Resumen por el autor, W. P. Davey.
Laboratorio de Investigación,
Compañia General Eléctrica, Schenectady, N. Y.

Prolongación de la vida de Tribolium confusum debida aparentemente a pequeñas dosis de los rayos X.

En un trabajo publicado anteriormente (Journ. Exp. Zool., t. 22, núm. 3, Abril 1917) se describieron experimentos que demuestran: 1) Que una cantidad suficiente de rayos X pueden acortar la vida de Tribolium confusum, y, 2) Que la duración de la vida después de la acción de dichos rayos puede expresarse por una fórmula matemática, cuya derivación teórica fué expuesta en dicho trabajo. El presente trabajo contiene los resultados de nuevos experimentos, los cuales demuestran: 1) Que es posible, aparentemente, el prolongar de un modo material la vida de Tribolium confusum susministrándole pequeñas dosis de rayos X. 2) Que la prolongación de la vida, cuando se administran diariamente pequeñas dosis, es mayor que en el caso de administrarse dosis mayores de una sola vez. 3) El efecto letal de una dosis de rayos X es menor si se divide en una serie de dosis pequeñas administradas diariamente que cuando se somete al organismo a la acción de una sola dosis mayor. 4) El autor describe un método de análisis gráfico de los resultados obtenidos, mediante el cual el número de causas de muerte puede determinarse por la cantidad de individuos muertos y también estudiarse el efecto de un agente externo sobre cada una de estas causas. 5) Habiéndose empleado la misma clase de organismo durante todo el experimento los resultados comunicados en el presente trabajo y en el publicado anteriormente demuestran que por una simple variación de la dosis, un agente puramente físico (rayos X), puede producir a voluntad: a) una estimulación; b) un efecto destructivo que tiene lugar solamente después de un periodo latente y c) un efecto destructivo instantáneo.

Translation by José F. Nonidez
Columbia University

AUTHOR'S ABSTRACT OF THIS PAPER ISSUED
BY THE BIBLIOGRAPHIC SERVICE, JUNE 2

PROLONGATION OF LIFE OF TRIBOLIUM CONFUSUM APPARENTLY DUE TO SMALL DOSES OF X-RAYS

WHEELER P. DAVEY

FOUR FIGURES

In a previous article[1] experiments were described which showed, 1) that x-rays, when given in sufficient quantity, were able to shorten the life of Tribolium confusum, and 2) that the length of life after x-raying could be expressed by a mathematical formula, the theoretical derivation of which was given. It is the purpose of this article to give the results of further experiments showing that it is apparently possible to lengthen materially the life of Tribolium confusum by giving sufficiently small doses of x-rays.

In the article quoted above curves were given showing that the minimum dose necessary to kill all the beetles was 500 $\frac{MAM}{25^2}$ at 50 KV.[2] Some of the less resistant beetles could be killed by smaller doses, but the curves for 100 and 200 $\frac{MAM}{25^2}$ at 50 KV. had portions in which the death rate was lower than that of the controls. Comment on this was reserved until it could be confirmed by further experiments. Ample confirmation has now been obtained.

The experiments undertaken fall into two groups: A, those in which very small doses of x-rays were given daily throughout the life of the beetles; B, those in which the x-ray dose was given all at one time, as in the work previously published. In each of

[1] Journal of Experimental Zoölogy, vol. 22, no. 3, April, 1917.

[2] I.e., 500 milliampere-minutes at 25 cm. distance at 50 'root-mean square' kilovolts.

these groups of experiments it has been shown possible to duplicate results time after time, subject only to those general limitations which are inseparable from biological work. Typical experiments in each group will be described below. Apparatus and technique were the same as in the work previously reported.

