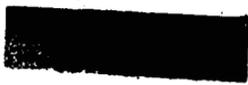


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REACTIONS OF HUMAN SKIN TO SINGLE DOSES OF BETA RAYS

BY

J. E. WIRTH, M.D., AND J. R. RAPER



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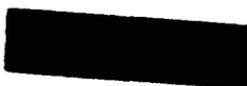
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REACTIONS OF HUMAN SKIN TO SINGLE DOSES OF BETA RAYS

By

J. E. Wirth, M.D. and J. R. Raper

Among 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. One of the main disadvantages of such a unit has been the extreme variation in doses of radiations to produce erythemas. This has been due, mostly, to the different methods used to measure a roentgen and to the varying interpretations of the degree of an erythema. The subject was reviewed by Laddy and Weatherwax⁽¹⁾ in 1924. They stressed the point that it was not an accurate means of measuring radiation and brought out many disadvantages. Earlier, Failla, Quimby and Dean, in a series of articles,^(2,3,4) suggested using a threshold erythema as a suitable expression since most persons could agree as to the presence or absence of a reaction, though they may not agree upon the degree of a given erythema. Since then Quimby and Paek⁽⁵⁾ have used the threshold erythema in other experiments.

One may recognize that such a unit is not an accurate measure of radiation, yet it is a useful means of comparing responses of the human skin to various forms of radiation. Wilhelmy⁽⁵⁾ discussed the response to low voltage x-rays and cathode rays rather extensively in 1936. In the longer wave length range, a threshold reaction must be distinguished from a threshold erythema. There has been uncertainty in 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 source of beta radiation, differences in interpreting erythemas and tanning or bronzing reactions, and

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Differences in the methods used to measure the quantity of radiation given. We have made an attempt 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 10 normal healthy adult volunteers (six females and four males). Exposures were made on four areas between the antecubital region of the left forearm and wrist of each person.

The method of preparation of the sources is as follows: Small shielded discs of phenol-formaldehyde plastic into which P^{32} had been intimately mixed, were used. The preparation and construction of the sources and the methods of measuring the beta radiation dose rate at the surface of plane sources are presented in detail in a separate account. (7)

Small circles, one inch in diameter, of special phosphorus-impregnated plastic (50% phosphorus by weight) were fastened in small aluminum cups and the exposed surface of the plastic of each was coated with plastic varnish. The discs were then activated with slow neutrons in the Clinton Pile by the reaction $P^{31} (n, \alpha) P^{32}$.

Measurements of surface dose rate were made with a special flat surface ionization chamber, calibrated for beta rays by the extrapolation chamber method (8).

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

First Series. Doses of 140, 170, 200 and 250 rep*, respectively, were given as measured at the surface of the plaque and on the skin. The

*rep = roentgen equivalent physical. Hereinafter wherever r appears, roentgen equivalent physical is intended.

