# THE PRODUCTION OF PERSISTENT ALOPECIA IN RABBITS BY X-RAYS OF VARIOUS DEGREES OF HARDNESS.

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These studies are a continuation of work reported recently[1] on the minimum dose of soft x-ray required to produce persistent alopecia of the abdominal skin of white rabbits. For the purposes of that work rays produced at 30 kilovolts, peak, were employed, and the critical dose was found to correspond to the production in air of $2.04 \times 10^{15}$ pairs of ions per gm. The rabbits were found to react accurately; although eighteen of the exposures fell within 2 per cent of the critical value, half on either side, no single case of inconsistent reaction occurred.

The present paper deals with similar experiments on the effect of somewhat harder rays. The various factors which have to do with the quality and intensity of the radiation are given in Table I. Column 1 shows the peak kilovoltage at which the rays were produced; Column 2, the current in milliamperes; Column 3 the thickness of the aluminium filter in mm.; and Column 4, the target distance in cm.

## *Apparatus.*

The same x-ray plant has been used in this work as in the previous work. The plant is known to operate with a high degree of consistency. The experiments were made at various times over a period of about 1 year, during which time four different tubes were used, and minor adjustments of the electrical equipment were made. As a means of following the tube efficiency and the effect of adjustment, the rate of ionization of air by the rays was measured from time to time. The apparatus used to make these measurements, together with studies of its trustworthiness, has been discussed.[2] The measurements were made with the ioniza-

[1] Clark, H., and Sturm, E., *J. Exp. Med.*, 1924, xl, 517.

[2] Clark, H., *Am. J. Roentgenol. and Radium Therap.*, 1924, xi, 445.

tion chamber in place of the exposed portion of the animal. A necessary correction for the effect of scattered radiation has been included in all values used in this paper. It varies from 2 per cent at 40 kilovolts, to 4 per cent at 70 kilovolts. The method of determining it has been described.[1]

### *Preparation and Treatment of the Animals.*

Only normal healthy white rabbits weighing between 1500 and 2100 gm. were used. The method of preparing and exposing them to the radiation has been described in detail.[1] Before exposure, the abdomen was shaved and covered with a screen of lead-filled rubber in which there are seven apertures, six round, 1 cm. in diameter, and one elongated for the purpose of identification. During exposure, the animal was shielded carefully from the heat of the tube and kept cool by a current of air at room temperature.

TABLE I.

| 1 | 2 | 3 | 4 |
|---|---|---|---|
| 40 | 15 | 0.5 | 27 |
| 50 | 12 | 1.0 | 27 |
| 70 | 8 | 1.5 | 36 |

## RESULTS.

In order to avoid the possibility of bias in making measurements and diagnoses, the work has been divided into two parts from the beginning. One of us (Sturm) has attended to the preparation and exposure of the animals, and to the observation of them thereafter, while the dosage measurements were made by the other (Clark). The two sets of records were not compared until each had been put into final form.

Fig. 1 is the record of the alopecia reactions of the animals. It comprises all of the experiments made at 40 and 50 kilovolts except a few preliminary ones in which the dose given proved to be too small to yield results of interest. The results at 70 kilvolts are not shown since in no case was the exposure sufficient to produce persistent alopecia. Each vertical column of circles gives the record of one rabbit, the seven circles corresponding to the seven skin areas treated. Each circle is so plotted on the vertical scale as to show the corresponding length of exposure in minutes. White circles represent temporary alopecia, the figures within showing the time interval after exposure, in weeks, before the regrowth of hair was observed. Black circles repre-

sent alopecia persistent for at least 10 weeks. In a few cases, a very slight regrowth was first observed at 9 weeks. In no case, however, was a similar observation made at 10 weeks, although most of the animals were kept under observation for some time thereafter. Reference to Fig. 1 shows that with one exception,—in which the regrowth was observed at 7 weeks,—all of the lowest black circles of each group lie on the same horizontal line, although the figures in the highest white circles are variable; five of the six 9's in the figure correspond to doses within 3 per cent of the critical dose as calculated below. It is assumed, therefore, that observations made at 10 weeks or thereafter constitute a fair criterion of persistency. Nine groups of animals are represented in Fig. 1—six at 40 kilovolts and three at 50 kilovolts. The four animals of each group were exposed on the same day to rays from the same x-ray tube.

