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Distribution and Retention of Cadmium^{109} by the Gastrointestinal Tract and Other Organs Following Intraperitoneal Cadmium Exposure

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Cadmium is known to be an environmental air pollutant and its toxic effect on pulmonary and renal system is well recognized (FRIBERG et al. 1971, 1973; FASSETT 1975; BONNELL 1955; Goyer et al. 1978; LANE & CAMPBELL 1954). The effects of chronic exposure to a low level of Cd constitute a continuing health concern (HIETANAN 1981; FRIBERG et al. 1973). The concentration of cadmium in food and drinking water varies from 12 ng/g to 3 µg/g (TRAVIS & ETNIER 1982; SCHROEDER et al. 1967). Despite various information on the organ distribution of Cd, relatively little published data are available in the literature about the gastrointestinal absorption and retention of cadmium (SHAIKH & SMITH 1980; ONOSAKA & CHERIAN 1981; MOORE et al. 1973). Estimates show that absorption of cadmium by the gastrointestinal tract are between 5-10% of the ingested dose (FRIBERG et al. 1971, 1973, HIETANAN 1981). Recent studies by SHAIKH & SMITH (1980) on the metabolic fate of orally administered cadmium in human volunteers indicated a long half-life of 26.3 years. Our recent studies indicated that some gastrointestinal hormones - cholecystokinin (CCK), pancreatic polypeptide (PP) and gastrin - were affected with cadmium was infused in combination with bombesin (BBS), a peptide known to stimulate the release of gastrointestinal hormones (CHOWDHURY et al., 1981). Whether Cd accumulates in parts of the digestive tract which synthesize these hormones is not known. This study was conducted to determine if Cd is accumulated and retained by organs of the gastrointestinal tract that synthesize these gastrointestinal hormones.

MATERIALS AND METHODS

Sprague-Dawley rats weighing 200-225 g were used in this study. The animals were maintained with Purina Lab Chow and tap water for a week. Thirty-six rats were divided into 3 groups containing 12 rats per group. Six rats from each group received saline while the other 6 rats received an ip injection of 4 mg Cd/kg bw + 3.75 µc of Cd^{109} in saline. Each exposed animal was housed in separate metabolic cages to collect 24 hr urine samples. Groups of animals were

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anesthetized at 24, 48 and 72 hr periods. Blood was collected through an incision through the abdominal aorta and then the animal was sacrificed. Tissue samples of liver, lung, kidney, brain, fundus, antrum, duodenum, jejunum, colon and pancreas were promptly collected and weighed individually.

Blood, plasma, urine and all tissue samples were monitored for radioactive Cd^{109} in an auto γ-counter (Model A-8000, Packard Instrument Co., Inc.). The counts were corrected with their respective controls collected at the same time intervals.

Percent distribution of cadmium^{109} was calculated from the corrected cpm of the individual organs, standardized for per gm of the organ weight. The data between control and the exposed animals were statistically evaluated applying a Student's "t" test (SNEDECOR & COCHRAN 1967). A p value of <0.05 was considered significant.

RESULTS AND DISCUSSION

The distribution of cadmium^{109} in blood and urine over the experimental period of 24 to 72 hr indicated a very little or no significant accumulation over these time periods. Accumulations of cadmium in the brain, lung, liver and kidney are presented in Table 1. Brain Cd levels were significantly elevated at 48 hr from 0.04% to 0.3% and returned to control values at 72 hr. Organs such as lung, liver and kidney showed a highly significant accumulation of cadmium as early as 24 hr after exposure and maintained the elevation through the experimental period. Lung accumulation was 0.23% at 24 hr, 0.26% at 48 hr and 0.37% at 72 hr. Liver accumulation was 4.48% at 24 hr, 3.11% at 48 hr and 5.69% at 72 hr. Kidney accumulation was 1.2% at 24 hr, 1.76% at 48 hr and 1.0% at 72 hr. Significant increases were observed in all these organs between 48-72 hr intervals.

Distribution of Cd^{109} per gm of gastrointestinal tract organs are shown in Figure 1-4 as percentages $\pm$S.E.M. Control values are shown as open bars and Cd-treated rats are shown as lined bars. The distribution of Cd^{109} in fundus of the exposed rats at 24, 48 and 72 hr were 0.81 ± 0.03, 0.15 ± 0.09 and 0.9 ± 0.15, and 0.22 ± 0.03, 0.22 ± 0.05 and 0.15 ± 0.02 in control ($p<0.05$) (Figure 1). In the antrum at 24, 48 and 72 hr Cd was 0.7 ± 0.5, 0.36 ± 0.08 and 0.81 ± 0.03, and was 0.15 ± 0.02, 0.084 ± 0.007 and 0.083 ± 0.006 in control rats. The levels in the fundus (stomach) were significantly elevated at 24 and 72 hr but not at 48 hr.

