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Absorption of Mercury from Ligated Segments of the Rat Gastrointestinal Tract[1] (39990)

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An understanding of the mechanisms involved in the absorption of different forms of mercury by the gastrointestinal tract is incomplete, although significant progress has been made for inorganic mercury (1). Clarkson and Cross (2) and Cikrt (3, 4) studied the uptake of inorganic mercury by duodenal and ileal intestinal everted gut sacs; Sahagian *et al.* (5, 6) examined the uptake in isolated strips of intestinal segments and in perfused everted intestinal sacs; and Cikrt (7) studied the absorption of inorganic mercury from ligated intestinal segments in the rat. General conclusions are that the uptake of inorganic mercury by the rat intestine exhibits the characteristics of a passive transport mechanism and that, although only a small percentage is absorbed, the duodenal and ileal sections are the optimal sites of absorption. Methylmercury, however, is readily absorbed (8–10), but absorption sites have not been determined.

Results of our attempts to kinetically analyze mercury transport in the rat suggested that methylmercury was absorbed from two or more large gastrointestinal compartments; the stomach appeared to be a major site of absorption (unpublished data). Consequently, this study was conducted to determine the major sites of methylmercury absorption in the rat gastrointestinal tract and to compare the sites of organic and inorganic mercury absorption.

Materials and methods. Fifty mature male Sprague–Dawley rats averaging 430 g were randomly assigned to 10 experimental groups and anesthetized with metofane after an overnight fast. The peritoneal cavity was surgically exposed and the intestine was carefully ligated to form three 8- to 10-cm intestinal segments, a stomach compartment, and a small intestinal segment for bile collection. Ligatures were placed at the pyloric–duodenal junction; approximately 4, 14, 30 to 40, and 40 to 50 cm distal to the pyloris; and approximately 2 and 12 cm proximal to the ileocecal junction. Before the second ligature on the segment to be dosed was closed, a needle was inserted into the lumen which passed through the ligature and into the segment. The isotope was injected after the ligature was secured. The incision was closed with wound clips and the animals were allowed to recover from the anesthetic under heat lamps.

Half of the rats were each dosed with 5 μCi of methylmercury chloride (CH_3-$^{203}HgCl$, 2.5 mCi/mg) either in the stomach, duodenal segment, jejunal segment, ileal segment, or intravenously; and the other half were similarly injected with 20 μCi of $^{203}HgCl_2$ (3.9 mCi/mg). The mercury compounds, dissolved in 0.5 *M* HCl, were diluted about 1:500 with physiological saline and 0.5 ml was injected into each segment. Doses were administered intravenously by tail vein and by gavage to the stomach after completion of surgery. One milliliter of blood was collected at 1, 2, and 4 hr after dosing. After 4 hr the rats were anesthetized and decapitated, and tissues were collected for analysis. The length of gastrointestinal segments was also measured.

Blood, liver, kidneys, stomach, and intestinal segments were counted in a deep-well automatic gamma spectrophotometer; the remaining carcass of each rat was counted in a large-volume tissue counter containing two 3 × 3-in. NaI crystals connected to a Packard pulse height analyzer and scaler. Total absorption was determined from the activity in blood, liver, kidneys, and carcass, and total endogenous mercury reappearing in the gastrointestinal tract was determined from the activity in the nondosed segments.

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Analysis of variance was applied to the data, and differences between means were determined by Student–Newman–Keul's multiple-range test.

Results. The concentration (% dose/ml) of mercury in the blood 1, 2, and 4 hr after dosing with methylmercury ($CH_3{}^{203}HgCl$) or inorganic mercury ($^{203}HgCl_2$) is shown in Table I. As expected, blood concentrations of methylmercury were greater ($P < 0.01$) than those of inorganic mercury for all dosing methods. One- and two-hour methylmercury blood concentrations of rats dosed in different gastrointestinal segments were not different, but the blood concentration of methylmercury at 4 hr was slightly higher ($P < 0.05$) from rats dosed in the duodenal segment (the segment of greatest absorption). There was no correlation between segment absorption and blood concentrations of inorganic mercury.

