SKIN REACTIONS TO ALTERNATE HEAT AND X-RAY EXPOSURES.*

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(Received for publication, June 27, 1925.)

We have previously reported some observations on the effect of simultaneous exposures to heat and x-rays on the skin reactions of guinea pigs.[1] The dosage of x-ray used in these experiments when given alone was not sufficient to cause even a mild erythema, while the heat exposure alone gave only a slight burn in 50 per cent of the animals. However, when the two agents were applied simultaneously, well marked burns resulted which healed very slowly. The time at which the burn developed and the character of the first stages were similar to a simple heat effect but the later appearance of the lesions and the slowness with which they healed suggested an x-ray burn.

It was the purpose of the present investigation to determine whether or not one of the physical agents mentioned is capable of sensitizing the tissues to the action of the other.

Method.

The character of the x-ray and the method of application have been previously described.[1,2] 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. Both chambers and the partitions were kept cool and ventilated by means of an electric fan. These precautions prevented any heat from the tube penetrating to 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 kilovolts

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

[1] Hawkins, J. A., and Clark, H., *J. Exp. Med.*, 1925, xli, 761.

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

and 22 milliamperes with a target distance of 27.5 cm. The duration of exposure was 11 minutes, giving a dosage which previous experiments had proved to be suberythemal.

The technique for holding the animals in place and at a definite target distance has already been described.[2]

Heat treatments were given by means of a flat hollow brass button, 3/4 inch in diameter and 3/8 inch thick, through which water from a constant temperature bath was passed. The circulation from the bath through the button and back again to the bath was maintained by means of an electric pump driven at a definite speed. The temperature of the water fell less than 0.5°C. in passing through the circuit. When in use the button was attached firmly to the abdomen of the animal by means of a broad elastic band which encircled the body. The heat treatment was thus confined to the portion of skin covered by the button. Throughout the experiments the temperature of the water in the button was maintained at 46°C.

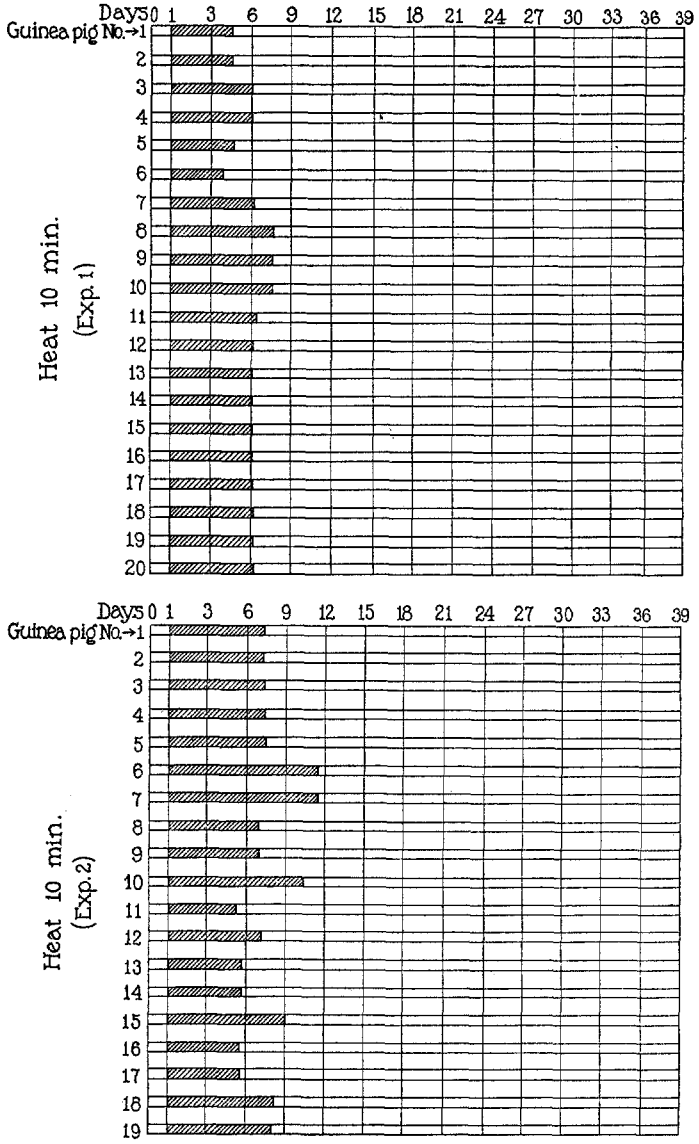
Experiment 1.—The abdomens of twenty guinea pigs were shaved and an area exposed for 11 minutes to x-rays of the intensity noted above. The brass button was then placed over part of the same area and water at 46°C. was circulated through it for 10 minutes. The heat in the same dosage was next applied to another area on the same animal but this area had received no previous exposure to x-rays. Thus the control exposures to x-rays and heat alone and the combined exposures to the two agents were made on each animal.

