (albumin) are almost purified because of the highly efficient effect of affinity chromatography. The band of fraction C showed a molecular weight of 66 kDa for albumin. The two major bands in fraction A are two isoforms of SeP with molecular weights of approximately 58 and 49 kDa. In fraction B, the staining gel indicated a number of protein bands. Therefore, affinity chromatography can give only an estimate of plasma Se in selenoproteins.

Although Se concentrations in serum of exposed and control groups are different, the fraction of Se entering SeP is approximately the same, ranging from 45 to 62% of total Se exposure, which is in agreement with other published data (Harrison et al. 1996; Plecko et al. 1999). The percentage of nonspecific binding of Se with albumin decreased, and the percentage of Se bound to GSH-Px increased from 28.7 to 33%. The Sec residue in selenoproteins as GSH-Px and SeP is codon-translationally incorporated via a predefined UGA codon, which has a specific covalent binding capacity. The Se concentration in the albumin fraction was approximately the same regardless of total Se exposure, which suggests that the nonspecific Se-binding capacity of albumin is stable and the remaining Se goes into the selenoprotein pool.

We found that Hg concentrations in various protein fractions of the control group were very low and close to the detection limit. We also found that a small fraction of Hg was bound to serum albumin (Table 3). Most Hg was present in the fractions containing SeP and GSH-Px. The SeP-containing fraction bound more Hg, whereas the Se:Hg molar ratio was much lower in the exposed group than in the control group (Table 2). These results indicate the strong interaction of SeP and Hg at high Hg exposure concentrations; at Hg exposures too low to affect the Se status, this interaction has not been reported (Falinoga et al. 2002).

Other studies have found that pure SeP binds with Hg, but our results do not support this finding. Although SeP is the main protein found in fraction A, a minor protein impurity may be associated with Hg. Generally, the highly purified SeP was obtained using immobilized monoclonal antibodies (Himeno et al. 1996) or multistep separation involved in heparin-affinity, anion-exchange, and metal-chelate affinity chromatography (Mostert et al. 1998). The process, with high salt concentrations and metal-chelate agarose, may result in denaturing protein fractions in serum, which represents a metabolic process and metal-chelate sequestration. Although SeP is the main protein containing sequestered mercury, its Hg-binding ability is limited, which is confirmed by our results. Thus, at very low Hg concentrations in serum, Hg may bind to a variety of different protein fractions, whereas the stronger competition and reactivity of the selenoprotein in selenoproteins explains why more Hg was observed in the SeP-containing fraction at higher Hg exposure concentrations.

**Figure 3.** Coomassie-stained SDS-PAGE gel for serum proteins after separation by heparin-Sepharose and blue-Sepharose affinity chromatography. Lane 1, protein standards (from top to bottom: 97.4, 66.2, 43.6, 31.1, 20.1, and 14.4 kDa); lane 2, sample buffer; lane 3, fraction A (mainly SeP); lane 4, fraction B (mainly albumin); lane 5, fraction C (containing GSH-Px).

**Figure 4.** The MDA concentration and GSH-Px activity in serum samples of the Hg-exposed people and control. Data are expressed as mean ± SD. *p < 0.05.

**Oxidative status in serum.** Activity of GSH-Px in serum of miners was significantly higher (p < 0.05) than that of the control group (84.6 ± 12.1 vs. 75.0 ± 14.1 U/mL/min). The lipid peroxidative product MDA increased significantly in the Hg-exposed group (7.12 ± 2.18 vs. 4.69 ± 1.55 nmol/mL, p < 0.05), as shown in Figure 4. The positive correlation between total Hg concentrations and MDA concentrations in serum was also observed in the present study (r = 0.568, p < 0.05). The oxygen-derived free radicals can induce the lipid peroxidation reaction of multiple-valent unsaturated fatty acids in plasma, which ultimately produces lipid peroxidation products such as MDA. Therefore, the MDA concentrations reflect the degree of oxidative injury in vivo. Although the results of the present study suggest that oxidative damage existed in the Hg-exposed individuals, exposures to other environmental contaminants may also contribute to elevated MDA concentrations.

