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Department of Pathology

Terminal Report

on

GROWTH, REPRODUCTION, MORTALITY, AND PATHOLOGIC CHANGES IN RATS FED GAMMA-IRRADIATED POTATOES

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ABSTRACT

For two years a colony of albino rats was fed diets of which one third contained potatoes which had been exposed to ionizing radiation for sprout inhibition. Growth, food consumption, reproductive performance, hematologic changes, mortality, and pathologic changes in these rats were compared with the same in animals fed a nonirradiated potato diet. The growth, reproductive performance, and pathologic changes up to 30 weeks of second- and third-generation animals were also compared with corresponding controls.

Three results emerged from this study. (1) There were no consistent effects due to irradiation of potatoes which could be established by these criteria. (2) There was a slightly greater mortality rate among males of the first generation fed the irradiated potato diets which was of questionable statistical significance and may be related to the poor condition of the irradiated potatoes relative to the nonirradiated controls. Second-generation males and females fed the irradiated potato diets also experienced a higher mortality rate but this is attributed to genetic factors. (3) An unusually high incidence of a necrotizing arteritis resembling "peri-arteritis nodosa" occurred in the first- and second-generation animals in this experiment. The combination of a genetic and a dietary factor is implicated in causing this disease, but irradiation of the potatoes is not a factor. Studies are currently in progress on hypertensive vascular disease in descendants of the animals used in the above experiment.

OBJECTIVE

The objective of this experiment was to test the wholesomeness of irradiated potatoes using albino rats as the experimental animals.

I. INTRODUCTION

The use of ionizing radiation to arrest sprout development in tubers and thereby to prolong their storage life has been extensively reported.[1-3] Since only about 7 to 15 kilorads are required to achieve this, many of the problems which involve prolonged research and development on the radiation sterilization of foods, which requires doses of 4000 kilorads or more, are avoided. For this reason, the irradiation of potatoes attracted attention early as a means of gaining civilian and military acceptance of other food preserved by radiation. Accordingly, potatoes were one of the first items on the list in the extensive program sponsored by the Office of the Surgeon General of the U. S. Army, on the basis of procedures set up by the Food and Drug Administration,[4] for evaluating the wholesomeness of a number of irradiated foods. A long-term feeding study using rats was prescribed, and the following is a report of the experiment, conducted in the Fission Products Laboratory over the past three years.

The potato varieties selected for the test were Idaho Russet Burbanks, Maine Russet Burbanks, and Maine Katahdins, and they were used in equal quantities. Two dose ranges of 13.5-20 and 27-40 kilorads of gamma radiation from reactor fuel elements were tested on each variety. The higher level was to provide a test of potatoes given an overdose. The evaluation of wholesomeness was based upon the growth, food consumption, reproductive performance, longevity, and hematologic and pathologic changes in rats fed a diet containing 73% of the above potatoes on a wet-weight basis for 2 years. In addition, growth and reproductive performance of second- and third-generation animals were to be determined.

II. EXPERIMENTAL

A. SOURCE AND STORAGE BEHAVIOR OF POTATOES

The potatoes used during the first year of the feeding experiment were from the 1955 harvest and were irradiated in December at the National Reactor Test Site, Arco, Idaho. Those used during the second year were from the 1956 harvest. All the potatoes from the first harvest and most of those from the second were stored at Presque Isle, Maine, under the supervision of Professor Matthew Highlands, University of Maine. An additional quantity of second-year lots were stored in Idaho under the supervision of Donald Hunsaker, Philips Petroleum Company, Idaho Falls. Nonirradiated lots of each variety were treated identically, except for the irradiation step, to serve as controls. The controls will be referred to as "OX" potatoes, and the irradiated lots, as "1X" and "2X."

The potatoes were stored and shipped either in 50- or 100-lb perforated paper-board drums with waxed bottoms or in bushel baskets with wooden covers. All "OX" potatoes were manually desprouted periodically. Further details on the storage conditions and storage behavior of these potatoes may be obtained through the U. S. Army Quartermaster Food and Container Institute.[5] The two varieties grown in Maine were subjected to shipping from that state to Idaho and back again for storage. As required for the feeding experiment, they were then shipped to Ann Arbor, Michigan. At The University of Michigan, they were accommodated through the courtesy of Mr. Herbert Wagner at the Food Service's regular potato-storage locker held normally at 40°F. In the laboratory they were held in a household type of refrigerator until made into diet.

The feeding part of the experiment began 3 months after the potatoes were irradiated. The skins and eyes as well as the whites were included in the potato diet. A month or more after the experiment was begun, some decay began to appear in the potatoes as received at the University. The decay at first was small in amount and difficult to remove, and any attempt to do so would have introduced more rather than less prejudice into the experiment. The amount of decay increased steadily in the potatoes as received, and starting with the twenty-fifth week of feeding, nearly all were culled and discarded. During the last 10 weeks of this 25-week period, the amount of decay occurring in the potatoes and the proportion of decayed material included in the diet were approximated by weight. The results for the 9 lots of potatoes are shown in Table I. With each variety there was a progressive increase in decay with the irradiation dose; the Katahdin variety appeared more susceptible than did the Burbank varieties. This is consistent with the results obtained in storage studies of irradiated potatoes.[4]

TABLE I

PERCENT DECAY BY WEIGHT OCCURRING IN POTATOES
AND INCLUDED IN THE DIET
FROM THE FIFTEENTH TO THE TWENTY-FIFTH WEEK OF FEEDING

Variety	Irradiation Dose*		
	OX	1X	2X
Maine Katahdin	0.7	5.4	8.3
Maine Russet Burbank	1.4	2.6	3.8
Idaho Russet Burbank	1.5	1.9	4.4
Whole diet**	0.9	2.4	3.9

*"OX," no irradiation; "1X," 13.5-20 kilorads; "2X," 27-40 kilorads.

**The potatoes were fed in equal quantities, and the average for the three varieties is reduced by the fraction (.72) of whole diet consisting of potatoes.

B. DIET FORMULATION AND PREPARATION

Most irradiated foods in the Surgeon General's program are tested, on a dry-weight basis, at 35% of the total diet solids. This is equivalent to 11.7% for each of the three varieties of potatoes tested in this experiment. The composition of the diet was as follows:

	Dry Weight, percent	Wet Weight, grams per batch
Maine Katahdin	11.7	1300
Maine Russet Burbank	11.7	1300
Idaho Russet Burbank	11.7	1300
Purified casein	15	355
Lactalbumin	10	235
Alphacel	5	120
Corn starch	14	330
Lard and other oils	15	355
Salt mixture	4	95
Vitamin mixture	1-2	25-45

The variation in solids content from potato to potato made sampling of individual batches of potatoes unreliable, and the presence of decay and other factors made estimates of solids content difficult on the basis of specific gravity.[6] The use of 1300 grams of each variety per batch is based on an average dry weight of 21% of all varieties as determined by oven-dried samples of various batches at this laboratory over a period of several weeks. The work of M. E. Highlands[4] showed that the solids content of the Idaho Russets, while in storage in Maine, varied from 18 to 26% over a 13-month period, Maine Russets, from 14 to 19%, and Maine Katahdins, from 14 to 17%. Irradiation dosage appeared to have little effect on the dry weight, however, and the average of all lots did not change (19.9% in December, 1956, and 20.1% in January, 1958).

For the first month and a half, the vitamin mixture consisted of the "Vitamin Diet Fortification Mixture" as compounded by the Nutritional Biochemicals Corporation, Cleveland. This contained all the vitamins known to be required, plus Vitamins D and C, and constituted 2% of the diet. After the first month and a half, Vitamins A, D, C, E, and choline were removed from the mixture; the first two were furnished in cod liver oil (1%) which was fed to provide a source of unsaturated fatty acid. Vitamin E was administered as an oral supplement in the form of alpha-tocopherol acetate and choline was added to the diet at 0.2% level from a 50% solution. What remained of the original vitamin mixture was added to the diet at a level of 0.85% (20 g/batch) and had the following composition:

	grams/kilo
Inositol	5.0
Menadione	2.25
p-Aminobenzoic acid	5.0
Niacin	4.5
Riboflavin	1.0
Thiamine HCl	1.0
Calcium pantothenate	3.0

	milligrams/kilo
Biotin	20
Folic acid	90
Vitamin B-12	1.35

	grams/kilo
Extender (casein)	974

After the first year of the experiment, the thiamine and biotin levels were increased twofold and the riboflavin level, threefold. These increases were made because of an ocular inflammation in the animal colony which may have been caused by marginal levels of these vitamins.

