SKIN REACTIONS TO SIMULTANEOUS TREATMENTS WITH RADIANT HEAT AND SOFT X-RAYS.

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In the course of experiments in which guinea pigs were exposed to x-rays it was observed in several instances by one of us (Hawkins) that whereas a given exposure to the rays, filtered through very thin cardboard, produced no visible effect on the skin even after several days, the same exposure to unfiltered rays in otherwise similar circumstances was followed a few hours later by the appearance of a burn. The difference in intensity of the x-radiations, filtered and unfiltered, amounting to 3 or 4 per cent of the ionizing power in air, can scarcely account for such widely different effects. The nature of the burns and the promptness with which they appeared suggested that they might have been caused in part at least by radiant heat from the tube. That healing did not occur promptly and properly indicated, however, that there had been some aggravation by the x-rays. In order to determine whether or not the combined action of x-rays and radiant heat has a more profound effect than either agent alone we have made some experiments on guinea pigs in circumstances such that the two kinds of radiation could be administered separately or together.

Method.

The x-rays were supplied by an outfit previously described,[1] the output of which is known to be constant in quality and intensity. The tube and the animal occupied two separate compartments of a lead-lined cabinet, the rays passing through an aperture covered with a filter of thin bristol board. The compartment containing the tube was sufficiently ventilated by means of a fan to keep the filter and other parts of the partition cool, thus preventing the heat of the

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

tube from reaching the animal. The tube was operated in all cases at 30 kilovolts and 22 milliamperes.

Radiant heat was supplied in some cases by electrically heated coils of nichrome wire and in others by an electric soldering copper. The source of heat was placed about 3 cm. above the abdomen of the animal, close to, but not actually in, the path of the x-rays. The position relative to the skin area to be exposed, and to the cabinet, was carefully maintained throughout each series of experiments. No attempt was made to measure the rise in temperature of the skin; the conditions of heating were carefully reproduced, however. The copper, when used, was preheated for the same length of time in every case, and both copper and coils were operated at constant voltage. All exposures were begun with the cabinet at room temperature and the cabinet doors were kept closed during the experiments to insure constant air current conditions. The fact that each exposure of heat, in the following experiments, lasted 1 minute longer than the corresponding x-ray exposure was necessary on account of the technique of handling the x-ray apparatus. Before each experiment the intensity of the heat was adjusted on the basis of a few preliminary trials to the critical value for producing little or no burn.

The technique of holding the animals in place and at a definite target distance has been described.[1] The abdomen was shaved before treatment and covered with lead-filled rubber except for the area, 7 by 5 cm., to be exposed. For further protection from the heat and Roentgen radiations a lead sheet with a hole corresponding to the one in the lead rubber was placed over the whole animal.

EXPERIMENTS.

Experiment 1.—An area on the abdomen of each of six guinea pigs was exposed for 11 minutes to the heat from a nichrome coil held about 3 cm. above the surface of the skin. A second series of seven pigs received a combined exposure to x-ray and heat, the duration of the exposures being 10 and 11 minutes, respectively. A third group of seven animals received a 10 minute exposure to x-ray alone. The target distance for the x-ray exposure in both of these groups was 35.4 cm., which gives, with the other factors, about 90 per cent of the estimated critical dose for producing slight scaling of the skin. For the control exposures of heat and x-ray alone the two agents were administered separately under conditions identical with those obtaining when given together.

Among the animals exposed to heat alone two of the six pigs developed burns which appeared immediately after the treatment but were healed completely between the 10th and 14th days. Of the seven animals receiving the combined x-ray and heat six developed extensive burns which did not heal completely till between the 42nd and 59th days after treatment. None of the animals exposed to x-ray alone showed visible skin changes (Chart 1).

