STUDIES ON X-RAY EFFECTS.

I. Destructive Action on Blood Cells.*

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Pusey,[1] Senn,[2] Brown,[3] Bryant and Crane,[4] and others,[5,6] have reported on cases of leucemia treated with the x-rays and all seem to agree that there is a definite reduction of the circulating leucocytes, following treatment. Most of the cases reported were, however, of the splenomyelogenous type and the myelocytes were the cells most affected. Capps and Smith[7] treated lymphatic leucemia with the Roentgen rays and noted a marked reduction of the circulating lymphocytes, after treatment, in five of their six cases.

Heineke,[8] the first to make careful histological examinations of animals following x-ray exposures, demonstrated that the lymphatic tissues of the body were primarily affected. He found degeneration of the lymph follicles in the spleen and lymph glands and a diminution of circulating lymphocytes. He correlated his observations by suggesting that the diminution in circulating lymphocytes is directly referable to the selective destruction of the lymphogenic tissues by the x-rays.

Helber and Linser[9] published blood counts made on a rabbit before and after x-ray treatment. A marked percentile and absolute reduction in the circulating

*This investigation was carried out by means of funds from the Rutherford Donation.

[1] Pusey, W. A., *J. Am. Med. Assn.*, 1902, xxxviii, 166.

[2] Senn, N., *N. Y. Med. J.*, 1903, lxxvii, 665.

[3] Brown, E. J., *J. Am. Med. Assn.*, 1904, xlii, 827.

[4] Bryant, B. L., and Crane, H. H., *Med. Rec.*, 1904, lxv, 574.

[5] For a review of the literature see Warthin, A. S., *Internat. Clin.*, 1906, iv, series 15, 243.

[6] For a further review of the literature see Pancoast, H. K., *Univ. Penn. Med. Bull.*, 1906–07, xix, 282.

[7] Capps, J. A., and Smith, J. F., *J. Am. Med. Assn.*, 1904, xliii, 981.

[8] Heineke, H., *Mitt. Grenzgeb. Med. u. Chir.*, 1905, xiv, 21.

[9] Helber, E., and Linser, P., *Münch. med. Woch.*, 1905, lii, 689.
Linser, P., and Helber, E., *Deutsch. Arch. klin. Med.*, 1905, lxxxiii, 479.

lymphocytes occurred. These cells, before treatment, represented 32 per cent of the white blood corpuscles, a total of 2,080 lymphocytes per c.mm. of blood. After treatment they had decreased to 6 per cent, or but 120 cells per c. mm. In a white rat there was a reduction of lymphocytes from 60 per cent, or 8,400 cells before, to 30 per cent, or 1,020 cells after x-ray treatment. These results were confirmed by other experiments.

Warthin[5] confirmed Heineke's work and added further evidence indicating that the x-rays have a specific destructive action on lymphoid tissues. He found the Malpighian bodies of the spleen to be first affected and later the lymph glands and bone marrow. Histologically, he noted fragmentation of the tissue lymphocytes, the particles being ingested by phagocytes. Mitotic figures were absent or very infrequently encountered in the lymphogenic tissues following x-ray treatment. After a short interval the lymph follicles, when present, were either inconspicuous or invisible in gross, and but few lymphocytic elements were found microscopically. The stroma of the organs affected was much in evidence, owing to the destruction and consequent disappearance of the lymphogenic cells. Heineke and Warthin both employed x-rays in lethal doses.

It has been shown that resistance to cancer[10] and tuberculosis,[11] in animals, is attended by an increase in number of the circulating lymphocytes and that the resistance, as well as the lymphocytosis, may be destroyed by x-rays in proper dosage.[11, 12] Likewise the natural resistance of animals to heteroplastic tissue grafts, which seems to be associated definitely with a local accumulation of lymphocytes, may be destroyed by the x-rays.[13]

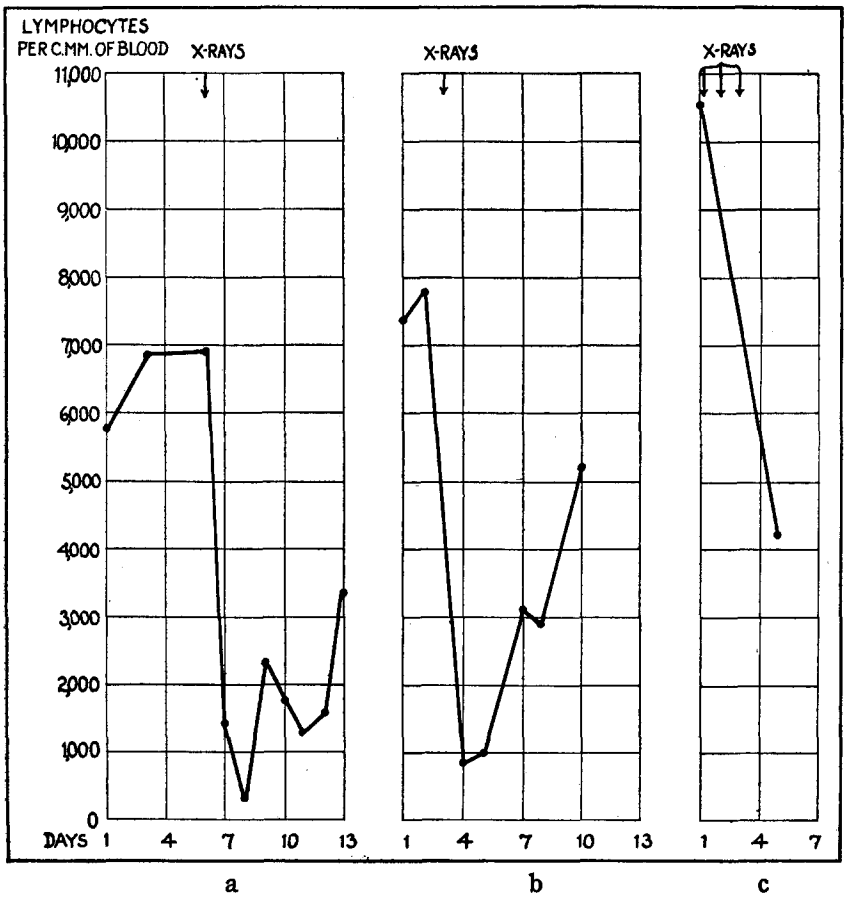
Inasmuch as (*a*) it is not possible to estimate the dosage employed in most of the older experiments concerning the effect of the x-rays on the blood, because gas tubes were used, (*b*) only a few blood counts have been published in these cases and their significance has not been adequately explained, (*c*) the x-rays are now being used with increasing frequency in therapeusis; it seemed important to obtain accurate information regarding the response of the blood to x-rays, and with this purpose the following results are recorded.