The distribution of Cd^{109} in duodenum and jejunum are shown in Figure 2. Accumulation of Cd^{109} in duodenum of the exposed animals at 24, 48 and 72 hr are 1.11 ± 0.23, 0.58 ± 0.22 and 0.78 ± 0.05, respectively and in controls values are 0.09 ± 0.003, 0.04 ± 0.012 and 0.1 ± 0.2, respectively ($p<0.05$). Distribution in jejunal tissue at identical time intervals were 0.97 ± 0.24, 0.29 ± 0.08 and 0.66 ± 0.1 in cadmium treated rats and 0.07 ± 0.02, 0.03 ± 0.007 and 0.05 ± 0.01 in controls ($p<0.05$).

Table 1. Percent Distribution of Cd^{109} Per gm of Rat Brain, Lung, Liver and Kidney

	24 hr			48 hr			72 hr		
	Control ± S.E.	Exposed ± S.E.	P Value	Control ± S.E.	Exposed ± S.E.	P Value	Control ± S.E.	Exposed ± S.E.	P Value
Brain	.052± .005	.067± .012	n.s.	.043± .006	.297± .037	.002	.051± .033	.105± .039	n.s.
Lung	.066± .023	.318± .049	.010	.049± .008	.262± .016	.0001	.022± .012	.373± .017	.0001
Liver	.028± .004	4.48 ± .538	.001±	.021± .003	3.113± .531	.004	.023± .003	5.689± .602	.001
Kidney	.008± .001	1.203± .4575	.001	.0085 ±.001	1.765± .245	.001	.0083 ±.001	.998± 0	.001

$P < 0.05$

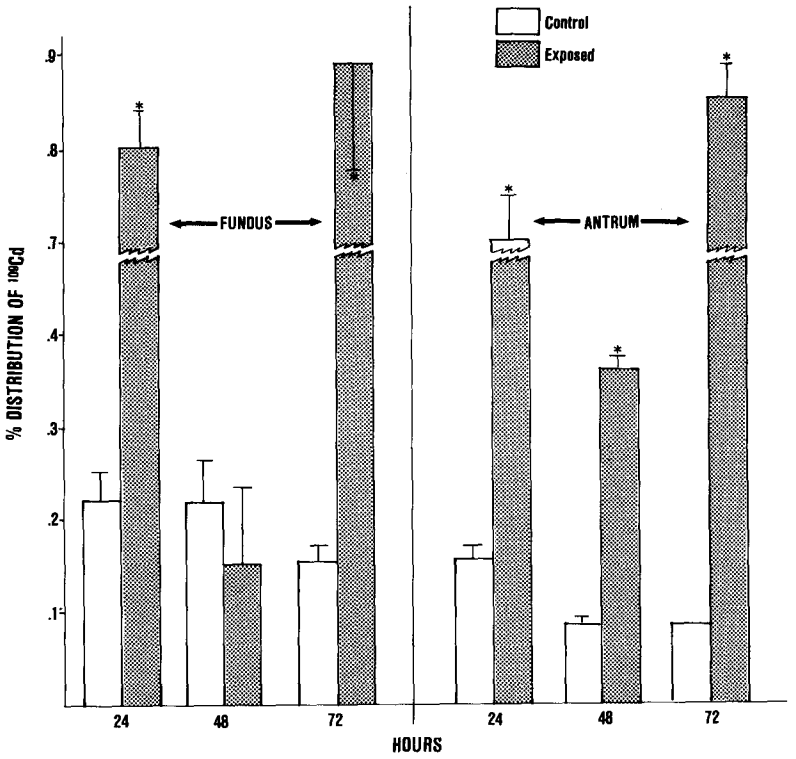

Figure 1. Percent distribution of Cd^{109} in fundus and antrum (stomach) in rats at 24, 48 and 72 hr. ☐ - control; ▨ - exposed.

Distribution of Cd^{109} in colon and ileum were significantly greater in cadmium treated rats when compared to controls at 24, 48 and 72 hr after treatment (Figure 3). Pancreatic tissue was 0.7±0.1 at 24, 0.5±0.06 at 48 and 1.96±0.15 at 72 hr; when compared with controls these values were significantly higher (Figure 4).

