COMBINED ACTION OF UV IRRADIATION AND 7,12-DIMETHYLBENZ(a)ANTHRACENE ON THE SKIN OF HAIRLESS MICE

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From 4 to 6 months after the beginning of combined treatment lasting 22 weeks, a decrease in the number of tumors was found in mice irradiated after application of 7,12-dimethylbenz(a)anthracene (DMBA). However, toward the end of the experiment this difference disappeared and no statistically significant differences were observed in the number of tumors in mice receiving DMBA alone or DMBA in any combination with UV irradiation. No tumors appeared in animals receiving UV irradiation only.

Cancer and precancerous keratoses of the skin are more frequent in the south than in the north. This fact is explained by the carcinogenic action of UV rays in the range of wavelengths between 2900 and 3441 Å [3].

Experimental tumors can be obtained in animals by excessive solar irradiation [1, 4] and by UV irradiation [2, 5].

Experimental tumors of the skin have been induced in animals by UV rays with wavelengths of between 2537 [3] and 3341 Å or more, i.e., over a wider range of wavelengths than has been established for man. However, much about the action of UV light still remains unexplained. For instance, the problem of the combined action of UV light and chemical carcinogens, which is the situation usually found in everyday life, has not yet been finally solved.

In the present investigation some aspects of the combined action of UV light and a chemical carcinogen were studied.

EXPERIMENTAL METHOD AND RESULTS

The experiments were carried out on hairless mice bred by the authors from an original strain obtained in Iversen's laboratory in Norway.

7,12-Dimethylbenz(a)anthracene (DMBA), as a 1% solution in benzene, was applied to the skin at three points of the animal's back. For this purpose, with a fine pipet the same dose of carcinogen was applied to the skin of the mice, always in a definite place (the skin was only just touched).

Altogether 131 animals, both males and females, were used in the experiment and were distributed into four groups.

The animals were irradiated under a BUF-30 lamp with a wavelength of 3660 Å, at a distance of 15 cm from the source for 30 min once a week. Before irradiation the mice were firmly secured to a frame and covered with a wooden screen with a wide slit through which the UV rays could fall on a particular area (always the same) of the back. Altogether, 22 weekly sessions of irradiation were given and DMBA was applied to the irradiated area at the ends and in the middle of the slit for 22 weeks.

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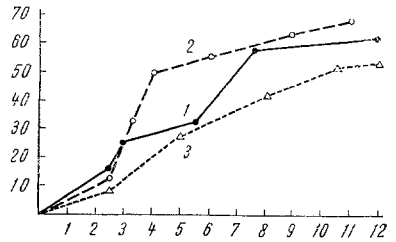

Fig. 1. Dynamics of appearance of skin tumors under the influence of combined UV irradiation and treatment with DMBA. Abscissa, time from beginning of experiment (in months); ordinate, number of animals with tumors (in percent). 1) DMBA; 2) UV irradiation plus DMBA; 3) DMBA plus UV irradiation.

The animals of group 1 were irradiated only with UV rays. Treatment with UV rays and DMBA was given consecutively on the same day to the animals of groups 2 and 3: group 2 was first irradiated with UV rays, then treated with DMBA, while group 3 was treated in the opposite order. The mice of group 4 were treated with DMBA solution only.

The animals were kept under observation for 1 year after the end of treatment, i.e., until the age of 19-20 months.

Irradiation for 30 min caused erythema and puffiness of the skin. The erythema rapidly subsided. After repeated irradiation the skin became thickened, keratinized, and pigmented. However, no tumors appeared in the animals irradiated with UV rays.

The sourse of neoplasia under the different experimental conditions is shown graphically in Fig. 1.

In the mice of group 4, after application of DMBA only, papillomas appeared 2.5 months after the beginning of the experiment: in 18.7% of males (three of 16 mice) and in 10% of females (one of ten mice).

In the animals of group 2 (UV + DMBA) the first papillomas were found at the same time: in 16.6% of males (two of 12 mice) and 22.7% of females (five of 22 mice).

In the mice of group 3 (DMBA + UV) the papillomas appeared rather later, after 2 weeks, and they were fewer in number than in the animals of groups 2 and 4: in 7.6% of males (one of 13 mice) and in 8.3% of females (one of 12).

Hence, by the 4th-6th month differences were found between the groups. In the mice irradiated with UV rays after application of DMBA, tumors began to appear later and in a smaller percentage of cases. Later this difference disappeared. It may be that under the influence of UV rays the carcinogen was partially destroyed and its dose reduced.

The results obtained at the end of the experiment showed that tumors still had not developed in the animals of group 1, in group 2 they were present in 23 (65.7%) of the 35 mice surviving until the appearance of the first tumor, in group 3 they were present in 21 (55.5%) of the 38 animals, and in group 4 in 16 (61.5%) of the 26 animals. The differences obtained were not statistically significant. In these experiments UV irradiation thus had no significant effect on carcinogenesis in the skin.

The results of microscopic investigation of the tumors obtained in the hairless mice showed that they are indistinguishable from such tumors in ordinary mice: the animals developed papillomas, some of which changed into a keratinizing squamous-cell carcinoma.

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