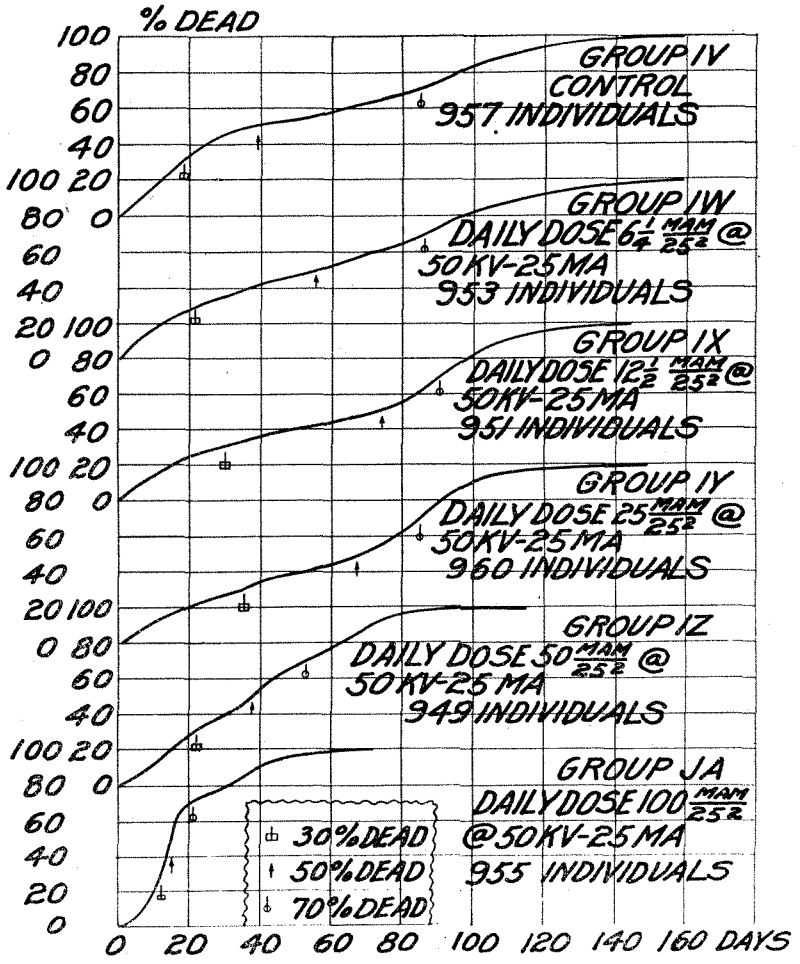

Fig. 1

A. PROLONGATION OF LIFE DUE TO SMALL DAILY DOSES OF X-RAYS

Six groups of approximately 950 individuals each were taken. These were known as groups IV, IW, IX, IY, IZ, JA.

Group IV was the control.

Group IW was given $6\frac{1}{4}\frac{MAM}{25^2}$ at 50 KV. – 25 MA. daily.

Group IX was given $12\frac{1}{2}\frac{MAM}{25^2}$ at 50 KV. – 25 MA. daily.

Group IY was given $25\frac{MAM}{25^2}$ at 50 KV. – 25 MA. daily.

Group IZ was given $50\frac{MAM}{25^2}$ at 50 KV. – 25 MA. daily.

Group JA was given $100\frac{MAM}{25^2}$ at 50 KV. – 25 MA. daily.

After 159 days the beetles were practically all dead. The data on the death rates were then collected and plotted as shown in figure 1. These graphs furnish ample proof that it is possible to reduce the death rate of Tribolium confusum by small daily doses of x-rays.

Table 1 gives readings from these graphs to the nearest whole number.

TABLE 1

NUMBER DAYS AFTER RAYING	PER CENT OF DEAD					
	Group IV, control	Group IW, $6\frac{1}{4}\frac{MAM}{25^2}$ at 50 kv. daily	Group IX, $12\frac{1}{2}\frac{MAM}{25^2}$ at 50 kv. daily	Group IV, $25\frac{MAM}{25^2}$ at 50 kv. daily	Group IZ, $50\frac{MAM}{25^2}$ at 50 kv. daily	Group JA, $50\frac{MAM}{25^2}$ at 50 kv. daily
10	17	17	14	11	12	20
20	34	29	25	21	28	69
30	46	35	30	28	39	79
40	51	42	36	34	55	90
50	54	47	40	39	67	96
60	58	53	44	44	77	99
70	63	59	48	52	88	100
80	67	65	56	63	96	
90	74	74	69	79	98	
100	84	83	84	91	99	

These readings, taken from the smooth curves of the graphs, do not differ from the actual experimental data by more than 1 per cent.

