STUDIES ON THE PHYSIOLOGICAL EFFECTS OF FEVER TEMPERATURES

II. The Effect of Repeated Short Wave (30 Meter) Fevers on Growth and Fertility of Rabbits*

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Plates 34 and 35

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The development of the short wave vacuum tube radio oscillator has opened many new fields for biological research. The study of the effect of short wave high frequency radiation (4 to 300 m.) on bacteria and their products, on plant and animal cells, as well as upon normal and diseased animals, is engaging the attention of many investigators. During the last 5 years approximately thirty reports on the biological effects of high frequency radiation have been published. A recent survey of this work was made by Szymanowski and Hicks (1). The production of therapeutic fevers by placing patients in a high frequency electrostatic field is still an experimental procedure, but the clinical work thus far done indicates that this procedure may have unusual possibilities. Before this method of treating disease in man can be accepted for clinical use sufficient proof must be established to demonstrate that there are no injurious results. Three possible biological effects of such radiation must be considered: first, the general heating effect; second, the possible selective heating due to special dielectric properties of different tissues at certain frequencies (principally above 60,000 kilocycles); third, a possible biological influence due to factors other than the temperature elevation of the cell. The latter is difficult

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to demonstrate because complicated arrangements are necessarily required to eliminate the heating factor. Nevertheless, Szymanowski and Hicks (1) believe they have succeeded in attenuating bacterial toxins by short wave radiation without the development of heat.

HISTORY

In 1893 d'Arsonval (2) reported that high frequency currents failed to stimulate tissues but only gave a sensation of heat. He was able to elevate the body temperatures of animals and with such currents to stimulate their metabolism. Schereschewsky (3) working with a vacuum tube oscillator studied the effect of short wave radiation on mice. He determined that wave lengths from 3.8 to 15 m. (80,000 to 20,000 kilocycles) had the most marked lethal effect on mice. He noted a rise in their body temperature but his explanation for the cause of death was that an electromechanical vibration destroyed the living cells of the body. He believed that this was a specific effect, especially since the rectal temperature of dead mice could be raised only from 0.1–0.7°C., while in the same length of time the rectal temperature of living mice was elevated from 5–6°C. Christie and Loomis (4) repeated similar work on mice, but maintained that the lethal effects were due to the heat generated by the high frequency current which was induced in the mice. They were unable to elicit any evidence of a specific effect. McKinley (5) made interesting observations on heating the adult and larval form of a beetle, *Tenebrio molitor*, with a short wave oscillator. The adult was killed in 1 minute and 19 seconds, while it took 7 minutes and 38 seconds to kill the larva. He explained this difference by the selectivity of the waves for nervous tissue which is abundant in the adult while the larval form is almost devoid of it. An exposure of 2 minutes and 1 second was required to kill the adult grasshopper, *Melanoplus femur-rubrum*, while the nymph of this same species was killed in 2 minutes and 15 seconds. The length of time required to kill these two forms was practically the same due to the similarity of their nervous structures. Therefore, McKinley postulates a specific effect or selectivity of the short waves apart from the elevation of internal temperature which he believes to be only a by-product of such radiation.

Knudsen and Schaible (6) studied the effect of fevers produced by short wave radiation on 28 white rats. They were heated to an average rectal temperature of 40.5°C. from 30 minutes to an hour, 5 times each week from 8 to 13 weeks. They state that it was difficult to keep the rats at any set temperature, and that during one treatment the temperature of five rats was elevated from 43.3–43.9°C., resulting in the death of one of the animals. They conclude that a temperature of 40.5°C. does not appear to retard the growth of rats when exposed for short daily intervals of ½ and 1 hour. They state that the reproductive organs of the male and female were not appreciably affected, and that no abnormal pathologic lesions were produced. However, it is also stated that a histological examination

of the male testes showed a retardation of spermatogenesis with exfoliation of the germinal epithelium and a proliferation of the Sertoli cells.

During the last 4 years we have studied the effect of short wave fevers on normal and diseased white mice, white rats, guinea pigs, rabbits, and dogs. We (7) have likewise observed the effect on man of such fevers when used for therapeutic purposes. It has been our general observation that no ill effects occurred except occasional slight superficial burns, unless too high a fever was produced for the species of animal irradiated. In 1929, as a preliminary study, we exposed a series of male and female guinea pigs at irregular intervals, producing a fever with a maximum temperature from 41–42°C. During the time they were receiving such treatments they were bred. The heatings were continued during their pregnancies which terminated normally. No apparent injury occurred to the fetuses *in utero*, since there were born just as large and normal litters with birth weights similar to those from untreated females. Although our impression at that time was that the fever-treated group was somewhat larger and sleeker than the untreated males and pregnant females, we did not have enough observations to be conclusive. Another difficulty we encountered was the inability to establish uniform fevers. We also had the same experience when rats and mice were irradiated. This was apparently due to the fact that such small experimental animals were not able to adjust themselves to the higher body temperatures and maintain them, due possibly to their ineffective temperature-regulating mechanism. The small body mass of such experimental animals must also be considered. Because of this preliminary observation on guinea pigs and the relative importance of determining the effects of short wave fevers on metabolism and fertility, a similar but more detailed study was made on twenty-four rabbits, including their young. Rabbits were used for this work because of their larger size and the fact that more uniform fever temperatures can be maintained in them than in the smaller species of experimental animals.