EXPERIMENTAL.

Experiment 1.—Eight areas, comprising both flanks of a Shetland pony, about 8 years old, were successively exposed in a single day to unfiltered x-rays generated by a Coolidge tube. The factors governing the dose at each exposure were:

[10] Murphy, Jas. B., and Morton, J. J., *J. Exp. Med.*, 1915, xxii, 204.
[11] Taylor, H. D., and Murphy, Jas. B., *J. Exp. Med.*, 1917, xxv, 609.
[12] Murphy, Jas. B., and Ellis, A. W. M., *J. Exp. Med.*, 1914, xx, 397.
[13] Murphy, Jas. B., *J. Am. Med. Assn.*, 1914, lxii, 1459.

spark-gap 8 inches, milliamperes 5, distance from the target to the skin 12 inches, and time 10 minutes. By computing the dose[14] from the factors given, it was found that the animal received over each area 20, or over the eight areas 160 Holzknecht



TEXT-FIG. 1, *a*, *b*, and *c*. (*a*) The effect of x-ray treatment on the circulating lymphocytes of a pony. (*b*) The effect of x-ray treatment on the circulating lymphocytes of a cat. (*c*) The effect of x-ray treatment on the circulating lymphocytes of a guinea pig.

units. The total number of lymphocytes per c. mm. of blood at each observation, during the period of study, is charted in Text-fig. 1, *a*. The per cent

[14] Remer, J., and Witherbee, W. D., *Am. J. Roentgen.*, 1917, iv, 303.

and total number of lymphocytes and polymorphonuclear neutrophilic leucocytes per c. mm. of blood at each determination are tabulated in Table I.

Experiment 2.—A healthy adult monkey (*Macacus rhesus*) was given a series of unfiltered x-ray treatments, extending over a period of 8 days. Seven doses were given, the dorsal and ventral surfaces of the body being alternately exposed. The factors at each treatment were: spark-gap 3 inches, milliamperes 10, distance from the target of the Coolidge tube to the skin 12 inches, and time 4 minutes. This dose represents, at each exposure 6, or a total of 42 Holzknecht units. Text-fig. 2 graphically illustrates the effect of the x-rays on the circulating lymphocytes in this animal, each determination referring to the total number of lymphocytes per c. mm. of blood. In Table II the blood counts, made at different times in the course of the experiment, are summarized to show more fully the changes in the circulating cells following treatment.

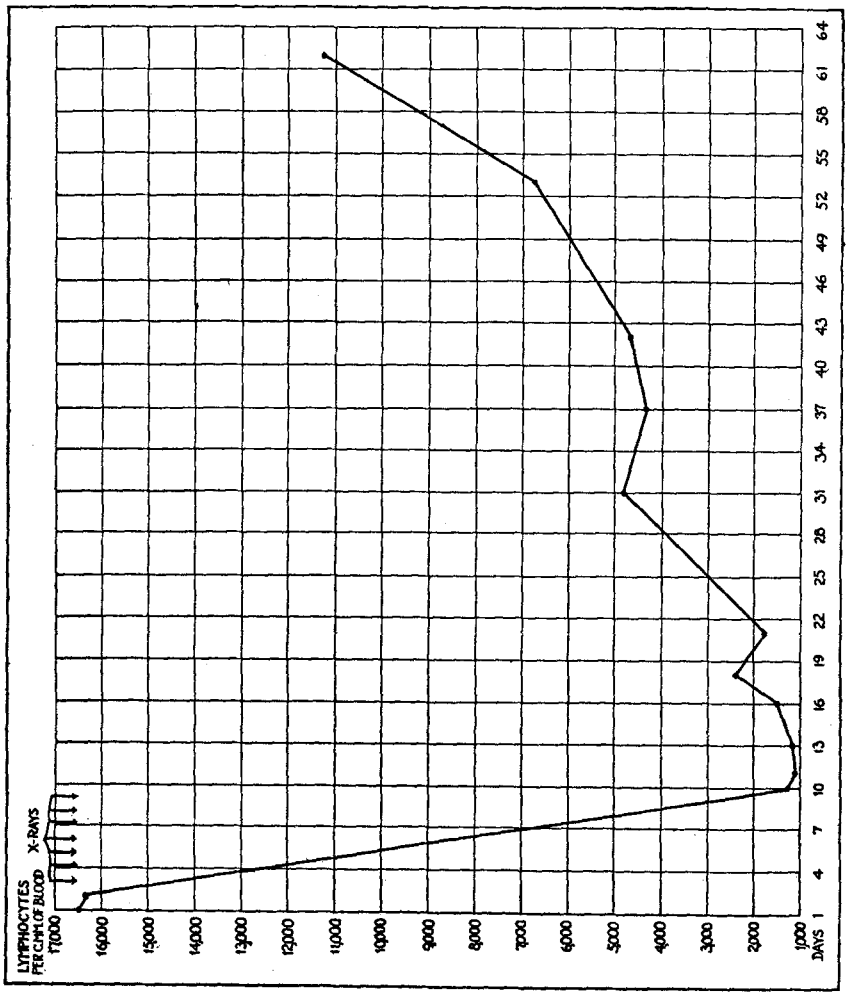
TABLE I.

Pony Receiving 160 Holzknecht Units.

Day of experiment.	Length of time after x-rays.	Lymphocytes.		Polymorphonuclear cells.	
		Per cent.	Total No.	Per cent.	Total No.
	days				
1		43.7	5,790	55.7	7,380
3		48.3	6,859	48.3	6,859
6		44.2	6,906	50.0	7,813
7	1	6.3	1,473	93.7	21,902
8	2	1.2	321	92.7	24,797
9	3	11.7	2,404	84.7	17,406
10	4	24.2	1,785	66.7	4,918
11	5	29.3	1,282	60.3	2,638
12	6	27.0	1,593	66.3	3,912
13	7	31.6	3,410	64.0	6,912

Experiment 3.—A full grown cat was given two treatments in a single day with unfiltered x-rays emitted by a Coolidge tube. One exposure was made on the dorsal and one on the ventral surface of the body. The factors at each exposure were: spark-gap 3 inches, milliamperes 10, distance from the target to the skin 12 inches, and time 1 minute. The dose, in this instance, was for each exposure $1\frac{1}{2}$, or a total of 3 Holzknecht units. Text-fig. 1, *b* is a curve showing the total number of lymphocytes plotted against the days on which blood counts were made. Table III gives percentages and actual numbers of white blood cells on the days recorded in Text-fig. 1, *b*.