Table II contains a summary of the ionization measurements together with all of the data from Fig. 1 which are of interest for the purpose of determining the critical dose. In addition to the work at 40 and 50 kilovolts, Table II contains the measurements and data relative to the longest exposures at 70 kilovolts. Column 1 contains the identification numbers of the various groups of animals for purposes of reference to Fig. 1. Columns 2 and 3 show the degree of hardness of the rays (kilovolts), and the number of the tube used, respectively. Column 4 contains the summary of the ionizing powers of the rays when the various tubes were used; the figures given are the numbers of pairs of ions (divided by $10^{14}$) produced per gm. of air per minute at the surface of the abdomen of the animal. The critical exposure time for each group of animals dealt with in Fig. 1, lies somewhere between the times which correspond to the highest white circles and the lowest black circles; Columns 5, 6, and 7 of Table II have to do with these highest white circles, and Columns 8, 9, and 10, with the lowest black ones. Of these, Columns 5 and 8 contain the number of circles considered; Nos. 6 and 9 contain the exposure times taken from Fig. 1; and Nos. 7 and 10 contain the products (divided by $10^{15}$) obtained by multiplying the exposure times of Columns 6 and 9 respectively by the ionization rates of Column 4.

We may make use of Columns 7 and 10 to estimate the critical dose for each kind of ray, in ionization terms. The critical dose must not

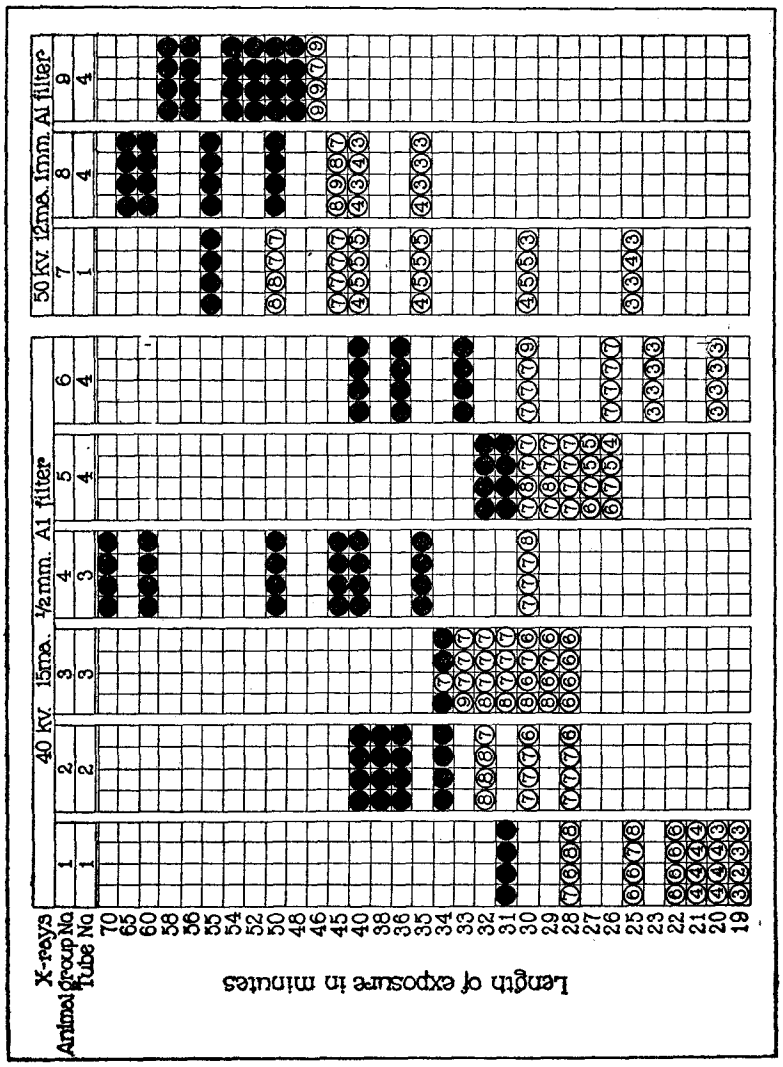
X-rays
Animal group No.
Tube No.
Length of exposure in minutes
40 kv. 15ma. ½mm. Al filter
50 kv. 12ma. 1mm. Al filter

FIG. 1.

be less than any of the values given in Column 7 nor greater than any of the values in Column 10. At 40 kilovolts no such value appears, either because the measurements are inaccurate, or because the animals do not react consistently, or because the output of x-ray is not constant. The discrepancy is not great, however; if we may assume that the value given in Column 7 for one animal (*), is too high by 2/3 of 1 per cent, the table becomes consistent for the critical value $3.68 \times 10^{15}$. This value is then defined by 19 black circles, and 9 white circles, all of which lie within 2.5 per cent of it. Since the critical value, as written, implies a higher degree of accuracy than can be claimed for the measurements, it may be taken as $3.7 \times 10^{15}$ pairs of ions per gm. At 50 kilovolts, the table is consistent; the critical dose may be taken as $4.5 \times 10^{15}$. At 70 kilovolts, the critical dose is at least greater than $5.10 \times 10^{15}$.