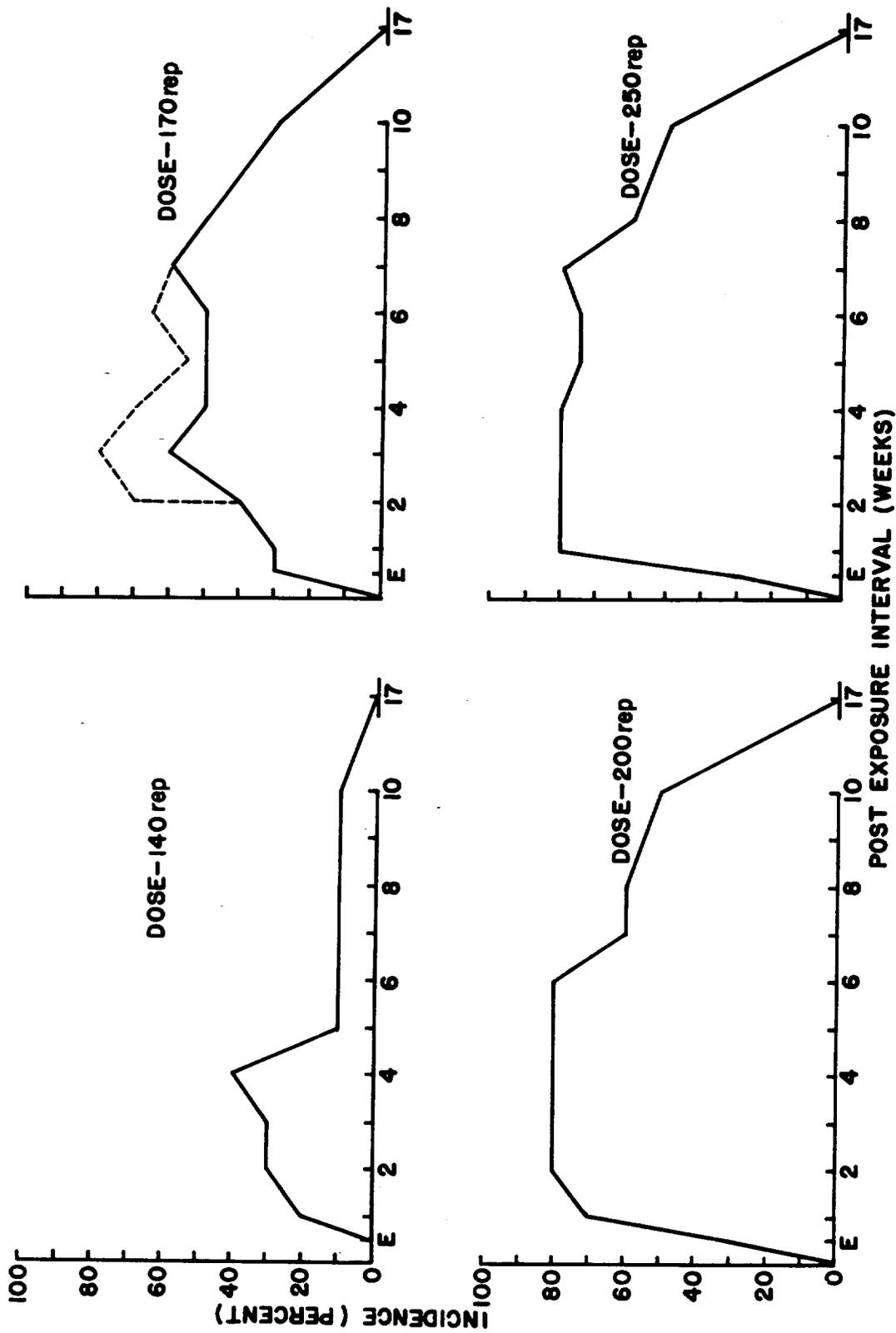
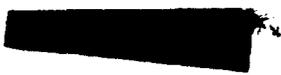


Fig. 1. Threshold skin reaction from beta radiation from P³².
 Exposures made at time 0. E = early reactions within 1 to 3 days post exposure. rep = roentgen equivalent physical.
 - - - - - Doubtful reactions. _____ Mild tanning.

exposure times varied from $2\frac{1}{2}$ minutes to $5\frac{1}{4}$ minutes. A clear zone of at least one-centimeter distance was allowed between each exposure. The areas were observed daily for a week; three times a week for another week; twice a week for three weeks; then at weekly intervals for a total observation period of 10 weeks. A final observation was made at 17 weeks post exposure. Only three people showed a primary response within the first 48 hours to doses of 170 r to 250 r. At the end of the first week 8 of the 10 cases receiving 200 and 250 r showed a reaction while not more than 2 to 3 showed any response at the end of the first week in the two lower doses. By the third and fourth week the number of reactions that were visible from the following doses were: from 140 r - a maximum of 4; from 170 r - a maximum of 6; from 200 and 250 r - 8 of the 10 showed a positive reaction. (See fig. 1).

It is notable that the reaction could not be spoken of as a 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 which could be referred to as only a mild tanning. A critical review of the reactions in the group receiving 170 r impresses one with the fact that not more than 50% to 60% showed definite reactions where the entire shape of the exposure plaque was clearly discernable. If the number of cases showing some pigmentation in irregular patches were added to the cases showing a definite reaction the total reached 80% on only the third week of observation. The effect of adding all borderline reactions to the number of positive reactions is illustrated graphically in the 170 r dose series in fig. 1 by the broken line.

The number of roentgens of beta radiation from P^{32} on the surface of the skin of this group of people to produce a visible reaction in 80% of those so exposed is, therefore, between 170 r and 200 r. It is interesting to note that 200 and 250 r produced reactions in 8 of the 10 persons exposed.



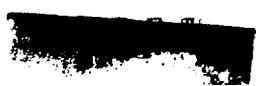
The skin of one person, in the series given 140 to 240 r showed no visible reaction at any time. The difference between 80% and 90% positive reactions in the 200 r and 250 r exposures is made up by variations in reporting the responses to certain exposures positive at one time and negative at another observation period.

The early onset and persistence of tanning after the primary reaction in this series is at variance with Dean's⁽³⁾ description of his series of cases treated with radon in a glass tube, where he obtained a subsidence of the early blush after 2 to 3 days and noted that the skin appears normal for a period of days or weeks before the secondary reaction comes on.

