Differences in Cadmium Transport to the Testis, Epididymis, and Brain in Cadmium-Sensitive and -Resistant Murine Strains 129/J and A/J

LAURA M. KING, WILLIAM A. BANKS, and WILLIAM J. GEORGE
Department of Pharmacology, Tulane University School of Medicine, New Orleans, Louisiana

Accepted for publication December 30, 1998 This paper is available online at http://www.jpet.org

ABSTRACT
Although most animals with scrotal testes are susceptible to cadmium-induced testicular toxicity, strain-related differences are seen in mice. Resistant murine strains demonstrate a decreased cadmium concentration in the testis and also in the epididymis and seminal vesicle. In this study we analyzed cadmium transport into tissues with a vascular barrier, the testis, epididymis, and brain, in an attempt to characterize the mechanisms of strain resistance to cadmium-induced testicular toxicity. In the resistant murine strain A/J, $^{109}$Cd transport (administered as $^{109}$CdCl$_2$) was significantly attenuated in the testis, epididymis, and brain, when compared to the sensitive murine strain 129/J. The unidirectional influx constant ($K_{in}$, in $\mu l$ g$^{-1}$ min$^{-1}$) for $^{109}$Cd was 0.01929 in the A/J testis as compared with 1.174 in the 129/J testis ($P < .0001$). The percentage of a $^{109}$Cd dose that reached the A/J testis by 60 min was over 10 times less than that which reached the 129/J testis. The transport system used by cadmium in the 129/J testis was saturable, with 20 $\mu$M unlabeled cadmium chloride inhibiting transport by over 60%. The transporter was competitively inhibited by zinc ($P < .00017$), but not by calcium, indicating a specificity in ion transport. Studies with isolated tubules and analysis of testicular fluid compartments demonstrated no significant difference in cadmium uptake or efflux between the strains when corrected for the amount of $^{109}$Cd entering the testis. Therefore, murine strain differences in testicular sensitivity to cadmium appear to be related to the variable presence of a transport system for cadmium in the testicular vasculature.

Cadmium is a nonessential trace element, and its toxicity may be due to induced alterations in cellular homeostasis of essential metal ions, such as copper, zinc, and calcium. The absence of homeostatic mechanisms for toxic metals such as cadmium also suggests the absence of selective, mediated transport processes. To traverse plasma membranes, cadmium must therefore utilize transport systems that normally carry endogenous metals or gain entry via nonselective pathways (Ballatori, 1991). Because of the similarity in the overall transport characteristics between zinc and cadmium, and because they inhibit each other's rapid phases of uptake, it has been suggested that these metals share a common transport pathway (Failla et al., 1979; Stacey and Klaassen, 1980). In endothelial cells, cadmium competitively inhibits zinc transport into the cells (Bobilya et al., 1992), and the two cations may share a common uptake mechanism (Blazka and Shaikh, 1991).

Cadmium distributes to tissues rapidly and has a high volume of distribution. Although the majority of cadmium enters the liver and the kidney, acute exposure to cadmium can result in a rapid testicular hemorrhagic necrosis. Strain resistance to this testicular toxicity has been found in mice. All mice found to be resistant have been descended from Bagg-albino stock, which implies that susceptibility is the normal state and resistance is a mutation (Taylor et al., 1973). Resistant murine strains demonstrate a decreased cadmium concentration in the testis (Lucis and Lucis, 1969; Hata et al., 1980; Chellman et al., 1984) and also in the epididymis and seminal vesicle (King et al., 1998).