The data obtained in the present study indicate that cadmium was accumulated and retained by the organs of the gastrointestinal tract in greater amounts than any of the other target organs except for liver and kidney. There appears to be significant uptake of cadmium by organs of the gastrointestinal tract besides liver and kidney. Accumulation of cadmium by liver and kidney has been well documented and known to be due to the synthesis of Cd-binding protein by these organs (KAGI & NORDBERG 1979; WEBB 1979). The exact mechanism for this increased binding of this metal to various parts of the GI tract is not yet known. It has, however, been suggested that cadmium may have a regulatory role in gastrointestinal hormonal release (CHOWDHURY et al. 1981). Whether or not cadmium may be taken up by the cells of gastrointestinal origin

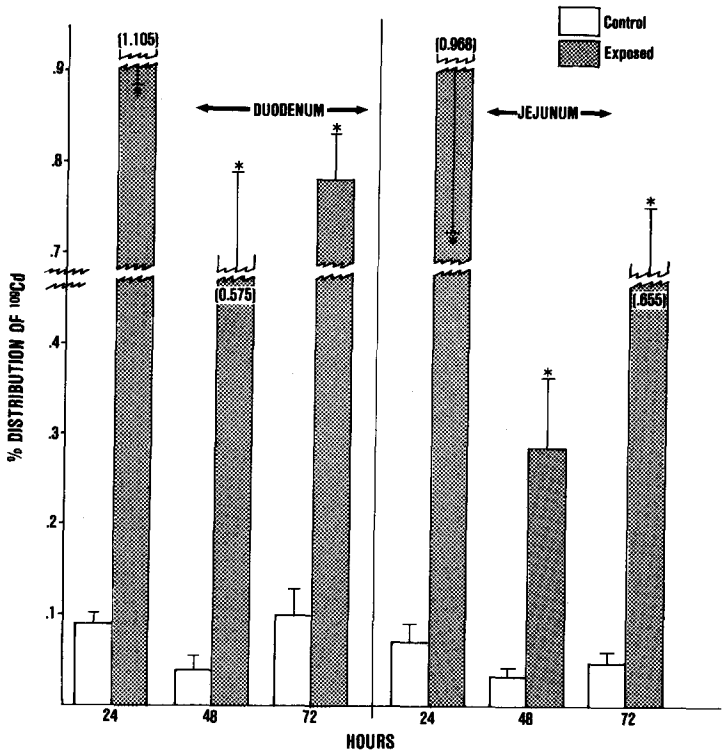

Figure 2. Percent distribution of Cd^{109} in duodenum and jejunum of rats exposed to cadmium chloride at 24, 48 and 72 hr. [ ] - control; [////] - exposed.

is yet questionable and the mechanism of its distribution suggests that retention of Cd by the GI tract may have some role in detoxification mechanism in either acute or chronic exposure.

Accumulation of cadmium by pancreas and other parts of the GI tract can be better explained with the recent report on isolation of intestinal (TOGUCHI & NAKAMURA 1982) and pancreatic metallothionein (YAU & MINNEAR 1977). Further reports by NOMIYAMA & NOMIYAMA (1982) have also provided the evidence of the presence of MT-like proteins in stomach, duodenum, intestine, lung and other organs. The studies by NOMIYAMA & NOMIYAMA (1982) were conducted in monkeys clinically exposed to cadmium. These findings indicate that the GI tract organs synthesize Cd-specific proteins and thus retains Cd in those organs. Earlier studies by MILLER et al. (1973) show a biphasic disappearance curve of blood cadmium following ip or iv Cd-exposure. The Cd-retention values calculated from the slower phase were in the range of 90-95%, however, the authors indicated the rapid phase of elimination of Cd as due to the unabsorbed cadmium and considered this unabsorbed cadmium to be deposited in the GI tract. Our current data indicate that retention