Experiment 4.—A guinea pig was exposed to unfiltered x-rays on 3 successive days, after an initial blood count had been made. On the 5th day, 48 hours after the last x-ray treatment, a second count was made; Text-fig. 1, *c* shows



TEXT-FIG. 2. The effect of x-ray treatment on the circulating lymphocytes of a *Macacus rhesus*.

graphically the fall in the total number of lymphocytes per c. mm. of blood following the administration of the x-rays. Table IV gives the actual figures determined at the two blood examinations. The factors at each treatment were:

TABLE II.

Monkey Receiving 42 Holzknecht Units.

Day of experiment.	Length of time after x-rays.	Lymphocytes.		Polymorphonuclear cells.	
		Per cent.	Total No.	Per cent.	Total No.
	days				
1		62.7	16,537	36.0	9,495
2		56.7	16,415	40.7	11,783
10	1	4.0	1,283	94.7	30,375
11	2	4.7	1,128	95.0	22,800
13	4	7.0	1,155	92.7	15,296
16	7	5.7	1,526	94.0	25,169
18	9	11.7	2,463	88.0	18,524
21	12	7.0	1,787	92.3	23,560
28	19	27.0	4,846	71.0	12,745
37	28	23.3	4,351	74.7	13,950
42	33	31.7	4,771	64.3	9,677
53	44	29.0	6,779	66.7	15,598
63	54	55.7	11,224	40.7	8,201

TABLE III.

Cat Receiving 3 Holzknecht Units.

Day of experiment.	Length of time after x-rays.	Lymphocytes.		Polymorphonuclear cells.	
		Per cent.	Total No.	Per cent.	Total No.
	days				
1		35.0	7,389	55.7	11,759
2		34.7	7,825	56.0	12,628
4	2	5.0	844	94.0	15,876
5	3	8.7	1,005	83.7	9,672
7	5	16.0	3,093	77.0	14,886
8	6	12.0	2,907	79.0	19,144
10	8	11.0	5,194	88.0	41,555*

* Distemper developed later in this cat and the high polymorphonuclear leucocyte count may be due to this.

spark-gap 2¼ inches, milliamperes 10, distance from the target of the Coolidge tube to the skin 12 inches, and time 3 minutes. This dose represents, approximately, 3 Holzknecht units.

In two experiments on mice a gas tube had been used to generate x-rays. The dose was necessarily indefinite and the only measure of the comparative amount of the x-rays received by each animal consists in the constant established by the fact that the mice included in each experiment were exposed simultaneously and for the same length of time. These experiments are included because they demonstrated the tendency of the circulating lymphocytes to decrease in number after animals had been exposed to the x-rays generated by gas tubes and because this decrease was, in many ways, similar to that observed in Experiments 1 to 4. Furthermore, there is a definite relation between the response of the various animals in a series, as determined by blood counts, to x-ray treatment.

TABLE IV.

Guinea Pig Receiving Approximately 3 Holzknecht Units.

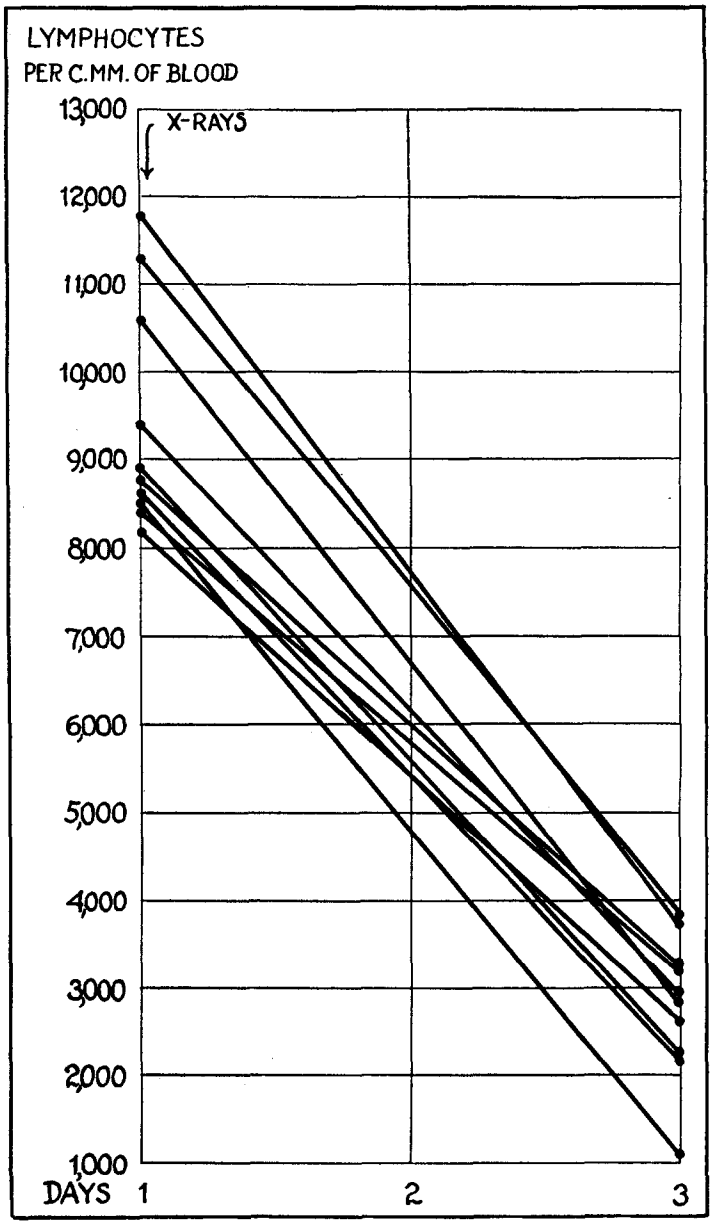
Day of experiment.	Length of time after x-rays.	Lymphocytes.		Polymorphonuclear cells.	
		Per cent.	Total No.	Per cent.	Total No.
	days				
1		36.7	10,606	61.7	17,831
5	2	16.3	4,283	81.3	21,138

Experiment 5.—Ten normal, adult, white rats were simultaneously exposed for the same length of time to unfiltered x-rays generated by a rather soft gas tube. Total white and differential blood counts were made on each animal immediately before and 48 hours after exposure. The effect of the x-rays on the circulating lymphocytes (total number per c. mm.) is shown in Text-fig. 3, where each line represents the difference, in a single rat, between the number of lymphocytes before and after treatment.