Although only about 1 to 2% of an acute cadmium dose is taken up by the testes, they are particularly sensitive; testicular necrosis is seen at cadmium concentrations as low as 0.15 $\mu$g/g testis (Gunn et al., 1968). The mechanism(s) for this effect have not been clearly elucidated. Several lines of evidence point to the testicular endothelium as the primary target of cadmium; early changes are seen in the endothelial cell junctions after cadmium exposure (Gabbanini et al., 1974), an increase in capillary permeability occurs within 1 to 2 h of cadmium exposure (Aoki and Fawcett, 1975) and the distribution of injury parallels the anatomical distribution of the blood supply to the testis and epididymis (Gunn and Gould, 1970). However, other authors contend that the seminiferous tubules...
epithelium is more sensitive to the effects of cadmium; the permeability barrier of the seminiferous tubules is compromised by cadmium before vascular damage occurs (Satchell and Waites, 1970), isolated Sertoli cells are more susceptible to the toxic effects of cadmium than interstitial testicular cells (Clough et al., 1990), and cadmium causes a failure of sperm release from the rat seminiferous epithelium at a dose that does not cause acute testicular necrosis (Hew et al., 1993).

In addition to the testis, acute cadmium toxicity is also manifested in the cranial and spinal sensory ganglia (Gabbiani, 1966). The ganglionic lesions closely resemble those in the testes with a similar sequence of development and hemorrhagic nature (Schlaepfer, 1971; Gabbiani et al., 1974). Because these studies of the ganglia were conducted in rats, it is not known if murine strain resistance to the ganglionic effects of cadmium exists. However, differences were noted in the cadmium sensitivity of endothelial cells in the rat sensory ganglia (Schlaepfer, 1971), and may also exist in murine strains.

The present study was conducted to determine if cadmium transport is altered in murine strains that differ in their testicular sensitivity to cadmium. We analyzed cadmium transport in vivo in the testis, epididymis, and brain to characterize the transport mechanisms of cadmium in tissues with a vascular barrier. By using low, non-necrotizing doses of radioactive $^{109}\text{Cd}$, the endogenous transport of cadmium was examined, and not the pathological sequence of events that occur with higher doses. These studies were intended to help determine the basis of strain resistance to cadmium-induced toxicity.

**Materials and Methods**

**Chemicals.** Cadmium chloride ($\text{CdCl}_2$), calcium chloride ($\text{CaCl}_2$), zinc chloride ($\text{ZnCl}_2$), and bovine serum albumin fraction V, were purchased from Sigma Chemical Co. (St. Louis, MO). Laboratory grade (type II) water was prepared using a Life Scientific Inc. water purification system (St. Louis, MO). Lactated Ringer’s solution was purchased from McGaw Inc., (Irvine, CA). The radiolabels $^{109}\text{CdCl}_2$, $^{125}\text{I}$, and $^{65}\text{ZnCl}_2$ were obtained from NEN Life Science Products (Boston, MA). $^{125}$I-labeled albumin (I-alb) was prepared by the chloramine-T method of Greenwood et al. (1983).

**Animals.** Male mice (8–20 weeks of age) were purchased from Jackson Laboratories (Bar Harbor, ME). Mice of the strain 129/J are sensitive to the testicular effects of cadmium, whereas those of strain A/J are resistant (Gunn and Gould, 1970; Hata et al., 1980; Chellman et al., 1984). Mice were housed in a vivarium at the Tulane University Center for Bioenvironmental Research, which is approved by the Association for the Assessment and Accreditation of Laboratory Animal Care International (AAALAC International). The animals were housed under conditions of controlled light (12-h light/dark cycle), air, and temperature (23°C). Animals had free access to food and water at all times. The “Guiding Principles in the Use of Animals in Toxicology” were followed in all animal experiments.

**Measurement of Cadmium Entry Rate.** This was carried out essentially as described by Banks and Kastin (1992). Briefly, mice were anesthetized with i.p. urethane (2 g/kg b.wt.) and the right carotid artery and left jugular vein were exposed. An injection of 0.2 ml of lactated Ringer’s solution containing 1% bovine serum albumin, $1 \times 10^6$ cpm $^{109}\text{CdCl}_2$ (a dose of approximately 0.4 $\mu$mol/kg), and $1 \times 10^6$ cpm I-alb was made into the jugular vein. Arterial blood was collected at regular time intervals after the i.v. injection from an incision in the carotid artery. Immediately after the collection of arterial blood, the mice were decapitated. Serum was obtained by centrifugation at 3000 rpm for 10 min at 4°C. The testes, epididymis, and brain were removed, weighed, and counted in a gamma counter with the serum. The specific activity of the $^{109}\text{CdCl}_2$ used in all studies was 1.12 mCi/mg.

