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Biological
Effects of
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Radiation

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EFFECTS OF EXTERNAL BETA RADIATION

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at the outstanding difference 5, 1. The latent period elapsing e onset of burn symptoms, might minor differences brought out in of beta-exposed rats to give evi- natocrit, when an elevated hem- verity of thermal burns, may be e latent period any changes in the recovery kept pace with their

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Chapter 12*

REACTIONS OF HUMAN SKIN TO SINGLE DOSES OF BETA RAYS

By J. E. Wirth and J. R. Raper

1. INTRODUCTION

In the various attempts to obtain a biological unit to express the response of tissues to radium and roentgen radiations, the erythema produced on human skin has been among the foremost effects investigated. One of the main disadvantages of such a unit has been the extreme variation in the doses of radiations necessary to produce erythemas. This has been mostly due to different methods used to measure a roentgen and to the varying interpretations of the degree of an erythema. The subject was reviewed in 1924 by Leddy and Weatherwax,¹ who stressed the fact that it was not an accurate means of measuring radiation and brought out many disadvantages. Earlier Failla, Quimby, and Dean,²⁻⁴ in a series of articles, suggested using a threshold erythema as a suitable expression since most investigators could agree as to the presence or absence of a reaction, though they might not agree upon the degree of a given erythema. Subsequently Quimby and Pack⁵ used the threshold erythema in other experiments.

It may be recognized that such a unit is not an accurate measure of radiation, yet is a useful means of comparing responses of the human skin to various forms of radiation. Wilhelmy⁶ discussed the response to low-voltage X rays and cathode rays rather extensively in 1936. In the longer-wavelength range a threshold reaction must be distinguished from a threshold erythema. There has been uncertainty as to the amount of beta radiation necessary to produce a threshold skin reaction in humans. Much of this has been due to the lack of a pure

*Based on Report MonH-98, May 24, 1946 (MDDC-508).

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source of beta radiation, differences in interpreting erythema: tanning or bronzing reactions, and differences in the methods used to measure the quantity of radiation given. An attempt was made to obtain an approximate figure experimentally by using a limited number of human subjects. The volar aspect of the left forearm was chosen as the most suitable site for observations on a group of normal healthy adult volunteers (6 females and 4 males). Exposures were made on four areas between the antecubital region of the forearm and wrist of each person.

2. MATERIALS AND METHODS

The method of preparation of the sources was as follows: shielded disks of phenol-formaldehyde plastic containing P^{32} were used. The preparation and construction of the sources and the methods of measuring the beta-radiation dose rate at the surface of the sources are presented in detail in a separate chapter.⁷ Briefly, circles, 1 in. in diameter, of the special phosphorus-impregnated plastic (50 per cent phosphorus by weight) were fastened in aluminum cups, and the exposed surface of the plastic of each was thinly coated with plastic varnish. The disks were then activated by slow neutrons in the Clinton Pile by the reaction $P^{31}(n,\gamma)P^{32}$.

Measurements of the surface dose rate were made with a flat-surface ionization chamber which was calibrated for beta radiation by the extrapolation-chamber method.^{7,8}

An exposure was made by setting the source directly on the skin for the length of time necessary to deliver the required dose. The dose thus delivered to the skin in contact with the source was uniform throughout the treated area; the aluminum shield surrounding the source disk prevented low-dose exposure to adjacent areas and other parts of the body.

3. EXPOSURE DATA

3.1 First Series. Doses of 140, 170, 200, and 250 rep, respectively, as measured at the surface of the plaque and on the skin, were given. The exposure time varied from 2.5 to 5.25 min. A clearance of at least 1 cm distance was allowed between each exposure area. The areas were observed daily for a week, three times a week for a second week, twice a week for 3 weeks, and then at weekly intervals for a total observation period of 10 weeks. A final observation was made at 17 weeks postexposure. Only three people showed a primary response within the first 48 hr to doses of 170 to 250 rep. At the end of the first week 8 of the 10 cases receiving 200 and 250 rep showed

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reaction, but not more than 2 to 3 cases showed any response at the end of the first week in the two lower doses. By the third and fourth weeks the number of visible reactions from the various doses were: from 140 rep, a maximum of 4; from 170 rep, a maximum of 6; and from 200 and 250 rep, 8 of the 10 (see Fig. 12.1).

