

## ROENTGEN RAY INTOXICATION.

### IV. INTESTINAL LESIONS AND ACUTE INTOXICATION PRODUCED BY RADIATION IN A VARIETY OF ANIMALS.

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When our x-ray experiments on dogs gave such uniform results both as to intestinal injury and clinical intoxication we became interested in the reaction to radiation of other common laboratory animals. We found that in a great variety of animals the intestinal epithelium was sensitive to the x-ray; indeed capable of injury and destruction by means of radiation with a clinical reaction due to a disturbed intestinal tract.

The series of animals given below is not sufficient to establish the lethal dose and intestinal pathology as accurately as has been done for the dog (Warren and Whipple (13)) but there is striking similarity which strengthens our belief in the fragmentary data indicating that human beings are likewise sensitive to these hard x-rays. The roentgenologist must be on his guard to recognize the evidence of this condition in human beings and having established toxic doses he must guard against permanent injury of the intestinal mucosa. The chronicity of the intestinal ulcerations is no less disturbing than that of the familiar x-ray skin burn, or ulcers.

A review of the experimental work done upon laboratory animals with various types of radiation is very confusing. There are several reasons for this. The most obvious is that there has been the greatest variety as to the source or amount of radiation used. The second obvious factor is the individual resistance or lack of sensitivity of different animals to various amounts and kinds of radiation. Most of the earlier investigators were interested in the effects of the softer

radiations from the lower powered Roentgen ray machines upon the skin, generative organs, spleen, and bone marrow.

Frogs and young amphibia have been used frequently. Fromme (3) found that 60 to 270 m.a.m. killed a young axolotl in 4 days. No reference to the use of reptiles was found.

Birds were exposed to radiation by Krause (1906 (5)) and by Perthes (1903 (9)) who reports that one chick died in 22 days after radiation.

Lazarus-Barlow (1920 (6)) in a preliminary report described changes in the intestinal mucosa and the general organism of rats, rabbits, cats, and dogs after exposure to large amounts of radium. The changes seem comparable to our experimental results with the Roentgen rays in the same animals. Meyer and Ritter (8) were the first to establish the lethal dose for mice—30 x (hard BW5 radiation)—4 to 10 days were the various antemortem periods. Many have noticed the intoxication with diarrhea, etc., but all save a few of the more recent authors (Fromme (3); Lazarus-Barlow (6); Denis *et al.* (1)) have neglected to make histological studies of the animals to discover the cause.

Rabbits were used by Warthin (11, 12), Perthes (9), Denis, Martin, and Aldrich (1), and Hussey (4). One given 600 m.a.m. by Warthin died 40 hours later. This is somewhat earlier than was to be expected. The experiments of Denis *et al.* show that for rabbits the equivalent of 300 m.a.m. over the abdomen at 10 inches is just below the minimal lethal dose. They found changes in the alkali reserve during the intoxication following radiation. Hussey (4) thought that 150 m.a.m. at 6 inches was the maximal sublethal amount for rabbits. He noted an alkali excess which paralleled the drop in leucocytes, especially the mononuclears.

Dogs were used by Regaud, Nogier, and Lacassagne (10) in the best piece of experimental work reported in the earlier literature. They described the more chronic lesions in the intestines and stomach. The significance of their findings has not been fully appreciated. Krause (5) and Warthin (11, 12) also used dogs. Their results are hardly useful in calculating a m.l.d. as their series of exposures is not uniform nor fully described. This is a common fault observed in much of the earlier work. Emsmann (1911 (2)) reports a diarrhea in a dog 2 days after ingesting 5,000 maché units of thorium X in water, followed by death on the 4th day. No changes were noticed in the intestine. This seems within the m.l.d. when compared to our experiments. Martin and Rogers (1923 (7)) found 200 m.a.m. (about 75 kilovolts) fatal to a dog by the 5th day with the usual symptoms.

#### *Method.*

In these experiments very large amounts of radiation have been applied in single doses over the abdomen or the whole body of various laboratory animals in the endeavor to destroy a sufficient amount

of intestinal epithelium to bring about total intoxication. The smallest dose which will kill the animal in the shortest space of time has been designated as the minimal lethal dose (M.L.D.) for this type of radiation. The same standard equipment and technique were used in these experiments as in all the other studies. The target-skin distance was always 25 cm. and the filter 2 mm. of aluminum. The spark-gap was between 21 and 23.7 cm. The E.M.F. varied between 85 and 95 kilovolts. The current filament was usually 8 milliamperes and the dose was computed in milliampere minutes.