The unidirectional influx constant ($K_i$ in units of $\mu$g $\text{cm}^{-2} \text{min}^{-1}$) from the blood into the tissue was determined by the multiple time regression analysis method of Patlak et al. (1983) as applied to the testicular influx of cytokines (Banks and Kastin, 1992). Briefly, this was determined by plotting the tissue/serum ratio (in $\mu$g/ml) against time (min). Because the concentration of Cd in serum decreases with time after i.v. injection, an integrated value for the level of radioactivity (exposure time) was used (Gjedde, 1981; Blasberg et al., 1983; Patlak et al., 1983). The equation for exposure time is:

$$\text{exposure time} = f_0 \int_0^t \frac{C}{p} \, dt = C_{\text{pt}}$$

where $C$ is cpm/µl of arterial serum at time $t$. The unidirectional influx constant ($K_i$) was determined after correction for the albumin space by the equation:

$$K_i = \frac{\text{Am}}{\text{Cpt}} - \frac{V_i}{V_s}$$

where $C_{\text{pt}}$ is cpm/µl of tissue and $C_{\text{pt}}/C$ is the tissue/serum ratio in $\mu$g/ml at time $t$ and $V_s$ is the initial volume of distribution within the tissue (in µl). Only the linear portion of the relation between $C_{\text{pt}}$ and exposure time is used to compute $K_i$. The percentage of the injection dose entering the testes ($C_{\text{t}}$) was determined after correction for the albumin space by the equation:

$$C_t = \frac{100(R_i - R_s)(S_i/I)}{I}$$

where $R_i$ and $R_s$ are the testes/serum ratios for $^{109}\text{Cd}$ and I-alb, respectively, $S_i$ is the cpm of $^{109}\text{Cd}$ per µl of serum, and I is the cpm of $^{109}\text{Cd}$ injected per mouse.

**Measurement of TIF/SNF.** Testicular interstitial fluid (TIF) and seminiferous tubule fluid (SNF) were collected as described by Turner et al. (1984), with minor modifications. Briefly, arterial serum was obtained as described previously from mice 15 min after i.v. injection of $^{109}\text{Cd}$ and I-alb. The testes were excised, and one testis was weighed and counted in the gamma counter as described previously. In the contralateral testis, a small puncture was made in the distal pole through the tunica albuginea. The testis was placed in a Micropore 0.45 µm separator that fit into a Micropore vial (Amicon Inc., Beverly, MA) and was centrifuged at 10,000 rpm for 10 min at 4°C. TIF drained from the testis and collected in the preweighed vial. Volumes of TIF averaged 1.5 to 2 µl.

The same testis was removed from the 0.45 µm separator and decapsulated. The seminiferous tubules were ligated, removed from the rete testis and proximal pole vasculature, and rinsed four times in cold saline to remove residual TIF. The rinsed tubules were blotted dry and ruptured by extruding them through the hub of a 3-ml syringe. The ruptured tubules were centrifuged at 12,000 rpm for 30 min at 4°C. SNF was collected as the supernatant over the compressed tubules and was removed by a micropipette. SNF volumes averaged 5 to 10 µl.

