

THE SKIN REACTIONS PRODUCED BY ALTERNATIONS OF HEAT AND X-RAY AT VARIOUS TIME INTERVALS*†

By JAMES A. HAWKINS, PH.D.

(From the Laboratories of The Rockefeller Institute for Medical Research)

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We have previously reported some observations on the effect of exposures to heat and X-rays on the skin reactions of guinea pigs. In the first series of experiments (1), in which the two agents were applied simultaneously, well-marked burns resulted, which healed very slowly, although the dosage of X-ray was not sufficient to cause even a mild erythema, and the heat exposures alone gave only a slight burn in 50 per cent of the animals. In the second series of experiments (2), in which the two agents were applied alternately, in order to determine whether or not one of the physical agents is capable of sensitizing the tissues to the action of the other, well-marked and persistent burns resulted in whichever sequence the agents were applied. It is thus apparent that either type of radiation is capable of augmenting the action of the other.

The present investigation was carried out to determine the duration of the sensitization of tissues produced by one agent to the action of the other.

Method

The character and measurements of the applications of X-ray and heat have been described previously (1-4).

During exposure the animal and X-ray tube occupied separate compartments of a lead-lined cabinet with an aperture for the passage of the rays, closed with thin bristol board. The chambers and partition were kept cool and ventilated

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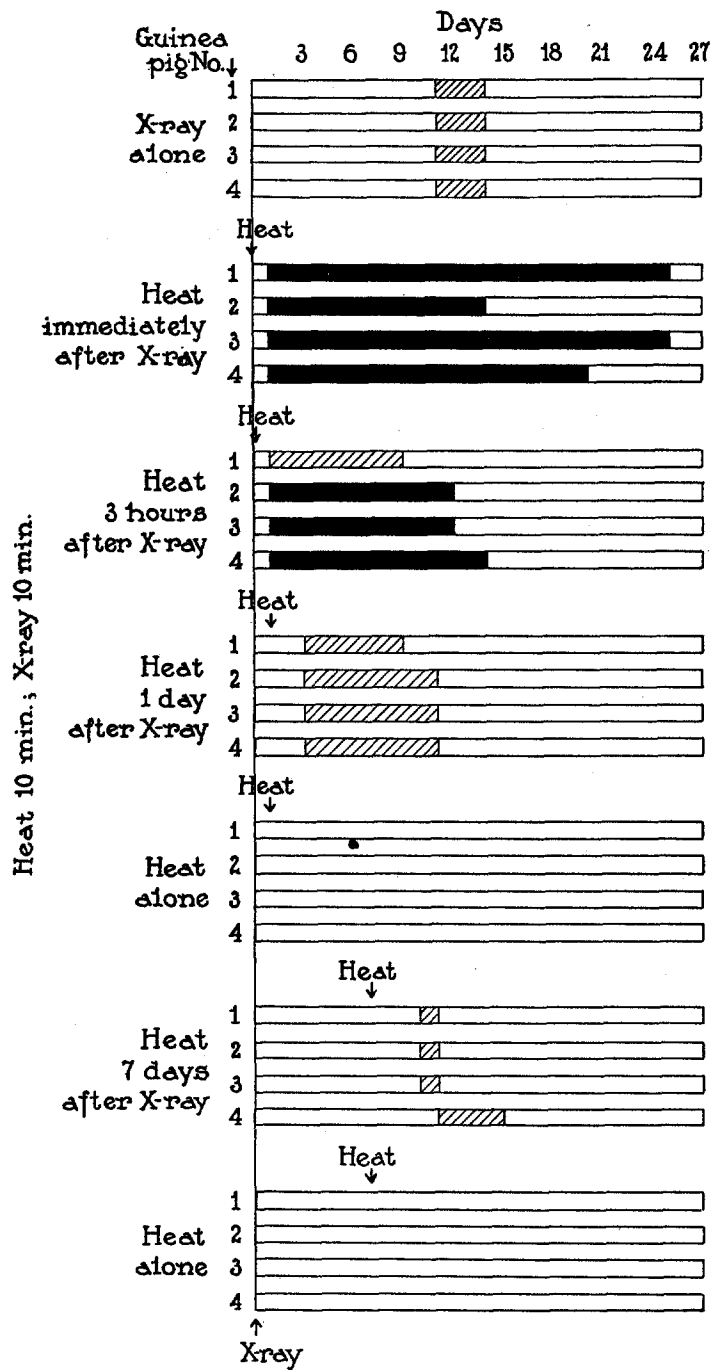
by means of an electric fan to prevent heat from the X-ray tube reaching the animal. The dosage used throughout the experiments was supplied by an outfit known to produce X-rays remarkably constant both in quality and intensity. The tube was operated at 30 kv. and 22 ma. with a target distance of 27.5 cm. The duration of exposure was 10 minutes, giving a dosage which previous experiments had proved to be suberythematous. The technique for holding the animals in place and at a definite target distance has already been described (3).