For the first month and a half the salt mixture consisted of "Salt Mixture U.S.P. XIV," prepared by the Nutritional Biochemicals Corporation. Since the potatoes in the diet furnished over 1% potassium (dry-weight basis),[7] it was desirable not to furnish additional potassium through the salt mixture. Thereafter, a salt mixture of the following composition was used at a 3.5% level:

	Percent
$CaHPO_4 \cdot 2H_2O$	48.0
NaCl	22.1
$CaCO_3$	15.0
$MgSO_4 \cdot 7H_2O$	8.7
Fe citrate$\cdot 6H_2O$	5.5
$MnSO_4 \cdot H_2O$	0.52
KI	.08
$CuSO_4 \cdot 5H_2O$	.07
$ZnCl_2$	.025
$CoCl_2$	.005

After one year of the experiment, calcium carbonate was removed from the salt mixture because of the possibility that it was promoting auto-oxidation of some of the vitamins.[8] The calcium was supplied by additional calcium phosphate. Potassium iodide was furnished in the choline chloride solution because it tends to oxidize in salt mixtures containing cupric salts and moisture. Zinc chloride and cobaltous chloride were also removed from the salt mixture because the large proportion of potatoes in the diet furnished these trace elements.[9,10] The simplified salt mixture, added to the diet at the 3.5% level, had the following composition:

	Percent
$CaHPO_4 \cdot 2H_2O$	67.2
NaCl	20.2
$MgSO_4 \cdot 7H_2O$	7.1
Fe citrate $\cdot 6H_2O$	5.0
$MnSO_4 \cdot H_2O$	0.5
$CuCO_4 \cdot 5H_2O$	0.06

To prepare the diet, the potatoes were freed of decay (except during the first few months of feeding), but not of the eyes or skin, washed quickly, cut up, and steamed for 10 to 15 minutes at low steam pressure. They were then pushed through a meat grinder having a plate with 3/16-in.-diameter holes, which cut the skins finely without making a paste of the whites. The dry ingredients were added to the cooked and mashed potatoes and, while being mixed, lard, in a melted state, and other liquids were added. When the batch of "dough" reached the completely cohesive stage (further beating makes it adhesive), it was rolled out in a flat stainless-steel pan 3.5 cm deep. The diet was scored on top into 180 cubes so that when the animals were fed on a per-cube basis, as an alternative to weighing out the diet, the portion of nutrients furnished to the animals was known in spite of variations in the thickness of the diet or moisture content.

The diet was stored in a refrigerator until use, sometimes covered with polyethylene or cheesecloth to control moisture accumulation on the surface. The diet was never used after the second day.

C. THE ANIMAL COLONY

The parent-generation colony was organized into 5 replicates. Each replicate consisted of 5 litters of Holtzmann strain rats (Madison, Wisconsin), and each litter had 4 males and 4 females. The replicates were started one week apart, the first on 14 March 1956; all rats were 22 days old when started. Each of the 3 potato diets was fed to one male and one female in each of the 25 litters. The groups thus constituted will be referred to as the "OX," "1X," and "2X" groups. The fourth male and fourth female of each litter were fed Purina Laboratory Chow, and these animals will be referred to as the "XL" (extralittermate) group.

The parent generation of animals was maintained for about 2 years. At 15 weeks of age, 4 of the 5 females fed each diet in each replicate were mated in weekly rotation with 4 males in the same group. The second-generation animals obtained from the second breeding of the parents were fed the parental diet until two breedings had been completed, after which it was no longer necessary to maintain them for the purposes of this experiment. They were then all fed the "OX" diet, and later the same diet with fresh market potatoes, to make certain observations of pathological interest.[11] The third-generation animals were also fed the experimental diets until their young had been weaned, at which time they too were continued on the fresh-potato diet. The fourth-generation animals were examined at weaning, but were not fed the irradiated-potato diet thereafter.

All animals fed the irradiated potato diets were housed in individual wire-bottom cages and provided with water and diet ad libitum. Animals fed Purina Laboratory Chow were housed five to a large cage, and were not mated. The animal quarters were air-conditioned (70°F) with ambient humidity. The usual standards of cleanliness, periodic cage and water-bottle washing, and shavings change were followed.

D. PROCEDURES USED

All animals were weighed weekly to the nearest gram on a Toledo balance.

Food consumption was measured for the first 12 weeks after weaning for first- and second-generation animals. Each animal's daily allotment of fresh food was weighed and samples from the same batch of diet were air-dried to constant weight. Food left in jars was collected daily and combined, after fecal matter was separated, with food spilled which was caught on a piece of mosquito screen; this was dried in air and its weight was subtracted from the total of food, dry basis, fed for the week as calculated from the daily fresh food weights and fraction of solids.

Reproduction data consisted of apparent pregnancies, pups born/litter, survival of pups to first and twenty-first days, and average body weights of pups at the seventh and fourteenth days of lactation for the last three of the six breedings, and at the twenty-first day for all breedings.

Each first-generation animal was examined externally each week, and all observations obtainable were recorded. Special attention was paid to respiratory condition, tumors, and abscesses.

Blood cell counts were made on one male and one female in each of the three dietary groups in each of the five replicates (i.e., 30 animals of the total colony of 150). Blood was obtained from the tail vessels. These counts were performed during the fourth, tenth, and eighteenth months of experiment.

All first-generation animals, whether found dead, sacrificed because of moribund condition or sacrificed to terminate the experiment, were subjected to complete necropsy. The tissues were submitted for histological examination to members of the Department of Pathology of The University of Michigan Medical School. Also included were members of the second generation which died or were sacrificed before the end of their second breeding period.

III. RESULTS

A. GROWTH

Growth curves for the first-, second-, and third-generation males and females fed the diets containing nonirradiated ("0X") potatoes and potatoes irradiated at two levels ("1X" and "2X") are shown in Fig. 1. Body-weight averages for the first generation are extended beyond the growth and reproduction phase to about 70 weeks, at which time the mortality complicates the significance of the curves. Differences between the curves would not be significant for females after the onset of pregnancy.

The three diets resulted in uniform growth, except first-generation females fed the "1X" diet, which showed a slight but statistically ($P < .01$) significant superiority in body weight. Table II shows means and standard deviations for first-generation animals up to 36 weeks, and shows the small but significant increase in weight of 1X females but of no other groups.

B. FOOD EFFICIENCY

The average gram body-weight gain per gram diet solids consumed for the 25 animals in each of the 6 groups is shown in Fig. 2 for the first 12 weeks following weaning. After 8 weeks, the fraction of food contributing to body-weight increase is small and normal fluctuations in growth rate lead to large differences in food efficiency. For the first 8 weeks, however, there is apparently no difference in the ability of each diet to furnish nutrition for optimum growth.

C. REPRODUCTION

Table III shows the reproductive performance for the first-, second-, and third-generation animals through the first and second breeding. Differences can be found between animals in the three dietary groups but these are not consistent. For example, apparent pregnancy was lowest for 1X females through all six breedings, and in the three instances where one group showed a relatively poor birth rate, this was always the 1X group. The average number of pups born per litter was uniformly good. The average number of pups surviving to one day after birth was lower for first breedings than the second, and it was especially low during the first breedings of the first and third generations; but there were no differences between dietary groups in this respect. The number of pups surviving to weaning was variable from breeding to breeding, particularly poor during the first breeding of the second and third generation, but again all groups behaved in a similar fashion. In both the first and second breedings of the third generation, however, the average weight of pups in the 2X group was somewhat less than that for the other groups.