Testicular fluid/tissue ratios were expressed as:

$$\frac{\text{cpm/ml (radioactivity in fluid)}}{\text{cpm/g (radioactivity in testis)}} = \frac{\text{g/ml}}{\text{g}}$$

**Measurement of $^{109}\text{Cd}$ Uptake/Efflux in Isolated Tubules.** Seminiferous tubules were isolated as described in Hoyes et al. (1995). Briefly, testes were decapsulated and very gently teased apart with fine forceps before suspension in incubation medium. Isolated tubules were incubated at 34°C with $5 \times 10^5$ cpm $^{109}\text{CdCl}_2$ (about 1.0 $\mu$Ci, a dose of approximately 0.2 $\mu$M) in minimal essential medium supplemented with L-glutamine (2 mM), sodium bicarbon-
ate (0.85 g/liter), nonessential amino acids, and vitamins with 5% fetal bovine serum, and buffered to pH 7.4 with 15 mM HEPES.

Tubules were incubated with $^{109}$Cd for 2 h. At the end of this time, the tubules were washed three times with ice-cold Hanks’ balanced salt solution. An aliquot was removed for $^{109}$Cd uptake determination. The rest of the tubules were reincubated in fresh ($^{109}$Cd-free) incubation media and aliquots of tubules were removed at regular intervals and treated as described previously, for the calculation of $^{109}$Cd efflux.

**Statistical Analysis.** Data are reported as mean ± S.E., unless otherwise specified. Means were compared by ANOVA. Regression lines were computed by the least-squares method and compared for statistical differences using the Prism program (GraphPad Software, Inc., San Diego, CA).

**Results**

**Influx of $^{109}$Cd into Testis, Epididymis, and Brain**

To characterize the nature of cadmium transport, multiple-time regression analysis was conducted from 1 to 60 min after injection of $^{109}$Cd and I-alb. The doses of cadmium were less than 1.0 $\mu$mol CdCl$_2$/kg, well below the threshold for the acute hemorrhagic reaction that occurs in the testes. I-alb was used to verify that the $^{109}$Cd treatment did not alter the permeability and integrity of the vascular barrier.

Cadmium transport in the testis (Fig. 1), epididymis (Fig. 2), and brain (Fig. 3) was significantly greater ($P < .0001$) in sensitive 129/J mice than resistant A/J mice, as shown by differences in $K_i$. No significant entry of I-alb into the tissues occurred during this time period, and albumin entry rates were not significantly different between strains in any tissue (Table 1).

**Percentage of $^{109}$Cd Injection Reaching the Testis**

The percentage of an injected $^{109}$Cd dose in the testes of the sensitive strain was significantly higher than that in the resistant strain (Fig. 4), with the area under the curve in 129/J mice (107.5) over 25 times greater than that in A/J mice (3.797). 129/J mice reached a plateau of percentage of injected $^{109}$Cd in the testes of 2.02% by 15 to 30 min, as has been previously reported (Chellman et al., 1984). Percentage of injected $^{109}$Cd in A/J testes reached a peak of 0.33% at 5 to 7 min, with levels declining after 15 min.

**Table 1**

<table>
<thead>
<tr>
<th></th>
<th>$K_i$</th>
<th>$V_i$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testis</td>
<td>$^{129}$J</td>
<td>$^{129}$J</td>
</tr>
<tr>
<td>$A/J$</td>
<td>0.39 ± 0.05</td>
<td>4.07 ± 0.52</td>
</tr>
<tr>
<td>$A/J$</td>
<td>0.32 ± 0.05</td>
<td>4.21 ± 0.36</td>
</tr>
<tr>
<td>Epididymis</td>
<td>$^{129}$J</td>
<td>$^{129}$J</td>
</tr>
<tr>
<td>$A/J$</td>
<td>0.34 ± 0.33</td>
<td>14.59 ± 2.23</td>
</tr>
<tr>
<td>$A/J$</td>
<td>0.85 ± 0.09</td>
<td>8.91 ± 0.84</td>
</tr>
<tr>
<td>Brain</td>
<td>$^{129}$J</td>
<td>$^{129}$J</td>
</tr>
<tr>
<td>$A/J$</td>
<td>-0.05 ± 0.04</td>
<td>7.53 ± 0.66</td>
</tr>
<tr>
<td>$A/J$</td>
<td>-0.06 ± 0.01</td>
<td>7.21 ± 0.12</td>
</tr>
</tbody>
</table>

Values expressed as mean ± S.D., $n = 20$ to 28.