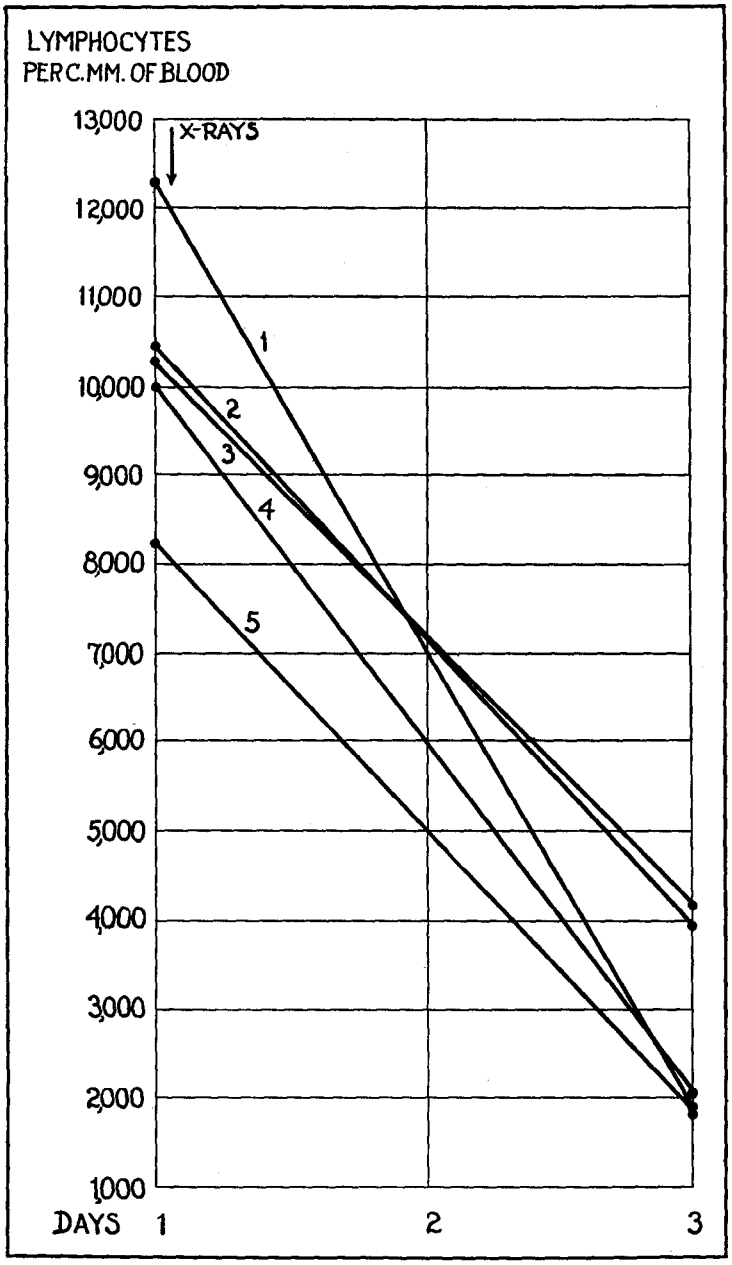
Experiment 6.—The procedure followed in Experiment 5 was repeated with five additional white mice and the results are shown in Text-fig. 4, in which the lines have the same significance as those in Text-fig. 3.

Experiment 7.—Four mice were simultaneously given seven treatments with unfiltered x-rays, the Coolidge tube being used. Blood counts were made on each animal before the first and 48 hours after the last x-ray exposure. The effect of the x-rays on the blood of each mouse is shown in the usual manner in Text-fig. 5; additional data of interest are given in Table V.[15] The factors at

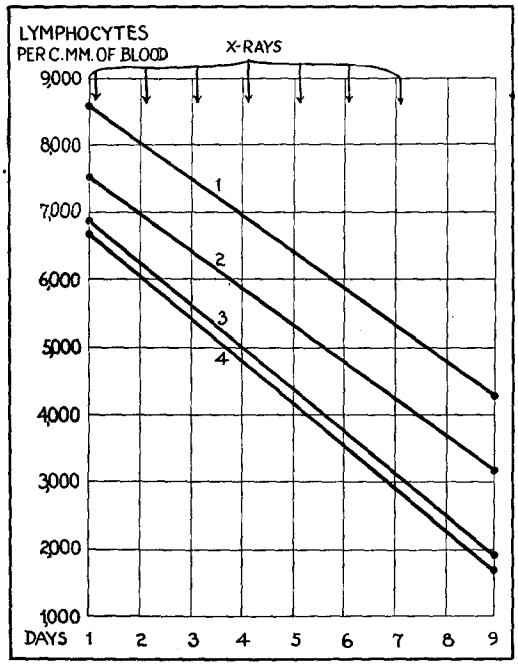
[15] The number of the animal in the curve and in the table corresponds, in this and the following experiments.



TEXT-FIG. 3. The effect of x-ray treatment on the circulating lymphocytes of ten white rats. In this and the following text-figures each line represents the difference in a single animal between the number of lymphocytes before and after treatment.



TEXT-FIG. 4. The effect of x-ray treatment on the circulating lymphocytes of five white mice.