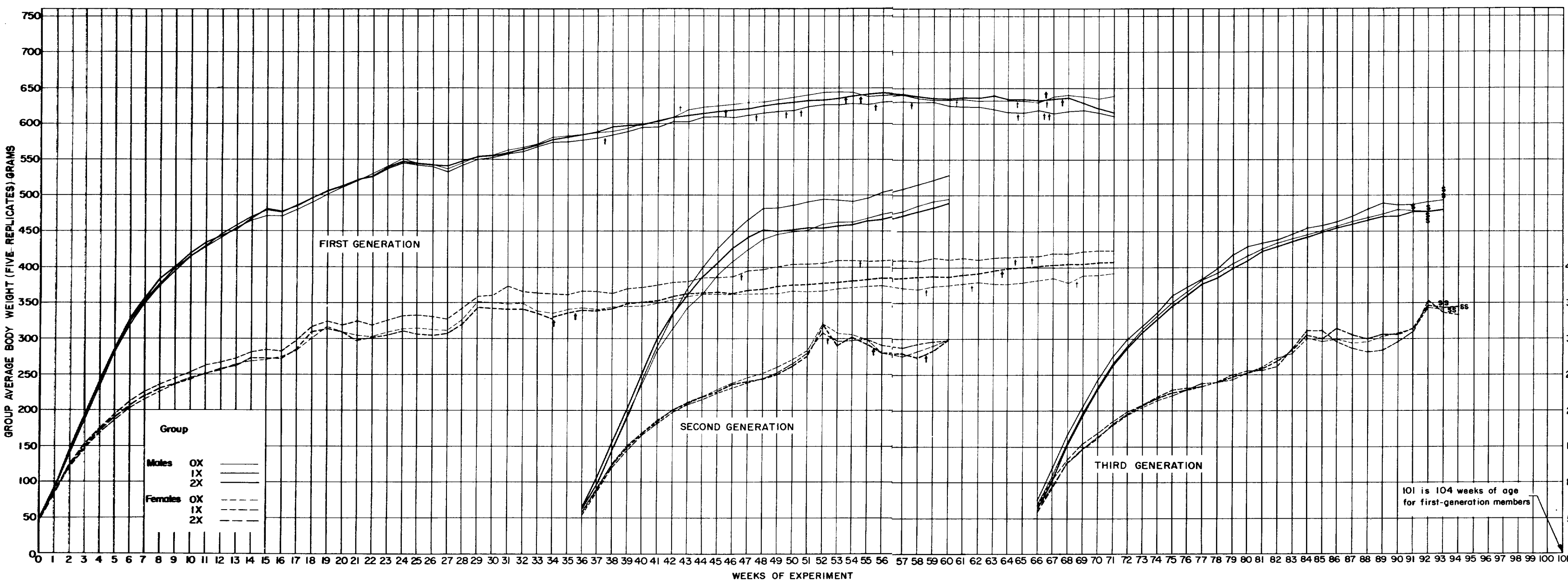

Fig. 1. Growth curves for first-, second-, and third-generation male and female rats fed diets containing irradiated potatoes.

TABLE II

MEAN BODY WEIGHTS AND STANDARD DEVIATIONS FOR FIRST-GENERATION MALES AND FEMALES UP TO THIRTY-SIX WEEKS

Week	Mean Body Weight, Grams, and Standard Deviation							
	Male Groups				Female Groups			
	0X	1X	2X	XL	0X	1X	2X	XL
0	49.0 ± 0.4	48.4 ± 0.5	48.3 ± 0.5		47.7 ± 0.4	47.7 ± 0.5	47.5 ± 0.5	
4	236 ± 4	241 ± 2	242 ± 3		168 ± 2	175 ± 2	172 ± 2	
8	376 ± 6	377 ± 5	384 ± 6	329 ± 4	227 ± 4	237 ± 3	231 ± 4	214 ± 2
12	441 ± 7	447 ± 7	442 ± 7	393 ± 4	257 ± 5	267 ± 4	258 ± 4	234 ± 3
16	473 ± 7	480 ± 7	476 ± 9	442 ± 5	275 ± 5	284 ± 4	274 ± 3	258 ± 3
20	526 ± 8	513 ± 8	516 ± 9	475 ± 5	307 ± 6	321 ± 5	311 ± 7	270 ± 4
24	554 ± 8	546 ± 7	549 ± 10	498 ± 6	314 ± 6	333 ± 5	312 ± 5	275 ± 4
28	548 ± 11	542 ± 9	546 ± 11	508 ± 6	327 ± 6	343 ± 6	324 ± 6	283 ± 4
32	565 ± 10	560 ± 9	564 ± 11	521 ± 8	350 ± 7	364 ± 6	341 ± 9	290 ± 5
36	586 ± 10	580 ± 8	587 ± 11		342 ± 6	368 ± 8	340 ± 6	

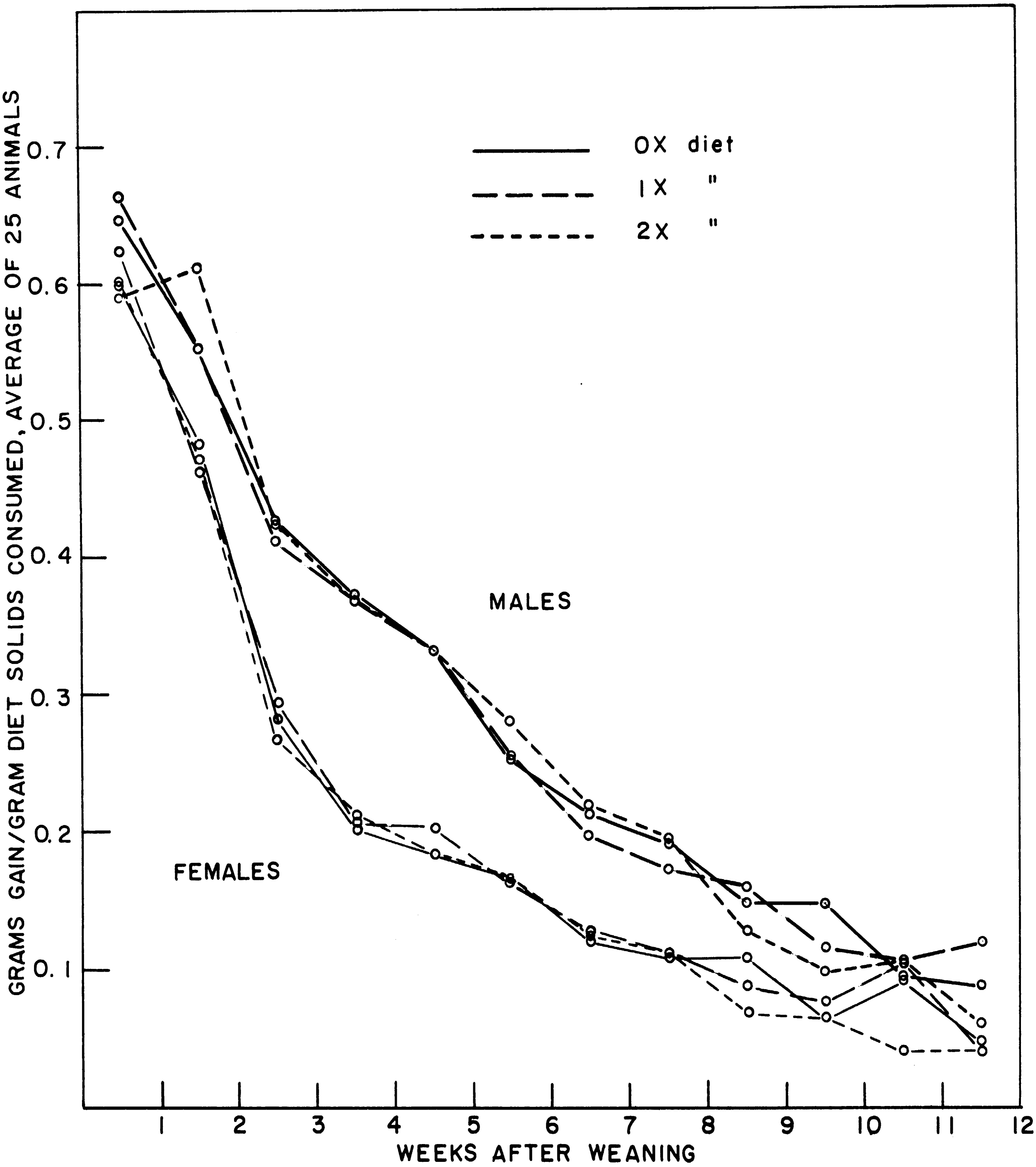

Fig. 2. Efficiency of utilization of food for growth by males and females of the first generation fed diets containing irradiated potatoes ("1X" and "2X") relative to those fed the control diet ("OX").

TABLE III

REPRODUCTIVE PERFORMANCE OF FIRST-, SECOND-, AND THIRD-GENERATION ANIMALS

	First-Generation Animals						Second-Generation Animals						Third-Generation Animals					
Breeding:	First			Second			First			Second			First			Second		
Diet:	0X	1X	2X	0X	1X	2X	0X	1X	2X	0X	1X	2X	0X	1X	2X	0X	1X	2X
1. Number of females bred	20	20	19	20	20	19	20	19	20	19	18	18	20	20	20	20	20	20
2. Number of males used	20	20	20	20	20	20	10	10	10	10	10	9	20	20	20	20	20	20
3. Percent of females bred which appeared to become pregnant	90	90	95	85	75	84	100	84.2	100	94.7	77.7	94.4	100	95	100	100	95	100
4. Percent of apparently pregnant females which gave birth	83	83	100	82	67	81	100	87.5	95.0	100	85.7	100	95	100	95	100	100	100
5. Average number of pups born per litter	11.2	9.6	10.7	10.4	11.9	10.5	10.9	10.3	11.1	9.8	9.2	9.8	10.1	10.4	10.7	9.9	9.6	9.5
6. Percent of pups born surviving birth and the first day after birth	80	78	77	86	92	95	91.3	92.4	90.0	93.8	92.7	97.6	78.5	77.8	68.3	90.1	90.2	91.6
7. Percent of pups surviving the first day which reached 21 days (weaning)	93	86	92	86	86	84	57.0	62.6	65.4	83.2	71.8	72.5	58.0	64.3	52.1	93.3	80.1	90.2
8. Average body weight of pups at 7 days	--	--	--	--	--	--	--	--	--	15.0	14.5	15.1	14.3	14.3	13.2	16.0	15.9	14.9
9. Average body weight of pups at 14 days	--	--	--	--	--	--	--	--	--	30.4	30.6	31.7	29.9	28.3	26.4	30.7	30.3	28.7
10. Average body weight of pups at weaning	51.4	53.7	52.9	50.1	47.0	48.1	47.3	49.6	44.9	51.1	53.5	54.5	49.1	48.8	44.3	50.4	51.0	45.7

D. BLOOD CELL COUNTS

Table IV presents three sets of blood cell counts made on a male and female representative from each of the 15 groups. Blood cell counts were made on these same animals at 4, 10, and 18 months of age, although by the last set of data some of the original members of the group had been sacrificed. In addition, blood cell counts for all parent animals surviving at 19 months are shown.