Total absorption, GI retention, and excretion of endogenous mercury into the gastrointestinal tract are shown in Table II. The duodenal segment absorbed over 80% of a local methylmercury dose, greater ($P < 0.01$) than any other segment. Nearly 60% of a local methylmercury dose was absorbed from the stomach, not statistically different from the ileal segment. Absorption from the jejunum was 35%, less ($P < 0.01$) than any other segment. Gastrointestinal retention was inversely proportional to absorption. Significant differences in absorption of inorganic mercury between gastrointestinal segments were not detectable.

Total endogenous excretion of methylmercury into the gastrointestinal tract was proportional to absorption, but excretion as a percentage of dose was significantly less ($P < 0.01$) when the dose was administered in the jejunal segment. However, when the data were expressed as a percentage of the absorbed dose rather than as a percentage of the total dose, no differences were seen in excretion between sites of absorption.

Table III lists the endogenous excretion of mercury into the intestinal segments after intravenous injections of methylmercury chloride or mercury chloride. More ($P < 0.01$) of both forms of mercury was excreted into the first duodenal segment (which contained all bile excreted during the experiment) per unit length than any other segment. This was presumably due primarily to bile excretion. Significant amounts of mercury were also excreted into other intestinal segments; the duodenal segment was the optimal site for intestinal excretion. In contrast to mercury absorption from the intestine, mercury excretion by intestinal tissue was the same for both forms of mercury per unit length, and the excretion of mercury in bile from inorganic mercury was greater ($P < 0.05$) than that of methylmercury.

Discussion. Methylmercury was readily absorbed from all segments of the gastrointestinal tract in the following pattern: duodenum > stomach = ileum > jejunum.

TABLE I. THE CONCENTRATION OF ^{203}Hg ($CH_3{}^{203}HgCl$ AND $^{203}HgCl_2$) IN THE BLOOD 1, 2, AND 4 hr FOLLOWING INTRAVENOUS INJECTIONS AND INJECTIONS INTO LIGATED SEGMENTS OF THE GASTROINTESTINAL TRACT (% DOSE/g ± SE).

Segment	1 hr	2 hr	4 hr
	Methylmercury		
iv	5.10 ± 0.36*, [a]	4.57 ± 0.48[a]	4.05 ± 0.70[a]
Stomach	0.61 ± 0.08[b]	1.08 ± 0.13[b]	1.25 ± 0.11[b]
Duodenum	0.41 ± 0.04[b]	0.98 ± 0.06[b]	2.10 ± 0.04[c]
Jejunum	0.47 ± 0.06[b]	0.82 ± 0.12[b]	0.91 ± 0.11[b]
Ileum	0.42 ± 0.08[b]	0.86 ± 0.18[b]	1.22 ± 0.34[b]
	Mercury chloride		
iv	1.90 ± 0.11[a]	1.40 ± 0.05[a]	1.16 ± 0.06[a]
Stomach	0.014 ± 0.006[b]	0.012 ± 0.007[b]	0.019 ± 0.009[b]
Duodenum	0.011 ± 0.005[b]	0.018 ± 0.006[b]	0.019 ± 0.006[b]
Jejunum	0.006 ± 0.003[b]	0.012 ± 0.005[b]	0.025 ± 0.014[b]
Ileum	0.014 ± 0.007[b]	0.014 ± 0.006[b]	0.013 ± 0.005[b]

* Mean ± SE. Means with the same subscript in the same vertical row are not different at the 5% level of significance.

TABLE II. Gastrointestinal Retention, Absorption, and Endogenous Excretion of Mercury after Injections of Methylmercury or Mercury Chloride into Ligated Segments.

Site of dose	GI retention (% dose)	Absorption[a] (% dose)	Total endogenous excretion[b]	
			% Dose	% Absorbed
		Methylmercury		
Stomach	35.9 ± 2.4*, c	58.6 ± 2.0c	3.60 ± 0.28c	6.14 ± 0.96c
Duodenum	15.8 ± 1.1d	83.1 ± 2.3d	4.65 ± 0.22c	5.60 ± 0.42c
Jejunum	58.4 ± 3.8e	34.8 ± 3.0e	2.18 ± 0.25d	6.26 ± 1.44c
Ileum	31.9 ± 3.2c	54.6 ± 6.4c	3.34 ± 0.30c	6.12 ± 1.10c
		Mercury chloride		
Stomach	91.1 ± 2.2c	3.66 ± 1.18c	0.314 ± 0.138c	8.85 ± 2.46c
Duodenum	90.0 ± 1.1c	2.33 ± 0.66c	0.218 ± 0.046c	10.64 ± 3.05c
Jejunum	90.7 ± 1.1c	2.00 ± 0.89c	0.134 ± 0.041c	9.92 ± 2.63c
Ileum	95.6 ± 2.4c	1.91 ± 0.93c	0.197 ± 0.060c	10.98 ± 3.68c

