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Detection of Minute Gastrointestinal Bleeding Utilizing Radioactive Iron, Fe^{59}.* (24036)

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A simple method for detecting minute gastrointestinal bleeding would provide a screening test for detection of ulcerated lesions of the alimentary tract not recognizable by conventional radiographic or other currently available diagnostic means. Such a test could be utilized for detection of the presence of silent cancers of mucous membranes of the gastrointestinal canal, or possibly of other tracts with external orifices. The use of radioactive ferrous citrate, Fe^{59}, for this purpose was investigated. Radioactive iron given orally may make its appearance in red blood corpuscles as early as 4 hours following ingestion(1). Radioactive iron given intravenously is also rapidly incorporated into the red blood cell(2). Bleeding from the mucous membrane of the alimentary tract should be recognizable by the appearance of increased radioactivity in the stool provided normal excretion patterns of the isotope by this route are determined.

The experiments reported herein indicate that occult bleeding in the gastro-intestinal tract can be detected by the use of radioactive ferrous citrate incorporated into the red blood cell. After preliminary study, the method appears to be more sensitive than the guaiac test for this purpose.

Method. Twenty healthy mongrel dogs weighing 10-15 kg, and divided into 3 groups, were utilized in this study. Group I consisted of 8 control animals, each of which received 25 microcuries of radioactive ferrous citrate (Fe^{59}) intravenously. Group II consisted of 6 test animals. Each of these received 25 microcuries of radioactive ferrous citrate intravenously and after 14 days also received 30 mg of histamine in beeswax intramuscularly daily. Ulcerations of the gastrointestinal tract occur regularly in the majority of animals so treated(3). Group III consisted of 6 normal dogs. Each of these received by gastric tube small amounts of Fe^{59} tagged blood obtained from one of the Group I animals. In all animals of Groups I and II following injection of the isotope and in Group III dogs following intragastric injection of the labeled blood, daily stool collections were made. An equal amount of water was added to each 24-hour stool sample and mixed thoroughly in Waring Blendor. Four ml of resultant mixture was then counted in a well-type scintillation counter, 1000 or more counts being recorded for each specimen. Values are expressed as number of counts/4 ml of stool-water mixture for 10 minutes, which actually represents the number of counts/2 ml aliquot of stool. Whole blood was removed by venipuncture from animals of Groups I and II at intervals, and one ml was counted in the scintillation counter. The guaiac test for occult blood was

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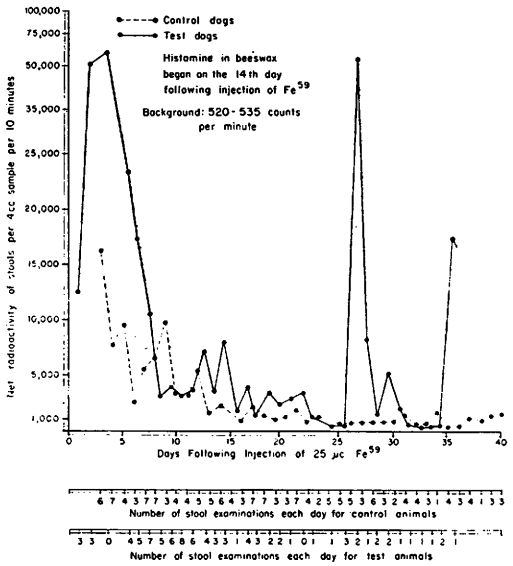

FIG. 1. Mean and extreme values of stool radioactivity in control and test animals.

also performed on all specimens. All animals were followed for 40 days or until death. During the study, all animals received regular kennel rations ("Kibbies") and no other food was given. Autopsy was carried out in all animals. Animals were excluded from Group I if intestinal parasites or other lesions were present, and no animals were included in Group II unless obvious mucosal ulceration of the gut was demonstrated later upon sacrifice. All animals fulfill the above criteria.

Results. Fig. 1 demonstrates the pattern of excretion of radioactive iron in the stools of Groups I and II dogs. Following injection of the isotope, prompt excretion through the gastrointestinal tract occurs; gradually, decreasing amounts are detectable in the stool of normal animals. After 21 days, excretion of radioactive iron by normal animals has reached consistently low levels. In none of 65 stool determinations done after this time were counts of more than 2500 above background recorded. Animals of Group II showed a similar pattern of excretion following injection of the isotope with gradually declining levels of stool radioactivity. However, following administration of histamine in beeswax, elevated excretion of the isotope in the stool was observed. Of a total of 45 stool determinations upon Group II dogs, performed 21 or more days following administration of the isotope, 17 showed counts greater than the 2500 level. Thirteen of these 17 were associated with a positive guaiac test and in 4 the guaiac test was negative. The radioactive iron method, in detection of an indeterminate amount of bleeding, was thus positive in 24% more of determinations than was the case with the guaiac test.