What variations existed among animals on the different diets did not persist over the period studied, and nearly without exception every range of values for any one count overlapped every other one.

E. MORTALITY

Mortality curves for first- and second-generation males fed each of the three diets are shown in Fig. 3 and for females, in Fig. 4. Each animal is represented by a horizontal bar, the length of the bar corresponding to the animal's age at death. Those animals which died or became moribund after termination of the experiment was begun are indicated by a dagger. There is, of course, no significance to the mortality curve after this point.

The mortality of second-generation animals was due principally to a vascular disease (see below), and those remaining after 16 months, although in apparent good health, were sacrificed to complete an evaluation of the extent of the lesions in the entire colony. They had been continued beyond 30 weeks of age on the control diet, as they were not intended to have been fed the experimental diets beyond this time. (The same practice was followed with the third generation, but there was no mortality before the thirtieth week of age, when they were all given the control diet, and showed little mortality for several months thereafter. The fourth-generation members were transferred to the control diet shortly after weaning, and, likewise, had no significant mortality.)

The one important difference among animals on the various dietary groups appeared in the survival rate at 21 months for first-generation members, and at 16 months for second-generation animals. These results are shown in Table V. In the first generation, the mortality was twice as great among males on the 1X and 2X diets as among those on the control diet, but there was virtually no difference among the female groups. The Student-Fisher t-test applied to the mortality rate of the male groups revealed no statistically significant difference between any two of them. In the second generation, most of the mortality occurred after the animals has been given the "OX" diet. Before the change, however, only one control had succumbed, while three had succumbed from the 1X and three from the 2X groups. Altogether, after 16 months, the difference between the female groups was rather marked, while there was less difference among the male groups.

TABLE IV

BLOOD CELL COUNTS OF REPRESENTATIVE ANIMALS AT FOUR, TEN, AND EIGHTEEN MONTHS OF AGE

(Each value is an average for 5 animals; figures in parentheses are minimum and maximum values in the group of 5 animals)

Group	Hemato-crit, %	Hemoglobin, grams %	Corpuscular Hemoglobin, %	White Blood Cells, Thousands per mm³	Differential Count: % of White Cell Count						Platelets
					P(1)	SL(2)	LL(3)	M(4)	E(5)	B(6)	
				Four Months							
MALES											
OX (5)	48.9	16.0	32.7	15.0	19	74	2	3	2	0	
1X (5)	47.9	15.9	33.2	13.3	14	79	3	3	1	0	
2X (5)	47.6	15.5	32.6	14.0	18	76	2	3	1	0	
Pellet (5)	48.3	16.2	33.5	14.7	13	80	3	3	1	0	
				Ten Months							
OX (5)	50.0	15.9 (14.8-17.4)	31.8	13,150 (9,800-18,400)	22 (17-30)	65 (63-73)	8 (2-15)	2 (1-3)	3 (2-5)	0	Adequate
1X (5)	49.8	16.5 (15.3-17.4)	33.2	12,110 (8,900-15,400)	26 (23-29)	60 (56-67)	8 (4-12)	4 (1-7)	2 (1-4)	0	Adequate
2X (5)	48.9	15.1 (13.7-16.3)	30.9	13,100 (8,800-19,000)	24 (11-40)	62 (55-70)	9 (3-15)	4 (2-8)	2 (1-4)	0	Adequate
				Eighteen Months							
OX (3)	49.6	16.0 (15.1-17.0)		15,500 (13,550-17,650)	42 (30-55)	39 (25-54)	7 (3-9)	9 (7-12)	4 (0-5)	0	Adequate
1X (2)	52.9	16.5 (16.4-16.5)		9,000 (5,700-12,200)	35 (31-39)	51 (49-52)	7 (6-7)	8 (5-10)	1 (0-1)	0	Adequate
2X (2)	48.9	15.9 (15.3-16.4)		22,300 (10,350-34,250)	51 (41-61)	31 (21-40)	9 (8-10)	9 (8-9)	1 (0-2)	0	Adequate
OX (10)	47.6	15.1 (9.4-17.4)		15,200 (7,750-27,700)	40 (29-59)	41 (23-53)	13 (5-27)	5 (1-10)	2 (0-3)	0	Adequate
1X (4)	48.0	15.5 (14.2-16.2)		10,750 (5,800-22,700)	34 (29-37)	46 (38-50)	15 (9-19)	5 (3-8)	1 (0-3)	0	Adequate
2X (6)	46.9	15.0 (12.6-18.3)		15,900 (9,750-20,350)	38 (22-60)	46 (30-66)	10 (2-21)	5 (0-8)	2 (0-5)	0	Adequate
XL (8)	46.1	14.6 (8.4-16.6)		17,800 (12,150-23,450)	36 (20-54)	40 (22-55)	13 (9-19)	9 (5-15)	2 (0-4)	0	Adequate
				Four Months							
FEMALES											
OX (5)	46.1	14.6	31.6	10.4	19	74	3	3	1	0	
1X (5)	48.1	15.4	32.0	10.2	12	80	3	3	2	0	
2X (5)	47.9	15.3	31.9	9.0	17	77	2	2	2	0	
Pellet (5)	46.4	14.7	31.7	14.9	16	77	2	2	3	0	
				Ten Months							
OX (5)	46.6	15.1 (14.4-16.3)	32.4	6,280 (4,000-9,200)	32 (12-49)	58 (37-81)	6 (4-8)	2 (1-3)	2 (0-4)	0	Adequate
1X (5)	47.4	15.4 (14.6-17.2)	32.5	6,480 (4,400-9,100)	20 (12-31)	65 (51-78)	9 (3-14)	4 (0-7)	2 (0-5)	0	Adequate
2X (5)	45.9	14.7 (12.7-15.7)	32.1	5,850 (3,600-8,300)	25 (11-32)	65 (55-74)	8 (1-19)	1 (0-2)	2 (0-3)	0	Adequate
				Eighteen Months							
OX (4)	49.3	15.7 (14.6-16.6)		7,000 (4,750-12,100)	46 (29-69)	33 (14-46)	13 (3-17)	6 (1-12)	3 (2-4)	0	Adequate
IX (4)	48.1	15.4 (15.1-15.8)		6,500 (5,400-7,500)	34 (31-36)	49 (46-53)	11 (8-15)	6 (3-9)	1 (0-2)	1 (0-1)	Adequate
2X (4)	47.6	14.9 (14.7-15.3)		6,900 (5,750-7,800)	34 (31-38)	43 (36-48)	17 (8-27)	5 (2-7)	2 (0-3)	0	Adequate
OX (10)	46.7	15.1 (13.8-16.7)		9,400 (7,000-16,500)	42 (31-66)	36 (14-51)	12 (4-27)	8 (4-16)	2 (1-4)	0	Adequate
1X (8)	45.9	14.7 (10.8-15.6)		8,200 (5,650-15,600)	39 (19-59)	41 (26-61)	11 (4-19)	7 (3-10)	3 (0-5)	0	Adequate
2X (11)	49.1	15.7 (14.9-17.8)		7,600 (3,700-11,550)	35 (26-52)	42 (25-60)	15 (8-29)	7 (2-11)	2 (0-7)	0	Adequate
XL (10)	47.8	15.6 (14.5-16.4)		10,900 (7,050-29,550)	39 (28-51)	34 (15-47)	15 (6-25)	5 (3-10)	6 (0-25)	0	Adequate

(1) Polymorphonucleocytes
(2) Small leucocytes
(3) Large leucocytes
(4) Monocytes
(5) Eosinophils
(6) Basophils