Heat treatments were given by means of a flat, hollow brass button, $\frac{3}{4}$ inch in diameter and $\frac{3}{8}$ inch thick, through which water from a constant temperature bath was passed. The circulation through the button, from and to the bath, was maintained by means of an electric pump driven at a definite speed. The heat treatment was confined to the portion of skin covered by the button, which was attached firmly to the abdomen of the animal by means of a broad elastic band that encircled the body. Throughout the experiments the temperature of the water in the button was maintained at 46°C.

Experiment 1.—The abdomens of four guinea pigs were shaved and an area exposed for 10 minutes to X-rays of the intensity noted above. The brass button was placed over different parts of the same area, at the following times: immediately, 3 hours, 1 day and 7 days after the X-ray treatment, and water at 46°C. was circulated through it for 10 minutes. The same animals were given the heat treatment at the same time intervals on areas which had had no X-ray exposure, as controls for the heat alone. Consequently, the control exposures to X-rays and heat alone, and the combined exposures to the two agents, were made on each animal.

The areas exposed to X-ray alone developed slight scaling of the skin on or about the 11th day after treatment, and this persisted for 4 days. In the areas exposed to heat immediately after X-ray, definite burns appeared on the 2nd day, and the healing of these burns took from 14 to 24 days. Three of the animals developed burns in the areas where heat was applied 3 hours after X-ray, which did not heal until between the 11th and 14th day. The other animals developed heavy scaling in this area which persisted for 9 days. In the areas exposed to heat 1 day after X-ray, scaling of the skin developed 2 days after heat treatment and lasted for 9 days. Three of the animals showed scaling in the areas exposed to heat 7 days after X-ray, the scaling appearing 3 days after heat treatment and lasting for 2 days. None of the animals showed visible skin changes in the areas exposed to heat alone. The results are graphically shown in Text-fig. 1.

Experiment 2.—The abdomens of four guinea pigs were shaved. The brass button was placed over different parts of this area at time intervals so spaced that 2 spots



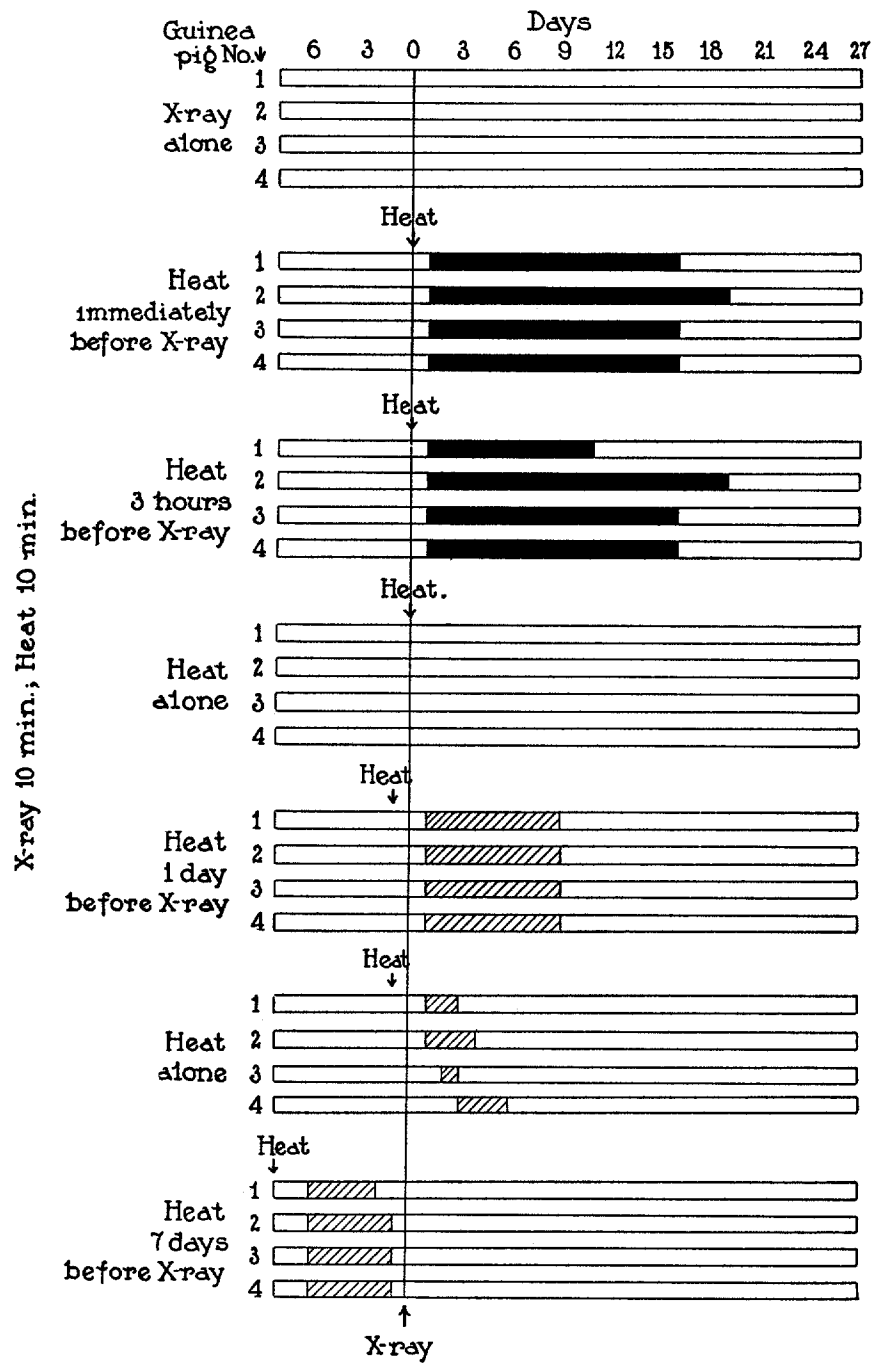
TEXT-FIG. 1. Each line represents the changes in an area of skin exposed to heat or X-ray or both. The duration of a burn is indicated by heavy lines, scaling by cross-hatch, while the unshaded lines indicate that there are no visible reactions.