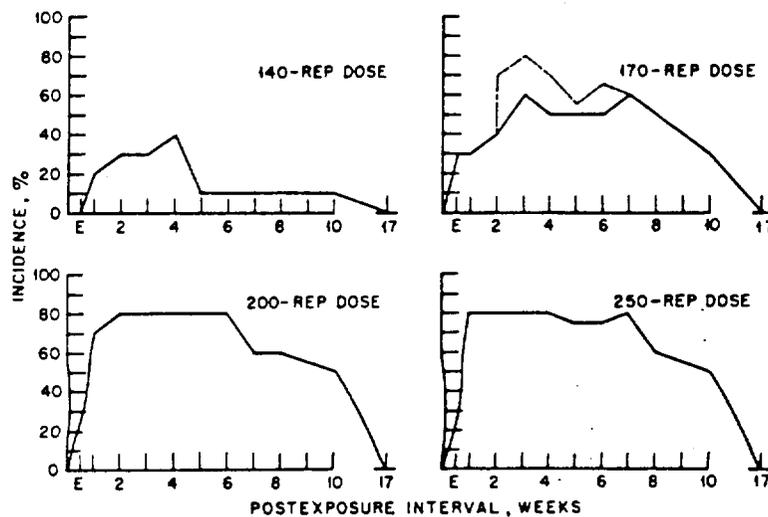


Fig. 12.1—Threshold skin reaction from P^{32} beta radiation. Exposures made at time 0. E, early reactions within 1 to 3 days postexposure; broken line, doubtful reactions; solid line, mild tanning.

It is notable that the reaction could not be spoken of as "threshold erythema." It appeared more like a mild tanning, with only 2 or 3 people of the 10 showing any signs of pinkness or redness. It was therefore believed that this was not a true threshold erythema but rather a threshold reaction that could be referred to as only a "mild tanning." A critical review of the reactions in the group receiving 170 rep is impressive for the fact that not more than 50 to 60 per cent showed definite reactions where the entire shape of the exposure plaque was clearly discernible. If the number of cases showing some pigmentation in irregular patches is added to the cases showing a definite reaction, the total reached 80 per cent only on the third week of observation. The effect of adding all borderline reactions to the number of positive reactions is illustrated graphically in the 170-rep dose series in Fig. 12.1 by the broken line.

The dose of P^{32} beta radiation (measured at the surface of the skin) which is required to produce a visible reaction in 80 per cent of this

group of people is therefore between 170 and 200 rep. It is interesting to note that 200 and 250 rep produced reactions in 8 of 10 per cent exposed. The skin of one person in the series given 140 to 240 rep showed no visible reaction at any time. The difference between 80 and 90 per cent positive reactions in the 200- and 250-rep exposures is due to variations in reporting the responses to certain exposures positive at one time and negative at another observation period.

The early onset and persistence of tanning after the primary reaction in this series are at variance with Dean's description³ of a series of cases treated with radon in a glass tube. He observed subsidence of the early blush after 2 to 3 days and noted that the reaction appears normal for a period of days or weeks before the secondary reaction comes on.

The observations made during the first 6 weeks were analyzed in April 1945, and, as a result, a second series of exposures to higher doses was made on May 21, 1945.

3.2 Second Series. Ten persons were given a series of four exposures each in doses varying from 635 to 1180 rep. Exposure time varied from 5 to 10 min. In seven cases the right forearm was used for the test, and in three cases the inner aspect of the mid-thigh was used. The differences in the response of these two sites to this series of radiation were less notable than were the variations of the reactions on the forearm of different subjects. Observations were made on this series at 3, 6, 10, and 24 hr postexposure and then daily for 10 days. Thereafter observations were made at 2-day intervals for 11 days, twice a week for 3 weeks, and weekly for 5 weeks. Observations were then made on the 70th and 98th days and at 4 and 8 months postexposure.