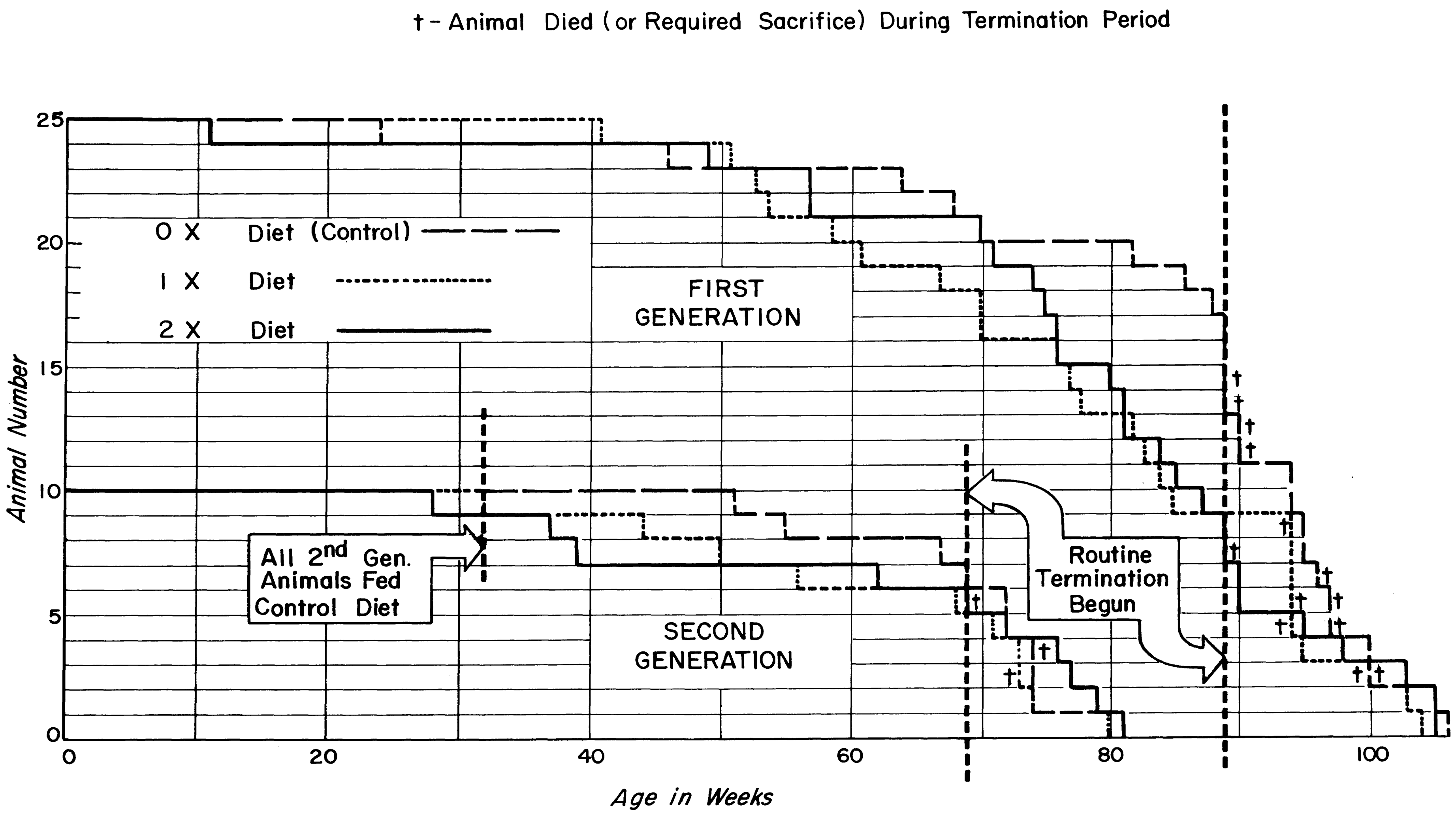

Fig. 3. Survival curve of first- and second-generation males fed irradiated potato diets.

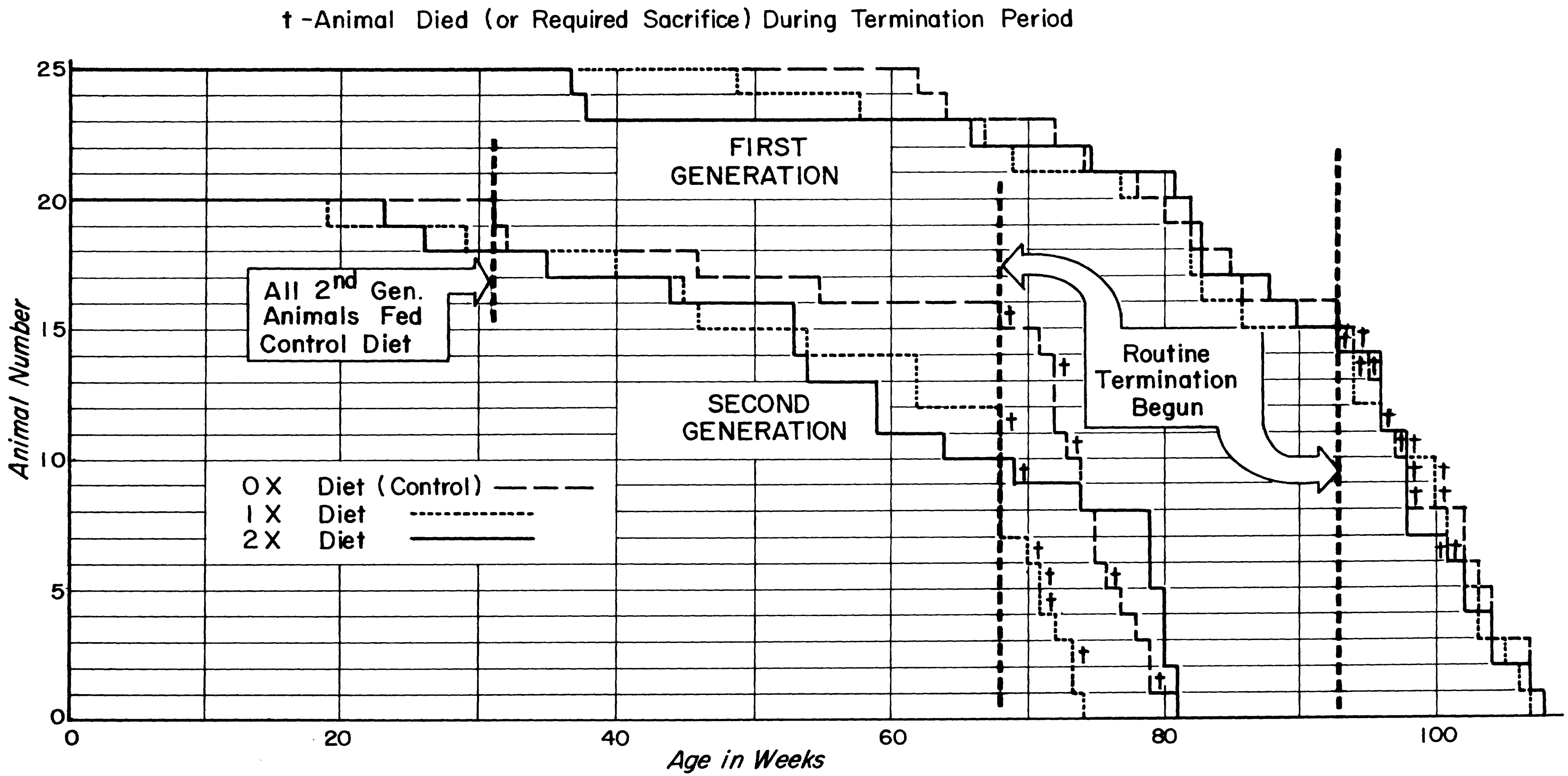

Fig. 4. Survival curve of first- and second-generation females fed irradiated potato diets.

TABLE V

MORTALITY DATA FOR FIRST- AND SECOND-GENERATION MALES AND FEMALES DURING PERIODS SPECIFIED

Diet	% Decay in Diets*	Percent Mortality of Animals at Time When Termination Began			
		First Generation		Second Generation	
		Males, 89 Weeks	Females, 93 Weeks	Males, 69 Weeks	Females, 68 Weeks
0X	0.9	32	36		
1X	2.4	64	40		
2X	3.9	64	40		
0X	~ 0.1			30	20
1X	~ 0.1			50	45
2X	~ 0.1			40	50

*During fifteenth to twenty-fifth week of life for first-generation animals and not at all during the life of second-generation animals.

F. GROSS TISSUE WEIGHTS

As part of the necropsy procedure, routine weights were taken of the opened heart, spleen, kidneys, lungs, liver, and, from males, testes. In Table VI the results appear for each group as the mean percentage of organ to body weight with standard deviation; data from the "XL" group are included.