Except while being x-rayed or counted, the beetles were kept in an incubator at 34 to 35°C. In order to make sure that the results were not affected by some possible 'temperature coefficient of life,'[3] the controls were taken out of the incubator while group JA was being rayed, and were kept out during the whole raying. Since group JA was rayed the longest time each day, this meant that the controls were cooled off for a longer time than groups IW, IX, IY, IZ. Therefore, if cooling off for a few minutes each day happened to tend to increase the length of life, then the controls were made to live longer than they otherwise would. The actual increase in length of life observed in groups IW, IX, and IY is, therefore, not due to any possible effect of temperature, but occurs in spite of it. After so many boxes of beetles in JA were dead that the time of raying group IZ was greater than the time of raying JA, the controls were kept out of the incubator while group IZ was being rayed.

Some data not given in the graphs may be of additional interest. Each group was divided into two subgroups of about the same number of individuals each. It was found that the idiosyncrasy was great enough so that the curves of the corresponding subgroups could not be exactly superimposed. However, it was found that this idiosyncrasy was always less than the changes in death rate caused by x-rays. By way of illustration, table 2 shows the percentage of beetles dead in each subgroup, *a*) on the day when 50 per cent of the controls were dead; (*b*) on the day when 50 per cent of the x-rayed group were dead. This table shows that the lowest death rate among the controls (group IV) was higher than the highest death rate among the beetles of groups IW, IX, IY.

It is interesting to note in this connection that the total dose received by these beetles was greatly in excess of that minimum dose which, when given all at once, would have caused premature death.

[3] Loeb and Northrup, Proc. Nat. Acad. Sci., Aug., 1916.

TABLE 2

GROUP	PER CENT OF TRIBOLIUM CONFUSUM DEAD			
	Approximately 50 per cent controls dead		Approximately 50 per cent x-rayed tribolium confusum dead	
	Subgroup (1)	Subgroup (2)	Subgroup (1)	Subgroup (2)
	39th day		56th day	
IV	47.7	54.2	52.8	60.0
IW	41.6	42.1	48.1	52.3
	39th day		74th day	
IV	47.7	54.2	59.9	70.3
IX	32.4	38.3	44.7	54.1
	39th day		67th day	
IV	47.7	54.2	58.6	68.2
IY	31.7	36.7	48.5	50.2
	39th day		38th day	
IV	47.7	54.2	46.8	53.4
IZ	52.9	54.5	50.1	52.4
	39th day		14th day	
IV	47.7	54.2	22.1	24.9
JA	88.5	91.7	43.7	46·8

A further analysis of the data of groups IV to JA will be of interest. The curves shown in figure 1 were each replotted on probability paper[4] (fig. 2). It was found that each curve was composed of portions of three accurate probability curves, joined end to end. It is as though there were three causes of death, or perhaps three definite groups of ages. These three portions of the death-rate curve will be termed A, B, and C. Portion C represents those beetles which lived the longest in their group.

[4] The ordinates of probability paper are so spaced that the ordinary curve of the probability integral is represented by a straight line.

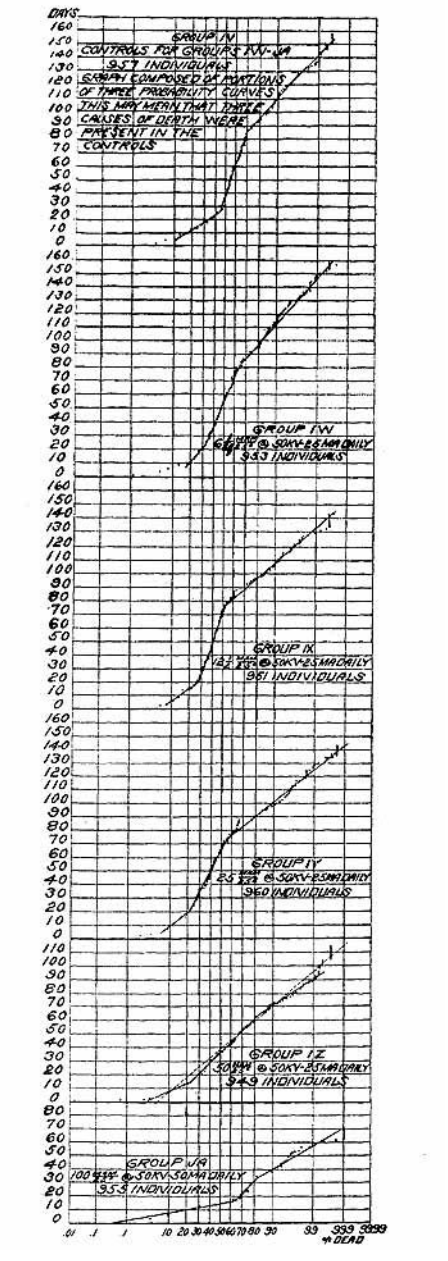
DAYS
GROUP IN
CONTROLS FOR GROUPS XN-IN
957 INDIVIDUALS
EACH COMPOSED OF MATINGS
OF THREE PROBABILITY CURVES
THIS MAY MEAN THAT THREE
CAUSES OF DEATH WERE
PRESENT IN THE
CONTROLS
GROUP IN
@ 50KV-2.5MA DAILY
953 INDIVIDUALS
GROUP IX
@ 50KV-2.5MA DAILY
961 INDIVIDUALS
GROUP IY
@ 50KV-2.5MA DAILY
960 INDIVIDUALS
GROUP IZ
@ 50KV-2.5MA DAILY
949 INDIVIDUALS
GROUP IA
@ 50KV-2.5MA DAILY
953 INDIVIDUALS
% DEAD