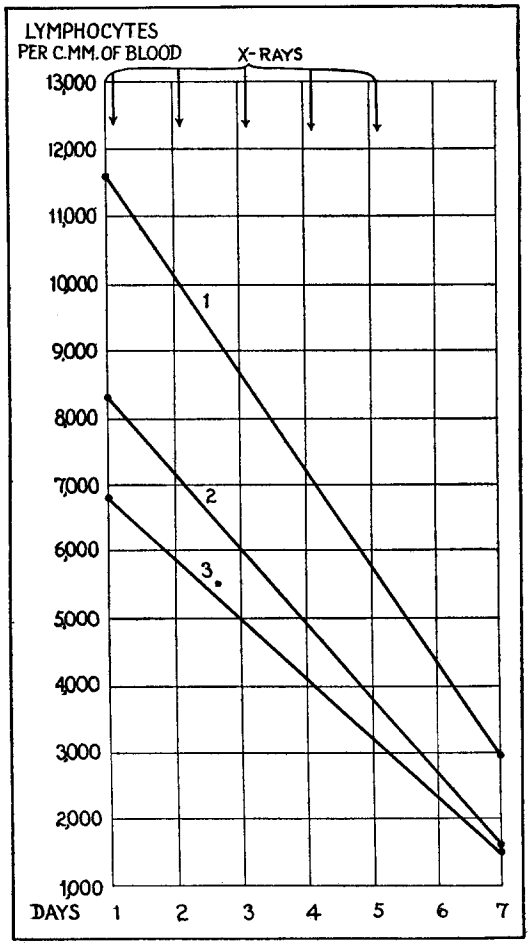
TEXT-FIG. 5. The effect of x-ray treatment on the circulating lymphocytes of four white mice.

TABLE V.

Four Mice Receiving 14 Holzknecht Units.

Mouse No.	Day of experiment.	Length of time after x-rays.	Lymphocytes.		Polymorphonuclear cells.	
			Per cent.	Total No.	Per cent.	Total No.
		days				
1	1		73.0	8,588	27.0	3,180
	9	2	55.3	4,301	44.7	3,477
2	1		90.3	7,527	9.6	800
	9	2	57.0	3,103	43.0	2,341
3	1		48.2	6,909	51.7	7,410
	9	2	42.0	1,914	58.0	2,643
4	1		51.0	6,687	49.0	6,424
	9	2	14.0	1,680	86.0	10,320

each exposure were: spark-gap 2¼ inches, milliamperes 10, distance from the target to the skin 12 inches, and time of exposure 2 minutes. This represents 2, at a single exposure, or a total of 14 Holzknecht units.



TEXT-FIG. 6. The effect of x-ray treatment on the circulating lymphocytes of three adult white rats.

Experiment 8.—Three adult white rats were exposed to the unfiltered x-rays generated by a Coolidge tube. The factors were: spark-gap 3 inches, milliamperes 10, distance from the target to the skin 12 inches, and time 4 minutes. This dose was repeated daily for 5 days. Each exposure represents 6, a total of

30 Holzknecht units being therefore given. White and differential blood counts made before the first and 48 hours after the last exposure are summarized in Table VI and total lymphocytes per c. mm. of blood at each determination charted in Text-fig. 6.

Experiment 9.—Three rabbits, after preliminary blood counts, were given seven daily, unfiltered doses of x-rays, each dose depending on the following factors: spark-gap 3 inches, milliamperes 10, distance from the target to the skin 12 inches, and time 4 minutes. This represents 6 at a single dose, or a total of 42 Holzknecht units. The dorsal and ventral surfaces of the animals were exposed to the rays on alternate days. Text-fig. 7 and Table VII refer to the blood counts on these animals.

Experiment 10.—Two rabbits were each given a single treatment with the unfiltered x-rays emitted by a Coolidge tube, which was controlled by the following factors: spark-gap 3 inches, milliamperes 20, distance from the target to the

TABLE VI.

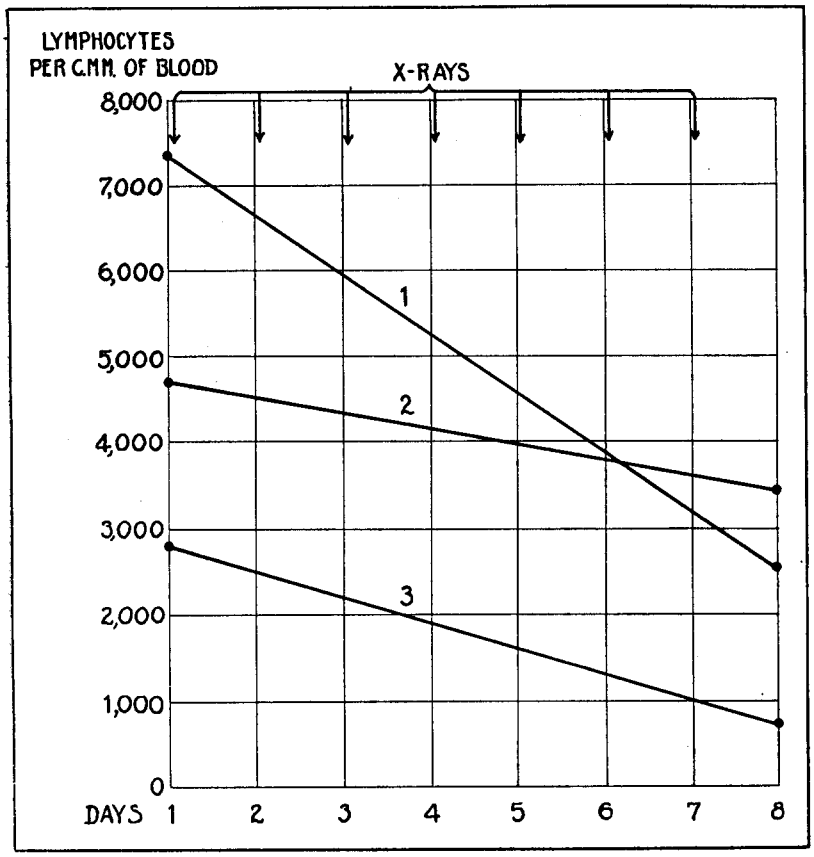
Three Rats Receiving 30 Holzknecht Units.

Rat No.	Day of experiment.	Length of time after x-rays.	Lymphocytes.		Polymorphonuclear cells.	
			Per cent.	Total No.	Per cent.	Total No.
		days				
1	1		89.7	11,683	10.3	1,342
	7	2	62.3	2,990	37.3	1,790
2	1		63.0	8,096	37.0	4,755
	7	2	16.3	1,593	83.7	8,182
3	1		79.2	6,831	20.7	1,785
	7	2	48.7	1,583	51.3	1,667

skin 12 inches, and time 4 minutes. This dose represents 11 Holzknecht units. Text-fig. 8 and Table VIII refer to the blood counts on these animals.