In the male groups, there appeared to be a significantly lower ratio of lung to body weight in the controls than with males fed the 2X diet (statistically significant to the 5% level). There are no other important differences, even between animals fed the potato diets and the Purina Lab Chow diet.

In the case of the females, the ratio of spleen and lung to body weights appeared significantly lower in the 1X females than with either the control females or those fed the 2X diet. Again, there were no important differences between animals fed the two types of diets. The only exceptions to this were that the heart and kidney weights of the females fed the Purina Lab Chow were lower than those of the 0X females, but not of the 1X and 2X females.

TABLE VI

MEAN PERCENTAGE OF ORGAN TO BODY WEIGHT OF SIX TISSUES FROM FIRST-GENERATION ANIMALS FED THE POTATO DIETS

Diet	Heart	Spleen	Kidneys	Lungs	Liver	Testes
			Males			
0X	.371 ± .017	.245 ± .028	.459 ± .042	.550 ± .043	3.34 ± .170	.295 ± .031
1X	.397 ± .021	.212 ± .013	.534 ± .056	.760 ± .106	3.43 ± .170	.304 ± .014
2X	.394 ± .018	.229 ± .013	.491 ± .032	.840 ± .145	3.45 ± .170	.288 ± .033
XL	.367 ± .016	.207 ± .013	.421 ± .036	.653 ± .092	3.72 ± .220	.299 ± .017
			Females			
0X	.462 ± .047	.278 ± .031	.393 ± .025	.712 ± .097	3.20 ± .160	
1X	.387 ± .039	.211 ± .015	.412 ± .055	.473 ± .027	3.12 ± .180	
2X	.401 ± .023	.294 ± .041	.365 ± .023	.626 ± .077	3.36 ± .180	
XL	.326 ± .013	.261 ± .040	.350 ± .012	.693 ± .120	3.05 ± .110	

IV. PATHOLOGIC CHANGES

Necropsy on each animal in this study included examination of cranial contents, cervical, thoracic, and abdominal viscera, and the extremities. The heart, lungs, liver, spleen, kidneys, and testes were weighed routinely. These data have been presented above with other quantitative data. A minimum of 30 to 40 tissue sections was examined from each animal, with the exception of those of the XL group, in which tissues from only 18 animals were submitted for complete microscopic examination. From the remaining animals of this group, those sacrificed at the termination of the study, only sections of kidney, adrenal gland, and pancreas were studied microscopically. This was done to reveal the presence of the necrotizing arteritis described below. Therefore the incidence of other diseases encountered in the XL group is useful in a qualitative rather than strictly quantitative sense. All tissues were fixed in 10% formalin, embedded in paraffin, and the sections stained with hematoxylin and eosin. Frozen sections of heart, lung, liver, kidney, and adrenal gland stained with Sudan IV were routinely processed.

During the course of this study, microscopic examination of tissues was performed by several members of the Department of Pathology. The data were summarized by one of us (GDA); the original slides were reviewed when necessary to confirm the comparability of diagnoses from the several pathologists. In summarizing the data on the kidneys and neoplasms, all the original sections were reviewed.

The summary of pathological findings presented below includes information concerning only first-generation animals. In keeping with the design of the experiment, of the 120 animals of the second generation, only the 7 that died prior to completion of the second breeding were submitted for microscopic examination. In each case, the major finding was the presence of the necrotizing arteritis described below.

In general, the pathological processes encountered in this study were similar to those that have been reported in other long-term studies of this species. The diseases observed in any one dietary group did not differ qualitatively from those encountered in the other groups. The incidences of the more frequently encountered and major diseases in the four groups are presented below in tabular form, while the pathologic changes in these diseases and the less common conditions are discussed under headings of organ systems involved.

A. BRAIN

Significant lesions of the brain were uncommon in all groups. Cerebral edema of varying degree, and mild focal leukocytic infiltration of the meninges were encountered in several animals of each group. In one animal of group 1X, a large brain abscess was associated with suppurative otitis media. The brains of two other animals of this group were infiltrated diffusely by a malignant glioma. The brain of one animal of group 2X was involved by direct spread of a neoplasm originating in the hypophysis.

B. CARDIOVASCULAR SYSTEM

1. Heart.—The cardiac lesions observed in the several groups were similar in type. Sclerosis of coronary arterial branches was noted in all groups and, with somewhat greater frequency in the 1X and 2X groups (Table VII). These figures, however, are not based upon a systematic grading and specific comparison of the vessels and the differences, therefore, may not be significant. Small foci of chronic interstitial inflammation occurred in the myocardium with a frequency roughly parallel to that of arteriosclerosis (Table VII). A peculiar focal endocarditis characterized by marked fibroblastic proliferation and infiltration of chronic inflammatory cells was found in five animals, three of group OX, one of group 2X, and one of group XL. Cartilaginous metaplasia in the region of cardiac valves was encountered in three animals, two of group 1X and one of group XL. Intracardiac mural thrombi were present in three animals of group OX and in two animals of group 2X. Some degree of degenerative fatty infiltration of myocardial fibers occurred in slightly less than one-half of the members of each group, and was unrelated to other cardiac lesions.

TABLE VII

INCIDENCES OF THE MOST COMMON NON-NEOPLASTIC PATHOLOGICAL PROCESSES IN THE FIRST-GENERATION COLONY

Incidences apply to 50 animals (25 males and 25 females) except for XL's as noted

	Dietary Group			
	OX	1X	2X	XL
Sclerosis of the coronary arteries	6	8	15	3*
Focal interstitial myocarditis	7	13	14	1*
Necrotizing arteritis				
Males	18	16	17	8
Females	12	15	9	2
Total	30	31	26	10
Severe bronchiectasis with associated pneumonitis and abscesses	5	11	10	5*
"Vascular nephropathy"	19	11	12	7
Otitis media	13	16	15	3*

*Incidence applies to a total of 18 rather than 50 animals.

2. Blood Vessels.—The frequent occurrence of a necrotizing arteritis in all the groups virtually overshadowed the other diseases encountered in this study. The presence of the disease was usually heralded upon gross examination by the tortuosity and nodularity of the arterial branches in the region of pancreas and mesentery, the site of most frequent involvement. The presence of lesions elsewhere in the cardiovascular system usually was not suspected grossly. However, subsequent microscopic examination revealed widespread lesions, of variable occurrence, in the intrinsic arteries and arterioles of heart, gastrointestinal tract, liver, kidneys, gonads, genitourinary tract, and more rarely, other areas.

Microscopically, the changes in the large pancreatic and mesenteric arteries resembled lesions which have been called "periarteritis nodosa." Varying stages of the process, from acute necrosis to advanced scarring, were observed. Characteristically, in an active lesion, there was subendothelial deposition of a "fibrinoid" material, extensive destruction of the media, with fibroblastic and angioblastic ingrowth, dense leukocytic infiltration, and adventitial and periarterial involvement by the inflammatory process. Thrombi were frequently present in affected arteries. Destruction of the wall often resulted in aneurysmal dilatation of the affected segment. Rupture of such an aneurysm rarely resulted in massive intraperitoneal hemorrhage.

In small arteries and arterioles in the splanchnic area and in distant organs, a somewhat different process characterized by fibrinoid necrosis and slight, if any, perivascular fibroblastic proliferation and infiltration of chronic inflammatory cells was encountered.

As seen in Table VII, the incidence of necrotizing arteritis was approximately equal in the groups receiving potato diets, whether irradiated or not, and was markedly lower in the control group receiving a "stock" diet. An apparent predilection for males was evident. This tabulation includes under the same heading all stages and degrees of severity of the process, and a variable pattern of organ involvement. The detailed analysis of this arteritis is beyond the scope of the present study, and will be presented in a later publication.[11]

C. RESPIRATORY SYSTEM

The well-known susceptibility of rats to respiratory infection was reflected in the high incidence of these changes in each of the experimental groups. Most frequently encountered were varying degrees of chronic tracheobronchitis often accompanied by slight dilatation of bronchi, and patchy pulmonary emphysema and atelectasis. In a number of animals of each group, greater in the 1X and 2X groups (Table VII), extensive destruction of pulmonary parenchyma had resulted from progression of the inflammatory process. The lungs of these latter animals were often noted at necropsy to be firm, nodular, and extensively consolidated. Microscopic examination revealed severe bronchiectasis with associated abscesses and foci of acute and chronic pneumonia. Proliferation of columnar epithelium was prominent, and squamous metaplasia was occasionally encountered. Often, little functional lung tissue remained in such areas.

Significant acute inflammation of the respiratory tract was relatively infrequent. Focal purulent bronchopneumonia was observed, apparently as an incidental terminal event in an occasional animal of each group.