Fig. 2

TABLE 3

GROUP	DAILY DOSE	PER CENT DIED		
		A	B	C
IV	Control	44	26	30
IW	$6\frac{1}{4}$	32	36	32
IX	$12\frac{1}{2}$	26	26	48
IY	25	21	35	44
IZ	50	23	61	16
JA	100	64	17	19

Table 3 gives the death rate per 100 in each group for A, B and C.

It is evident that the smallest daily dose (group IW) decreases the death rate of 'A' and that those beetles which are kept from dying of 'A', die of 'B.' Deaths from cause 'C' are practically unaltered. A larger daily dose (group IX) causes about half of those which would normally die of 'A' to die of 'C.' A still larger daily dose (group IY) causes half of those which would have died of 'A' to die of 'B' and 'C.' A still larger daily dose (group IZ) acts much like the previous dose in causing almost half of those which would have died of 'A' to die of 'B,' but it differs from it in that some of those which would have died of 'C' are prematurely killed. The largest daily dose employed (group JA) caused about a third of those which would have died of 'B' and 'C' to die of 'A.'

It is hard to interpret all this. It may be that life cannot exist except in the presence of a small amount of radio-activity. The radio-activity of the earth may not have been of the optimum value, so that some benefit was derived from the x-rays received each day. The following is an effort at an alternative explanation. The evidence given by group JA shows that the lethal action of x-rays is tied up in some way with cause of death 'A.' It is well known that the lethal action of x-rays is more marked on cells in the process of division than on those in the resting state. Therefore, small daily doses (larger than a certain minimal value) can kill off those few cells which happen to be in a state of division at the time of raying. The death of

these few cells stimulates the production of more to take their places between the periods of raying. Therefore, small daily doses, instead of increasing the death rate from cause 'A,' actually decrease it by stimulating the processes of repair. The whole individual beetle, therefore, has a smaller chance of dying from 'A' and is compelled to die of either 'B' or 'C.' When the daily dose is increased to such a value that the daily destruction of cells is equal to or greater than the production of new cells, premature death occurs, from causes 'B' or 'A' (see groups IZ and JA).

B. PROLONGATION OF LIFE DUE TO SMALL SINGLE DOSES OF X-RAYS

Five groups of approximately 850 individuals each were taken. These were known as groups JB, JC, JD, JE and JF.

Group JB was the control.

Group JC was given $100 \frac{MAM}{25^2}$ at 50 KV. – 50 M.A.

Group JD was given $200 \frac{MAM}{25^2}$ at 50 KV. – 50 M.A.

Group JE was given $300 \frac{MAM}{25^2}$ at 50 KV. – 50 M.A.

Group JF was given $400 \frac{MAM}{25^2}$ at 50 KV. – 50 M.A.

The beetles were rather old, so that the controls were all dead on the fortieth day of the experiment. There were so few beetles still alive after the thirty-fifth day that the results of the last five days are not of the same order of accuracy as those of the first thirty-five days.

