Effect of Cobalt upon Iron Absorption (34873)

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Cobalt decreases iron absorption as effectively as equimolar quantities of carrier iron (1–4). The site and mechanisms of this inhibition are unknown. Previous investigations have demonstrated that cobalt does not inhibit iron absorption by a toxic effect upon the gut or by intraluminal competition for substances which enhance absorption. Since cobalt is not incorporated into ferritin and is poorly bound by transferrin, it is unlikely that these proteins are responsible for the inhibition of iron absorption by cobalt (4). One possibility is that these metals share a common absorptive pathway in intestinal cells. This hypothesis was tested by studies of the mucosal uptake of iron in the presence and absence of cobalt.

Methods. Absorption studies were performed in 200- to 300-g male rats of the Walter Reed Carworth Farm strain that had been fasted overnight. The rats were given intragastric doses of iron or cobalt under light ether anesthesia with a 17-gauge olive-tipped endoesophageal needle. Each test dose was 0.5 ml of distilled water which contained 0.5 μCi 59 Fe as $FeCl_2 \cdot 4H_2O$. In one experiment 5 μmoles of iron ($FeCl_2 \cdot 4H_2O$) was administered either with or without 25 μmoles of cobalt as $CoCl_2 \cdot 6H_2O$. In another experiment, various amounts of iron (0.005–50 μmoles) were administered with or without 50 μmoles of cobalt in the test dose.

After dosing, each rat was placed in a vented quart container, and the whole-body radioactivity was measured in a small animal liquid scintillation detector (ARMAC, Packard). In one experiment iron absorption was quantified by comparing a similar measurement made 1 week later to the measurement obtained immediately after dosing (5). In another experiment, the rats were killed 4 hr after dosing. Then the gastrointestinal tract was excised intact and the carcass returned to the quart container for a second assay of whole body radioactivity. The small intestine of each rat was incised lengthwise, washed in Tris buffer (pH 8.4) and placed in a 250-ml water-filled bottle. Radioactivity was quantified in a whole-body liquid-scintillation detector.

Iron deficiency was induced by feeding animals an iron-depleted powdered milk diet for 2 weeks.

Comparisons between treated and untreated animals were made by Student's *t* test. There were 8–10 rats in each group.

Results. Figure 1 shows the results of iron-absorption studies in rats given various oral doses of iron with and without 50 μmoles of cobalt. In rats receiving only iron, iron absorption increased in a biphasic manner with increasing doses of carrier iron. The first portion of the curve has been interpreted to represent absorption facilitated by a saturable carrier, whereas the second portion has been thought to be diffusion (6–7). The addition of cobalt to the test doses of iron produced a linear dose-related response with a slope similar to that seen for the absorption curve in rats receiving high doses of iron alone.

Table I shows the results of studies in normal and iron-deficient rats which received 5-μmole doses of radioiron with and without 25 μmoles of cobalt. Significantly less radio-

[1] In conducting the research described in this report, the investigators adhered to the Guide for Laboratory Animal Facilities and Care, as promulgated by the Committee on The Guide for Laboratory Animal Facilities and Care of the Institute of Laboratory Animal Resources, National Academy of Sciences, National Health Council.