Experimental Method

This procedure was designed to determine whether any gross abnormalities in growth or fertility occur from the continual use of short wave fevers produced in an electrostatic field (10,000 kilocycles).

The second and third generations were observed for any possible developmental changes resulting from injury to the gonads or to other organs during fetal life. Such effects might result from the increased heat of the fever or from some inherent specificity of the short radio waves.

Twenty-four healthy immature rabbits born to normal, large, adult Belgian hares were chosen from our stock. The mates of six litters, labelled A, B, C, D, E, and F respectively in the order of the kindling date of the litter, consisting of twelve bucks and twelve does, were divided into two groups. The first group contained ten controls, while the second was comprised of fourteen rabbits to be given fever treatments. Since the number and sexes in each litter varied, it was necessary to make an arbitrary division of the sexes and matings in the control and treated groups. Wherever possible litter mates of the treated groups were paired and treated together, assuming that the maximum effect would thus be produced in the young born to them, providing any changes resulted from this form of radiation. In one case a treated buck (No. 11-84) was bred to two control females (Nos. 11-85 and 11-86). The matings and data concerning the number and frequency of the fevers appear in Table I.

The technique of irradiation was as follows: The rabbits were exposed in a wooden box (orange crate) in the electrostatic field of the high frequency oscillator operating at a frequency of 10,000 kilocycles (30 m.). An orange crate, in addition to being inexpensive, offers both ventilation and drainage and the wood, being a good dielectric, does not heat to any great extent. The irradiation was supplied by two oscillators in a Hartley circuit. In one a push-pull circuit was used, while the other gave only half-wave rectification. The D.C. plate voltage on the oscillating tubes was from 1,800 to 2,000 volts, and the plate current was from 2 to 4 milliamperes. The high frequency waves oscillated between two aluminum plates (14 x 20 inches) set upon the cabinet, producing an electrostatic field in which the animals were heated. The high frequency current in the leads to these plates varied from 2 to 4 amperes, depending upon the number and size of the animals in the field, as well as on the distance between the plates. The output of the machine was adjusted in each irradiation to the optimum heating field strength, no set values except frequency being possible under the present conditions. One of the machines was kindly loaned to us by Dr. W. R. Whitney of the General Electric Research Laboratory, where it was designed. The other was built by Mr. F. W. Bishop of our laboratory staff. Both machines operate at the frequency stated above. Oscillation is indicated by the glowing of a neon bulb set near one of the high frequency leads.

The fever treatments were begun on litter mates at ages varying from 29 to 171 days and continued either 2, 3, or 5 times per week until the pregnancy terminated. The bucks likewise were given no more fevers after their mates had kindled. The rabbits in Litters C, D, E, and F were not treated for about 1 month during

TABLE I

Effect of Repeated Short Wave Irradiation on Fertility and Growth of Rabbits

Rabbit No.	Sex	Litter	Mated with Rabbit	Age at beginning of treatment	No. of treatments per wk.	Total No. of treatments	Duration of treatment	Maximum temperature	Age of rabbits at kindling	No. in litter	Weight of litter	No. raised	Weight at beginning of treatment	Weight at 1 year	Gain in weight
				days			*hrs.*	*°C.*	*days*		*gm.*		*gm.*	*gm.*	*per cent*
11-16	F.	A	11-20	123	3	22	23½	41.9	331	6	244	0	1662	2105	21.04
11-18	M.	A	Normal F.	123	Control	—	—	—	—	—	—	—	1882	2200	14.45
11-20	M.	A	11-16	123	3	26	33	41.7	—	—	—	—	1725	1913	9.82
11-15	M.	B	11-17–9	171	3	22	24½	41.4	—	—	—	—	2344	2600	9.84
11-17	F.	B	11-15	171	Control	—	—	—	239	7	301	3	2400	3054	21.41
11-19	F.	B	11-15	171	3	26	32⅙	41.6	251	6	280	0	2364	2980	20.67
11-83	F.	C	11-84	80	3	36	75½	41.9	183	7	162	0	1099	3500	68.60
11-84	M.	C	11-83–5–6	80	3	36	68½	42.1	—	—	—	—	985	2915	66.20
11-85	F.	C	11-84	80	Control	—	—	—	223	9	288	0	1160	3415	66.02
11-86	F.	C	11-84	80	Control	—	—	—	182	8	256	0	1045	3300	68.33
11-87	M.	D	11-88	46	2	30	51⅓	42.4	—	—	—	—	555	3910	85.80
11-88	F.	D	11-87	46	2	31	53½	42.3	210	3	123	3	500	3900	87.18
11-89	F.	D	11-90	46	5	67	136½	42.0	204	6	351	5	452	3945	88.54
11-90	M.	D	11-89	46	5	67	135¾	42.0	—	—	—	—	585	4289	86.33
11-91	M.	D	11-97	46	Control	—	—	—	—	—	—	—	581	3290	82.34
11-92	M.	D		46	Control		Died 83 days of coccidiosis						400		
11-93	F.	E	11-98	44	2	31	57½	42.4	207	3	158	0	442	4185	89.44
11-94	F.	E	11-98	44	2	39	78½	41.7	255	8	279	0	568	3870	85.32
11-95	F.	E	11 96	44	Control	—	—	—	172	6	250	0	476	3850	87.63
11-96	M.	E	11-95	44	Control	—	—	—	—	—	—	—	533	3700	85.59
11-97	F.	E	11-91	44	Control	—	—	—	216	5	185	0	540	3450	84.34
11-98	M.	F	11-93–4	29	2	39	74½	42.3	—	—	—	—	353	4800	92.65
11-99	M.	F	Normal F.	29	Control	—	—	—	—	—	—	—	322	4820	93.31
12-00	M.	F		29	Control		Died 255 days of pneumonia						200		