The first ten days of the experiment, group JC ($100 \frac{MAM}{25^2}$ at 50 KV.) had the same death rate as the controls. After the tenth day the death rate was considerably less than that of the controls. The two groups were divided into two equal subgroups, and although it was found that the idiosyncrasy was such that the subgroups were not exactly alike, still, after the

tenth day, the highest death rate of JC was lower than the lowest death rate of the controls.

During the first seventeen days of the experiment, group JD ($200 \frac{MAM}{25^2}$ at 50 KV.) had a higher death rate than the controls. After the seventeenth day the death rate of group JD was less than that of the controls. After the twentieth day the death rate of JD was identical with that of JC. When divided into two equal subgroups, as described above, it was found that after the twenty-second day the highest death rate of group JD was less than the lowest death rate of the controls.

During the first twenty-nine days of the experiment the death rate of group JE ($300 \frac{MAM}{25^2}$ at 50 KV.) was greater than that of the controls. After the twenty-ninth day the death rate of JE was less than that of the controls.

The death rate of group JF ($400 \frac{MAM}{25^2}$ at 50 KV.) was at all times greater than that of the controls.

These results are shown graphically in figure 3. Figure 4 contains an analysis of these same curves by means of probability paper, showing that, as in the case of experiment A, the curves are composed of accurate portions of probability curves placed end to end.

All of the above results seem to be a direct confirmation of the curves given in the previous paper (loc. cit.). The effect of concentrated single doses is not nearly so marked as the effect of a series of small 'homeopathic' doses. This seems to be much the same law as is already well known in serum therapy and in the action of certain drugs. In the case of serum therapy, this law has been shown to be identical with the law of adsorption. If it could be rigorously shown that the effects of exposure to x-rays follow the same general law, we should conclude that the x-rays are responsible for the production of some substance, perhaps in the blood, which is later adsorbed.

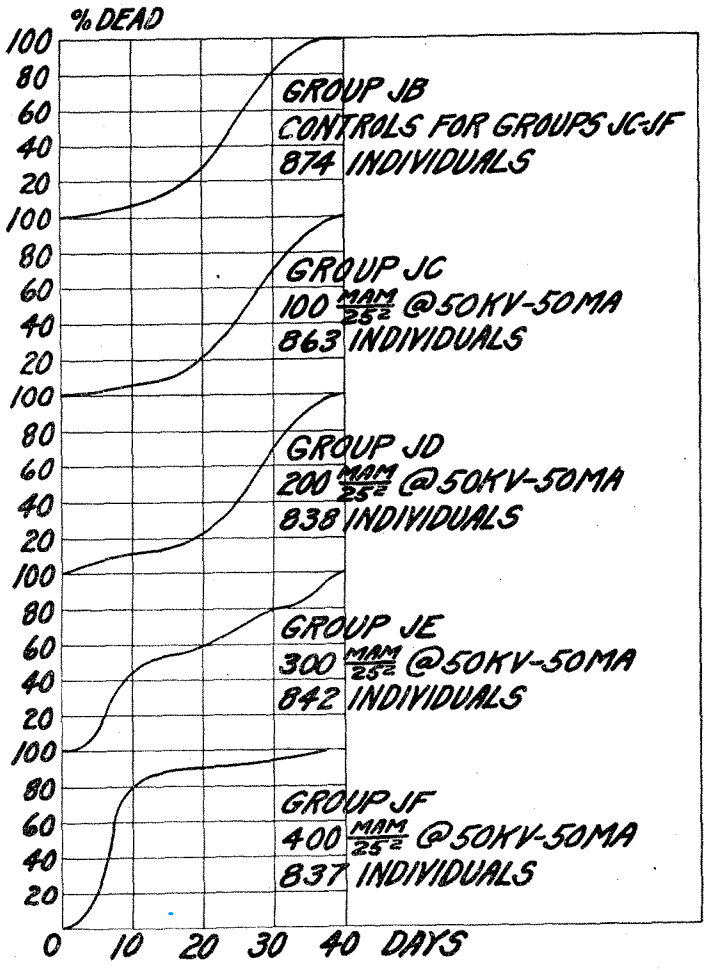
% DEAD
100
80
60
40
20
GROUP JB
CONTROLS FOR GROUPS JC-JF
874 INDIVIDUALS
GROUP JC
100 MAM/25² @ 50KV-50MA
863 INDIVIDUALS
GROUP JD
200 MAM/25² @ 50KV-50MA
838 INDIVIDUALS
GROUP JE
300 MAM/25² @ 50KV-50MA
842 INDIVIDUALS
GROUP JF
400 MAM/25² @ 50KV-50MA
837 INDIVIDUALS
0 10 20 30 40 DAYS

