PRODUCTION OF EPITHELIAL TUMOURS BY A COMBINATION OF BETA RADIATION AND PAINTING WITH BENZPYRENE

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In a previous paper (1) it has been shown that if mice be painted with 0.5 per cent solution of 3:4-benzpyrene \(^1\) in benzoI twice a week for ten weeks, and on the sixtieth day a dose of from 176 to 1584 \(r\) gamma radiation be

![Diagram of a mouse showing painted skin and radiation application](image)

**Fig. 1.** Mouse viewed from above, showing long area of painted skin (A + C), with the upper half covered by the square radium applicator (A) which extends over unpainted skin (B, B) on either side.

Other areas receiving various doses of radiation are indicated by X.

applied, both benign and malignant tumours occur; no tumours follow painting for the same period without irradiation. In the present paper, this observation is extended to beta radiation, and the conditions for the formation of epithelial tumours by this double treatment are now more precisely defined.

An area along the back behind the head, 4 cm. long by 1 cm. wide, was painted with benzpyrene twice a week for ten weeks. On the sixtieth day a single dose of beta radiation was applied with a square applicator containing 60 mg. of radium, 2 \(\times\) 2 cm. in area, screened with 0.12 mm. silver. Forty minutes’ exposure was given, corresponding to 6000 \(r\) units to the surface of the skin. This was applied to half the painted area and adjacent unpainted

\(^1\) Originally termed 1:2-benzyprene but now designated 3:4-benzpyrene in the interest of a uniform nomenclature (see Am. J. Cancer 29: 221 (footnote), 1937).
skin on either side. In all, 20 mice were treated: in 10 the upper half of the painted skin was irradiated, and in 10 the lower half; one died early in the experiment and is not included in the report.

![Diagram](image)

**Fig. 2. Painted Areas in Seven Tumour-Bearing Mice, Viewed from Above with the Heads of the Animals Away from the Observer**

The ruled half indicates that which was under the radium applicator, A in Fig. 1; the unrulled half, that which was not covered by the radium, C in Fig. 1. Black dots indicate the place of origin of the warts. Circles round the dots indicate squamous epitheliomas. The figures to the left of the dots give the day of origin figured from the application of radium.

The conditions of the experiment are illustrated in Fig. 1. In this instance the upper half of the painted area was irradiated. In determining the results, several different areas of skin must be considered. In the first place, there are the two areas under the radium applicator: A the painted and B the unpainted (Fig. 1). In neither of these areas did any epithelial tumours occur. All around the applicator, which was applied touching the skin, is a third area, X X X, which received varying quantities of radiation according to the distance from the radium. As will be seen, the dosage here varied from about 40 r at 2 cm. from the applicator up to about 2800 r close to its edge. No tumours occurred in these areas. Lastly there remains to be considered that part of the painted skin not under the radium applicator, C, which, as will be seen, received radiation varying from 2800 r close to the applicator,
FIG. 3. DISTRIBUTION OF BETA RADIATION IN R/MINS. FROM THE EDGE OF THE APPLICATOR, WHERE IT IS ABOUT 70 R/MINS., OUTWARD FOR A DISTANCE OF 13 MM., WHERE IT IS ABOUT 10 R/MINS.

With an exposure of forty minutes the dose varied from 2800 r close to the radium, down to about 400 r at 13 mm. On this distribution curve are shown the points of origin of the tumours both benign (dots) and malignant (dots with circles). This figure was kindly prepared by Dr. Gray, physicist to the hospital.

down to a few r at the points farthest distant from the radium. In this area many epithelial tumours were observed.

Twelve warts occurred in 7 out of the 19 mice, and 9 of these were cancerous. In the case of mouse No. 7 the growth was more like a spindle-cell sarcoma than a spindle-cell epithelial tumour. Especial attention is drawn to the distribution of the tumours (Fig. 2); all occurred near to the radium applicator; none at any great distance.
If now we examine the radiation energy set free in this area of skin, it is found to have the distribution shown in Fig. 3. The figure shows that warts occurred on the painted skin which had received from 800 to 2800 \( r \) units, and more especially on the skin which had received about 2400 \( r \) units. No warts occurred below 800 \( r \) units, and as has been seen, none occurred at 6000 \( r \) units under the radium. Only a very narrow line of skin, between the edge of the applicator and its face, received between 2800 and 6000 units, so that the experiment does not indicate what the production of tumours would be within this range. At 6000 \( r \) units, under the applicator, the skin showed transient ulceration, healing taking place from the surrounding unpainted epidermis; it is probable that this destruction of the epidermis accounts for the absence of tumours here.

The time of origin of the tumours is given in Fig. 2. This is decidedly less than when painting alone is employed, in which circumstances, tumours seldom arise before a hundred days. It is also to be noted that only 3 tumours appeared after a hundred days, and none after a hundred and fifty days; whereas with painting alone they continue to appear for much longer periods of time.

This curtailed period of tumour development suggests that the warts were caused by the single exposure of radium. If this be so, then good opportunity is given to investigate the latent period, since the time of application of the cancer-producing agent is given with precision. It should be possible to decide accurately whether the tumours arise from many or single cells, by a method previously followed (2), observing the growth rate of the tumours, calculating back to the time when they would be single cells, and determining whether or no this corresponds with the time when the radiation was given.

The results show that it is probably dangerous to treat precancerous lesions with doses of radiation lower than are required to kill all the epithelial cells; they indicate further the possible danger of exposing such lesions to sunlight, since ultraviolet radiation is known to be carcinogenic and may well have the same action as beta and gamma radiation.

**Conclusions**

The experiments show some of the conditions necessary for the production of epithelial tumours in mice by the combined action of painting with benzpyrene twice a week and a single exposure to beta radiation.

An amount of painting insufficient to produce warts, combined with a single exposure of from 800 to 2500 \( r \), results in the production of tumours both benign and malignant.

**References**