Experiment 11.—Two rabbits at a single exposure were treated with x-rays filtered through 3 mm. of aluminum, the dose approximating 5 Holzknecht units. This was determined by the following factors: spark-gap 9 inches, milliamperes 5, distance from the target to the skin 12 inches, and time 5 minutes and 20 seconds. Text-fig. 9 and Table IX refer to the circulating lymphocytes and polymorphonuclear leucocytes in these animals, before and 48 hours after exposure.

Experiment 12.—Three monkeys were each exposed to the unfiltered x-rays generated by a Coolidge tube for a total of seven treatments. Monkeys 1 and 2 had daily exposures, while Monkey 3 was given the seven treatments in 4 days. The factors at each treatment were: spark-gap 3 inches, milliamperes 10, distance from the target to the skin 12 inches, and time 4 minutes. At each exposure 6, or a total of 42 Holzknecht units were therefore given to each animal. Text-fig. 10 and Table X give the data for these monkeys.

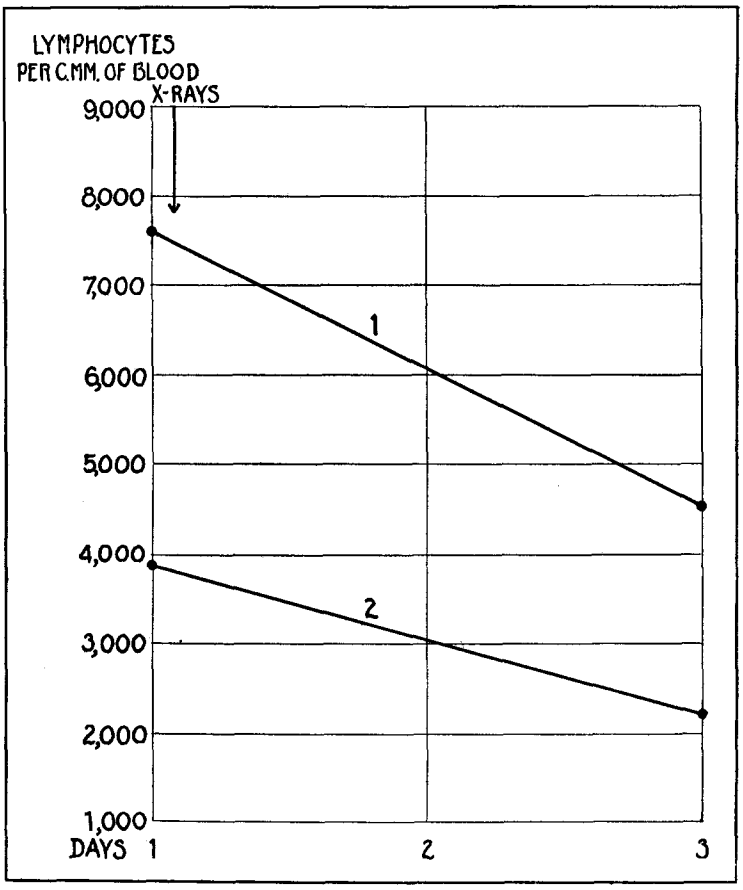


TEXT-FIG. 7. The effect of x-ray treatment on the circulating lymphocytes of three rabbits.

TABLE VII.

Three Rabbits Receiving 42 Holzknecht Units.

Rabbit No.	Day of experiment.	Length of time after x-rays.	Lymphocytes.		Polymorphonuclear cells.	
			Per cent.	Total No.	Per cent.	Total No.
		days				
1	1		55.3	7,383	42.0	5,607
	7	2	54.3	2,570	39.3	1,870
2	1		44.7	4,716	47.7	5,032
	7	2	39.7	3,462	55.7	4,857
3	1		29.7	2,866	64.0	6,176
	7	2	24.3	758	66.7	2,081

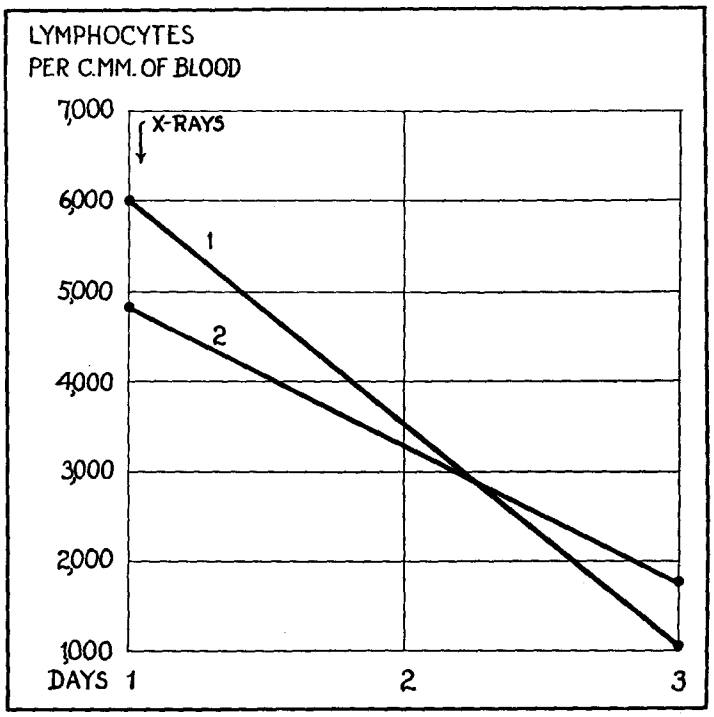


TEXT-FIG. 8. The effect of x-ray treatment on the circulating lymphocytes of two rabbits.

TABLE VIII.

Two Rabbits Receiving 11 Holzknecht Units.