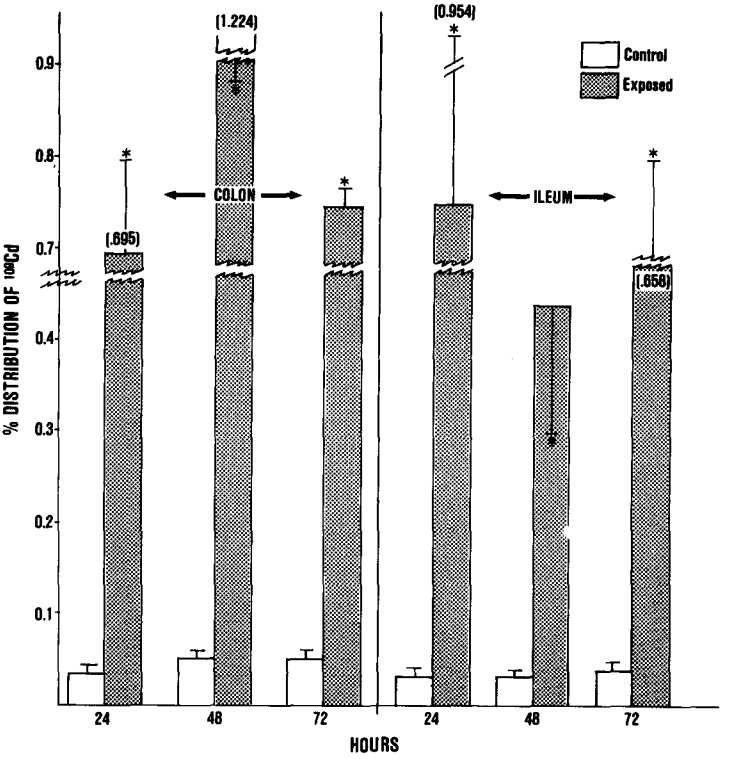

Figure 3. Percent distribution of Cd^{109} in colon and ileum of rats at 24, 48 and 72 hrs. ☐ - control; ▨ - exposed.

of Cd by the GI tract does not change in appreciable quantities between 24-72 hr and supports the mechanism of retention of cadmium in GI tract organs by the production of specific Cd-binding proteins.

The results obtained from tissue accumulation of cadmium in the present study are consistent with accumulation reported by earlier investigators (HIETANAN 1981; BUHLER et al. 1981; SHAIKH & SMITH 1980). Some investigators have shown that most unabsorbed cadmium accumulates in the GI tract at a very early stage, possibly within 4 hrs of injection before being excreted (BURCH & WALSH, 1959). This study indicate that cadmium accumulated significantly with the 72 hr experimental period and excretion, if any, appeared to be very slow within the experimental period. The exact role of Cd and Cd-binding proteins in areas of the GI tract are not fully understood but they may play a role in the release of GI hormones. The data reported in the current study, however, will not support that hypothesis.

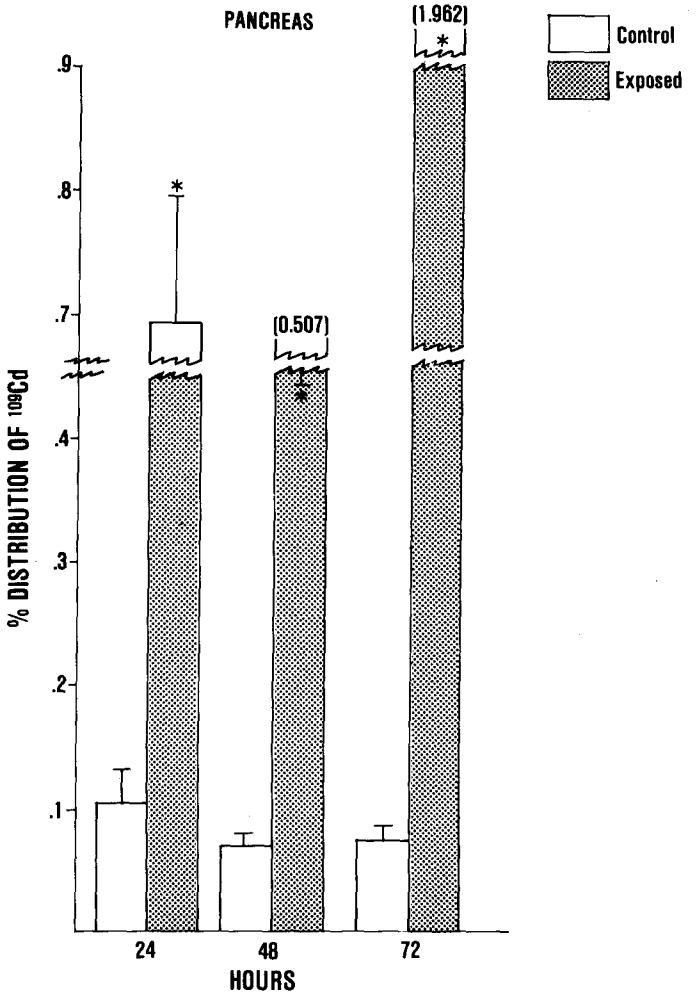

Figure 4. Percent distribution of Cd^{109} in pancreatic tissue of rats exposed at 24, 48 and 72 hr. ☐ - control; ▨ - exposed.

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