[a] Sum of activity in blood, liver, kidneys, and carcass.
[b] Total activity in all nondosed gastrointestinal segments.
* Mean ± SE. Means with the same subscript in the same vertical row are not different at the 5% level of significance.

TABLE III. Endogenous Excretion of Mercury into the Gastrointestinal Tissue after Intravenous Injections of Either Methylmercury or Mercury Chloride.

Segment	Methylmercury		Mercury chloride	
	% Dose/cm	% Dose/g	% Dose/cm	% Dose/g
Duodenum (bile)	0.081 ± 0.008*, a	0.248 ± 0.027a	0.169 ± 0.024a	0.613 ± 0.990a
Duodenum	0.036 ± 0.003b	0.444 ± 0.017b	0.078 ± 0.015b	1.410 ± 0.230b
Jejunum	0.023 ± 0.002b	0.340 ± 0.025a	0.029 ± 0.002c	0.520 ± 0.041a
Ileum	0.025 ± 0.005b	0.283 ± 0.015a	0.042 ± 0.006c	0.661 ± 0.082a
Stomach		0.121 ± 0.020c		0.191 ± 0.017c
Cecum/colon		0.171 ± 0.015c		0.321 ± 0.038b

* Mean ± SE. Means with the same subscript in the same vertical row are not different at the 5% level of significance.

Inorganic mercury was not readily absorbed, and no significant difference existed between segments.

The significance of the high absorption of methylmercury from the stomach is difficult to evaluate, since the surface area of the stomach may differ from that of intestinal segments and the emptying time of methylmercury from the stomach may be very rapid in the normal animal. Methylmercury in a normal diet is probably protein bound (10) rather than ionic and may not be as readily absorbed from the stomach until the proteins have been digested. Thus the residence time of the readily absorbable form of methylmercury could reduce absorption in the stomach. It is apparent, however, that the absorption of methylmercury from the stomach is likely to contribute a sizable portion of total methylmercury absorption.

The pattern of metal absorption from the gastrointestinal tract differs for various elements and even for different chemical forms of the same element. This study demonstrates that, unlike methylmercury, inorganic mercury was not readily absorbed from the stomach or other intestinal segments. Thus methylmercury was absorbed more readily from all segments of the gastrointestinal tract studied, a relationship which has been observed many times in whole animal studies (8–10). Whanger *et al.* (11) found that inorganic and organic selenium were absorbed equally from the gastrointestinal tract and that essentially no selenium was absorbed from the stomach. Among other metals studied only copper is readily absorbed from the stomach (12).

The major route of mercury excretion is via the feces, and both methylmercury (13, 14) and inorganic mercury (15) are excreted in the bile. Autoradiographic studies by Berlin and Ullberg (16) have also shown an accumulation of intravenously injected mercuric chloride in the mucosa of the entire intestinal tract. Our data indicate that both methylmercury and inorganic mercury are excreted by intestinal tissue as well as in bile.

Summary. The ligated segment technique was used to compare the gastrointestinal absorption of methylmercury and mercury chloride in the rat. Methylmercury was more readily absorbed (15-35 times greater, depending on the absorption site) than inorganic mercury from all ligated segments. The relative order of methylmercury absorption from ligated segments was as follows: duodenum > stomach = ileum > jejunum. Differences in absorption of inorganic mercury between gastrointestinal segments were not observed. Endogenous excretion of both forms of mercury into intestinal tissue were equal. Our data indicate that the absorption of methylmercury from the stomach is significant relative to other parts of the gastrointestinal tract and that the stomach must be considered a major site of absorption.

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