Strain Difference in Sensitivity of Mice to Renal Toxicity of Inorganic Mercury

TOSHIKO TANAKA-KAGAWA, MIEKO SUZUKI, AKIRA NAGANUMA, NOBUAKI YAMANAKA and NOBUMASA IMURA

Department of Public Health, School of Pharmaceutical Sciences, Kitasato University, 5–9-1 Shirokane, Minato-ku, Tokyo 108, Japan (T.T.-K., M.S., N.I.), Department of Molecular and Biochemical Toxicology, Faculty of Pharmaceutical Sciences, Tohoku University, Aoba-ku, Sendai 980–77, Japan (A.N.) and Department of Pathology (I), Nippon Medical School, 1–1-5 Sendagi, Bunkyo-ku, Tokyo 113, Japan (N.Y.)

Accepted for publication December 29, 1997 This paper is available online at http://www.jpet.org

ABSTRACT

Inorganic mercury has a high affinity for the kidneys and causes acute renal failure. The present investigation was designed to determine the cause of the strain difference in sensitivity of mice to the renal toxicity of inorganic mercury. Renal damage caused by HgCl₂ was estimated by histopathological and biochemical assessment, such as increase in blood urea nitrogen and plasma creatinine levels, and was found to be more remarkable in C3H/He than in C57BL/6 mice. Increase in renal lipid peroxidation in C3H/He was greater than that in C57BL/6 mice. However, no strain difference was observed in renal activities of glutathione (GSH) peroxidase, superoxide dismutase and GSH S-transferase in HgCl₂-untreated mice. The GSH content and activities of catalase and GSSG reductase in kidney of HgCl₂-untreated mice were higher in C3H/He than in C57BL/6. Background level of renal metallothionein content and the extent of metallothionein induction by HgCl₂ showed no strain difference. On the other hand, renal mercury accumulation was higher and urinary mercury excretion was lower in C3H/He than in C57BL/6. The activity of renal γ-glutamyltranspeptidase (γ-GTP), which plays a key role in renal mercury accumulation, was higher in C3H/He than in C57BL/6. Furthermore, the increase in blood urea nitrogen by HgCl₂, renal mercury accumulation and renal γ-GTP activity in B6C3F1 mice were intermediate between those of the parent strains. These results suggest that the strain difference in renal toxicity of inorganic mercury seems to be caused by the discrepancy in renal mercury accumulation, and therefore, renal γ-GTP may be an important factor determining the susceptibility of mice to the toxic action of inorganic mercury.

The metabolism of xenobiotics including heavy metals and their effects on living organisms can vary greatly by differences in species, strain, sex and age. Many of the variations seen in the metabolism of these compounds are considered to be the result of genetic differences, but the concrete causes for these differences are not well understood.

Inorganic mercury accumulates preferentially in kidneys and causes acute renal failure. Several investigators have reported strain differences in tissue distribution (Doi et al., 1983), excretion rate (Yasutake and Hirayama, 1986) and susceptibility to the toxicity (Yasutake and Hirayama, 1988) of methyl mercury in mice. However, strain difference in the distribution and susceptibility to the toxicity of inorganic mercury remains to be elucidated. The purpose of the present study, therefore, is to investigate the strain difference in sensitivity of mice to the toxicity of inorganic mercury.

Received for publication September 2, 1997.

1 This work was supported in part by Kitasato University of Research Grant for Young Researchers. This work was presented at the 114th Annual Meeting of The Pharmaceutical Society of Japan in April 1994.

ABBREVIATIONS: BUN, blood urea nitrogen; GSH, glutathione; γ-GTP, γ-glutamyl transpeptidase; MT, metallothionein; SBD-F, ammonium 7-fluorobenzo-2-oxa-1,3-diazole-4-sulfonate; TBA-RS, thiobarbiturate-reactive substances; GSH-Px, glutathione peroxidase; GST, glutathione S-transferase; GSSG, oxidized glutathione; SOD, superoxide dismutase.

Mercury compounds cause oxidative damage in renal proximal tubule cells, which has been characterized by depletion of reduced GSH (Gstraunthaler et al., 1985), increased mitochondrial hydrogen peroxide production, lipid peroxidation (Lund et al., 1993) and the oxidation of reduced porphyrins (Woods et al., 1990). Therefore, strain difference in the extent of mercury-induced lipid peroxidation as well as in the levels of several cellular antioxidative factors, including SOD, catalase, GST and GSH-Px were investigated in this study.