Albumin transport was not significantly different ($P > .05$) in any tissue between the strains.

**Entry of $^{109}$Cd into the TIF/SNF**

Distribution of cadmium was measured in the TIF and SNF of the testis. When measured as the percentage of injected $^{109}$Cd, the TIF and SNF ratios were significantly different between the two strains (Table 2). However, when corrected for the amount of $^{109}$Cd entering the testis, proportionally equivalent amounts of $^{109}$Cd entered the testicular fluid compartments of both strains. The TIF/testis ratio (g/ml) and the SNF/whole testis ratio were not significantly different in either strain. Similarly, the SNF/testis ratio (g/ml) and the SNF/whole testis ratio were not significantly different in either strain.

![Fig. 1](https://i.imgur.com/1234567.png)  
**Fig. 1.** 109Cd Transport in testis. Transport of $^{109}$Cd in testis of 129/J and A/J mice 1 to 60 min after an i.v. injection of 2 $\mu$Ci $^{109}$CdCl$_2$. Exposure time is increased over real time and is used to reflect a constant plasma $^{109}$Cd concentration. Each symbol represents one animal.

![Fig. 2](https://i.imgur.com/8765432.png)  
**Fig. 2.** 109Cd Transport in epididymis. Transport of $^{109}$Cd in epididymis of 129/J and A/J mice 1 to 60 min after an i.v. injection of 2 $\mu$Ci $^{109}$CdCl$_2$. Exposure time is increased over real time and is used to reflect a constant plasma $^{109}$Cd concentration. Each symbol represents one animal.

![Fig. 3](https://i.imgur.com/4321567.png)  
**Fig. 3.** 109Cd Transport in brain. Transport of $^{109}$Cd in brain of 129/J and A/J mice 1 to 60 min after an i.v. injection of 2 $\mu$Ci $^{109}$CdCl$_2$. Exposure time is increased over real time and is used to reflect a constant plasma $^{109}$Cd concentration. Each symbol represents one animal.
In vitro studies with isolated tubules were performed to correct for the differences in testicular cadmium uptake between the two strains. By isolating seminiferous tubules, the integrity of the Sertoli cell barrier can be assessed separately from the vascular component of the blood-testis barrier. There were no significant differences between $^{109}$Cd uptake in isolated seminiferous tubules from $^{129}$/J (0.83 ± 106 cpm/g) or from $^{A}$/J (1.11 ± 106 cpm/g). $^{109}$Cd efflux was comparable in the two strains, with a maximal $^{109}$Cd efflux of 45% of control by 15 min (Fig. 5).

**In Vivo Characterization of the Cd Transporter in the Testis of $^{129}$/J Mice**

**Saturability.** Dose-response studies were performed using a tracer amount of $^{109}$Cd, with increasing concentrations of unlabeled cadmium, to a maximum concentration necessary to cause testicular necrosis. The transport of $^{109}$Cd in the $^{129}$/J testis was inhibited in a dose-responsive manner, with significant inhibition occurring with the concurrent administration of 20 μmol CdCl₂ (Fig. 6).

**Competition with Zn.** To evaluate competitive inhibition of cadmium transport in the testes, ZnCl₂ (20 μmol/kg) was given concurrently with $^{109}$Cd. As shown in Fig. 7, the concurrent administration of ZnCl₂ significantly ($P = .00017$) inhibited the transport of $^{109}$Cd in the $^{129}$/J testes, resulting in a 28% reduction in transport.