Rabbit No.	Day of experiment.	Length of time after x-rays.	Lymphocytes.		Polymorphonuclear cells.	
			Per cent.	Total No.	Per cent.	Total No.
		days				
1	1		66.3	7,591	31.3	3,584
	3	2	54.7	4,568	41.3	3,449
2	1		51.2	3,878	48.0	3,636
	3	2	32.3	2,196	65.6	4,461

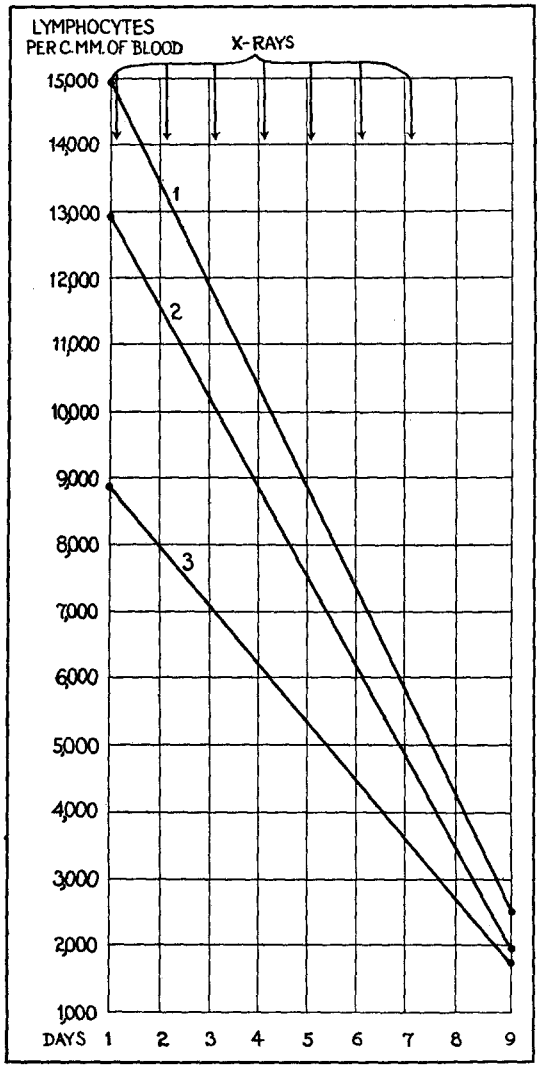


TEXT-FIG. 9. The effect of x-ray treatment on the circulating lymphocytes of two rabbits. The x-rays were filtered through 3 mm. of aluminum.

TABLE IX.

Two Rabbits Receiving Approximately 5 Holzknecht Units (Filtered).

Rabbit No.	Day of experiment.	Length of time after x-rays.	Lymphocytes.		Polymorphonuclear cells.	
			Per cent.	Total No.	Per cent.	Total No.
		days				
1	1		87.3	6,002	11.0	756
	3	2	44.7	1,017	50.7	1,153
2	1		54.0	4,860	39.7	3,573
	3	2	27.2	1,761	65.0	4,209



TEXT-FIG. 10. The effect of x-ray treatment on the circulating lymphocytes of three monkeys.

TABLE X.

Three Monkeys Receiving 42 Holzknecht Units.

Monkey No.	Day of experiment.	Length of time after x-rays.	Lymphocytes.		Polymorphonuclear cells.	
			Per cent.	Total No.	Per cent.	Total No.
		days				
1	1		59.7	14,925	34.3	8,575
	9	2	17.7	2,509	77.0	10,915
2	1		54.0	12,960	42.0	10,080
	9	2	15.0	1,980	77.5	10,230
3	1		54.7	8,861	43.7	7,079
	6*	22	17.7	1,744	81.3	8,008

* In this animal the seven treatments were given in 4 days.

DISCUSSION.

The immediate effect of the x-rays, in the dose employed in these experiments, is a sudden decrease in the circulating lymphocytes, evident in every curve and table in the series. The curves all represent total numbers of lymphocytes, small and large varieties combined, per c. mm. of blood. When the lymphocytes are studied in terms of percentage of total white blood cells the results are not so striking, and, while in most instances there is a definite fall in percentage as well as in actual numbers of these cells after x-ray treatment, an occasional instance is encountered where the percentile change is slight or absent. For example, whereas the total lymphocytes of Rabbit 1, Table VII, decreased from 7,383 before to 2,570 after exposure, the corresponding fall in percentage of lymphocytes was small; *i.e.*, from 55.3 to 54.3 per cent. The latter fall is well within the limits of counting error and is therefore negligible. It seems, therefore, that an estimation of the total number of lymphocytes per c. mm. of blood, determined by multiplying the total white count by the combined percentage of large and small lymphocytes, before and after x-ray treatment offers a more accurate indication of the effect on the blood than can be determined by following percentage figures only. This means, in other terms, that while the x-rays, in most instances, affect the lymphocytes selectively, occasional cases occur in which together with the lymphocytes the granular blood cells are also destroyed.

When the total number of circulating lymphocytes is plotted against the time in days a curve is formed which reaches its lowest level 48 hours after the administration of the x-rays (Text-figs. 1, *a*, *b*, and 2). Following this fall there is a primary rise, which reaches its acme from 3 to 5 days after the last x-ray exposure (3 days in Experiment 1, 9 days in Experiment 2, and 4 days in Experiment 3). A secondary fall then occurs, which reaches its lowest level from 5 to 12 days after treatment, and this is followed by a secondary and, as far as has been determined, permanent rise, which persists for at least 54 days after x-ray treatment (Text-fig. 2). The slight variation in the time relations of the various phases of the curves, shown in Text-figs. 1, *a*, *b*, and 2 are probably due to the fact that in Experiments 1 and 3 the entire dose of x-rays was given in a single day, while in Experiment 2 the seven doses were dispersed over an interval of 8 days. A comparison of Text-figs. 1, *a* and 2 shows that the primary rise occurred on the 3rd and on the 9th day respectively, while the secondary fall reached its lowest limit on the 5th and on the 21st day. It seems possible that the destructive action of the x-rays on the lymphocytes is first felt by these cells in the general circulation and in the spleen (this corresponds to Warthin's view[5]), and that this accounts for the primary fall. In the meantime the lymphogenic cells of the other organs, lymph glands, bone marrow, etc., contribute cells to the blood, these being responsible for the secondary transient rise. When all the lymphogenic tissues have been affected by the x-rays the secondary fall in these cells is apparent in the blood, but it does not reach the extremely low level characteristic of the primary fall, because of beginning regeneration in the spleen. Regeneration of all the lymphogenic tissues later contributes to the permanent rise. It requires a considerable period of time before the lymphocyte-forming tissues regenerate entirely. In Experiment 2 for instance, the tissues are not contributing the normal numbers of lymphocytes to the circulation 54 days after the last x-ray treatment. The curve representing blood lymphocytes (Text-fig. 2) can be seen to be rapidly approaching the pre-treatment level at this time, however, and probably, had the observations been prolonged over a sufficiently long period of time, the lymphocytic elements would again have been present in the blood in normal numbers. When the x-ray treatments are distributed

over a number of days the issues are somewhat confused, and because of overlapping of phases the curves are not so sharply defined as when the entire dose is given in a single day. The primary fall in circulating lymphocytes, which in the case of the animals given x-rays in several doses is really the result of a series of primary falls, one following each treatment, is complete after 48 hours. However, the other phases, as may be seen from Text-fig. 2, are somewhat lengthened on this curve as contrasted with those given in Text-fig. 1, *a* and *b*.