#### EXPERIMENTAL OBSERVATIONS.

*Dogs.*—In a series of sixteen dogs the average minimum lethal dose for 20 to 40 pound dogs was found to be 350 M.A.M. It is very common for dogs of this size to survive 320 M.A.M. but with evidence of severe intoxication. Much larger doses of radiation than 350 M.A.M. do not shorten the antemortem period of 4 to 5 days nor increase the severity of the intoxication syndrome—vomiting, tarry or bloody diarrhea, prostration, and death. At autopsy the mucosa of the small intestine is roughened, dark red in color, and quite thin. Histologically the villi show absence of the covering epithelium and the crypts are filled with exudate and injured and necrotic epithelium,—signs of epithelial regeneration are apparent; mitotic figures are frequent; ruptured capillaries are conspicuous. With small x-ray doses the destruction of the epithelium is apt to be patchy. With large doses it is widespread. The progress of this injury from 2 hours after radiation until the death of the animal has been reported fully in previous studies (Warren and Whipple (13)).

The erythema dose at 95 kilovolts is approximately 90 to 100 M.A.M. at 10 inches skin-target distance with a 2 mm. aluminum filter.

*Cats.*—Cat 19-4c, weight 4 kilos; adult male. 320 M.A.M. radiation administered over abdomen produced a moderate intoxication on the 3rd day. This increased on the 4th and 5th days and was accompanied by some diarrhea and drooling. The cat was completely recovered by the end of the week. The stools continued to be formed after this time. 3 weeks after radiation the hair fell out over a part of the right thorax and abdomen, and the skin became pigmented. The cat steadily lost weight and at the end of 7 weeks weighed only 2½ kilos. It was killed under ether anesthesia. At autopsy the viscera were essentially negative except that the mucosa of the small intestine appeared to be thinner and more granular than usual. There were no ulcerations in evidence. Microscopically, however, pronounced injury and destruction of the villi could be seen in many areas of the small intestine. There was rather diffuse injury to the crypt epithelium in the mucosa of the duodenum, jejunum, and ileum. Attempts at regeneration were atypical and these epithelial cells were pale and somewhat basophilic. In several places the muscularis mucosæ was bare. The muscle wall was atrophic

and thin, showing that this dose had caused some injury to the smooth muscle of the intestine as well as to the epithelium. The spleen and lymph follicles showed necrotic centers in the Malpighian bodies and atrophy of the pulp elements.

This is a sublethal amount of radiation producing widespread patchy injury to the small intestine which was demonstrable at the end of 7 weeks. This injury to the mucosa was probably responsible for the conspicuous loss of weight.

Cat 19-1c, weight 1½ kilos; young female. 400 m.a.m. radiation was administered over the abdomen at 90 kilovolts with a 2 mm. aluminum filter. The animal appeared intoxicated on the 3rd day and was found dead on the 4th. No diarrhea or vomitus. Autopsy showed no gross abnormalities except in the small intestine. The mucosa, especially in the duodenum, upper jejunum, and middle ileum, was diffusely injected and dark red in color. The surface was still velvety and there were no ulcerations. There were quite a few live segmented worms present. The mucosa of the stomach and colon was pale and apparently normal. The feces in the colon were fluid though not blood-stained.

Microscopically the duodenum, jejunum, and ileum showed marked and widespread collapse of the crypts. The villi where present were short, thick, and clubbed. The epithelial cells remaining in the crypts were large, pale, and tended to take the basophilic stain. Mitoses were frequent. There was some infiltration of the submucosa with a few leucocytes and phagocytes. Ruptured capillaries contained fibrin plugs in many cases. The spleen and lymph follicles showed pulp atrophy and phagocytosis of the degenerating nuclei. The mature ova were necrotic while the immature ova were unchanged.

This is a lethal dose for a rather small cat. A smaller amount, probably 350 m.a.m., would probably have been lethal. The injury to the intestinal mucosa is marked and rather widespread.