Metallothionein is a metal-binding protein of low molecular weight thought to play a role in the homeostasis of essential metals such as zinc and copper (Bremner and Beattie, 1990). It may be involved in the detoxification of heavy metals, and scavenge free radicals. Inorganic mercury induces synthesis of MT and binds to it (Piotrowski et al., 1974). The renal toxicity of inorganic mercury was prevented significantly by preinduction of MT synthesis in rats (Zalups and Cherian, 1992). Renal MT may bind to Hg(II) and suppress its toxic action in the kidney cells. Therefore, in the present...
study strain differences in MT levels and its induction were also investigated.

Mercury compounds have high affinity to SH groups (Bach and Weibel, 1976). Recent data obtained from both mice (Tanaka et al., 1990) and rats (Zalups and Barfuss, 1995) indicate that exogenous GSH causes an increase in the renal tubular uptake of mercury. Our previous data indicate that when hepatic GSH is depleted specifically with 1,2-dichloro-4-nitrobenzene before the administration of inorganic mercury, the renal accumulation and toxicity of inorganic mercury are diminished significantly (Tanaka et al., 1990). These results suggest that hepatic GSH, as a source of plasma GSH, plays an important role in the renal uptake of mercury. In several recent studies, inhibition of renal γ-GTP by pretreatment with acivicin has caused a decrease in the renal uptake and/or accumulation of mercury and an increase in the urinary excretion of mercury in mice administered inorganic mercury (Tanaka et al., 1990; Tanaka-Kagawa et al., 1993) or methyl mercury (Naganuma et al., 1988; Tanaka et al., 1992a; Tanaka-Kagawa et al., 1993) and rats administered inorganic mercury (Zalups, 1995). These results suggest that mercurials in the lumen of proximal tubules which are filtered through the glomeruli or translocated from tubular cells exist as a mercury-GSH complex. This mercury-GSH complex may also serve as a substrate for γ-GTP and the final product, mercury-cysteine, may be taken up by renal cells after degradation of the GSH moiety in the same manner as in the metabolism of GSH itself. We have also reported that age-, sex- and strain-related differences were observed in renal mercury content of mice treated with methyl mercury which was correlated significantly with the renal γ-GTP activity (Tanaka et al., 1991, 1992b). These findings suggest the possibility that similar strain differences as described above should also be observed in the sensitivity of mice to inorganic mercury.

**Methods**

**Chemicals.** Glutathione was obtained from Boehringer Mannheim GmbH (Indianapolis, IN). Other chemicals were obtained from Wako Pure Chemical Industries Ltd. (Osaka, Japan).

**Animals.** Male mice of two inbred strains, C57BL/6 and C3H/He and their F1, B6C3F1 (C57BL/6 female × C3H/He male), were used in the experiments 4 weeks after birth. They were supplied through Charles River, Japan Inc., Tokyo, and kept in metabolism cages (one mouse per cage) in a room equipped with a 12-hr light cycle. They received laboratory chow (CE-2, CLEA-Japan) and water ad libitum.

**Survival study.** C3H/He and C57BL/6 mice were injected with HgCl₂ (35 μmol/kg s.c.) and the survival rate for 5 days was examined.

**Renal toxicity studies.** C3H/He and C57BL/6 mice were treated with HgCl₂ (20 μmol/kg s.c.) and blood samples were collected from animals under ether anesthesia at 12, 24, 48 and 72 hr after the injection. Blood was collected from the femoral vein into heparinized containers. Blood samples were separated into plasma and red blood cells by centrifugation (800 × g, 5 min). BUN and plasma creatinine values as indicators of renal damage were determined by the NADH-coupled enzymatic method using urease (Hallett and Cook, 1971) and colorimetric determination based on the Jaffé reaction (Jaffé, 1886) using a commercially available assay kit (Wako Pure Chemicals Ind., Osaka, Japan), respectively.

**Lipid peroxidation in the kidneys was determined by quantitating the TBA-RS by the method of Ohkawa et al. (1979).** In separate experiments, C3H/He, C57BL/6 and B6C3F1 mice were treated with HgCl₂ (20 and 25 μmol/kg s.c.) and blood samples for BUN determination were collected from animals under ether anesthesia at 48 hr after the injection.