**Competition with Ca.** The specificity of the cadmium transport system in the testis was assessed by using CaCl₂ (20 μmol/kg) given concurrently with $^{109}$Cd. The concurrent administration of CaCl₂ did not significantly affect the transport of $^{109}$Cd in the $^{129}$/J testes (Fig. 8), with a pooled $K_i$ of 1.16622 μg⁻¹ min⁻¹ and a pooled $V_i$ of 7.11938 μl/g.

**Discussion**

The tissues chosen for study (testis, epididymis, and brain) were selected because they contain restrictive vascular barriers limiting the permeability of the tissue to large proteins and other molecules. The presence of vascular boundaries indicates the need for specialized transport of substances into and out of the tissue. The blood-brain barrier is well known, having been first described at the turn of the century (Biedl and Kraus, 1898). It is comprised of endothelial cells connected by tight junctions which serve to restrict the passage of substances from the vasculature into the cerebral interstitial...
Each symbol represents one animal. The pooled vascular permeability in the sensory ganglia, but without acute cadmium exposure induces a similar increase in transport system for metal ions across vascular barriers. The testicular reaction seen after acute cadmium exposure does not cause acute testicular edema or hemorrhage. Differences in testicular cadmium distribution are seen very early, within the first 5 min, and at doses of cadmium that do not cause acute testicular edema or hemorrhage. The permeability of the seminiferous tubules to cadmium is inherently different in sensitive 129/J mice as compared with the resistant strain A/J. These two strains have been shown previously to differ in their sensitivity to the testicular toxicity of acute cadmium exposure (Taylor et al., 1973). Because only tracer doses of cadmium were used in the present study, it can be assumed that the transport of $^{109}$Cd in these mice reflects intrinsic processes and not a pathological manifestation. The permeability of 129/J tissues is not increased over that of A/J tissues, as shown by the negligible transport of I-alb of both strains. The results in Fig. 4 confirm that sensitive mice accumulate a higher proportion of cadmium in the testes. They also demonstrate for the first time that these strain differences in testicular cadmium distribution are seen very early, within the first 5 min, and at doses of cadmium that do not cause acute testicular edema or hemorrhage.

In addition to the testis, the strain differences in cadmium transport were also seen in other tissues with vascular barriers—the brain and epididymis; thus, the blood-testis barrier is not unique in its variable handling of cadmium. This may signify that resistant animals have a more selective/restrictive transport system for metal ions across vascular barriers. The testicular reaction seen after acute cadmium exposure may be reflective of anatomical constraints rather than a particular target in the vasculature. This may be concluded because acute cadmium exposure induces a similar increase in vascular permeability in the sensory ganglia, but without the ischemic changes. Acute administration of cadmium induces cerebral edema with protein leaks and apparent disruption of the blood-brain barrier. Petechial hemorrhages in the parietal cortex occur within 2 h of cadmium exposure, accompanied by thinning and vacuolization of capillary walls and widening of interendothelial gaps (Webster and Valois, 1981). Ischemia occurs in the testis because it contains a fibrous tunica, which acts as a structural barrier to the dispersion of interstitial fluid. The increased fluid builds up and causes an increase in interstitial pressure, which compresses the vascular supply and leads to ischemia. The ganglia lacks such a barrier and the diffusion of fluid may counteract an increase in local interstitial pressure and thus serve to maintain the ganglionic blood flow (Schlaepfer, 1971).

The permeability of the seminiferous tubules to cadmium was similar in both strains when measured in vivo, as shown in Table 2. There was a proportionally equivalent distribution of cadmium into the interstitial and tubular fluid compartments of the testis. By using the amount of $^{109}$Cd entering the testis to calculate the interstitial fluid/tissue and seminiferous fluid/tissue ratios, it was shown that proportionally equivalent amounts of $^{109}$Cd entered the testicular fluid compartments of both strains. However, when these same fluid/tissue ratios were calculated as the percentage of the injected $^{109}$Cd dose, the strain differences became apparent. Thus, the significance of the endothelial vascular barrier emerges. Cadmium distributed evenly into the testicular fluid compartments of both the sensitive and resistant murine strains. However, more cadmium entered the testes of the sensitive strain, and thus was able to accumulate in both fluid compartments to a greater extent. This also confirms the ability of $^{109}$Cd to cross into the seminiferous tubules, which agrees with published reports (Lee and Dixon, 1973; Jackson et al., 1995). Because $^{109}$Cd is able to gain entry into the seminiferous tubules, it may have an impact on spermatogenesis. This is especially relevant in light of the low doses of $^{109}$Cd used in this study.