On the 24th day following injection of 25 microcuries of the isotope, counts of peripheral blood averaged 6675 counts/ml/minute for control animals and 5591 counts/ml/minute for animals receiving histamine in beeswax.

Data from Group III animals are shown in Table I. Amounts as small as 1 ml of Fe^{59} tagged blood given to animals by gastric tube were detectable by the ensuing high levels of radioactivity in the stool. Most of the blood was excreted within 24 hours of administration and stool counts fell to low levels promptly thereafter. Amounts of blood less than 10 ml were not detectable by the guaiac test when administered in this manner. From these data the radioactive iron method would appear to be at least 10 times more sensitive

TABLE I. Stool Radioactivity following Intragastric Administration of Fe^{59} Tagged Blood in 6 Animals.

Amt of blood given (ml)*	Net stool activity in counts/4 ml/10 min.	Days after blood given	Guaiac test
10	4,867	1	0
	10,606	2	+
	835	3	0
	5,765	4	0
5	5,212	1	0
	40,607	2	0
5	1,244	1	0
	151	2	0
	214	3	0
3	12,605	1	0
	1,489	2	0
	46	3	0
1	13,517	1	0
	910	2	0
	1,004	3	0
1	1,822	1	0
	72	2	0
	922	3	0

* Radioactivity of blood given: 6,540 counts/cc/min.

Background count: 520-535 counts/min.

than the guaiac test for detection of known minute amounts of blood in the stool.

Discussion. Not all of the injected radioactive iron is incorporated into red blood cells. Hahn and associates(4) have shown that 35 to 70% of injected isotope becomes incorporated in peripheral circulating red blood cells. However, if a sufficient period of time is allowed to elapse following injection of radioactive iron, the excretion pattern of the isotope in the stool may subsequently be utilized for detection of bleeding from the alimentary canal, since elevated levels of stool radioactivity after 21 days are indicative of abnormal sources of iron loss.

The method appears to be considerably more sensitive than the guaiac test, utilizing amounts of the isotope and the technic for determination of stool radioactivity described herein.

It is conceivable that the sensitivity of the method might even be enhanced somewhat by modifying the technic of examination by ashing and counting the entire 24-hour stool. If proved correct, this modification could permit administration of smaller amounts of the isotope. In the presence of a positive test, a comparison of esophageal, gastric and colonic washings could prove to be of real help in localizing the source of the bleeding from the tract. It is proposed presently to undertake clinical investigation of the efficacy of the method in the detection and localization of silent malignancies of the gastrointestinal canal.

Summary. 1. Excretion patterns of intravenously administered radioactive iron in the stool of normal dogs and in dogs with histamine induced bleeding of the gastrointestinal tract have been compared. 2. Levels of stool radioactivity have been measured following intragastric administration of known amounts of isotope-labelled blood. 3. Radioactivity in the stool can be utilized for detection of occult bleeding. 4. Comparative evaluation following administration of known small quantities of isotope-labelled blood (Fe^{59}) indicates definitely that this test is considerably more sensitive than the guaiac test.

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Pressor Substances in Kidneys of Renal Hypertensive Rats with and Without Adrenals. (24037)

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In the rat, sustained hypertension develops after clamping the artery of one kidney, leaving contralateral kidney untouched(1). It has also been demonstrated that the content of pressor substances (renin) in aqueous extracts prepared from kidneys is normal or enhanced in the clamped kidney, while it is reduced or absent in the contralateral untouched kidney which, however, shows typical morphological changes(2). Furthermore, it is well known that experimental renal hypertension of the Goldblatt type is dependent on presence of functioning adrenal cortex. In the adrenalectomized animal, hypertension does not develop or blood pressure falls to normal values if the adrenals are extirpated after establishment of hypertension(3). In former experiments we observed that in rats in which hypertension has been produced by overdosage of cortexone and salt, pressor active substances disappeared from the kidneys (4). The experiments reported here were

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