**Histopathological examination.** Four mice each in C3H/He and C57BL/6 strains were sacrificed on days 1 (24 hr), 2, 3, 5, 10 after the dorsal subcutaneous injection of HgCl₂ (20 μmol/kg). Four normal aged-matched, unmanipulated mice in each group were studied as controls. After removal of the kidney, tissue blocks were fixed in 20% formalin and embedded in paraffin, and sectioned at 2–3 μm. Hematoxylin-eosin and periodic acid-Schiff stains were performed for light microscopic studies.

**Determination of tissue distribution and urinary excretion of mercury.** C3H/He and C57BL/6 mice were injected with HgCl₂ (20 μmol/kg s.c.). Urine was collected in metabolism cages (one mouse/cage) and also by bladder puncture. Kidney, liver, brain, heart, lung and spleen were removed 1, 4, 8, 12, 24, 48 and 72 hr after HgCl₂ injection. In a separate experiment, C3H/He, C57BL/6 and B6C3F1 mice were injected with HgCl₂ (20 μmol/kg s.c.). Urine was collected in metabolism cages (one mouse/cage) and also by bladder puncture. Kidney, liver, brain, heart, lung and spleen were removed at 2, 4, 8 and 16 hr after HgCl₂ injection. Mercury contents in tissues, blood and urine were determined by the reductive vapor-atomic absorption method using a mercury analyzer (RA-2, Nippon Instruments Co., Tokyo, Japan) after wet digestion with nitric acid.

**Determination of renal GSH concentration.** Renal GSH concentration was measured by high-performance liquid chromatography with SBD-F as a fluorogenic reagent (Toyoo’oka and Imai, 1983) as described previously (Tanaka-Kagawa et al., 1993).

**Measurement of enzyme activity.** Activities of catalase, GSH-Px, GST, GSSG-reductase and SOD in kidney of HgCl₂-untreated mice were measured. For measurement of the activity of GSH-Px, GST and GSSG-reductase, kidneys were homogenized in 9 volumes of 0.25 M sucrose solution, and the homogenates were centrifuged at 105,000 × g for 1 hr at 4°C. GSH-Px activity in the supernatant was determined by the method of Lawrence and Burk (1976) with H₂O₂, tert-butyl hydroperoxide or cumene hydroperoxide as a substrate. GST activity in the cytosol was determined by the method of Habig et al. (1974) by using 1-chloro-2,4-dinitrobenzene as a substrate. GSSG-reductase in the cytosol was determined by the method of Carlborg and Mannervik (1985). For assay of the activity of catalase and SOD, kidneys were homogenized in 24 volumes of 20 mM potassium phosphate buffer (pH 8.0) containing 14 mM sodium borate and 0.2 mM ethylenediaminetetraacetic acid, disodium salt. Catalase activity was assayed by the method of Miehren and Berg (1988). SOD activity was determined by the method of Ohyanagi (1984). Because Cu/Zn-SOD is blocked by cyanide, the activity measured in the presence of 25 mM potassium cyanide corresponds to Mn-SOD activity and that measured in the absence of cyanide corresponds to the sum of Mn-SOD and Cu/Zn-SOD activities. γ-GTP activity in the 800 × g supernatant was determined by the method of Tate and Meister (1974) with γ-glutamyl-p-nitroanilide as substrate.

Protein was determined colorimetrically using Coomassie blue binding (Bio-Rad Protein Assay, Bio-Rad Laboratories, Richmond, CA), with γ-globulin as a standard.

**Determination of MT.** MT content was determined by the 3H binding assay (Kotsonis and Klaassen, 1977) as modified by Naganuma et al. (1987) as described previously (Tanaka-Kagawa et al., 1993).

**Statistics.** Data are expressed as means ± S.D. from four to eight mice. Data were statistically analyzed by one- or two-way analysis of variance. When P values obtained with the analysis of variance were found to be statistically significant (P < .05), the Scheffe’s multiple comparison post hoc test was used. Student’s t test was used to determine the significance of the difference in activities of antioxidative enzymes in mouse kidney between C3H/He and C57BL/6 mice.
Results

Strain difference in susceptibility to mercury toxicity. Figure 1 shows the strain difference in lethal toxicity of HgCl$_2$. Five days after administration of HgCl$_2$ (35 µmol/kg s.c.) all mice of the C57BL/6 strain survived, whereas 40% of C3H/He strain mice died.