each were exposed to heat 7 days, 1 day, 3 hours and immediately before the X-ray treatment. Water at 46°C. was circulated through the button for 10 minutes. A whole area containing a heated spot for each period was then exposed for 10 minutes to X-ray of the intensity noted above. Thus the control exposures to X-rays and heat alone and the combined exposures to the two agents were made on each animal.

The areas exposed to heat alone, as controls for the period immediately before X-ray, showed no skin reaction. The areas exposed to heat alone, as controls for the period 1 day before X-ray, developed slight scaling of the skin in two animals on the 1st day, and in the other two on the 2nd and 3rd days. This scaling persisted for 3 days. In the areas exposed to heat immediately and 3 hours before X-ray definite burns appeared on the 2nd day. The healing of these burns took from 10 to 17 days. In the areas exposed to heat 1 day before X-ray slight scaling of skin developed on the 2nd day and persisted for 8 days. In the areas exposed to heat 7 days before X-ray slight scaling of skin appeared and lasted for 5 days. This scaling had disappeared before X-ray treatment was given and no further skin changes resulted. No visible skin changes appeared in the areas exposed to X-ray alone. The results are tabulated in Text-fig. 2.

From these experiments it is seen that there is a very marked difference in the reaction of the areas which received X-ray or heat alone and those exposed to both types of radiation in sequence, a fact that has been shown before (2). The maximum effect of each agent alone was a slight scaling of the skin. There is a marked difference in the areas exposed to both agents where the treatment with one agent preceded the other by 3 hours, as compared with the areas exposed to heat or X-ray alone. A burn invariably resulted in the areas exposed to both agents, when the treatment with one followed the other immediately or in 3 hours. There was only a slight difference in the areas exposed to both agents, where the one preceded the other by 1 day, as compared with the areas that were exposed to heat or X-ray alone. Scaling of the skin developed in these areas and persisted for several days longer than in the areas exposed to heat or X-ray alone. There is no visible augmentation of effect on the skin when the treatment with either agent preceded the other by 7 days.

The sequence in which the agents were applied seemed to make no



TEXT-FIG. 2. For explanation see Text-fig. 1.

difference in the intensity of the reaction. It is apparent from these observations that either type of radiation is capable of sensitizing the skin to the action of the other, within certain limits.

DISCUSSION

In previous experiments (1) in which the skin of guinea pigs was exposed to X-ray and heat radiation simultaneously, burns were produced which had the appearance of heat burns, but were much more extensive. In a second series of experiments (2), in which the exposures were in sequence, extensive burns resulted, the reaction being the same regardless of which agent was applied first. The fact that burns developed so soon after the treatment, and their general appearance during the first few days, gave them a close resemblance to a heat reaction, but the later appearance, the slowness of healing and the type of resulting scar were more characteristic of an X-ray effect. Thus the lesions produced had some of the features characteristic of the action of both agents.

The present experiments were undertaken to see if some insight into the nature of the effect of radiant energy on the living cell could be obtained. Burns similar to those in previous experiments were obtained even when one agent was applied 3 hours after the other. Scaling of the skin resulted when the interval was as great as a day and this scaling was heavier and lasted for a longer time than that produced by either heat or X-ray alone. It can be concluded that the sensitizing effect persisted in some degree for 24 hours. Heat applied 1 week before X-ray caused no visible augmentation of the skin reaction to the latter. This was to be expected. No apparent skin changes followed the application of heat to areas X-rayed 1 week previously, though the effects of the raying were beginning to appear.

It is evident that either type of radiation is capable of sensitizing to the action of the other. The result was the same regardless of whether the heat or the X-ray treatment was given first. No interpretation of the phenomenon is ventured.

SUMMARY

Areas on the abdomen of the same guinea pig were exposed to suberythreal doses of soft X-rays, to heat of an intensity below the critical

dose for the production of burns, and to both radiations in sequence with various time intervals between the exposures.

The only effect of exposure to X-ray or heat alone was a slight scaling of the skin. The areas exposed to heat and X-radiation developed well-marked and persistent burns when the exposure to one agent was made within 3 hours of the other. Scaling of the skin developed when the exposure to one agent was made 1 day after the other. This scaling was more marked and lasted longer than the scaling produced by either agent alone. The results were the same no matter in which sequence the agents were applied.

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