TABLE II.

| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 40 | 1 | 1.19 | 4 | 28 | 3.33 | 4 | 31 | 3.69 |
| 2 | 40 | 2 | 1.10 | 4 | 32 | 3.52 | 4 | 34 | 3.74 |
| 3 | 40 | 2 | 1.10 | 1* | 34 | 3.74 | 3 | 34 | 3.74 |
| 4 | 40 | 3 | 1.05 | 4 | 30 | 3.15 | 4 | 35 | 3.68 |
| 5 | 40 | 4 | 1.20 | 4 | 30 | 3.60 | 4 | 31 | 3.72 |
| 6 | 40 | 4 | 1.20 | 4 | 30 | 3.60 | 4 | 33 | 3.96 |
| 7 | 50 | 1 | 0.90 | 4 | 50 | 4.50 | 4 | 55 | 4.95 |
| 8 | 50 | 4 | 0.955 | 4 | 45 | 4.30 | 4 | 50 | 4.78 |
| 9 | 50 | 4 | 0.955 | 4 | 46 | 4.39 | 4 | 48 | 4.58 |
| | 70 | 1 | 0.49 | 4 | 80 | 3.92 | | | |
| | 70 | 3 | 0.51 | 4 | 100 | 5.10 | | | |

To sum up the foregoing, the critical dose is $3.7 \times 10^{15}$ pairs of ions per gm. at 40 kilovolts, $4.5 \times 10^{15}$ at 50 kilovolts, and over $5.10 \times 10^{15}$ at 70 kilovolts.

## DISCUSSION.

These experiments, taken with the earlier ones,[1] show that, as regards the alopecia reaction, rabbits respond, under constant conditions of treatment, with little or no individual variation. They show also that when rays of different degrees of hardness are considered, the

critical dose, expressed in terms of ionization, is not constant; at 30, 40, 50, and 70 kilovolts the critical doses are 2.04, 3.7, 4.5, and over 5.1 respectively (all multiplied by $10^{15}$ pairs of ions per gm.). It is of interest to note also that the alopecia, erythema, and pigmentation reactions do not run parallel to each other. At 30 kilovolts, the critical alopecia dose produced little erythema—none in most cases. At higher voltages, it produced progressively more pronounced erythema. At 30, 40, and 50 kilovolts, it produced no pigmentation, but at 70 kilovolts, one-half of the animals receiving doses above $3.05 \times 10^{15}$, which is, of course, far below the critical dose, became pigmented.

There is no evident explanation of these results. The dosage values given refer to the surface of the animal. Hard rays produce more ionization within the body of the animal than soft rays, for the same surface ionization; and to produce the same surface dosage, the exposures are necessarily longer. It seems quite clear that x-rays produce primary changes in matter only through the medium of ionization produced by secondary beta rays, and that the amount of ionization produced is proportional to the energy absorbed irrespective of the hardness of the ray. It seems clear also that the relation between the ionization of the skin tissues and that of air is within reasonable limits independent of the quality of the ray. The complex effects of x-rays on animals probably result from simple primary reactions.

## SUMMARY.

1. The minimum dose of x-ray, of each of three degrees of hardness, required to produce persistent alopecia of the abdominal skin of normal white rabbits has been studied. 40 kilovolt rays filtered by 0.5 mm., 50 kilovolt rays filtered by 1 mm., and 70 kilovolt rays filtered by 1.5 mm. of aluminium were employed. The 70 kilovolt work is unfinished.

2. Under constant conditions of treatment, the animals were found to react with a high degree of consistency.

3. The values of the critical minimum doses expressed in terms of air ionization (pair of ions per gm. of air divided by $10^{15}$), for rays produced at 30, 40, 50, and 70 kilovolt peak, are 2.04, 3.7, 4.5, and over 5.1 respectively. The 30 kilovolt value is taken from a previous paper.[1]

4. It is shown that the alopecia reaction does not run parallel to the erythema and pigmentation reactions.