Both BUN and plasma creatinine levels measured as biological indicators of renal damage dramatically increased in C3H/He mice treated with HgCl$_2$ (fig. 2). In contrast, BUN levels increased slightly, and no significant increase was observed in plasma creatinine levels of C57BL/6 mice after HgCl$_2$ injection (fig. 2).

Figure 3 shows morphological changes in the renal tissue after HgCl$_2$ administration. The proximal tubule cells mainly in portions of the S2 and S3 segments were injured in C3H/He mice (fig. 3D). The changes, including swelling, degeneration, necrosis and sloughing of tubular epithelial cells, were observed in C3H/He mice 24 hr after the injection of HgCl$_2$ (fig. 3, D and E). These changes progressed at day 2 to day 3 after the injection of HgCl$_2$ and no rupture of the tubular basement membrane was detected in the periodic acid-Schiff-stained specimens (data not shown). Then, regeneration of tubular cells was observed at day 5 (data not shown). However, the changes in renal tissue were less evident in C57BL/6 mice (fig. 3F, at 24 hr) throughout the whole experimental period. No obvious change was detected in glomeruli of both C3H/He and C57BL/6 mice. These results indicate that the renal toxicities caused by HgCl$_2$ were more severe in C3H/He mice than in C57BL/6 mice.

Numerous studies have suggested that oxidative tissue damage is a principal underlying action of mercury-induced nephrotoxicity (Woods et al., 1990; Lund et al., 1993). TBA-RS levels of the kidney, an indicator of lipid peroxidation, in C3H/He/mice increased to 2.5-fold at 1 hr and 4 hr after HgCl$_2$ injection (fig. 4). However, no remarkable increase in renal TBA-RS level was observed in C57BL/6 mice treated with HgCl$_2$, although 1.6-fold increase was seen at 1 hr after treatment (fig. 4).

To investigate the possible mechanism underlying the strain difference in renal damage after mercury treatment, background levels of free radical scavenging factors were measured in both strains of mice untreated with HgCl$_2$. As shown in table 1, no significant strain difference was observed in renal activity of GSH-Px, SOD and GST. Moreover, activities of catalase and GSGG reductase were higher in C3H/He than in C57BL/6, which is more resistant to HgCl$_2$ than C3H/He. Strain difference accounting for the higher sensitivity of C3H/He mice to renal toxicity of inorganic mercury was not observed in GSH concentration of HgCl$_2$-treated mouse kidney (table 2). No strain difference in renal MT content was observed in HgCl$_2$-untreated mice, and renal MT content in both strains of mice was similarly increased for 24 hr after HgCl$_2$ treatment (table 3). At 48 and 72 hr after HgCl$_2$ treatment, renal MT content in C57BL/6 mice was lower than that in C3H/He mice (table 3). Thus, resistance of C57BL/6 mice to lethal and renal toxicity of HgCl$_2$ can not be ascribed to these biological factors.

Mercury distribution and excretion. The percentage of injected mercury found in kidneys and urine at various times after injection is shown in figure 5. Renal mercury level was highest at 4 hr after HgCl$_2$ administration in both C3H/He and C57BL/6 mice, but distribution of mercury to the kidneys was dramatically lower and urinary mercury excretion was markedly higher in C57BL/6 mice than in C3H/He mice (fig. 5). No apparent difference in mercury content in liver, heart, lung, spleen, testis, brain, plasma and red blood cells was observed between C3H/He and C57BL/6 mice at 4 hr after HgCl$_2$ injection (data not shown). These results suggest that the relative insensitivity of the C57BL/6 mouse to HgCl$_2$ toxicity simply may be related to the lower mercury accumulation in the kidneys than that in C3H/He mice.

We have reported previously that hepatic and plasma GSH and renal γ-GTP can be determinants of renal mercury uptake in mice treated with methyl mercury. To investigate the strain difference in factors regulating renal mercury accumulation, background levels of tissue GSH concentration and renal γ-GTP activity were determined. No significant strain difference was observed in plasma and hepatic GSH concentration (data not shown), whereas renal γ-GTP activity in C57BL/6 mice was lower than in C3H/He mice (fig. 6).