an epidemic of diarrhea due to coccidiosis. This occurred in the controls and treated rabbits alike when they were about 90 days old. On the day of the first treatment all of the rabbits in a litter were weighed and thereafter at weekly intervals. Rectal temperatures were taken at the beginning and at 15 minute intervals during the period of the exposure and afterward until the temperature of the rabbit had returned to normal. The current was shut off and the animals were removed from the field to make these observations. At each treatment we endeavored to produce a rectal temperature with fastigium of 41.5°C., but occasionally the temperature varied from 41–42°C. The highest temperatures measured during the series of irradiations are recorded in Table I, and it will be observed that in two instances temperatures of 42.4°C. were reached.

The exposure of the animals repeatedly over a long period of time necessitated care to prevent burns from contact with the aluminum plates. It is important not to allow the urine to wet the feet of the rabbits. It contains enough salts to make an excellent condenser, and the concentration of eddy currents in the liquid is sufficient to cause severe burns. While the position of the animal between the aluminum plates makes some difference in the rate of heating, the movement of the animal in the crate is usually sufficient to make local overheating negligible during the treatment.

When the rabbits were young it was possible to irradiate four at a time in the compartments of an orange crate, but as they grew larger mated pairs were heated to maintain similar conditions in both sexes. The control rabbits were likewise brought to the treatment room each day with the animals to be treated. Their temperatures were taken several times, as were those of the irradiated rabbits, in order to handle the former animals as much as the treated animals.

When pregnancy terminated the young in each litter were counted and weighed, and, if they survived, observations were made on their growth and fertility until a third generation was born. The litters comprising the third generation were also counted, weighed, and observed for survival and growth.

Pairs were kept together until pregnancy was definitely established, after which the rabbits were separated. All rabbits were otherwise kept in separate cages and fed on a stock diet of an abundance of whole oats. In the summer months fresh cut green alfalfa was fed daily in addition, while during the rest of the year dried alfalfa and chopped cabbage were fed on alternate days. Fresh water was always available in the cages. All of the animals were fed at the same time each day.

EXPERIMENTS

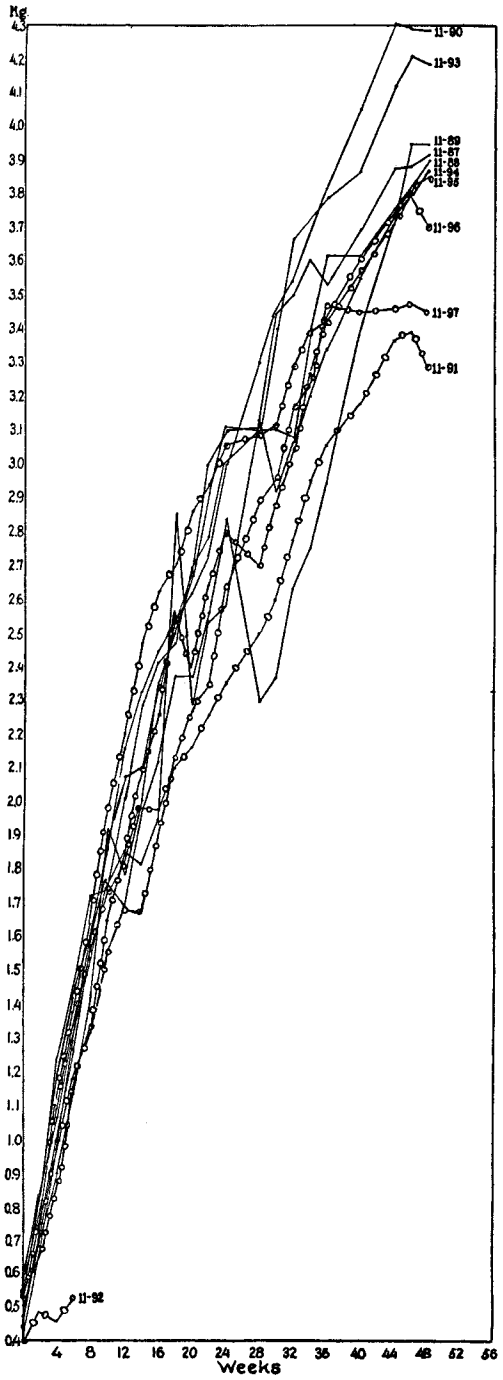
Experiment 1. Litter A.—Rabbits 11-16 female and 11-20 male were paired. Beginning at 123 days of age they were given 3 short wave fevers each week with a total of 22 and 26 exposures respectively, with a total amount of 23½ and 33 hours irradiation. At the age of 331 days the female gave birth to six normal, living young totalling a weight of 244 gm. She refused to nurse them and raised none of the litter. The other male in this litter, No. 11-18, was used for a control.