Cat 19-3c, weight 2½ kilos; adult female. 480 m.a.m. radiation was administered over the abdomen. On the 2nd day the cat became definitely intoxicated. Vomitus and tarry stools appeared that afternoon. The cat was very sick on the 3rd day and was killed under ether. It was evident clinically that the cat would die early on the 4th day. Autopsy showed a pale, slightly granular mucosa in the small intestine with the exception of the lower ileum where there were many slightly depressed hemorrhagic areas. There was no extensive denudation of the mucosa evident in gross and the appearance did not deviate much from the normal except for the hemorrhagic areas. Microscopically, however, the crypt epithelium had suffered marked injury in all of the intestine except a portion of the ileum and the colon, where was noted only slight injury. The Malpighian bodies of the spleen and lymph nodes showed pale hypertrophied centers. There was a slight amount of pulp atrophy with much phagocytosis going on. The remainder of the viscera were negative.

This amount of radiation is excessive for a lethal dose. These lesions are exactly comparable to those in a dog sacrificed on the 3rd day following a large lethal dose of radiation.<sup>1</sup>

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<sup>1</sup> Warren and Whipple, Paper I, this series.

*Rabbits.*—Two rabbits given 400 and 600 M.A.M. respectively died on the 7th and 13th days. The first one (No. 19-1r) was quite intoxicated on the 2nd and 3rd days and lost 2 pounds in weight in the next few days before death. At autopsy nothing abnormal could be made out in the mucosa of the intestine. Histologically not only was there patchy destruction of the mucosa of the small intestine but there was also a widespread injury to the epithelium of the cecum. The picture resembled that described in the other animals.

This dose of radiation is very near the M.L.D. The animal was very sick on the 2nd and 3rd days and barely pulled through each day up to its death 4 days later.

The second rabbit (No. 19-2r) though given the larger amount of radiation (600 M.A.M.) did not show the intoxication, loss of weight, and marked intestinal injury that the first one did. The result was probably due to a decreased amount of radiation as the machine was found several days later to be defective. The lesions, however, were similar to those in the other rabbit though less marked in extent.

*Guinea Pigs.*—Guinea Pig 19-2g, weight 525 gm.; adult female. Received 228 M.A.M. radiation over the whole body apparently without any immediate effect. 6 days later the guinea pig had a greenish diarrhea which later became black. During the last 10 days the guinea pig lost weight rapidly and became inactive. It was sacrificed on the 25th day following radiation. The hair began to fall out on the 11th day after radiation. At autopsy nothing abnormal could be made out except for fatty infiltration of the liver. The intestines were rather thin walled and flabby but gave no evidence of ulceration. Microscopically the crypts of the cecum and to some extent those of the duodenum and colon showed large pale atypical cells. There was no destruction of the epithelium of the villi.

It is interesting that these large, pale, distinctly abnormal crypt cells seen in the duodenum and colon resembled similar cells seen in dogs 2 days after radiation. This amount of radiation is just short of the M.L.D.

Guinea Pig 19-3g, weight 500 gm.; white, adult female. 400 M.A.M. radiation given over the whole body. The guinea pig remained apparently normal until the 4th day when it became toxic and developed a tremor of the limbs and head. It seemed very sick. There was no diarrhea. The guinea pig was found dead the following morning. At autopsy the mucosa of the small intestine was brick-red in color and covered here and there by a thick tenacious mucus. The villi seemed absent, leaving a rather raw surface which no longer presented a velvety texture. The cecum and colon were not abnormal; their mucosa was greenish and velvety. The remainder of the viscera were normal. Microscopically the epithelium of the small intestine was almost all destroyed, leaving a few epithelial cells here and there in the collapsed crypts. The epithelial cells of the colon mucosa appeared larger and paler than normal. There was no destruction of the colon villi. The other viscera were normal. This somewhat excessive dose produced a marked and widespread destruction of the epithelium of the small intestine.

*Rats.*—Six rats (Nos. 1 to 6) were given 100 M.A.M. radiation and one was sacrificed every day. There were no signs of intoxication and no gross lesions. Microscopically, however, the crypt cells of the duodenum, jejunum, and cecum were large and pale with large round pale nuclei containing one to two nucleoli. They were most evident and prominent in the small intestine of the rat killed on the 5th day. There was no distortion or change in the shape of the villi. The spleen contained somewhat more pigment than usual in the 5th and 6th day rats.