To investigate whether the sensitivity of mice to renal
toxicity of inorganic mercury is controlled genetically, renal damage caused by HgCl₂ was estimated in C3H/He, C57BL/6 and their hybrid F1 generation, B6C3F1 mice. Level of increase in BUN (fig. 7) in B6C3F1 mice was intermediate between C3H/He and C57BL/6. Furthermore, renal mercury accumulation and urinary mercury excretion of B6C3F1 mice injected with HgCl₂ tended to be intermediate between those of the parent strains except for the renal mercury content at 2 hr after HgCl₂ treatment (fig. 8). Renal γ-GTP activity of B6C3F1 also showed the intermediate value (fig. 6).

**Discussion**

Although organ distribution and toxicity of inorganic mercury have been studied by numerous investigators, strain differences in susceptibility to the toxicity of inorganic mercury have not been reported previously. The data presented in this paper demonstrate that C57BL/6 mice are considerably more insensitive to HgCl₂-induced lethal and renal toxicity than C3H/He mice, and the relative insensitivity of the C57BL/6 mice may simply be related to the lower mercury

---

**Fig. 3.** Light microscopic assessment of the strain difference in nephrotoxicity 24 hr after the administration of HgCl₂ (20 μmol/kg s.c.). (A, B) Renal cortex of a C3H/He mouse untreated with HgCl₂. (C) Renal cortex of a C57BL/6 mouse untreated with HgCl₂. (D) Renal cortex of a C3H/He mouse treated with HgCl₂. Proximal tubular cells are injured mainly in the S2 and S3 segments, as shown by decreased staining areas. (E) Renal cortex of a C3H/He mouse treated with HgCl₂. Prominent injuries of proximal tubular cells, including swelling, degeneration, necrosis and sloughing. (F) Renal change of a C57BL/6 mouse treated with HgCl₂. Tubular damages are less evident than in C3H/He mice. (hematoxylin-eosin stain, A and D original magnification, ×12; B, C, E and F, ×40)
accumulation in the kidneys than that in C3H/He mice. Strain differences in renal mercury accumulation may result from different activity of renal γ-GTP, which plays an important role in renal mercury accumulation.

Levels of BUN and plasma creatinine which indicate renal failure dramatically increased 2 days after HgCl₂ injection in C3H/He mice. Changes in renal morphology after HgCl₂ injection were also more evident in C3H/He mice than in C57BL/6 mice. Morphological changes caused by HgCl₂ were observed in tubular cells but not in glomeruli in both C3H/He and C57BL/6 mice by light microscopic studies in the present investigation. Autoradiographic studies (Berlin and Ulberg, 1963) previously showed that Hg(II), administered as HgCl₂ to mice, rapidly accumulated in the renal cortex, and that the highest concentration was detected in the S3 segment of the proximal tubules. It is well known that a sublethal dose of HgCl₂ causes necrosis of pars recta in the kidneys of rats and mice. Changes in renal morphology after HgCl₂ injection were also more evident in C3H/He mice than in C57BL/6 mice. Strain differences in renal mercury accumulation may result from different activity of renal γ-GTP, which plays an important role in renal mercury accumulation.

### TABLE 2

<table>
<thead>
<tr>
<th>Renal GSH concentration (μmol/g tissue)</th>
<th>C3H/He</th>
<th>C57BL/6</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>hr</strong></td>
<td><strong>μmol/g tissue</strong></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>4.00 ± 0.12</td>
<td>3.16 ± 0.22**</td>
</tr>
<tr>
<td>1</td>
<td>5.08 ± 0.67</td>
<td>2.43 ± 0.35**</td>
</tr>
<tr>
<td>4</td>
<td>7.68 ± 0.30</td>
<td>4.61 ± 0.35**</td>
</tr>
<tr>
<td>8</td>
<td>5.76 ± 0.77</td>
<td>4.40 ± 0.57</td>
</tr>
<tr>
<td>12</td>
<td>4.76 ± 0.59</td>
<td>4.77 ± 1.17</td>
</tr>
<tr>
<td>24</td>
<td>4.44 ± 0.57</td>
<td>3.19 ± 0.67</td>
</tr>
<tr>
<td>48</td>
<td>4.12 ± 0.59</td>
<td>4.32 ± 1.05</td>
</tr>
</tbody>
</table>