Experiment 2. Litter B.—Rabbits 11-15 male and 11-19 female were paired and beginning at 171 days of age were given 3 fevers each week. The male received 22 exposures, while the female had 26. The total number of hours irradiation was $24\frac{1}{2}$ and $32\frac{1}{3}$ respectively. At 251 days of age No. 11-19 had a litter of six normal, living young totalling a birth weight of 280 gm. She gave them no care and all died within 3 days. A female, No. 11-17, was kept as a control. She was bred to Rabbit 11-15, the same male that was used to mate the fever-treated female in this litter. At 239 days of age she bore seven normal, living young totalling a weight of 301 gm. Three of the seven were raised.

Experiment 3. Litter C.—Rabbits 11-83 female and 11-84 male, beginning at 80 days of age, were given fever treatments 3 times weekly. A total of 36 fevers were produced, the female receiving a total exposure of $75\frac{1}{2}$ hours while the male received a total of $68\frac{1}{2}$ hours. The female conceived and gave birth to a litter of seven rabbits with a total litter weight of 162 gm. Parturition occurred during the night and when found in the morning only one of the litter was living. It died 3 hours later. Two females, Nos. 11-85 and 11-86, in this same litter were used for controls. They were bred to Rabbit 11-84. They conceived and bore normal litters of nine and eight weighing 288 and 256 gm., at 223 and 182 days of age respectively. Neither female raised any of her young. Rabbit 11-85 killed and ate all of her young within 24 hours. All of the litter born to No. 11-86 were living. The mother destroyed three within 4 hours after birth and the remainder within 48 hours.

Experiment 4. Litter D.—Rabbits 11-87 male and 11-88 female were paired and given biweekly, beginning at 46 days of age, 30 and 31 fevers totalling $51\frac{1}{3}$ and $55\frac{11}{12}$ hours irradiation respectively. At 210 days of age the female gave birth to three young totalling 123 gm. in weight. All of the young were raised to maturity. Rabbits 11-89 female and 11-90 male of this same litter were paired. They were given short wave fevers 5 times each week. 67 fevers were given each, totalling $136\frac{7}{12}$ and $135\frac{3}{4}$ hours respectively. At 204 days of age the female (No. 11-89) had a litter of six with a total birth weight of 351 gm. Five of these were raised to maturity, the sixth dying 1 week after birth from an unknown cause. Two males, Nos. 11-91 and 11-92, were used for controls. Rabbit 11-92 died at the age of 83 days from coccidiosis. The other control matured normally. The growth curves of the treated and control rabbits in this litter are seen in Graph 1.