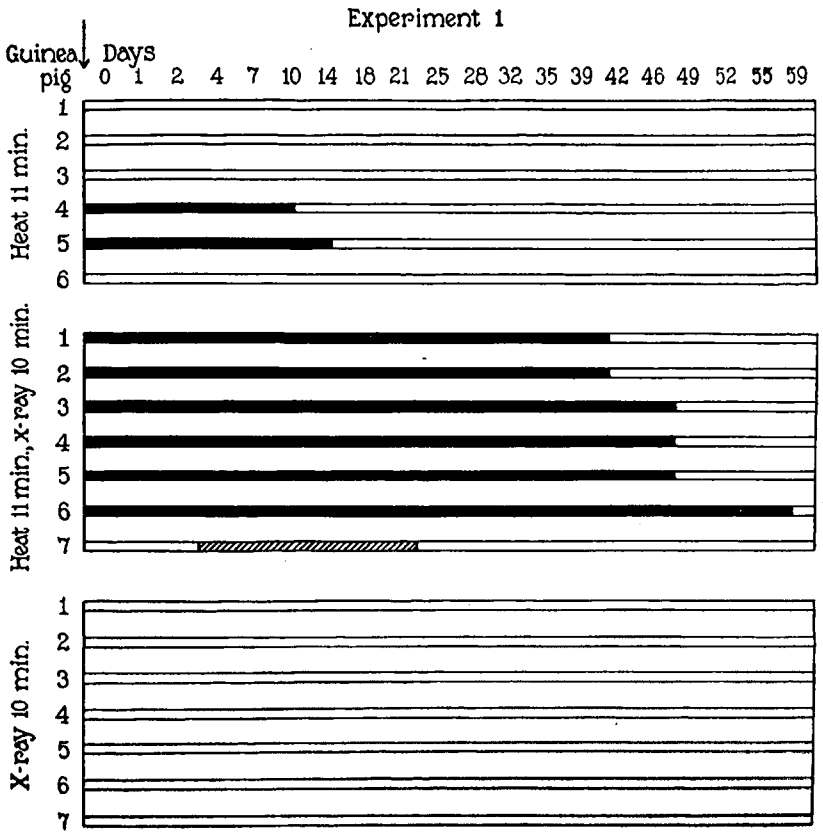

CHART 1. Each line represents the history of a single individual animal from the time of exposure till the end of the experiment. The heavy lines indicate burns; the cross-hatch, scaling but otherwise intact skin; and the unshaded line indicates no reaction, or a healed lesion in the skin.

Experiment 2.—An area on the abdomen of each of ten guinea pigs was exposed for 11 minutes to the heat from an electric soldering copper held 3 cm. from the skin. Another lot of eleven animals were exposed in a similar fashion to heat for 11 minutes and x-ray for 10 minutes, the exposures being made simultaneously. As the x-ray dosage used for this experiment was the same as that of Experiment 1, no control was included for the effect of this agent alone.

All of the heated animals with two exceptions developed burns but these did not appear till 24 hours after exposure and were completely healed between the 10th and 23rd days. Among the eleven animals receiving the combined treatment all developed burns, which, with two exceptions, appeared immediately

after exposure. The healing in this group was somewhat irregular. In three animals it was complete between the 21st and 28th days, but in the remaining eight not until between the 42nd and 59th days (Chart 2).

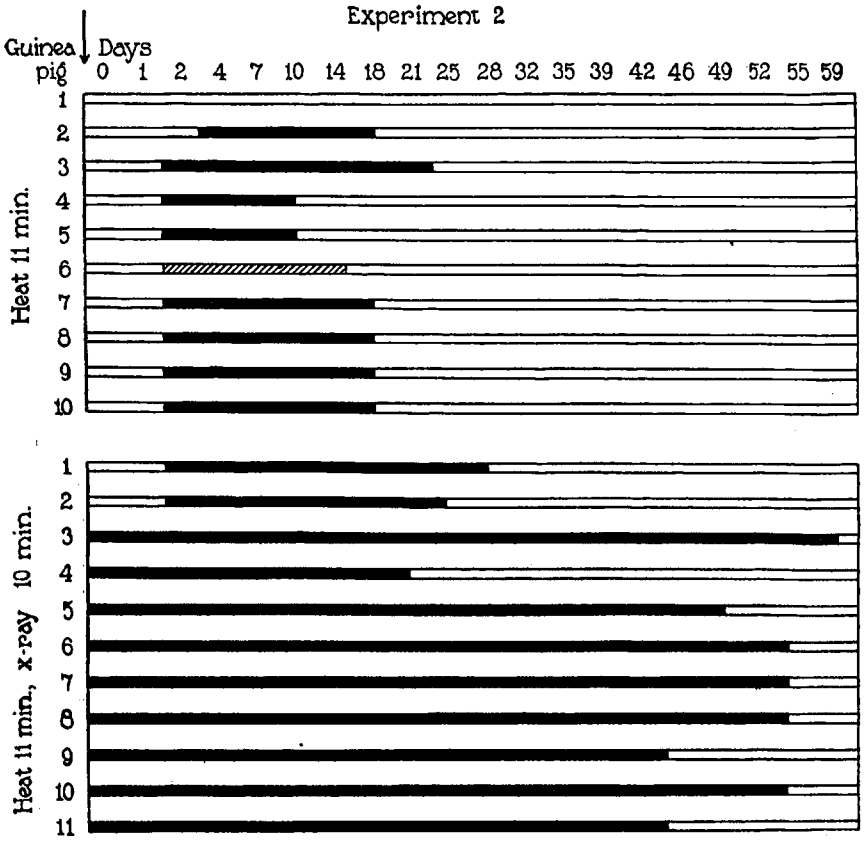

CHART 2. See explanation of Chart 1.

Experiment 3.—The source of heat in this experiment was the same soldering copper as that used in Experiment 2, but the distance from the skin was increased to 4.5 cm. and the length of exposure to 16 minutes. Of the five animals exposed to this dosage of heat only one developed a burn and this appeared the 2nd day and was healed by the 14th day after treatment. The other four guinea pigs all showed slight scaling but no break in the skin.