In vitro studies with isolated seminiferous tubules confirm the results obtained by testicular fluid measurement, and verify that cadmium is able to cross the Sertoli cell barrier. By isolating seminiferous tubules, the Sertoli cells are removed from the vasculature and cadmium exposure in the two strains is identical. When seminiferous tubules from both strains were exposed to cadmium, no differences were found in $^{109}$Cd uptake rates or retention. Similar results have been found in rats, with a comparable rate of $^{109}$Cd transport reported in isolated rat Sertoli and interstitial cells (Clough et al., 1990). In addition, isolated rat testicular interstitial cells demonstrated a dose-dependent uptake of cadmium, with a substantial efflux of cadmium over a 60-min period (Waalkes and Poirier, 1985). However, cadmium transport rates may be tissue- and cell-specific; Failla et al. (1979) detected no measurable efflux of $^{109}$Cd in rat hepatocytes that had been exposed to cadmium for 20 h. The addition of unlabeled cadmium to the incubation media failed to stimulate $^{109}$Cd release, suggesting minimal exchange diffusion in these cells.

Because cadmium did not enter the testes of the resistant strain to any great extent, the sensitive strain was used to characterize the transport system used by cadmium in the testes. Most mammals with scrotal testes are sensitive to the...
acute cadmium-induced testicular toxicity, as sensitive mice are a good model for these studies. The transport of 109Cd was significantly inhibited by concurrent administration of 20 μmol CdCl2/kg, suggesting a saturable transport system. It was also subject to competitive inhibition, with zinc and cadmium competing for a similar transport mechanism in the testis. Zinc and cadmium are transition metals, with similar size and properties, and the competition between the two ions has been shown in a number of cell types, including isolated rat interstitial cells (Waalkes and Poirier, 1985). Whereas the transport system in the current study is competitively inhibited by zinc, it is not affected by calcium. This may indicate that the 109Cd transport system in sensitive animals is not utilized by nonspecific divalent cations, but is selective for zinc (and cadmium). A recent study has reported that cadmium influx is not competitively inhibited by calcium in the corneal endothelium (Weidner and Sillman, 1997).

These studies give further support to the hypothesis that the primary target of cadmium toxicity is the vasculature (Gunn and Gould, 1970; Gabbiani et al., 1974; Aoki and Fawcett, 1975). However, the testicular vasculature has not been shown to be unique in its sensitivity to cadmium because we found that other tissues that contain vascular barriers, the epididymis and the brain, also demonstrate a strain-dependent alteration in cadmium transport.

Cadmium may be entering these tissues by using a transport system that normally carries zinc. The resistant murine strain may have an impaired zinc transport system, and therefore not transport cadmium as rapidly as the sensitive strain. Conversely, the resistant strain may have a mutation in the zinc transporter which makes it more selective, and therefore not transport cadmium as rapidly as the sensitive strain. Conversely, the resistant strain may have a mutation in the zinc transporter which makes it more selective, and therefore not transport cadmium as rapidly as the sensitive strain. Conversely, the resistant strain may have a mutation in the zinc transporter which makes it more selective, and therefore not transport cadmium as rapidly as the sensitive strain.

References


Send reprint requests to: L.M. King, USDA-ARS, LPSI, Germplasm and Genetic Resources Laboratory, 200, Room 112, BARC-East, Beltsville, MD 20705. E-mail: likeness@lps.iars.usda.gov.