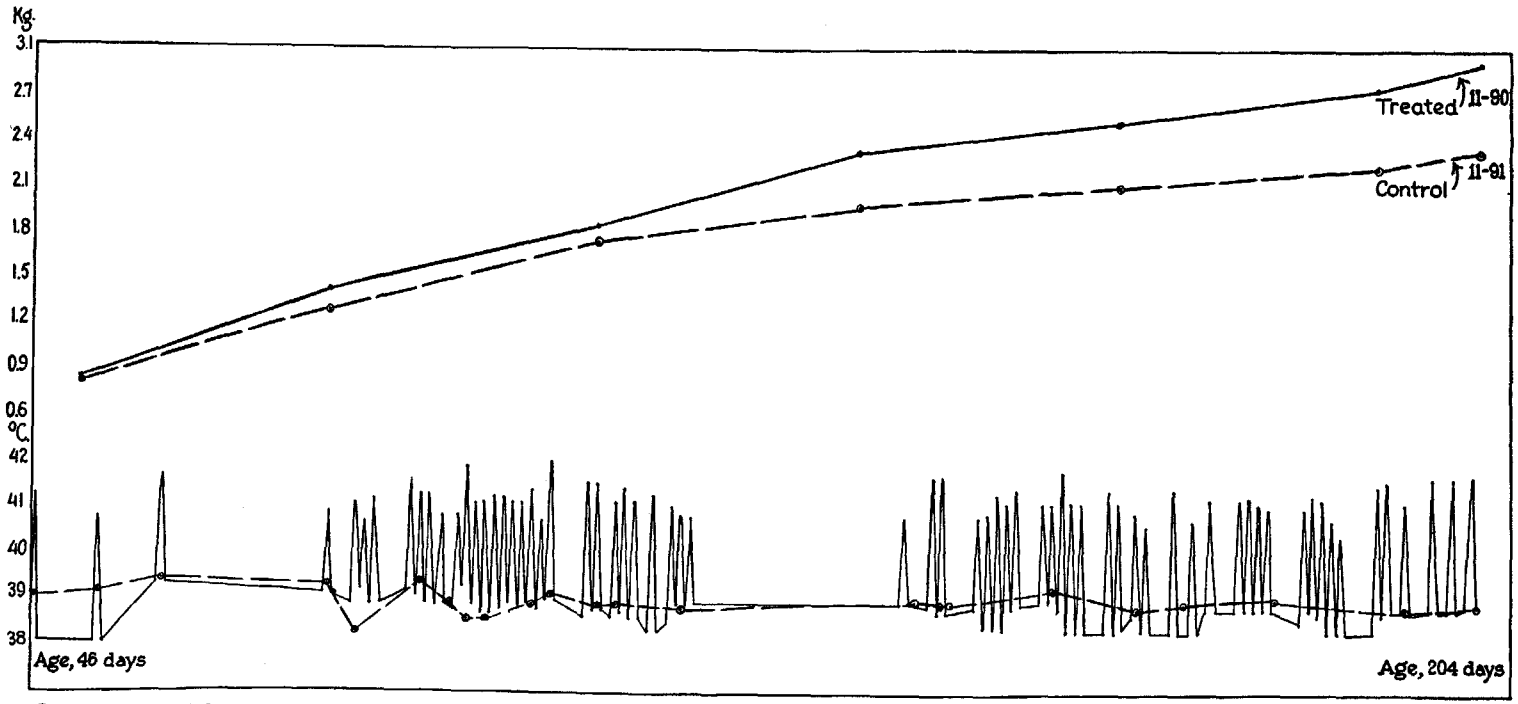
Experiment 5. Litter E.—Rabbits 11-93 and 11-94 females were bred to Rabbit 11-98 male (Litter F) and treated biweekly 31 and 39 times, totalling $57\frac{5}{12}$ and $78\frac{11}{12}$ hours respectively. The first fever was given at 44 days of age. At 207 days of age No. 11-93 gave birth to three normal, living young totalling a weight of 158 gm. Two of the litter died in 2 days and the third on the 4th day after birth. Rabbit 11-94 had a litter of eight rabbits weighing 279 gm. at birth. Neither female raised any of her young. The three other rabbits in Litter E served as controls. Female 11-95 was bred to Male 11-96, and Female 11-97 was bred to Male 11-91 (Litter D). At 172 days of age Rabbit 11-95 gave birth to six young totalling a weight of 250 gm. All were dead except one when found



GRAPH 1. Bimonthly weight curves of control and of short wave (30 m.) fever-treated rabbits.

——— fever-treated.

○———○ controls.



GRAPH 2. Weight and temperature curves on one control male (No. 11-91) and his litter mate (No. 11-90), a fever-treated rabbit, both from Litter D, showing the multiple fevers given over a period of 158 days.

———— fever-treated.

o———o controls.

and the latter died a few hours later. Rabbit 11-97 gave birth to five young totalling a weight of 185 gm. when she was 216 days old. The mother refused to nurse the litter and to care for them, which resulted in their death within 48 hours after birth.

Experiment 6. Litter F.—The three males in Litter F, Nos. 11-98, 11-99, and 12-00, were used as follows: Rabbit 11-98, as mentioned above, was bred to the two treated females in Litter E (Nos. 11-93 and 11-94). Rabbit 11-98 was given 39 fevers biweekly, totalling 74½ hours irradiation. Rabbit 11-99 was used for a control, while No. 12-00, also a control, died at the age of 255 days from pneumonia.

RESULTS

It will be noted from Table I and from the growth curves of the controls and of the treated rabbits in Graph 1, that no evidence of injury was caused by repeatedly irradiating rabbits in an electrostatic field of short radio waves (30 m.), thereby elevating their body temperature from 41–42°C. for a considerable length of time. Weekly weights were observed until they had attained their maximum weight at maturity (age when body weight maintained practically a uniform level). In the majority of cases the rabbits exposed to repeated short wave fevers gained a greater maximum weight than did the controls. However, the treated bucks did not attain as great a weight as that of the treated does 3 or 4 months after kindling. The coats of the irradiated group of rabbits were smoother and sleeker than those of the non-irradiated group. In practically every instance one not familiar with the experiment could easily differentiate the two groups by the better general appearance and size of the fever-treated rabbits. The latter appeared more vigorous, healthier, and better nourished (see Fig. 1).

