Radioiron Excretion by the Skin and Kidney of Dogs. (17717)

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Many publications support the concept that the body absorbs iron in significant amounts as a rule only when its iron stores are depleted(1-3), and that small amounts of iron escape in the urine and bile(4). A recent article(5) states that human subjects under "minimal sweating" conditions can excrete 6.5 mg of iron per day, or 13% of the iron ingested. Since the dog has been used in many experimental studies of iron metabolism it seemed pertinent to measure the iron excretion by the skin in this species which is nearly devoid of sweat glands.

The experiments tabulated below indicate clearly that no significant amount of radioactive iron is excreted by the dog's skin when iron is given by mouth or vein.

Methods. The radioiron procedures and other methods used in this laboratory have been described elsewhere(6). The isotopes used consisted almost entirely of Fe^{55}. The dogs were thoroughly scrubbed in a baby bathinette, using tap water and a commercial detergent. The entire washings were collected, evaporated to a small volume, and transferred to Kjeldahl flasks for wet ashing with sulfuric and perchloric acids. Prior to electroplating, the iron was extracted with isopropyl ether(7). Urine and feces were similarly treated. Intravenous iron solutions were prepared in gelatin(8). The dogs used were all normal female mongrels with normal hematocrits and presumably adequate iron stores. Dog 43-141 had a year previously received radioiron and had absorbed and utilized a small amount. The other dogs had received none. During the course of the experiments, the animals were caged in the laboratory which was usually around 26°C. No attempt was made to control the humidity.

Experimental observations. Routes of administration and radioiron recovery data appear in Table I. The findings are in harmony with work published elsewhere. In the first 2 experiments in Table I, only 0.03 and 0.02% of radioactive iron could be found in the washings taken one day after the intravenous injection of 5.23 and 5.03 mg of iron containing the isotope. In the second experiment only 0.01% could be found after a week.

It will be noted that the washings taken prior to the iron administration in the first experiment contained 900 counts per minute of radioiron. This was thought at the time to have been derived from the radioiron administered at an earlier date. To our surprise, however, the washings taken prior to iron administration in Exp. 2 contained a similar amount of radio-activity. A check revealed that the separatory funnels used in the ether extraction were slightly contaminated with radioiron. Consequently, the traces of radioiron found in the washings of these 2 experiments may have come partially or entirely from this source. Since even traces of iron contaminating the glassware are picked up—710-418 counts per minute or 0.0016-0.0009 mg of radioiron in Exp. 1 and 2—it is scarcely probable that any significant amount of iron eliminated by the skin could escape detection.

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TABLE I.
Recovery of Radioiron in Body Washings and Urine Following Intravenous and Oral Administration of Radioiron.

Exp.	Dog	Wt in kilo	Hematocrit, %	Route of iron administration	Radioiron, mg*	Body washings: Before iron Counts per min.	After iron administration: One day Counts per min.	One day % of dose	One week Counts per min.	One week % of dose	Urine Counts per min.	Urine % of dose
1	43-121	12	49	i.v.	5.23	900	710	.03	—	—	37,000	1.6†
2	49-61	12	51	i.v.	5.04	540	418	.02	229	.01	35,200	1.6†
3	49-131	11.7	54	oral	10.6	0	1240	.02	720	.02	3,000	0.06‡

58% of the dose in Exp. 3 was found in the feces.
* The activity of the iron used was about 450,000 counts per min. per mg.
† Urine collected for 24 hrs.
‡ " " 48 "

In Exp. 2 determination of total plasma iron 5 minutes after the injection gave a value of 554 γ per 100 ml of which 442 γ per 100 ml could be accounted for from the administered radioiron. Since only traces of radioiron might have been excreted through the skin following intravenous administration, oral administration was tested. A third dog weighing 11.7 kilos was given 10.6 mg of radioiron as ferric chloride by stomach tube (Exp. 3). New separatory funnels were used and no activity was found in the washings prior to radioiron feeding. Only 0.02% of the dose was found in the washings taken at one day and one week. The plasma radioiron one hour after feeding was 15 γ per 100 ml. In one week 2.5% of the dose was found in the circulating red cells.

In Exp. 3, 58% of the dose was found in the feces collected during a 3-day period. This low value(1) probably resulted from too short a collection period. Since no precautions were taken to prevent contamination of the dog by feces, other than by their prompt removal from the cage, some, if not all, of the radioiron found in the washings could have come from this source. Urinary radioiron data are given in the last column of Table I. In Exp. 1 the urine was collected by catheterization; in Exp. 2 and 3 it was collected in a metabolism cage. In each of the 2 tests following intravenous injection the 24-hour urines contained 1.6% of the radioiron administered. After oral feeding, only 0.06% of the administered radioiron appeared in the urine in 48 hours. The high values following intravenous administration are presumably due to the higher plasma iron values for the few hours following injection.

The urinary excretion of radioiron was many times that found in the dermal washings, even assuming that all such radioiron was excreted by the skin.

Discussion. From the data presented it is quite obvious that an insignificant amount of radioiron, if any, appears in washings from dogs given a single dose of radioiron by vein or mouth. The maximum amount found corresponded to 0.03% of the dose and may well have resulted largely from contamination of

the glassware in the first 2 experiments, or of the skin by feces in the third. It would seem reasonable to assume that any dermal loss of iron would be mediated in part at least by the plasma transport mechanism, yet in the intravenous experiments in which the plasma iron was raised to very high levels, no appreciable loss through the skin occurred.

It should be noted that an oral dose of 10 mg of iron to a 10 kilo dog corresponds roughly to a 70 mg dose to an average man, a level relatively higher than the iron fed daily by Mitchell and Hamilton(5).

It is difficult to reconcile the final conclusion of Mitchell and Hamilton(5) that the skin and sweat glands are important excretory organs for iron with the finding that the absorption of iron occurs with difficulty and can be influenced by bodily needs. This has been amply demonstrated with radioiron in the dog(1), rat(3), and human(2) subject. The reutilization of iron released from destroyed erythrocytes following the administration of phenylhydrazine(9), transfusion of non-viable red cells(10), and normal wear and tear(11), has been shown repeatedly. The occurrence of transfusion hemosiderosis, both clinically and in normal dogs(12), indicates little or no ability on the part of humans and dogs to excrete iron. Moreover, the high tissue iron found by Finch and his co-workers(13-15) in rats and dogs fed a corn grit and lard diet is incompatible with much loss of iron from the body by any route, including the skin.

Summary. Following intravenous or oral administration of single doses of radioiron to dogs, little or no radioiron can be washed from the skin and hair, thus indicating that no significant amounts of iron are excreted through the skin in 1 to 7 days.

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Some Effects of Subcutaneous Tocopherols in Normal and Tocopherol-Deficient Mice. (17718)

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Pregnant mice will resorb their fetuses when fed a tocopherol-deficient diet long enough to deplete the body stores of this vitamin; such animals, however, when treated with tocopherols will have normal litters(1,2). Although parenteral administration of tocopherols has been used effectively in preventing or repairing the histopathologic changes in voluntary muscle due to tocopherol deficiency in several species, the effect of treatment by this route on the maintenance of pregnancy has not been fully explored, due primarily to the greater effectiveness of the oral over the parenteral route of administration(3-8). To supplement

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