The observations made during the first six weeks were reported at a monthly meeting in April, 1945, CH-2808, and as a result of the discussion, a second series of exposures of higher doses was made on May 21, 1945.

Second Series. Ten persons were given a series of 4 exposures each in doses varying from 635 r to 1180 r. Exposure times varied from 5 to 10 minutes. In 7 cases the right forearms were used for the test, and in 3 cases the inner aspect of the mid thighs were used. The differences in response of these two sites were less notable from this form of radiation than were the variations of the reactions on the forearms of different subjects. Observations were made on this series at 3, 6, 10, and 24 hours post exposure, 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 day, and at four months, and 8 months post exposure.

Primary Reaction. (Erythema followed by Tanning). With all four doses (635 r, 813 r, 1000 r, and 1180 r) a primary blush or mild erythema was noted within 6 hours in 100% of the people. This primary blush persisted for 2 to 4 days in the highest doses, but in the lower doses per-



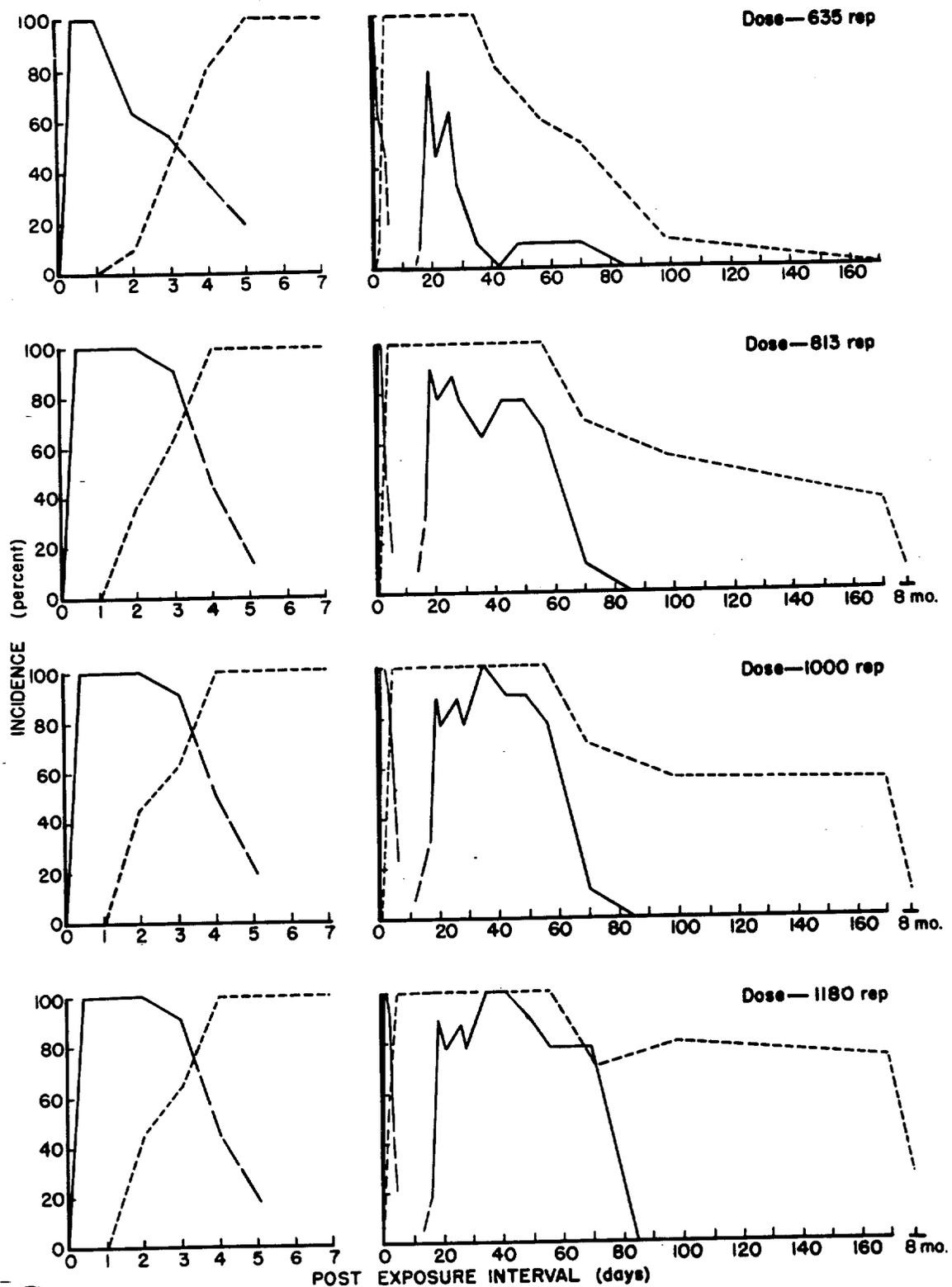


Fig. 2. Threshold erythema from beta radiation from p^{32} .
 Exposures made at time 0. Graph on left is an expansion of
 the first few days of the graph on the right to illustrate
 details of the early response. - - - Tanning. _____ Reddening.
 - · - · - Uncertain because of superimposed tanning.