Regardless of the appearance of the two groups, the most reliable information is the percentage of gain in weight. It is difficult to make comparisons in Litters A and B because of their small numbers and because they were from 4 to 6 months old when the experiment was undertaken. However, the fever-treated Female 11-16 (Litter A) gained 21.04 per cent of her weight, while the untreated control doe in this litter, No. 11-18, gained only 14.45 per cent in weight in the same period. The treated buck gained 9.82 per cent. In Litter B the irradiated buck, No. 11-15, gained 9.84 per cent, while his doe, No. 11-19, likewise treated, made a percentage gain in weight of 20.67 per cent. The untreated doe, No. 11-17, showed a gain of 21.4 per cent,

which is slightly more than that of her treated sister. The percentage of gain in weight of the rabbits in Litters C, D, E, and F was similar although that of the treated rabbits, with one exception, was greater. The variation in percentage of weight gained between the irradiated and non-irradiated rabbits was never more than 6 per cent, while the average gain was from 2 to 3 per cent. The treated buck, No. 11-98 (Litter F), failed by 0.66 per cent to obtain as great a gain in weight as did his brother, No. 11-99. It is evident that 5 fevers given per week had no greater effect on the rabbits than 2 fevers per week. Of course, individual variation as to type and conformation of the rabbits must be considered. However, at the time when the litters were divided it was our aim to apportion them as equally as possible. The average percentage of gain in weight being practically always in favor of the rabbits given repeated fevers leads us to believe that the fevers stimulated their metabolism.

The protocols fail to show that repeated short wave fevers interfered with either the fertility of the bucks and does or with the size of the resultant litters when compared to the control group. The observations of Moore (8) indicate that the elevation of the temperature of the testes is a dangerous procedure, but in these experiments we failed to see any evidence of sterility being produced by the repeated elevation of the body temperature from 41–42°C. Rectal temperatures were recorded in these experiments, but by the use of thermocouples we have shown that normally the temperatures of the testes are from 1.5–2.5°C. lower than that of the rectum. Therefore, it is apparent that at no time during the irradiation was the temperature sufficiently elevated to injure the testes. The average age at which females become sexually mature and conceive is from 6 to 8 months. Allowing 31 days for the period of gestation, the controls conceived from 142 to 209 days of age, while the fever-treated rabbits conceived from 153 to 225 days of age. Thus, the average kindling age of the fever-treated females was 14 days older than that of the controls. This apparent delayed conception may be explained upon the basis of the frequent handling which may have disturbed the sexual relations of the male and female. However, an attempt was made to handle the controls as much as the irradiated group. As previously stated, when the fever-treated rabbits were brought from the animal house to the laboratory, the control

litter mates were brought with them and their temperatures were taken when they reached the laboratory and just before they were returned to the animal house. Nevertheless, the temperature of the irradiated rabbits was observed at intervals from 15 to 30 minutes during the exposure. Thus, the treated group was handled more because of the increased frequency with which their rectal temperatures were taken. With the exception of the differences above mentioned, we are aware of no change of the environmental factors in the two groups other than the repeated elevation of the body temperature by irradiation in an electrostatic field of short radio waves.

The average number of young born to the five control does was seven, while the average number in the litters born to seven fever-treated females was five and one-half. However, the average weight of the young from the irradiated females was 41 gm., while that of the young from the control females was 36.5 gm. It has been our experience that the average birth weight of young rabbits is inversely proportional to the size of the litter; that is, the larger the litter the smaller the average birth weight of the young. No definite deductions can be made from these data concerning the sizes of the litters, but if the fevers stimulated the metabolism of the adult, as will be discussed later, a similar factor may have had an effect on the growth of the fetuses *in utero*.

Only one of the control does, No. 11-17 (Litter B), raised three of her seven young, while two of the fever-treated does, Nos. 11-88 and 11-89 (Litter D), raised their litters. Rabbit 11-88, which received 2 fevers per week, raised all of her young, and Rabbit 11-89, given 5 fevers per week, raised five of her six young. It is disappointing that more of the treated and control females did not raise their litters, but because this failure was prevalent in both groups it is certainly not significant. All of the rabbits in the second generation matured to healthy and fertile adults. The litter of five contained three males and two females. They were inbred, with the exception of the extra male, who was bred to a normal female. In all of these matings the third generation was normal.

As a rule the treated and control females kindled living young, but occasionally a litter was born during the night and when the first observation was made of the nest, one or more of the litter was found

dead. None of the young showed any evidence of gross abnormality. The does of both groups had an abundance of milk but would not nurse the litter. Often the mothers cast them from the nest and gave the young no care. Since this attitude of the mother was similar in both groups, it is evidently not due to the irradiation or resultant fevers.