From 24 to 48 hours after x-ray treatment there is, in most instances, a considerable increase in the polymorphonuclear neutrophilic leucocytes, which is well seen in the figures of Tables I and II. This is not evident in the rabbits followed (Tables VII, VIII, and IX) nor in the rats (Table VI). In mice (Table V) there is a tendency for these cells to exhibit a post-treatment rise, but this is not striking. The blood of the guinea pig showed a moderate increase in these cells after x-ray exposure.

When there is a primary rise in polymorphonuclear leucocytes, it is followed by a primary fall, which reaches its lowest level at a time when the lymphocytes are beginning to rise, the 6th day after x-ray exposure in Experiment 1, and the 3rd day in Experiment 2 (Tables I and II). Later there is a gradual rise to normal, about which level the number of neutrophilic cells fluctuates within wide limits. This is well seen in Table II. The polymorphonuclear cells are much less affected than the lymphocytes even when large doses of x-rays are given, and after the primary stimulation and later depression the return to the normal number per c. mm. occurs at a time when the lymphocytes are still at a very low level (Tables I and II). This seems to confirm Warthin's contention[5] that the bone marrow is affected somewhat later and to a more limited extent than the lymphogenic tissues proper. Circulating eosinophils and basophils, as well as large mononuclear and transitional leucocytes, usually share in the stimulations and depressions of the neutrophilic cells. This is what would be expected, as they all belong to the granular series and all originate in the bone marrow.

A glance at the curves shown in Text-figs. 3 to 10 leaves little to be said regarding the regularity with which the circulating lymphocytes of a series of animals of the same species respond to the same

dose of x-rays. Exceptions to the general rule of a quantitative relation between the reactions of the several animals of a series are uncommon. Apparently Rabbit 2 in Text-fig. 7 and Rabbits 1 and 2 in Text-fig. 9 belong in this category. The latter animals received the only treatment with a filtered dose of x-rays in the entire group reported, and it is not possible to draw conclusions from this single instance. The lymphocytic fall is evident, however, in both animals. Rabbit 2 in Text-fig. 7, then, is the only exception encountered and no explanation is apparent. There is a decrease in the circulating lymphocytes of this animal, following treatment with the x-rays, but this is not so great as in the companion rabbits, Nos. 1 and 3. Exceptions are naturally encountered in all biological experiments, and as this is the only striking instance found in the entire study it seems safe to disregard it and to accept the other results as manifesting accordance to a general law, inasmuch as they are regular and constant.

In Experiment 9 x-rays equivalent to 42 Holzknecht units destroyed, if all the rabbits are included, an average of 55.1 per cent, or, if Rabbit 2 is disregarded and the others (Nos. 1 and 3) with comparable lymphocyte curves are considered, an average of 69.4 per cent of the total number of circulating lymphocytes in the 48 hour interval following treatment. In the monkeys, given the same dose, Experiment 12, Table X, the effect of the x-rays was much more pronounced, 82.7 per cent of the circulating lymphocytes having disappeared 48 hours after treatment. It would seem that the monkey is more susceptible to the x-rays, in as far as the lymphocytic reaction represents an accurate measurement of the degree of susceptibility, than the rabbit. In the pony a dose of 160 Holzknecht units destroyed 95.4 per cent of the circulating lymphocytes, as determined 48 hours after treatment. In the monkey, Experiment 2, Text-fig. 2, Table II, 42 Holzknecht units were sufficient to destroy 93.1 per cent of the lymphocytes of the blood. This contrasts sharply with the three monkeys in Experiment 12, Text-fig. 10, Table X, in which the same dose destroyed an average of 82.7 per cent, and in the animal most affected, No. 3, but 84.7 per cent.

The lymphogenic tissues of the cat seem to be more susceptible than those of any other animal studied, inasmuch as 3 Holzknecht

units were sufficient to destroy 89.2 per cent of the circulating lymphocytes. In some of the experiments it was not possible to determine accurately the doses of x-rays given, but from the information at hand it seems that different species of animals vary considerably in their response to a given dose of x-rays. Those studied here would seem to follow a series, progressing from the most to the least susceptible, somewhat as follows: cat, monkey, guinea pig, rabbit, rat, mouse, and pony.

SUMMARY.

1. X-rays in large doses affect the lymphocytes before any of the other circulating cells.

2. There is a sharp fall in the total number of circulating lymphocytes, which is complete 48 hours after x-ray treatment.

3. Following the immediate decrease in the circulating lymphocytes there is a primary rise, followed by another fall, which in turn is followed by a permanent rise of these cells to normal.

4. The effect of the x-rays on different species of animals varies considerably, but in those studied, cat, monkey, guinea pig, rabbit, rat, mouse, and pony, the selective action on the lymphocytes was in all instances apparent.

5. When several animals of the same species are given the same dose of x-rays, the effect on the circulating lymphocytes seems to be quantitatively parallel, when determined by blood counts.

6. The polymorphonuclear neutrophilic leucocytes, when affected at all, increase in number immediately after the administration of the x-rays and then tend to decrease below their normal level. This decrease is followed by a return to normal many days before the lymphocytes reach their original level.

7. The other cells of the blood follow the neutrophilic curve.

8. Percentage figures, as determined by differential blood counts, do not give an accurate indication of the effect of the x-rays. It is only when these are multiplied by the total white blood count that a figure, representing the total number of cells of the series per c. mm. of blood, is obtained, which varies to the stimulus in a constant manner, the variations being practically quantitative.