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sisted only for a day in 100% of the cases, and by the end of the second, day was present in only 60%. 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, as it was masked by tanning which gradually increased while the erythema was subsiding. (Long broken line in fig. 2). By the 4th to 5th day the tanning was definite in all cases, and this tanning persisted for the shortest time in the 635 r dose, for a longer period in the 813 r dose, and for a still longer period in the 1000 and 1180 r doses. (See fig. 2, broken line!)

Secondary Reaction. (Erythema and additional tanning). By the 19th and 20th day 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 the 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% of the cases receiving 635 r, but was present in 90% of those receiving 813 r and above. The erythema from 813 r and 1000 r persisted for nearly 60 days, while that for 1180 r persisted for 70 to 80 days. The exact time of disappearance cannot be stated definitely because of the coexisting tan. One could not 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 week post exposure. These were followed by a dry spotty desquamation of the most superficial layers of epithelium. The difference in response between male and female subjects was less notable than the difference in response between blonde and brunette skins. Similar doses produced more erythema in blonde skin than in brunette. The series of cases was too small to draw any conclusions as to the differ-

ence of intensity or persistence of tanning between blonde and brunette skin.

Tanning. The tanning, even from the small doses of 200 to 250 r, persisted on some people for as long as 10 weeks, but all disappeared entirely by the 17th week. In the higher doses, such as 1180 r, the tanning remained longer than 160 days in some 70% of the cases, while at 8 months there was still some persistent tanning in 25%. The differences in duration of the tanning reaction from doses of 635 and 1180 r may be seen readily from the dotted lines on the graphs in fig. 2.

Threshold Erythema. If one accepts as the criterion for a threshold erythema that 80% of those exposed show an erythema, then a dose somewhat greater than 635, and probably in the region of 813 r, may be considered the threshold erythema dose for beta rays from a one inch 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 suggested by Harris, Leddy and Sheard. (9)

Summary and Conclusion. 1. In determining responses of human skin to beta radiation a distinction must be made between a threshold reaction and a threshold erythema. 2. A threshold reaction (mild tanning) can be produced in 80% of those exposed to the beta radiation from a one inch diameter P^{32} contact plaque by a dose of 200 rep, and in only 60% of those exposed to 170 rep. 3. A threshold erythema may be produced under similar circumstances in 80% of those exposed to 813 rep. and in 60% of those exposed to 635 rep. 4. A larger number of cases than used here are necessary to determine correct figures within a narrower range. 5. The above preliminary experiments indicate the levels at which a larger series of cases should be exposed.

B I B L I O G R A P H Y

- (1) Leddy, E.T., and Weatherwax, J.L.: Erythema Dose as the limit in Deep Roentgen Therapy Dosimetry. Am. Jour. Roentgenol. & Rad. Ther., 12, 514-518, (1924).
- (2) Failla, G., Quimby, E.H., and Dean, A.: Radiation Therapy. Am. Jour. Roentgenol. and Rad. Ther., 9, 479-497, (1923).
- (3) Dean, A.L., Jr.: Results of Skin Tests Made to Determine an Objective Dose for Radium Radiations. Am. Jour. Roentgenol. and Rad. Ther., 10, 654-661, (1923).
- (4) Quimby, E.H., and Pack, George T.: Skin Erythema for Combinations of Gamma and Roentgen Rays. Radiology, 13, 306, (1929).
- (5) Quimby, Edith H., and Pack, George T.: Further Studies on the Skin Erythema with Combinations of Two Types of Radiation. Radiology, 15, 30-38, (1930).
- (6) Wilhelmy, E., Uber die Reaktionen de Haut auf Langwallige Rontgenstrahlen und Kathoderestrahlen. Strahlentherapie, 55, 498-523, (1936).
- (7) Raper, John R., Zirkle, R.E., and Barnes, E.K.: Technique of External Irradiation with Beta Rays. CH-3098 (June 30, 1946).
- (8) Parker, Herbert M.: Some Physical Aspects of the Effects of Beta Radiation on Tissue. CH-930 (Sept. 10, 1943).
- (9) Harris, Milo, M.D., Leddy, Eugene T, M.D., and Sheard, Charles: The Spectrophotometric Analysis of the Color of the Skin following Irradiation by Roentgen Rays. Radiology. 19, 233-256. (1932).