A slight scaling of the skin resulted from the heat exposure, which appeared about the 2nd day and lasted from 4 to 8 days (Text-fig. 1). In the areas exposed first to x-ray and then to heat scaling developed on the 2nd day and definite burns appeared on the 4th. The healing of these burns was somewhat irregular. In sixteen pigs it was completed between the 15th and 19th days, but in the remaining four the lesions were not covered till between the 32nd and 39th days (Text-fig. 2). The areas exposed to x-ray alone developed slight scaling of the skin on about the 7th day after treatment and this persisted for from 4 to 5 days (Text-fig. 3).

Experiment 2.—Heat was applied for 10 minutes to two widely separated areas on the abdomen of each of nineteen guinea pigs by means of the brass disc with the water circulated at a temperature of 46°C. Then an area on the abdomen was exposed to x-radiation so that one of the previously heated spots was included in the x-rayed area. The dosage was the same as that used in Experiment 1. Thus we had on each animal an area exposed to heat alone, x-ray alone, and one exposed first to heat and then to x-ray.

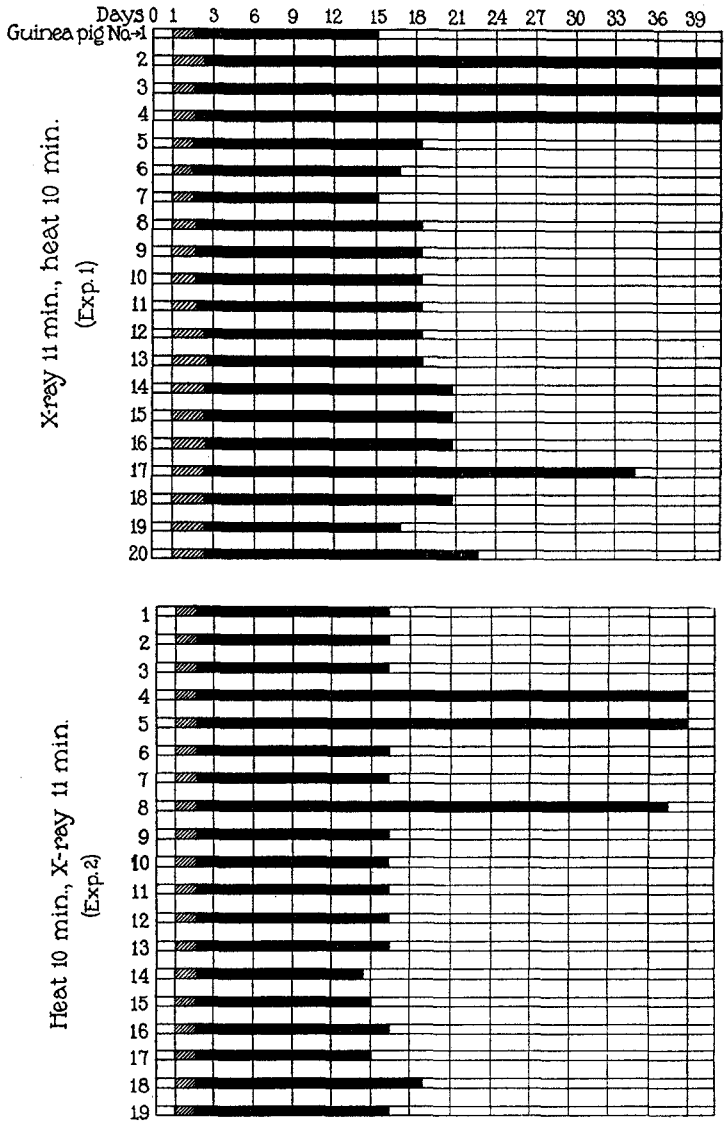
The results obtained in this experiment were identical with those in Experiment 1 and are shown in Text-figs. 1 to 3.

From these experiments it is seen that there is a very marked difference in the reaction of the areas which received either x-ray or heat alone and those exposed to both types of radiation in sequence. The maximum effect of either agent alone was a slight scaling of the



TEXT-FIG. 1.

TEXT-FIGS. 1 TO 3. Each line represents the history of a single individual area from the time of exposure until the end of the experiment. The heavy lines indicate burns; the cross-hatch indicates scaling but otherwise intact skin; and the unshaded area indicates that there was no reaction or else a healed lesion in the skin.