3.3 Primary Reaction: Erythema Followed by Tanning. Within 6 hr after four doses (635, 813, 1000, and 1180 rep) a primary blush or erythema was noted within 6 hr in 100 per cent of the people. In the highest doses, the primary blush persisted for 2 to 4 days in 100 per cent of the cases and by the end of the second day was present in only 6 per cent. A slight degree of tanning began in all cases by the second day. It was impossible to tell at what stage the redness disappeared completely since it was masked by tanning that gradually increased. On the fourth and fifth days the tanning was definite in all cases, and tanning persisted for the shortest time in the 635-rep dose, a longer period in the 813-rep dose, and for a still longer period in the 1000- and 1180-rep doses (see broken lines in Fig. 12.2).

and 200 rep. It is interesting to note that reactions in 8 of 10 persons in the series given 140 to 240 rep. The difference between 80 rep. and 250-rep exposures is not apparent in the responses to certain exposures during the observation period.

Following after the primary reaction, Dean's description³ of his observations in a glass tube. He observed a primary blush or reddening in a few days and noted that the skin began to tan a few weeks before the secondary

6 weeks were analyzed in the series of exposures to higher

given a series of four exposures of 1180 rep. Exposure time on the right forearm was used in the aspect of the mid-thigh was used at these two sites to this form the observations of the reactions. Observations were made at 2-day intervals for the first 5 weeks. Observations were made at 4 and 8 months

described by Tanning. With all the reactions, a primary blush or mild reddening occurred in 100 per cent of the people. This was present in only 60 per cent of the cases by the second day. Redness disappeared completely and gradually increased while tanning gradually increased (see solid line in Fig. 12.2). By the 4th day, tanning was complete in all cases, and this was true in the 635-rep dose, for a still longer period in the series given 1180 rep. (see solid line in Fig. 12.2).

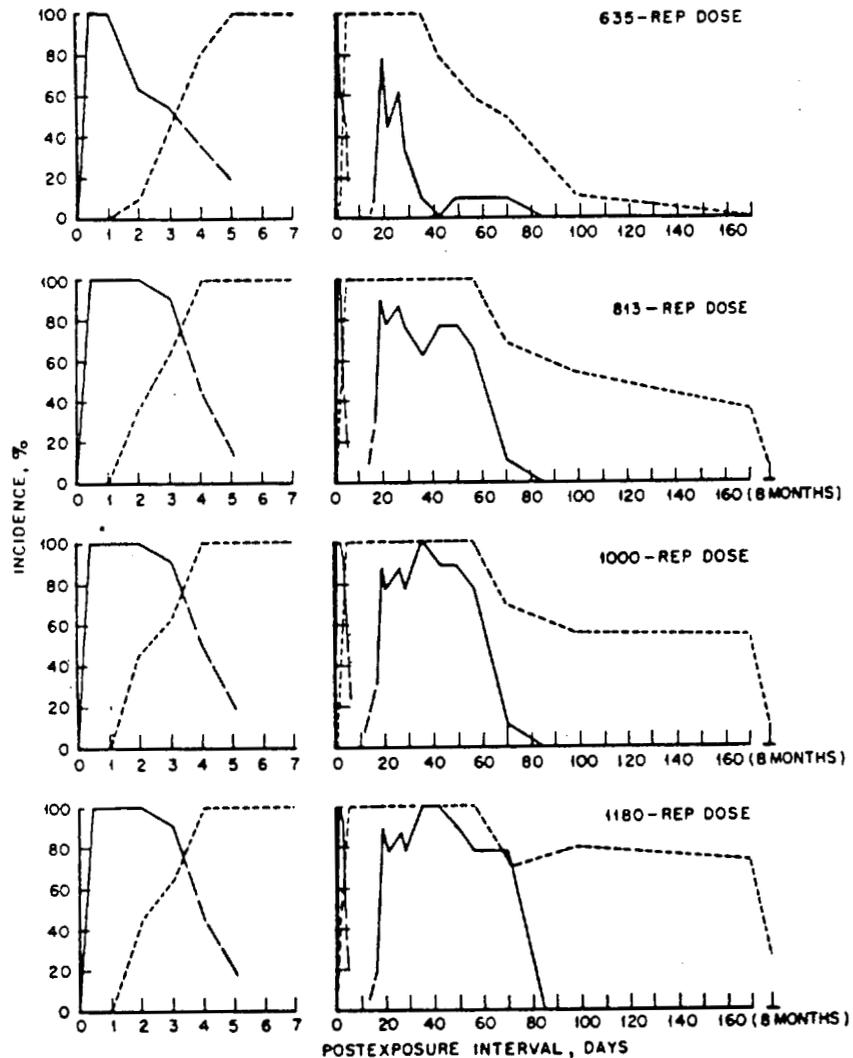


Fig. 12.2—Threshold erythema from P^{32} beta radiation. Exposures made at time 0. Graph on the left is an expansion of the first few days of the graph on the right to illustrate details of the early response. Broken line, tanning; solid line, reddening; broken portions of solid line, uncertain because of superimposed tanning.