D. DIGESTIVE SYSTEM

1. Salivary Glands.—Significant alterations were infrequent in the salivary glands of any group. Sclerosis or fibrinoid necrosis of small interstitial arteries was seen occasionaly in animals with necrotizing arteritis in other organs. One female or group IX was found to have a malignant mixed tumor, or carcinosarcoma, apparently arising in parotid gland.

2. Gastrointestinal Tract.—The most frequently observed lesions of the gastrointestinal track consisted of sclerosis and fibrinoid necrosis in small intramural arteries and arterioles. These lesions occurred in all experimental groups as part of the syndrome of necrotizing arteritis described above. Despite the severity of the vascular lesions, they were not associated with infarction of the bowel. In a single animal with arteritis, a focal area of gangrene of small intestine was found. However, in another animal with no demonstrable arteritis, focal hemorrhagic infarction of small bowel occurred. One instance of segmental infarction of colon, apparently due to mesenteric venous thrombosis, was found.

In two animals, one a male of group OX and the other a male of group XL, malignant neoplasms of apparent gastric origin were found. The former was a highly undifferentiated neoplasm, apparently a carcinoma, while the latter was a well-differentiated adenocarcinoma. A spindle cell sacroma arising in colonic wall occurred in a male of group OX.

3. Liver.—Lipid was demonstrable in the livers of over 80% of the animals of each group. No systematic attempt was made to grade the degree of lipidosis which was quite variable, and most frequently minimal. The lipid was deposited for the most part in the form of minute droplets in the cytoplasm of parenchymal cells, and occasionally Kupfer cells, with a tendency to concentrate in central lobular areas.

Sclerosis and, less often, necrosis of small hepatic arterial branches were noted occasionally in animals having necrotizing arteritis in other organs.

Two primary hepatic neoplasms were encountered, both in females of group IX. One tumor was a hepatoma, the other a cavernous hemangioma.

4. Pancreas.—The most prominent pancreatic lesions, occurring in all groups, consisted of periarteritis nodosa-like lesions of larger arteries, and

fibrinoid necrosis of smaller arteries and arterioles as outlined above. Closely associated with these lesions were foci of chronic interstitial pancreatitis.

Islet cell adenomas were discovered in six animals, one of group OX, four of group 1X, and one of group 2X. None of these neoplasms produced metastases.

E. GENITOURINARY SYSTEM

1. Kidneys.—A distinctive type of nephropathy was encountered in animals of each of the dietary groups, and was found to be related to the presence of necrotizing arteritis in these animals. At necropsy, the affected kidneys were found to be somewhat enlarged and mottled. Their cortical surfaces were pebbled or granular due to the presence of contracted scars alternating with microcystic areas. Microscopically, these contracted areas consisted of scarred glomeruli, atrophic tubules, increased interstitial connective tissue, and focal lymphocytic infiltrates. Small intrarenal arteries and arterioles were sclerotic and fibrinoid necrosis was not infrequently encountered. Tubules were widely dilated, contained abundant proteinaceous material, and the epithelium exhibited various retrogressive changes. Hemosiderin was deposited in the epithelium of occasional tubules.

When the sections of kidneys of all animals in the study were collectively reviewed, this "vascular nephropathy" was found with the incidence given in Table VII. With but one exception, this renal abnormality was associated with necrotizing arteritis elsewhere in the body, and even in this single animal, there was necrosis in a few small pancreatic arteries which, however, were surrounded by infiltrating carcinoma of gastric origin, rendering the significance of the necrosis uncertain. For purposes of this study, lesser degrees of nephrosclerosis were not systematically ranked. A detailed analysis of these lesions will be included with the subsequent report of the vascular disease in these animals.

A variety of renal lesions was encountered independently of the vascular disease. Minor degrees of focal chronic inflammation were present in animals of each group. Degenerative fatty infiltration of tubular epithelium occurred in approximately one-half of the animals of each group, with no constant relation to other renal abnormality. Focal calcification of calyceal mucosa or actual calculi were encountered twice in group OX, in three animals of group 1X, once in group 2X, and twice in group XL. A single renal neoplasm, a spindle cell sarcoma was discovered in a female of group OX.

2. Reproductive Organs.—The most prevalent abnormality of gonads and genital tracts of both sexes consisted of fibrinoid necrosis of small arteries and arterioles seen in all groups as a feature of the syndrome of necrotizing arteritis described above. Chronic endometritis was encountered in several females of each group, and suppurative inflammation of preputial or bulbovestibular glands was found with like frequency.

3. Mammary Glands.—Significant lesions of mammary glands were limited to the females, and consisted almost entirely of adenofibromas. The incidence of these neoplasms was approximately equal in the various groups (Table VIII). The histologic pattern varied widely, from predominantly fibrous tumors to almost purely adenomatous growths, many of which exhibited marked secretory activity. The neoplasms were histologically benign, except one tumor from an animal of group OX, in which malignant change in both components had occurred, producing a carcinosarcoma. Metastases were not observed.

TABLE VIII

INCIDENCES OF NEOPLASMS IN THE FIRST-GENERATION COLONY

Incidences apply to 50 animals (25 males and 25 females) except for XL's where the incidence applies to only 18 animals.

	Dietary Group			
	OX	1X	2X	XL
Pituitary tumors	6	8	7*	1
Adrenal tumors	4	6	2*	2
Thyroid "adenomas"	6	6	5	1
Islet cell adenomas	1	4	1	0
Mammary adenofibromas	9*	11	8	3
Miscellaneous additional neoplasms				
Benign	1	2	0	0
Malignant	3	6	1	1
Total neoplasms				
Benign	26	37	21	7
Malignant	4	6	3	1

*1 malignant.

F. ENDOCRINE GLANDS

Epithelial neoplasms of the various endocrine glands constituted a frequent finding in animals of both sexes in each group. Several animals were found to harbor two or more of these endocrine adenomas simultaneously. The incidence of these neoplasms (Table VIII) was approximately equal in groups OX, 1X, and 2X, and while the data are incomplete for group XL, similar neoplasms were found in that group.

Adenomas of the anterior lobe of the hypophysis varied from microscopic foci to large growths replacing almost the entire gland. These neoplasms were sharply circumscribed though not encapsulated, and frequently compressed the adjacent glandular cells. The component cells were larger than those in the adjacent normal gland and had pale cytoplasm. Special stains for differentiation of cell types were not performed. These neoplasms were benign, except one in a female in the group 2X in which there was local infiltrative growth.

Of 14 adrenal neoplasms, nine were considered to be medullary in origin. Although the distinction was not based upon appropriate special stains, five neoplasms were thought to be cortical in origin. In only one animal, a female of group 2X, was there metastasis from an adrenal tumor. Independent of the neoplasms, foci of hemorrhage and necrosis were encountered in the adrenals of approximately 10% of the animals of each group.

A peculiar epithelial proliferation in the thyroid gland was encountered with approximately equal frequency in groups OX, 1X, and 2X (Table VIII). In these glands, large, pale-staining cuboidal or polyhedral cells, growing in a medullary or slightly aveolar pattern extended between and around thyroid follicles in foci of varying size. Although pleomorphism was present and division figures were encountered, none of these growths extended beyond the involved thyroid lobe. They were, therefore, tabulated as benign "adenomas."

Varying degrees of hyperplasia of parathyroid glands, possibly related to renal lesions or to neoplasms of other endocrine glands, were noted in animals of each group.

The occurrence of pancreatic islet cell adenomas has been described above.

G. BONE MARROW, SPEEN, AND LYMPH NODES

The degree of cellularity of the bone marrow was somewhat variable in all groups. Likewise, varying degrees of lymphoid hyperplasia were encountered in speen and lymph nodes. Deposition of hemosiderin in spleen and lymph nodes was a prominent feature in each group. No abnormalities more specific than these were encountered.

H. SKIN

Chronic, nonspecific cutaneous ulcers and sinus tracts were observed occasionally on the extremities. A few epidermal inclusion cysts were encountered. Three cutaneous neoplasms appeared, a fibroepithelial papilloma in a female of group OX, a squamous cell carcinoma in a female of group IX, and a low-grade sarcoma in a male of group 2X.

I. EARS

Chronic purulent otitis media was common in each of the groups (Table VII). Although generally of apparently incidental importance, otitis media was associated with brain abscess in one animal.

J. EYES

Significant ophthalmic disease was infrequently encountered. Corneal vascularization or scarring was found in one or two animals of each group, and early cataractous changes were present in a like number. Suppurative panophthalmitis was present in a single animal of group 1X.