Days 0 1 3 6 9 12 15 18 21 24 27 30 33 36 39
Guinea pig No→1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
X-ray 11 min., heat 10 min.
(Exp. 1)
1
2
3
4
5
6
7
8
9
10
11
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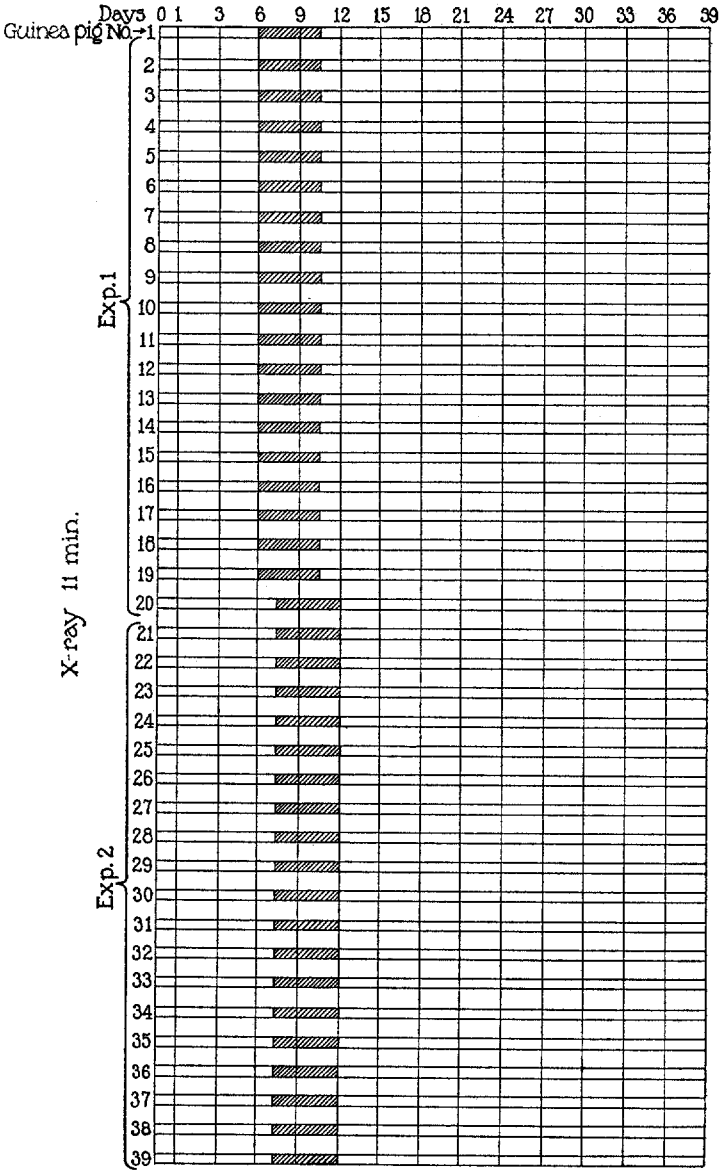
13
14
15
16
17
18
19
Heat 10 min., X-ray 11 min.
(Exp. 2)

TEXT-FIG. 2.


Days 0 1 3 6 9 12 15 18 21 24 27 30 33 36 39
Guinea pig No.-1
2
3
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14
15
16
17
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19
20
21
22
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27
28
29
30
31
32
33
34
35
36
37
38
39
Exp. 1
Exp. 2
X-ray 11 min.

TEXT-FIG. 3.

skin. In the areas exposed to both agents a burn invariably resulted. It seemed to make no difference in the intensity of the reaction whether the heat was followed by the x-ray exposure or the x-ray followed by the heat exposure. The burns appeared as white spots corresponding in size to the area covered by the brass disc. They became evident on the 2nd day after treatment and broke down usually on the 4th day. The majority of the lesions healed in from 15 to 18 days, leaving a thick scar. In about 50 per cent of the animals, some weeks later, the areas broke down a second time with the formation of chronic ulcers which healed very slowly. It is apparent from these observations that either type of radiation is capable of augmenting the action of the other.

DISCUSSION.

The mechanism in the cell which brings about the response to radiant energy is not understood. Bovie,[3] in the discussion of his observation that ultra-violet light sensitized paramecium to heat, suggests that the radiation induces some rearrangement of the atoms within the cell so that they may change from a passive to an active stage. The process of rearrangement by which the complex cell protoplasm returns to the normal equilibrium after x-ray exposure is undoubtedly slow. The heat radiation may intensify the atomic chaos so that the cell is destroyed before adjustment can take place. In the case of the present results the reaction was the same regardless of whether the heat or x-ray exposure was made first, in which respect they differ from Bovie's observation that ultra-violet light sensitizes to heat applied later, whereas the application of the two agents in reverse order is without effect.

The nature of the lesions produced in our experiments suggests the effect of both agents. The fact that they develop so soon after treatment and their general appearance during the first few days give them a close resemblance to a pure heat effect, but the later appearance of the burns, the slowness of healing, and the type of resulting scar are more characteristic of an x-ray effect. The observations would seem to be capable of further analysis with a possibility of yielding some insight into the nature of the effect of radiant energy on the living cell.

[3] Bovie, W. T., and Daland, G. A., *Am. J. Physiol.*, 1923, lxvi, 55.

SUMMARY.

Different areas on the abdomen of the same guinea pigs have been exposed to suberythema 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.

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. The results were the same no matter in which sequence the agents were applied.