There was a slight change also in the x-ray dosage in this experiment, the target distance being increased to 36.7 cm. and the time to 15 minutes. This dose was sufficient to cause some scaling. The combined treatment with the two agents produced burns in all of the five animals exposed. The lesions appeared the 1st

day but the healing showed some irregularity, the process being complete in one animal by the 21st day, in two others by the 28th and 32nd day, respectively, and in two only at the 59th day (Chart 3).

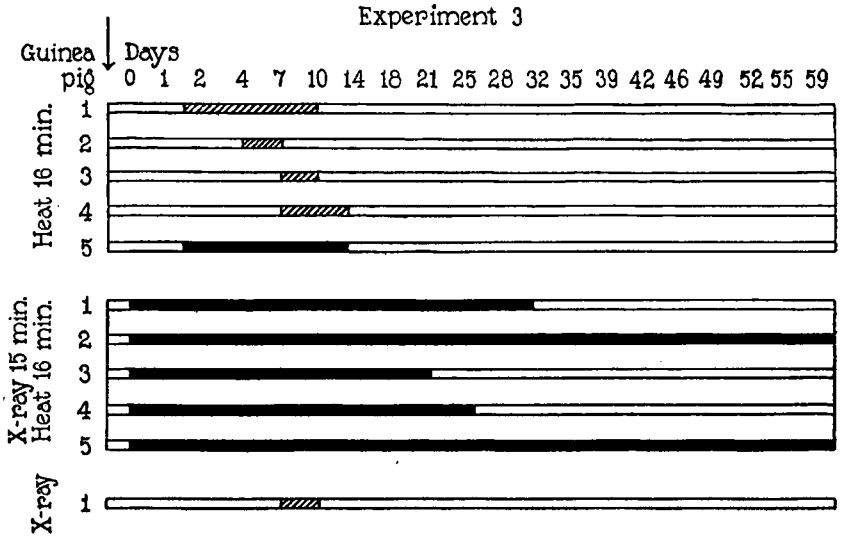

CHART 3. See explanation of Chart 1.

From these results it is seen that there is a marked difference between the developments in animals receiving either heat or x-radiation alone, and those receiving both radiations simultaneously. The x-rayed animals used as controls in Experiments 1 and 2 showed no skin reaction throughout the observed period, the hair growing in on the exposed area by the 14th day after treatment. In Experiment 3 the x-ray dosage given was sufficient to produce slight scaling with no erythema. The animals which were exposed to heat radiation alone, exhibited slight burns in 50 per cent of the animals treated. The burn appeared as a small white thickened area on the 2nd or 3rd day after treatment, which broke down and ulcerated on the 4th or 5th day and healed completely between the 10th and 14 days after exposure, leaving practically no scar. The irregular results from the heat treatment were to be expected because many factors were involved and the estimated dose was close to that which would regularly produce a burn.

In the experiments in which the guinea pigs were exposed to heat and x-radiations, simultaneously, all the animals developed well marked burns except one which had persistent heavy scaling for 2 weeks. The skin of these animals showed small hemorrhagic spots in the exposed area immediately after treatment. 1 or 2 hours later a large edematous area had appeared which broke down in 2 or 3 days. The lesions resulting were similar to those produced by heat radiation alone but were much more extensive. They healed much more slowly, the majority taking from 35 to 50 days, and when healed left a thick scar.

DISCUSSION.

No interpretation of the phenomenon is ventured. Whether one sort of radiation sensitizes the tissue to the action of the other can be learned only by giving the treatments in sequence. Experiments of this kind are now in process.

It is of interest to note that Rohdenburg and Prime[2] working with certain transplantable mouse and rat tumors have found that the combined effects of a certain exposure to heat and x-rays *in vitro* were lethal, although either exposure alone was without effect. A phenomenon somewhat similar perhaps has been observed by Bovie and Daland,[3] who have shown that by an exposure to fluorite rays *Paramecium caudatum* is rendered extremely sensitive to heat, so that it is injured or killed by an amount of heat which would not affect a normal unradiated individual.

SUMMARY.

Guinea pigs have been exposed to suberythema doses of soft x-rays, to radiant heat of intensity about critical for producing slight burns, and to both radiations simultaneously. No erythema was produced in the skin of the animals exposed to x-rays alone and only slight burns resulted in 50 per cent of the animals exposed to heat radiation alone. The animals exposed to heat and x-radiation simultaneously developed well marked burns which healed much more slowly than those produced by heat alone.

[2] Rohdenburg, G. L., and Prime, F., *J. Cancer Research*, 1921, vi, 101.
[3] Bovie, W. T., and Daland, G. A., *Am. J. Physiol.*, 1923, lxvi, 55.