The antioxidative properties of selenoproteins have attracted increasing interest. Extracellular GSH-Px reduces hydrogen peroxide and tert-butyl hydroperoxide and shows some activity against phospholipid hydroperoxide. Although SeP reduces phospholipid hydroperoxide, it has no effect on hydrogen peroxide and tert-butyl hydroperoxide. SeP is also reported to function as a peroxynitrite scavenger or cell survival factor in primary cultures of neurons (Yan and Barrett 1998). The imbalance of redox status, especially profound oxidative DNA damage, was found among Hg-exposed individuals (Chen et al. 2005). In the present study the significantly elevated MDA in serum indicates oxidative stress induced by Hg exposure. However, the elevated antioxidant enzymes or proteins such as GSH-Px and SeP could eliminate the increased reactive oxidative
species. Thus, we propose that selenoproteins may have two important roles in protecting against Hg toxicity. First, they may bind more Hg through their highly reactive selenol group, and second, their antioxidative properties help compensate the reactive oxygen species induced by Hg in vivo.

REFERENCES

Agency for Toxic Substances and Disease Registry. 1999. Toxicological Profile for Mercury. Atlanta, GA:Agency for Toxic Substances and Disease Registry.

Bierregaard P, Andersen BW, Rankin JC. 1999. Retention of methyl mercury and inorganic mercury in rainbow trout Oncorhynchus mykiss (W): effect of dietary selenium. Aquatic Toxicol 45:171–180.

Bradford MM. 1976. A rapid and sensitive method for the quantitation of microgram quantities of protein using the principle of protein dye binding. Ann Biochem 72:248–254.

Brune D, Nordberg GF, Vesterberg O, Gerhardsson L, Wester PO. 2001. Determination and distribution of human plasma selenoproteins. Fresenius J Anal Chem 369:281–286.

Burk RF, Foster KA, Greenfield PM, Kiker KW, Hannon JP. 1974. Binding of simultaneously administered inorganic selenium and mercury to a rat plasma protein. Proc Soc Exp Biol Med 145:762–765.

Burk RF, Hill KE, Motley AK. 2001. Plasma selenium in specific and non-specific forms. Biofactors 14:107–114.

Chen CY, Zhang PQ, Hou XL, Chai ZF. 1999. Subcellular distribution of selenium and Se-containing proteins in human liver. Biochim Biophys Acta 1427:205–215.

Clarkson TW. 1997. The toxicology of mercury. Crit Rev Clin Lab Sci 34:369–403.

Dalhe UK, Hill EG, Holman RT. 1982. The thioctic acid reaction and the autoxidants of polysaturated fatty acid methyl esters. Arch Biochem Biophys 216:253–261.

Drach G, Bose-O’Reilly S, Beinhoff C, Roiger D, Maydl S. 2001. The Mt Diwata study on the Philippines 1999—assessing mercury intoxication of the population by small-scale gold mining. Sci Total Environ 267(1–3):151–168.

Falnoga I, Kosal AB, Stibili V, Horvát M, Stegner P. 2002. Selenoprotein P in subjects exposed to mercury and other stress situations such as physical load or metal chelation treatment. Biom Trace Elem Res 89:25–33.

Falnoga I, Tusek-Znidaric M, Horvát M, Stegner P. 2000. Mercury, selenium, and cadmium in human autopsy samples from Idrija residents and mercury mine workers. Environ Res A 84:211–218.

Gao YY, Chen CY, Zhang PQ, Chai ZF, He W, Huang YY. 2003. Detection of metalloproteins in human liver cytosol by synchrotron radiation X-ray fluorescence after SDS-PAGE separation. Anal Chim Acta 495:131–137.

Hafeman DG, Sunde RA, Hoekstra WG. 1974. Effect of dietary selenium on erythrocyte and liver glutathione peroxidase in the rat. J Nutr 104:580–587.

Harrison D, Littlejohn D, Fell GS. 1996. Distribution of selenium in human blood plasma and serum. Analyst 121:189–194.

He YL. 1996. Se contents and distribution in soils of Guizhou Province. Acta Pedolog Sin 33(4):391–397.

Hoja S, Chittum H S, Burk RF. 1996. Isomers of selenoprotein P in rat plasma, evidence for a full-length form and another form that terminates at the second UGA in the open reading frame. J Biol Chem 271:15769–15775.