Six rats (Nos. 7 to 12) were given 200 M.A.M. of radiation and one was sacrificed every day. They developed a diarrhea and looked sick from the 3rd day on, and the last rat was found dead on the morning of the 6th day. Nothing could be made out in gross except in the 5th and 6th day rats whose small intestines in places presented a red or hemorrhagic mucosa. Microscopically there was evidence of abnormality in the crypt cells of the duodenum on the 1st day after radiation. The crypt cells were large and pale and increased in number. On the 2nd day there was evidence of degeneration and regeneration so that though the crypts were somewhat collapsed they were lined by sheets of large pale crypt cells. From the 2nd day on the injury to the villi was more and more evident until it reached the climax on the 6th day when the duodenal villi were stubby and the crypts markedly distorted and lined with atypical cells. The ileum showed ruptured blood vessels in great numbers. The spleen became more and more pigmented up to the 6th day. The ova were necrotic after the 3rd day and the spermatozoa after the 5th day.

A third set of six rats (Nos. 13 to 18) was exposed to 300 M.A.M. and one was sacrificed every 24 hours for 6 days. The symptoms of intoxication with diarrhea appeared on the 4th day and the sixth rat was found dead on the morning of the 6th day. Autopsy revealed several reddish patches in the small intestine in the 4th, 5th, and 6th day rats. Microscopically marked changes were noted on the 1st day following radiation in the crypt cells of the duodenum. These continued to increase in extent from this time on. The injury was very irregular in distribution and was not constant throughout the intestines, nor in the sections, from animal to animal. The fifth rat, for instance, showed remarkable destruction of the crypt epithelium with collapse of the villi in the small intestine. The cells were large and pale and spread out in thin layers over the abnormal villi. The 6th rat, which had died, showed no injury in the sections taken, though in gross there were the same red raw looking sections especially in the ileum. This patchy injury has been noted in other animals in lethal experiments. This is a large M.L.D. while 200 M.A.M. is evidently a small M.L.D., the average being somewhere between.

A fourth series of five rats (Nos. 19 to 23) was exposed to  $400 \pm$  M.A.M. radiation and one sacrificed every day. Diarrhea and intoxication appeared on the 3rd day and the 5th day rat was not sacrificed and found dead on the 8th day. Nothing was noted in gross. Microscopically all the rats which had had diarrhea (Nos. 21, 22, and 23) showed marked injury to the duodenum with destruc-

tion and collapse of the villi. The epithelium remaining was atypical and made up of sheets of large pale cells with large circular nuclei containing usually two nucleoli. The injury was very irregular. In some sections the crypt cells were very heavily stained and murky, though intact, while the transition cells between the tips and crypts were growing rapidly and often piled up in two or three layers. These cells were large and pale and with large pale round nuclei showing one to two nucleoli.

It was found that there was a short circuit in several of the secondary coils of the transformer so that we are certain of neither the amount nor the quality of the radiation these rats received (Rats 19 to 23).

One rat (No. 24) given  $600 \pm$  M.A.M. developed a profuse brown watery diarrhea on the 3rd day and died early in the 4th day. Autopsy showed the mucosa of the ileum to be red and engorged for about one-half its length. Microscopically the duodenum and ileum showed profound destruction of the villi with only a few epithelial cells left here and there in the crypt remnants. There were several ruptured capillaries all nicely thrombosed seen in sections. The pulp of the spleen and the lymph nodes was almost completely absent and the sinuses were filled with blood. Even with this large dose the intestinal injury was rather patchy and irregularly distributed. This is probably the shortest antemortem period for rats. Usually for doses nearer the M.L.D. the antemortem interval seems to be 5 to 6 days.

In brief, the rats show the same clinical syndrome—intoxication, diarrhea, and death—and the same histological picture of destruction of intestinal epithelium, that dogs do. The crypt cells too are most severely injured. None of these animals showed evidence of septicemia with the development of purulent or necrotic foci in various organs.

*Birds.*—Pigeon M-2b received 300 M.A.M. radiation on March 17, and again on April 14, 1919. A watery diarrhea developed about 5 days after the first exposure and continued throughout the rest of the experiment. On May 6 the pigeon was given 400 M.A.M. and on May 20, 600 M.A.M. more. The bird died 4 weeks later. This bird received within a period of 9 weeks 1,600 M.A.M., the last two allotments of which were directed at the abdomen primarily. There was a slight amount of anemia following each exposure due probably to the few cubic centimeters of blood taken from the wing vein daily for blood counts. There was no change noted at any time in the nucleated red corpuscles. The white count dropped somewhat after each exposure and then returned almost to the previous figures. Clinically the bird was more affected by the first exposure of only 300 M.A.M. than by any of the others. Even then it was only slightly less active than usual. The diarrhea was at no time blood-stained but was mostly made up of watery or mucoid material. At autopsy nothing abnormal could be made out in gross. Histologically, the villi of the duodenum were long and filamentous. The epithelium seemed intact and unchanged. A few of the crypts in the gizzard at its lower end were lined by atypical pale thin cells. There is a surprising lack of evidence of injury done this pigeon by radiation.