Welch (9) studied the effect of keeping rabbits in an incubator at temperatures from 41.5–41.8°C. for 3 weeks. He observed a loss of weight, but called attention to the differences between his artificial fever and that produced in the course of an infectious disease. In the former, heat loss was decreased, while in the latter it is not definitely known what changes in the heat-regulating mechanism occur. Nevertheless, it is evident that in the course of an infectious disease with elevation of body temperature, there is an increased heat production with or without a decreased heat loss in the body. He further quotes Naunyn as having kept a rabbit alive 13 days with an average body temperature of 41.5°C. In 1923 Walker (10) reported that an elevation of body temperature of 2° or 3°C. by the use of diathermy was accompanied by a 10 to 15 per cent increase in metabolism. Dubois (11) determined that during the course of a fever coincident with most infectious diseases, metabolism behaves according to Van't Hoff's law. He observed a 13 per cent increase for every 1°C. rise in body temperature. However, McCann and Barr (12) found that the basal metabolic rate in tuberculosis was within normal limits. Nasset, Bishop, and Warren (13) showed that when the body temperature of dogs was elevated from 5–7°C. by diathermy, the blood sugar was depleted, the non-protein nitrogen was increased, while the CO_2 content of the blood was diminished. These findings indicate a markedly increased metabolic rate during such fevers. That the short radio waves used to elevate the temperature of the rabbits have no specific effect on metabolism, and that the resultant heat of such irradiation is responsible for the increased weight, is indicated by the work of Luce-Clausen (14). She observed that near infra-red radiation (720 to 1120μ) accompanied by no noticeable rise of rectal temperature stimulated the growth of rachitic rats.

Although we know from previous experience with the production of short wave fevers in rabbits that it is possible to cause a loss of weight

from elevating the body temperature too high and maintaining it too long, we attempted to prevent such injury from overheating in this experiment. We anticipated an increased gain in weight in these rabbits because we have noted a gain in weight in those patients subjected to high frequency fevers as a therapeutic measure. We believe that the increased percentage of gain in weight of the fever-treated rabbits must be explained upon the basis of a stimulation of metabolism, or to an increased oxidation brought about by the increased acceleration of all body functions during the febrile reaction. However, these factors may also have caused a greater intake of food. It must be remembered that the type of fever produced in our experiments is very similar to that produced naturally in pathologic physiology. The short radio waves produce an internal heating that is entirely different from the elevation of the body temperature by warm air or warm water baths resulting from heat conductors.

SUMMARY AND CONCLUSIONS

1. The repeated elevation of body temperatures of male and female rabbits to 41° and 42°C. from 2 to 5 times per week by short radio waves (30 m.), beginning from 29 to 171 days of age and extending through their first period of gestation, failed to injure their growth or to interfere with mating, fertilization, or the development of young *in utero*. Litter mates were kept for controls.

2. The rabbits exposed to the short wave fevers showed, in the majority of cases, a greater percentage gain in weight than did the control litter mates.

3. The kindling age of the treated group was, on an average, 2 weeks older than the non-treated group.

4. The fever-treated females averaged five and one-half young per litter with an average weight of 41 gm., while the untreated females averaged seven per litter with an average weight of 36.5 gm.

5. The repeated elevation of body temperature by short radio waves is a safe procedure when temperatures greater than those within physiological limits are not employed.

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EXPLANATION OF PLATES

PLATE 34

FIG. 1. Litter D. Photographed Dec. 16, 1931. Age 14 months. Nos. 11-87, 11-88, 11-89, and 11-90 repeatedly irradiated with short wave (30 m.) fevers from 46 days of age until termination of first pregnancy. No. 11-91, control, untreated litter mate.

PLATE 35

FIG. 2. Litter E. Photographed Dec. 16, 1931. Age 14 months. Nos. 11-93 and 11-94 repeatedly irradiated with short wave (30 m.) fevers from 44 days of age until termination of first pregnancy. Nos. 11-95, 11-96, and 11-97, controls, untreated litter mates.