3.4 Secondary Reaction: Erythema and Additional Tanning. the 19th and 20th days it was quite evident that a secondary reaction was taking place. At first it was impossible to tell whether this was merely a deepening of tanning reaction already present or whether there was an erythema appearing in addition to the tanning. By the 21st day there was no question whatever but that there was a definite erythema. This was present in a little less than 20 per cent of cases receiving 635 rep but was present in 90 per cent of those receiving 813 rep and above. The erythema from 813 and 1000 rep persisted for nearly 60 days, and that for 1180 rep persisted for 78 days. The exact time of disappearance cannot be stated definitely because of the coexisting tan. It was impossible to avoid being impressed by the difficulty of distinguishing between the true erythema and the tanning associated with the primary and secondary reactions. None of the reactions went to the stage of bleb formation, but in the highest dose minute vesicles formed in three persons at the fifth and sixth weeks postexposure. These were followed by a dry spotty desquamation of the most superficial layers of epithelium. Differences in response between male and female subjects was less notable than the difference in response between blond and brunet skins. Similar doses produced more erythema in blond skin than in brunet. The series of cases was too small to permit drawing any conclusion as to the difference of intensity or persistence of tanning between blond and brunet skins.

3.5 Tanning. The tanning, even from the small doses of 200 and 250 rep, persisted on some people for as long as 10 weeks but disappeared entirely by the 17th week. In the higher doses, such as 635 rep, the tanning remained longer than 160 days in some 70 per cent of the cases, and at 8 months there was still some persistent tanning in 25 per cent. The differences in duration of the tanning reaction from doses of 635 and 1180 rep can be seen readily from the broken lines on the graphs in Fig. 12.2.

3.6 Threshold Erythema. If it is accepted as the criterion for threshold erythema that 80 per cent of those exposed show an erythema, then a dose somewhat greater than 635 rep and probably in the region of 813 rep may be considered the threshold erythema dose for beta rays from a 1-in.-diameter plaque of P^{32} . In a larger series of cases it may be possible to determine this more accurately with the aid of colored filters to distinguish between the tanning reaction and the true erythema in a manner similar to the one used by Haxel, Leddy, and Sheard.⁹

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and Additional Tanning. By it that a secondary reaction is possible to tell whether this was already present or whether addition to the tanning. By the fact that there was a definite decrease less than 20 per cent of the dose in 90 per cent of those re-exposed from 813 and 1000 rep per-son. 180 rep persisted for 70 to 100 days cannot be stated definitely whether it is possible to avoid being immunized between the true erythema and secondary reactions. (bleb formation, but in the case of free persons at the fifth and sixth followed by a dry spotty desquamation of epithelium. Difference between subjects was less notable than between blond and brunet skins. Similar results on skin than in brunet. The drawing of any conclusions as to the difference between blond

and the small doses of 200 to 300 rep long as 10 weeks but disappear at higher doses, such as 1180 to 1500 rep in 70 per cent of those in 100 days in some 70 per cent of those with ill some persistent tanning. The duration of the tanning reaction is dependent on readily from the broken

is accepted as the criterion for a secondary reaction. Those exposed show an erythema at 335 rep and probably in the range of the threshold erythema dose for P^{32} . In a larger series of experiments more accurately with the same dose in the tanning reaction and in the one used by Harris

4. SUMMARY

In determining responses of human skin to beta radiation, a distinction must be made between a threshold reaction and a threshold erythema. A threshold reaction (mild tanning) can be produced in 80 per cent of those exposed to the beta radiation from a 1-in. P^{32} contact disk by a dose of 200 rep and in only 60 per cent of those exposed to 170 rep. A threshold erythema may be produced under similar circumstances in 80 per cent of those exposed to 813 rep and in 60 per cent of those exposed to 635 rep. A larger number of cases than that used here is necessary to determine correct figures within a narrower range. The above preliminary experiments indicate the levels at which a larger series of cases should be exposed.

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