K. NEOPLASMS

A total of 105 neoplasms was encountered in 74 animals. With the exception of an adenocarcinoma of uncertain origin in an OX female and a thoracic fibrosarcoma in a 1X female, the neoplasms have been described above. Together the adenofibromas of mammary gland and the neoplasms of endocrine glands accounted for approximately 90% of the total number. The simultaneous occurrence of neoplasms of various endocrine glands and of adenofibromas with neoplasms of endocrine glands accounted for the majority of instances of multiple neoplasms in a single animal. The total incidence of benign and malignant neoplasms in the several groups is given in Table VIII.

V. DISCUSSION

One disadvantage of irradiation is its enhancement of the rate of decay of foodstuffs which normally spoil by enzymatic rather than microbial action. When the potatoes for this experiment were obtained and irradiated, the conditions under which irradiation of potatoes could be conducted without appreciable decay occurring were not appreciated. These conditions are: (1) delay irradiation as long as practicable after harvesting to permit suberization to heal harvest injuries; (2) use a minimum dose, e.g., 5000 rads which inhibits all but a tolerable amount of sprouting; and (3) minimum handling of the potatoes after irradiation because suberization and periderm formation are also inhibited by irradiation.

The potatoes used in this experiment were irradiated in December, about three months after harvest. A longer pre-irradiation storage period would have permitted maximum suberization and an opportunity to cull damaged potatoes. The dose used was several times that necessary for sprout control. The high dose, however, did serve as a safety factor for the wholesomeness test. Of all the factors, however, the one which most seriously compromised the experiment was the excessive amount of shipping and handling to which these potatoes were subjected after irradiation, as mentioned early in the report. Whether or not the high mortality rate of first- and second-generation animals stemmed from the conditions of potatoes fed will be discussed below.

The sub-optimum condition of the potatoes, however, did not appear to affect the nutritional value of the diet. Growth, food efficiency, and reproductive performance were optimum. With minor exceptions, no differences in these criteria could be traced to irradiation of the potatoes in the diet. The first-generation females fed the "1X" diet appeared to attain a significantly higher body weight than did females fed the other two diets, but this effect did not appear with the females of the second and third generation fed the same diet.

Nothing appeared from the periodic blood cell counts which revealed an important difference among the various groups. Practically all ranges of values overlapped. The males fed the 1X diet maintained a lower white blood cell count throughout most of this period, but considering the small numbers and the variations involved, this is not of statistical significance. With regard to organ weight-body weight ratios, there was only the higher lung weight in the males fed the irradiated diets, and this may have been influenced by the increased incidence of respiratory infection in these groups, as noted later.

With regard to the fact that the mortality rate of two generations of both male and female rats fed the irradiated potato diets was consistently, if in some cases only slightly, higher than those fed the control diets, a conclusion of unwholesomeness of such potatoes cannot be necessarily drawn. Irradiation promoted decay in the potatoes used in this experiment, and some of this was present in the diet early in the experiment. Delayed effects of this decay may account for the higher mortality of the males fed the irradiated diets. Although the effect was not proportional to the amount of decay included, and although there was little if any effect on the females, this factor cannot be ruled out.

This factor cannot explain the second-generation mortality since the practice of removing all decay from the potatoes fed started before the second-generation was born. There may, however, be another reason for that mortality pattern. This appears in Table IX, which shows the relation of mortality of second-generation animals to that of their parents by the nineteenth month of the experiment. At this time, the mortality in the second-generation control group reached 7%, that in the 1X group, 27%, and that in the 2X group, 23%. The table

TABLE IX

NUMBER OF SECOND-GENERATION ANIMALS (LEFT OF HYPHEN) AND NUMBER DEAD AS OF 15 OCTOBER 1957 (RIGHT OF HYPEHN) ACCORDING TO WHETHER NEITHER, ONE, OR BOTH PARENTS HAD DIED BY SAME DATE, BY DIETARY GROUP

Diet	Parents Dead		
	Neither	One	Both
0X	18-1	12-1	0-0
1X	7-0	17-6	6-2
2X	4-0	22-5	4-2

shows that, considering all groups together, the mortality rate of second-generation animals, both of whose parents were still living, was only 3%, of those of whose parents one had died, 32%, and of those of whose parents both had died, 40%. In the control group where one parent had died, it was usually the mother; in the 1X and 2X groups it was usually the father, a point ruling out a predominant effect of maternal diet upon the survival of offspring.

If it is reasonable to assume that early offspring mortality is related in some way to early parental mortality, then it should also be noted from the table that more than half (60%) of the second-generation animals in the control group happened to have come from parents both of which were still living, and none from parents both of which had died. In the groups fed the 1X and 2X diets, however, only 23% and 13%, respectively, had come from parents both of which were living, and 20% and 13%, respectively, had come from parents both of which had died. The parent-generation males and females were random-mated, and it was a matter of chance which particular males and females became parents. It thus appears that second-generation animals fed the irradiated potato diets quite by accident had a larger share of parents whose survival or resistance to disease was low. Whether the mortality in both generations was primarily due to the vascular disease which in turn was under genetic influence is the subject of a later paper.[11]

The question of what accounted for the apparently accelerated mortality of first-generation males in groups 1X and 2X after about 16 months is significant. While it is difficult to designate an immediate mechanism of death in an older animal with long-standing disease, the major pathological findings at necropsy must be construed to be of ultimate causal significance. These findings have been analyzed for those males already dead at a time when the differences in the mortality rate of groups 1X and 2X from the others had become clearly established. By this time, about 16 months, 42 of the 75 males had died or were sacrificed. The major findings are presented in Table X.

In spite of the higher mortality of the males fed the irradiated potato diets, similar to that shown in Table VII for 19 months, there is no great difference in the incidence of the arteritis. In some animals it was difficult to assign precedence to the respiratory infection or the arteritis, but there was a considerably greater incidence of major respiratory infection in the 1X and 2X animals relative to the controls than there was of the arteritis. Since two-thirds of the males fed each of the potato diets, irradiated or not, were susceptible to some degree of necrotizing arteritis, it appears that the more frequent presence of severe respiratory infection in the 1X and 2X males may have been a factor accounting for the additional mortality.

With regard to the pathological findings in general in this study, the diseases encountered in each group were of the same type as encountered in the other groups although of somewhat different incidence in some instances. No qualitative differences in the pathological findings could be attributed to irradiation of the diet. However, several disease processes stand out by virtue of their

TABLE X

MAJOR PATHOLOGICAL FINDINGS IN THE FIRST 42 FIRST-GENERATION MALES WHICH DIED OR WERE SACRIFICED (BY ABOUT 16 MONTHS)

	Dietary Group			
	OX	1X	2X	XL
Number of deaths	6	14	13	9*
Number in which the following was the major pathological finding				
Arteritis	4	4	6	2
Arteritis with respiratory infection	1	4	4	0
Respiraratory infection alone	0	2	2	1
Miscellaneous	0	1	0	2
No cause of death evident	1	3	1	4*

*Three were sacrificed in apparent good health for comparative purposes only.

frequency in all groups, or by virtue of a somewhat higher incidence in the 1X and 2X groups.

The high incidence of a severe and widespread necrotizing arteritis in groups OX, 1X, and 2X all but eclipsed other pathological findings. The incidence of this disease in the three groups was approximately the same, and thus irradiation of the potatoes in the diets of groups 1X and 2X cannot be considered to be the etiologic factor. A similar process has been described in this species under various conditions.[12-14] The much lower incidence of this disease in animals of group XL and the fact that they were affected much later in life than animals in the other three groups suggest that the high incidence of the disease may be related to factors in the potato diets unrelated to irradiation. The detailed analysis of this arteritis, since unrelated to irradiation, is beyond the scope of this study, and will be considered in a subsequent publication.

The great susceptibility of this species to respiratory disease is well known.[15] As shown in Table VII, severe bronchiectasis was common in all groups and was somewhat greater in the 1X and 2X groups. As pointed out above, severe respiratory disease may have been a factor in the apparently increased early mortality of the males of group 1X and 2X. However, the occurrence of respiratory disease in general in the rat is extremely frequent, and our tabulation takes into account only the "end stage" of respiratory disease, and not the frequently observed lesser degrees of inflammation. These facts must be considered when evaluating the significance of the apparently increased incidence of respiratory disease in the 1X and 2X males.

Middle ear infections were extremely common in all groups, regardless of diet (Table VII). This incidence is comparable to that reported from other colonies,[16] and there was no evidence suggesting any effect of irradiation of the diet in this regard.

The high incidence of neoplasms in this study was of interest, but certainly not unprecedented.[17,18] The frequent occurrence of adenofibromas of mammary gland[17-19] and of neoplasms of endocrine glands[20] has been reported previously; these two groups of neoplasms account for most of those encountered in this study. There was no suggestion of any significant difference in the incidence of neoplasms related to irradiation of dietary components.

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