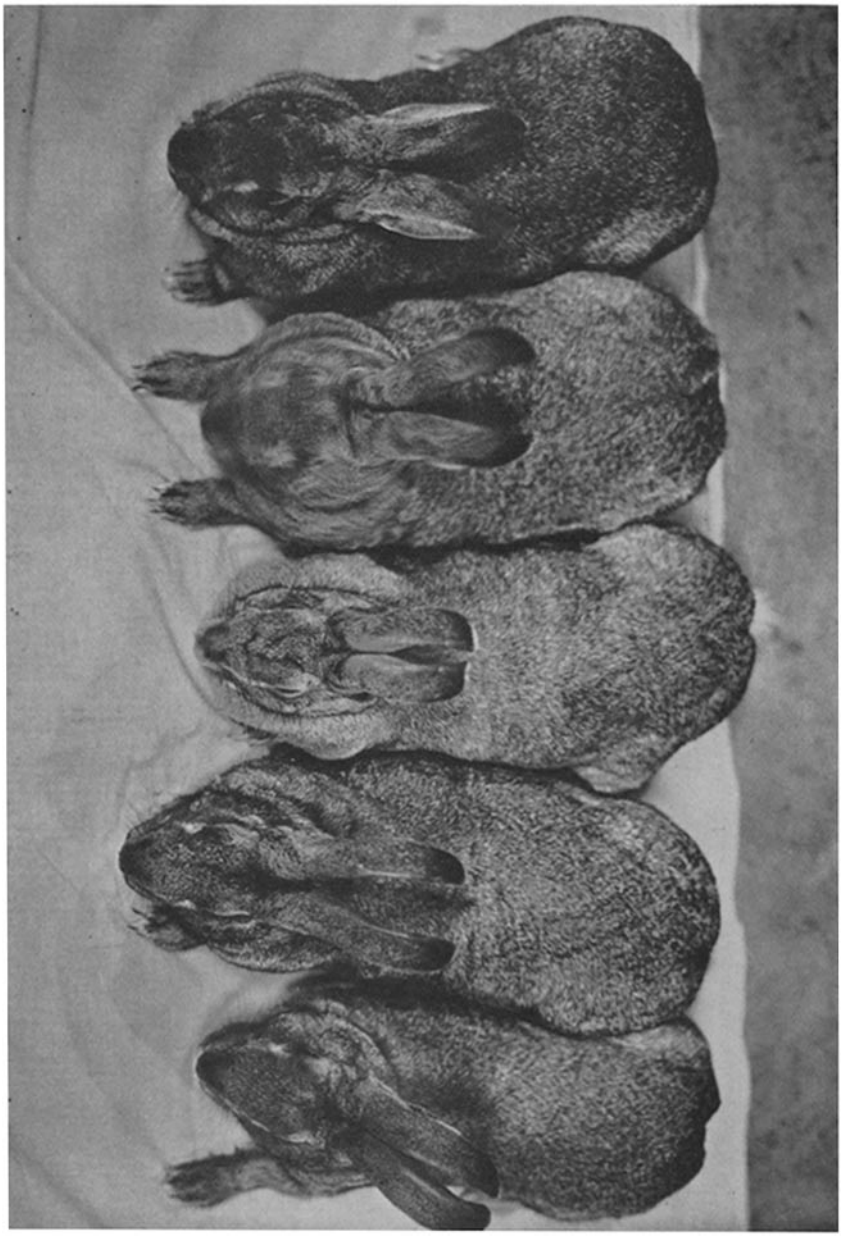

FIG. 1

(Boak *et al.*: Effects of fever temperatures. II)

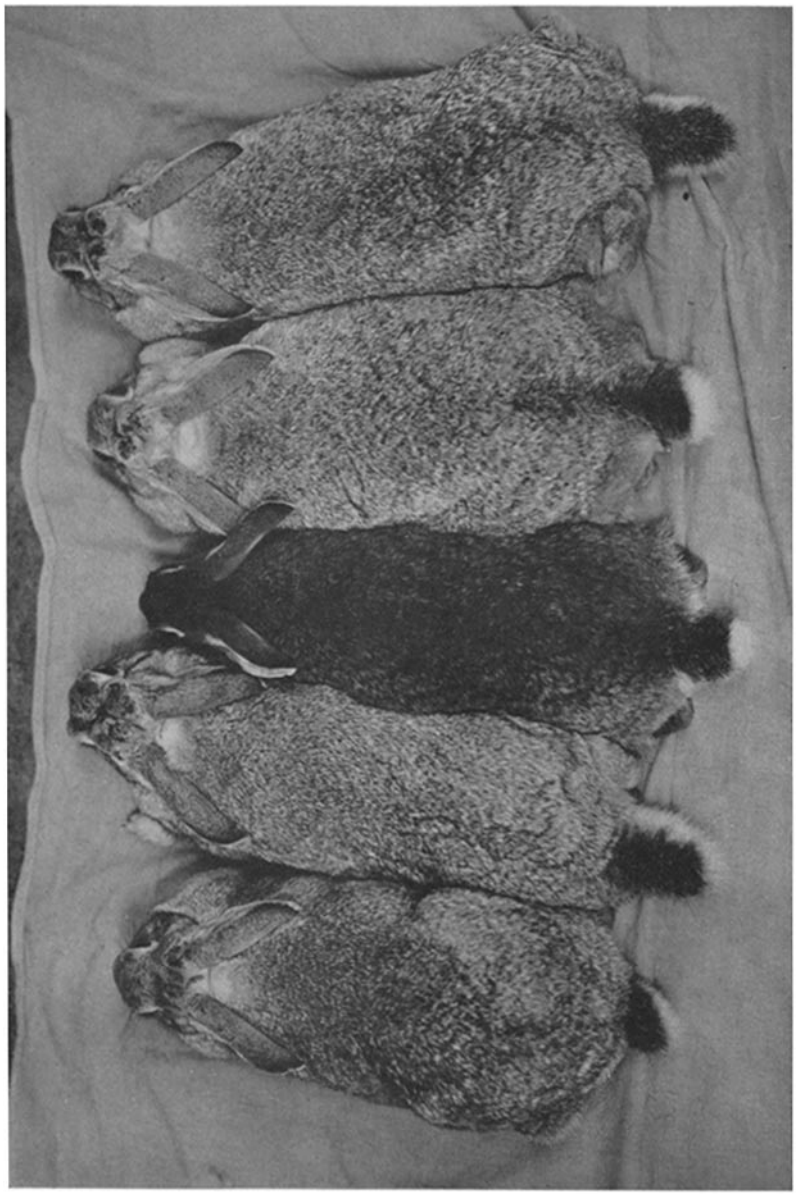

FIG. 2

(Boak *et al.*: Effects of fever temperatures. II)