Fig. 3

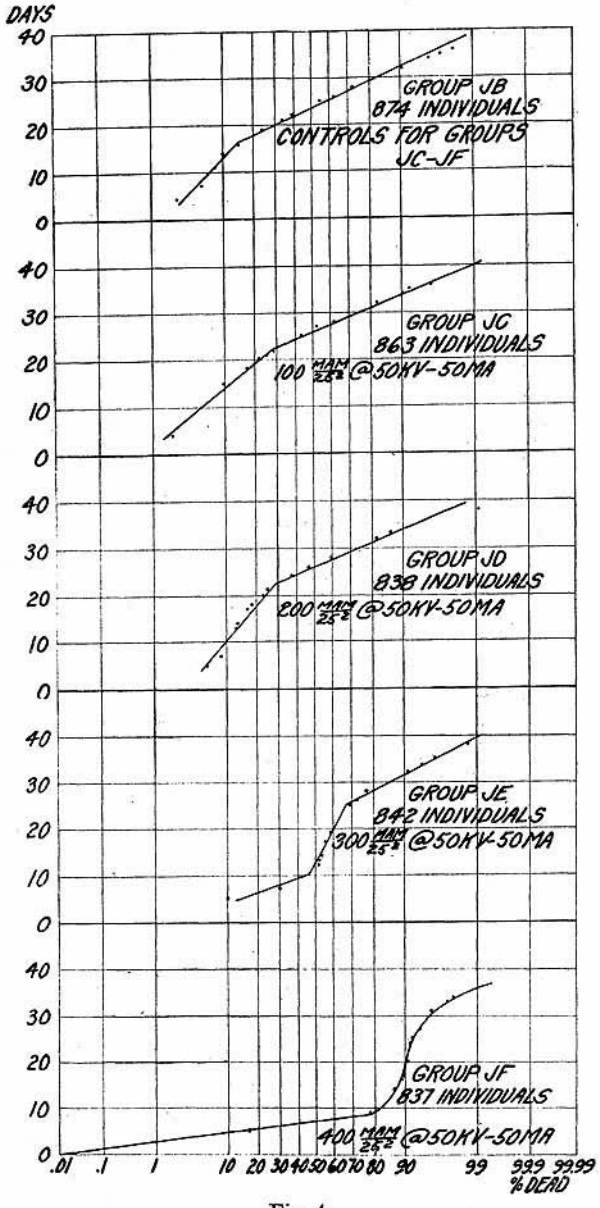
DAYS
GROUP JB
874 INDIVIDUALS
CONTROLS FOR GROUPS
JC-JF
GROUP JC
863 INDIVIDUALS
100 MAM/25² @50KV-50MA
GROUP JD
838 INDIVIDUALS
200 MAM/25² @50KV-50MA
GROUP JE
842 INDIVIDUALS
300 MAM/25² @50KV-50MA
GROUP JF
837 INDIVIDUALS
400 MAM/25² @50KV-50MA
.01 .1 1 10 20 30 40 50 60 70 80 90 99 99.9 99.99
% DEAD

Fig. 4

SUMMARY

1. It has been shown that the life of Tribolium confusum may be prolonged by the use of a purely physical agent, i.e., x-rays.

2. The prolongation of life due to a series of small daily doses is greater than that of larger doses given all at once.

3. The lethal effect of an x-ray dose is less if it is split up into a series of small daily doses than if it is given all at once.

4. A method of graphical analysis of results has been described by which the number of causes of death may be determined from the death rate, and by which the effect of an external agent upon each of these causes may be studied.

5. Using the same kind of organism throughout the whole experiment, the work reported in this and the previous paper has shown that, by merely varying the size of the dose, a purely physical agent (x-ray) may be made to produce at will, 1) a stimulation; 2) a destructive effect which occurs only after a latent interval, and 3) an instant destructive effect.

Research Laboratory,
General Electric Co.,
Schenectady, N. Y.