No. 19-3b, a large hen, was given 350 M.A.M. over the abdomen and was found dead 16 hours later. At autopsy it was thought that the mucosa of the duodenum was somewhat injected. Nothing else abnormal was seen. Histologically the nuclei of the crypts in the mucosa of the small intestine were all large, pale, and with their chromatin in masses they appeared pycnotic. Around the crypts in the interstitial tissue were masses of chromatin evidently from disintegrated cells. The cells lining the crypts were still in place. There was no polynuclear cell reaction. This hen was active, fat, and apparently in good condition when she was given radiation. The early fatality we are unable to explain. The changes in the intestine of this fowl and the next bird are similar to early changes reported in dogs.<sup>2</sup>

A pigeon (No. 19-5b) was given 800 M.A.M. radiation over the abdomen. The feces became fluid the next day and continued so. On the 6th day the diarrhea became profuse and on the 11th day there was a rapid loss of weight and profuse watery diarrhea. The bird looked very sick and sat with its feathers ruffled up. At autopsy there were no evident abnormalities other than marked emaciation. Histologically only one section of the duodenum showed destruction of the villi with atypical cells in the injured crypts. Another section showed a rather atypical pale and irregular epithelium covering stubby rounded villi. This bird though given much more than the others seems to have received a sub-lethal amount. Perhaps 100 or so M.A.M. more would approach the M.L.D. more closely. Study of the red corpuscles in this bird demonstrated no changes.

*Reptiles.*—A group of five grass snakes was exposed to various amounts of radiation up to 900 M.A.M. without any effect except that they became rapidly emaciated. One, receiving 800 M.A.M. a week after the changing of its skin, died in 20 days. Nothing abnormal could be detected in the mucosa cells of this snake nor in those two given 900 M.A.M. and sacrificed 26 days afterward.

*Amphibians.*—A series of five adult frogs was given 560 M.A.M. of radiation. One sacrificed on the 2nd day showed slight changes in the cells of the crypts of the duodenum and colon. Another sacrificed upon the 3rd day showed the same cells to be pycnotic and to have multiplied somewhat. The cells were large and pale and there were generally one or two large nucleoli in the large pale nuclei. These cells stand out prominently from the normal cells which are smaller, more cuboidal, and contain very densely staining oval nuclei. The remainder of the frogs were kept 3 weeks longer without showing any symptoms. One of these was then exposed to 800 M.A.M. 24 days after the previous radiation. It died 19 days later after showing tremors, ataxia, paralysis, and a wrinkled, dried up skin. Autopsy done several hours after death showed a remarkably advanced autolysis which obscured the microscopic picture completely. The other two frogs continued active and well and showed no abnormalities on sacrifice 1 month later.

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<sup>2</sup> Warren and Whipple, Paper II, this series.



TABLE I.  
*Roentgen Radiation.*  
*The Minimum Lethal Dose.\**

Animal.	No. of animals.	M.L.D.	Onset of symptoms of intoxication.	Death after radiation
		M.A.M.	days	days
Frogs.†	3	Over 800	3-5	18-20
Snakes.†	5	" 800	4-8	18-20
Birds.†	4	" 800	4-5	10-11
Rats.	24	200-300	3-4	5-6
Guinea pigs.	3	300-350	3-4	4-5
Rabbits.	2	350-450	2-3	4-5
Cats.	3	350-400	2-3	4
Dogs.	16	350	2-3	4

\* 95 kilovolts; 8 milliamperes; 10 inch spark-gap; 10 inch skin-target distance; 2 mm. aluminum filter. The amounts of radiation and the intervals of time indicated represent the average.

† 800 milliampere minutes was the most radiation given any single animal at one time. It is evidently somewhat less than the M.L.D. for frogs, snakes, and birds.

TABLE II.  
*Comparative Dosage\* for Sensitive Tissues.*

Dose.	Experimental values.			Calculated average values.			Erythema dose for man according to Seitz and Wintz.†
	Guinea pig.	Cat.	Dog.	Guinea pig.	Cat.	Dog.	
	M.A.M.	M.A.M.	M.A.M.	per cent	per cent	per cent	per cent
Erythema dose.‡	175	300	100	100	100	100	100
Light intestinal injury.	220	320	100	120	107	100	135
Muscle dose.§	—	320	200	—	107	200	180
M.L.D.	300-350	350-400	350	200	117	350	?