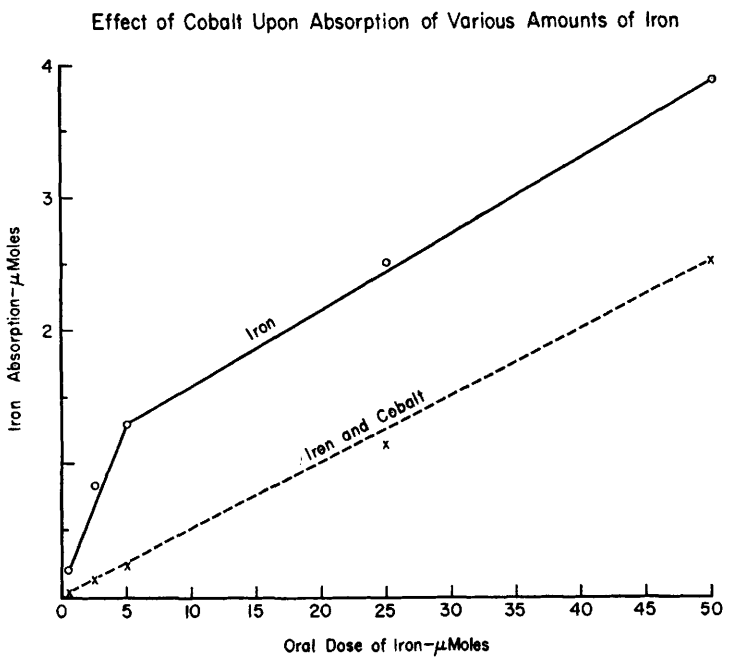

FIG. 1. Quantity of iron absorbed from oral test doses of radioiron containing various amounts of carrier iron with and without 50 μmoles of cobalt.

iron was observed in both the carcass and small intestine of animals receiving cobalt with test doses of radioiron, indicating that cobalt diminished the mucosal uptake of the iron from the lumen of the gut.

Discussion. A greater percentage of iron is absorbed from small quantities of iron than from larger oral doses of iron, although the absolute iron uptake increases as the iron concentration in the dosing solution is raised (5, 8). The biphasic dose-response curve observed with incremental increases in the oral test dose of iron is interpreted to represent facilitation of absorption of small doses of iron by a saturable carrier, whereas larger doses are absorbed mostly by a nonsaturable process such as diffusion (6, 7). The addition of cobalt to test doses of iron causes a disappearance of the initial facilitated phase of this curve suggesting that cobalt saturates a shared absorptive pathway. The lowered iron uptake into both the intestinal mucosa and carcass of animals receiving cobalt with test doses of iron indicates that there is diminished mucosal uptake of iron. It is unlikely that cobalt primarily blocks iron transfer from intestinal cells to blood. If this were the mechanism of action for cobalt, the content of absorbed iron in the intestine of cobalt-treated rats would presumably be greater than that for the controls not given cobalt. The normal absorption of other metals and

TABLE I. Iron Absorption 4 hr After Oral Dose of Iron.

	Oral dose	Fe in small intestinal wall (μmoles)[a]		Fe in carcass (μmoles)[a]	
Normal rats	5 μmoles Fe	.280 ± .035		.410 ± .06	
	5 μmoles Fe + 25 μmoles Co	.145 ± .015	$p < .01$	.120 ± .02	$p < .001$
Iron-deficient rats	5 μmoles Fe	.215 ± .043		1.655 ± .177	
	5 μmoles Fe + 25 μmoles Co	.115 ± .045	$p < .05$	.320 ± .005	$p < .001$

[a] Mean ± 1 SEM.

the continued effect of cobalt upon iron absorption in the presence of excess amounts of ascorbic acid suggest that cobalt does not affect iron absorption by exerting a toxic effect upon the gut or by competing for intraluminal substances which enhance iron absorption (4). Cobalt does not stimulate ferritin synthesis or incorporate into apoferritin, making it unlikely that ferritin is the common saturable pathway (4, 9). Identification of this common carrier might provide information of importance regarding the regulation of intestinal absorption by mucosal cells.

Summary. The addition of cobalt to oral test doses of radioiron decreases iron absorption. Studies were performed in rats to determine the site and mechanisms of this inhibition. Significantly less radioiron was observed in both the carcass and small intestine of rats fed cobalt with test doses of radioiron than in animals receiving iron alone. This indicates that cobalt diminished the mucosal uptake of iron from the intestinal lumen. Iron absorption studies in rats receiving various doses of iron with and without added cobalt suggested that cobalt was capable of saturating a common pathway in intestinal absorptive cells for the absorption of both metals.

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