Hoja S, Chittum H S, Burk RF. 1996. Nonoccupational source of mercury intoxication [Letter]. Clin Chem 42:1248.

Hol PJ, Vamnes JS, Gjerdet NR, Eide R, Isrenn R. 2001. Dental amalgam and selenium in blood. Environ Res 87(3):141–146.

Horvát M, Nolde N, Fajon V, Jerke V, Logar M, Lojen S, et al. 2003. Total mercury methylmercury and selenium in mercury poluted areas in the province Guizhou China. Sci Total Environ 304:231–256.

Iyengar V, Wolltje J. 1988. Trace elements in human clinical specimens: evaluation of literature data to identify reference values. Clin Chem 34(6):474–481.

Jia G, Wang TC, et al. 2005. Increased oxidative DNA damage, as assessed by urinary 8-hydroxy-2-deoxyguanosine concentrations, and serum redox status in persons exposed to mercury. Clin Chem 51(4):759–767.

Kryukov GV, Castellano S, Novoselov SV, Lobanov AV, Zehetb, Guigo R, et al. 2003. Characterization of mammalian selenoproteins. Science 300:1439–1443.

Laemmli UK. 1970. Cleavage of structural proteins during the assembly of the head of bacteriophage T4. Nature 227:680–685.

Ma S, Hill KE, Caprioli RM, Burk RF. 2002. Mass spectrometric characterization of full-length rat selenoprotein P and three isoforms shortened at the C terminus. Evidence that three UGA codons in the mRNA open reading frame have alternative functions of specifying selenocysteine insertion or translation termination. J Biol Chem 277(15):12749–12754.

Matskowitz J, Lombeck I, Abel J. 1999. A novel method for the purification of selenoprotein P from human plasma. Arch Biochem Biophys 357:226–300.

Plecko S, Nordmann M, Rukgauer M, Kruse-Jarres JD. 1999. Determination and distribution of human plasma selenoproteins. Fresenius J Anal Chem 362:517–519.

Sakakura C, Suzuki KT. 1999. Biological interaction between transition metals (Ag, Cd and Hg), selenide/sulfide and selenium protein. J Jpn Biochem 710–619–622.

Sekman K, Laakissainen R, Salonen JT, Kantola M, Lotjonsen S, Harri M, et al. 1998. Mercury-binding capacity of organic and inorganic selenium in rat blood and liver. Bio Trace Elem Res 69(3):197–210.

Suzuki KT, Sakakura C, Yoneda S. 1998. Binding sites for the (Hg-Se) complex on selenoprotein P. Biochem Biophys Acta 1429:102–112.

Tsui JS, Williams PR, Edwards MR, Allamneni KP, Kelch MA, Paustenbach DJ, et al. 2003. Evaluation of mercury in urine as an indicator of exposure to low levels of mercury vapor. Environ Health Perspect 111(4):823–830.

U.S. Environmental Protection Agency. 2001. Blood and hair mercury levels in young children and women of childbearing age—United States 1999. JAMA 285:1438–1437.

Whanger PD. 2001. Selenium and the brain: a review. Nutr Neurosci 4:81–97.

World Health Organization. 1990. Environmental Health Criteria 101: Methyl Mercury. Geneva:World Health Organization.

World Health Organization. 1991. Environmental Health Criteria 118: Inorganic Mercury. Geneva:World Health Organization.

Yan J, Barrett JN. 1996. Purification from bovine serum of a survival-promoting factor for cultured central neurons and its identification as selenoprotein-P. J Neurosci 16(21):8602–8611.

Yoneda S, Suzuki KT. 1997. Detoxification of mercury by selenium by binding of equimolar Hg-Se complex to a specific plasma protein. Toxicol Appl Pharmacol 143:274–280.

Zhang PD, Chen CY, Zhao JJ, Li B, Gu LY, Chai ZF. 2004. Correlation of mercury selenium and other elements in the tissues of fishes from the regions at different mercury exposure level in China. Environ Sci Tech 38(4):159–165.

Zhao JJ, Chen CY, Zhang PQ, Chai ZF, Gu LY, Li M. 2004. Comparison of selenium and mercury distribution in porcine tissues and their subcellular fractions studied by NAA and HG-AFS. J Radioanal Nucl Chem 259:459–463.