** Values are mean ± S.D. (n = 6) **

### TABLE 3

<table>
<thead>
<tr>
<th>Renal MT concentration (Hg bound nmol/g tissue)</th>
<th>C3H/He</th>
<th>C57BL/6</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>hr</strong></td>
<td><strong>μmol/g tissue</strong></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>14.8 ± 1.8</td>
<td>11.6 ± 4.7</td>
</tr>
<tr>
<td>8</td>
<td>59.5 ± 10.2</td>
<td>63.6 ± 10.1</td>
</tr>
<tr>
<td>12</td>
<td>160.4 ± 15.3</td>
<td>146.1 ± 35.5</td>
</tr>
<tr>
<td>24</td>
<td>172.1 ± 27.8</td>
<td>163.6 ± 6.5</td>
</tr>
<tr>
<td>48</td>
<td>208.9 ± 27.5</td>
<td>155.9 ± 19.0**</td>
</tr>
<tr>
<td>72</td>
<td>183.7 ± 40.5</td>
<td>102.3 ± 5.9**</td>
</tr>
</tbody>
</table>

** Values are mean ± S.D. (n = 6) **

** Significantly different from C3H/He (P < .01).
function. In the present study levels of BUN and plasma creatinine increased in C3H/He mice by HgCl₂ treatment, although no morphological changes were observed in glomeruli by light microscopy. The elevation of BUN and plasma creatinine levels may result from glomerular damage that cannot be detected by light microscopic observation in the present study or from reduction of the glomerular filtration rate caused by tubuloglomerular feedback. The tubuloglomerular feedback hypothesis (Thurau and Boylan, 1978) proposes that proximal tubular damage results in failure of the normal reabsorption of the filtered sodium chloride, and the concentration of this substance, therefore, rises in the distal tubules. The elevated sodium chloride is sensed by the macula densa which responds by inducing the release of renin leading to local generation of angiotensin II. The angiotensin II causes arteriolar constriction, decreased filtration pressure and a reduction in the glomerular filtration rate (Thurau and Boylan, 1978).

Glutathione is the major cytosolic low molecular weight sulphhydril compound which acts as a cellular reducing reagent and is protective against numerous toxic substances including heavy metals. Treatment of animals with an inhibitor of GSH synthesis or GSH depletors markedly sensitized mice to Hg (II) toxicity (Berndt et al., 1985; Naganuma et al., 1990), which suggests that cellular GSH is a major determinant of Hg (II) toxicity. In the present study, renal TBA-RS level as an indicator of oxidative damage was increased by HgCl₂ treatment. Glutathione may play an important role in the prevention of mercury-induced oxidative damage as a direct scavenger or by scavenging as a collaborating factor with GSH-Px. Thus GSH may be one cause of the strain difference in renal damage induced by HgCl₂. However, we observed no difference in renal GSH concentration between the two strains of mouse which would account for the higher sensitivity of C3H/He mice to renal toxicity of inorganic mercury.

The kidney damage caused by inorganic mercury was prevented by preinduction of renal MT because intracellular mercury in the kidney is firmly trapped by the MT (Zalups and Cherian, 1992). Furthermore, the sensitivity to the renal toxicity of HgCl₂ was enhanced markedly in the transgenic mice that are deficient in the MT-I and MT-II genes (MT-null mice) (Satoh et al., 1997). These findings suggest that MT is an important protective factor against the renal toxicity caused by inorganic mercury. In the present study, no strain difference was observed in renal MT content of HgCl₂-un-treated mice. Furthermore, the extent of MT induction was similar in the C3H/He and C57BL/6 strains. These results suggest that the strain difference in sensitivity to HgCl₂ was not caused by renal MT levels in these strains of mice.

Several recent studies suggested that the renal γ-GTP plays an important role not only in renal uptake but also in renal storage of mercurials (Tanaka-Kagawa et al., 1993: Zalups, 1995). As reported previously (Tanaka et al., 1991), renal γ-GTP activity in C57BL/6 mice was lower than that in C3H/He mice. The present study revealed that renal γ-GTP activity in B6C3F1 mice was intermediate between the activities in the parent strains. Furthermore, this study observed that renal mercury accumulation and renal damage in B6C3F1 mice treated with HgCl₂ were also intermediate. These facts indicate that the strain difference in sensitivity to HgCl₂-induced toxicity may be explained by the discrepancy in renal mercury accumulation. Furthermore, renal γ-GTP, as a determinant of renal mercury accumulation, may be an important factor in determining the susceptibility of mice to mercury toxicity.

References