\* 90 to 100 kilovolts; 8 milliamperes; 10 inch spark-gap; 10 inch skin-target distance; 2 mm. aluminum filter.

† Seitz, L., and Wintz, H., *Münch. med. Woch.*, 1918, lxxv, 89.

‡ The erythema dose in laboratory animals is the amount which causes superficial desquamation of the skin; this is less than that producing a first degree burn and greater than that causing depilation.

§ The muscle dose is the smallest amount which produces atrophy of the fibers of the smooth muscle of the intestinal wall.

## DISCUSSION.

The experiments given above show that the common laboratory mammals are sensitive to the x-rays in much the same dosage, and with similar clinical reaction and relatively uniform intestinal pathology (Tables I and II). Guinea pigs and rats are a little more susceptible to the radiation than are dogs, cats, and rabbits. The M.L.D. is correspondingly less in rats and guinea pigs. We have no evidence that the intoxication and intestinal injury are modified by body weight or body surface. We note little if any difference between a dog of 20 or 40 pounds in weight and a cat or rabbit of 4 to 8 pounds.

By contrast with the above group of mammals we observe that birds, frogs, and reptiles are very resistant to radiation. These animals can tolerate with little disturbance 1 or even 2 M.L.D. of radiation for the dog or cat. This peculiar resistance of birds, frogs, and reptiles is worthy of further study. We regret that our experiments are not adequate to give the answer to this riddle. One's first thought is that the feathers of birds and the skin of snakes may be very resistant to the x-rays and act as efficient screens. There is some experimental evidence to support this suggestion but no evidence that the frog's skin is impenetrable to the x-rays. The histology of these exposed animals indicates a less acute and extensive injury of intestinal epithelium by the longest x-ray exposures (800 milliamperes minutes). It seems probable that the intestinal tract of these animals differs fundamentally in its sensitivity to x-rays as compared to the dog or cat.

We hoped that these enormous doses of x-rays might bring out interesting changes in the nucleated red corpuscles of the birds but can only report negative observations. Our experiments indicate that the white blood cells of birds react to the x-ray exposures in somewhat the same fashion as do the white blood cells of the dog and cat. The red blood cells of birds in spite of the rich chromatin deposit in the nucleus are not injured by the x-ray and escape as completely as do the non-nucleated red cells of the dog and cat.

The whole question of repair of the intestinal epithelium following an x-ray injury is deserving of much study and is fascinating to the histologist. At times the repair seems to be complete with restora-

tion to normal but with longer doses healing may be long delayed and permanent ulcers may be formed which show no evidence of healing for months and may in fact lead to intestinal perforations. The x-ray offers a simple means of producing ulcers of the stomach, intestine, or colon which will resist healing as do peptic, duodenal, or other chronic ulcers of the intestinal tract.

In these experiments we note differences in sensitivity to the x-rays in different parts of the intestinal tract. For example, the cecal mucosa of the dog is relatively more resistant than is that of the small intestine. In the rabbit the cecal mucosa is quite extensively injured and seems as sensitive to radiation as the small intestine. We may recall that the physiology of the cecum in these two animals is vastly different and this may explain the differences in sensitivity to the x-ray.

One is impressed by the patchy injury of the intestinal tract noted in dogs dying from a M.L.D. of radiation. Larger doses give a much more uniform distribution of the intestinal injury. We may choose to explain this on the basis of the intestinal contents or the position of various intestinal coils in relation to the cone of radiation or on the score of intestinal activity, etc., but the fact remains that there is no convincing explanation for this observation at present.

#### SUMMARY.

These experiments show that the common laboratory animals are about equally sensitive to the x-ray given over the abdomen. The clinical reaction following a M.L.D. is very similar and the intestinal pathology almost identical. The rat and guinea pig are slightly more sensitive to the x-ray than are the dog, cat, and rabbit.

By contrast birds, frogs, and reptiles are very resistant to the x-ray and may tolerate two or three doses of radiation lethal for dogs. We can offer no convincing explanation for this fact which is discussed above.

These data strengthen our belief in the scattered and incomplete observations on human cases which indicate that the human intestinal tract is likewise sensitive to radiation. This fact must be given careful consideration in conditions where abdominal or pelvic radiation is being used because such injury done to intestinal epithelium is always serious and in some cases irreparable.

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