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CARCINOGENESIS INDUCED BY POLYCYCLIC  
AROMATIC HYDROCARBONS IN MALE AND  
FEMALE (CBA × C57/BL)<sub>F</sub><sub>1</sub> MICE

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UDC 616-006.6-092.9-02:  
[615.277.4:547.6

Sex differences were found in the development of skin tumors induced by 3-methylcholanthrene and benz(a)pyrene in (CBA × C57/BL)<sub>F</sub><sub>1</sub> mice. Males were more susceptible to the induction of skin tumors than females.

KEY WORDS: carcinogenesis; 3-methylcholanthrene; benz(a)pyrene; sex differences.

Sex differences in the statistics of malignant neoplasms have been found in both clinical and experimental studies [4]. Excluding the reproductive organs, cancer is found much more frequently among men than among women. This applies to malignant neoplasms of the liver, lungs, stomach, rectum, pancreas, urinary bladder, skin, etc. The exceptions are carcinoma of the thyroid gland and melanoma, which are more common in women.

Experimental findings also confirm the presence of sex differences in the development of both spontaneous tumors and tumors induced by chemical carcinogens in hamsters, rats, and mice. There is comparatively little information in the literature on the effect of the sex of experimental animals on the development of cutaneous chemically induced carcinogenesis. For instance, according to Bates [1], male mice are more susceptible to the carcinogenic action of 7,12-dimethylbenzanthracene than females. A similar fact has been observed by other workers studying hamsters [3] and rats [2] following subcutaneous injection of 3-methylcholanthrene.

The object of this investigation was to study whether sex differences occur in the frequency of skin tumors induced by polycyclic aromatic hydrocarbons (PAH) in hybrid (CBA × C57/BL) mice.

#### EXPERIMENTAL METHOD

Mice aged 2 months were used. The carcinogens were 3-methylcholanthrene (3-MC) in 0.5% solution in benzene and benz(a)pyrene (BP) in a 0.6% solution in benzene. In the experiments of series I 3-MC was applied to a previously shaved area of skin in the interscapular region in a dose of 0.02 ml daily until the appearance of malignant tumors. In the experiments of series II 3-MC was applied once in the same dose followed 2 weeks later by applications of a 1% solution of croton oil in benzene once a week in a dose of 0.02 ml until the 20th week of the experiment. In series III BP was applied in a dose of 0.02 ml weekly until the 24th week of the experiment. The following parameters were determined: The time of appearance of the first papilloma and the first carcinoma, the mean latent period of their development, the mean number of papillomas per mouse until the time of appearance of the first carcinoma, the percentage of mice with papillomas in the 20th week, and the percentage of mice with carcinomas in the 24th week. Statistical analysis was carried out by Student's method.

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Laboratory of Carcinogens, Institute of Nutrition, Academy of Medical Sciences of the USSR. (Presented by Academician of the Academy Sciences of the USSR N. A. Fedorov.) Translated from Byulleten' Eksperimental'noi Biologii i Meditsiny, Vol. 82, No. 10, pp. 1244-1245, October, 1976. Original article submitted March 23, 1976.

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TABLE 1. Cutaneous Carcinogenesis Induced by 3-MC and BP in Male and Female (CBA  $\times$  C57/BL) $F_1$  Mice

Series No.	Number and sex of mice	Time of appearance, weeks		Mean latent period of development, weeks		Mean number of papillomas per mouse	% of mice with	
		of first papilloma	of first carcinoma	of papillomas	of carcinomas		papillomas by the 20th week	carcinomas by the 24th week
I	48♂♂	4	13	12.4 $\pm$ 0.52	21.1 $\pm$ 0.37	4.75 $\pm$ 0.31	100	100
	49♀♀	7	19	14.8 $\pm$ 0.36	22.7 $\pm$ 0.26	3.71 $\pm$ 0.20	100	30
	34♂♂	10	—	14.1 $\pm$ 0.73	—	1.91 $\pm$ 0.22	50 $\pm$ 7.3	—
II	46♀♀	10	—	15.4 $\pm$ 0.78	—	1.20 $\pm$ 0.08	43 $\pm$ 7.2	—
	50♂♂	9	20	16.0 $\pm$ 0.31	22.8 $\pm$ 0.34	5.00 $\pm$ 0.33	100	86 $\pm$ 5.8
III	45♀♀	15	21	20.0 $\pm$ 0.37	24.5 $\pm$ 0.37	2.61 $\pm$ 0.15	70	43 $\pm$ 7.2

Legend. —) No carcinomas present.

## EXPERIMENTAL RESULTS

The results are given in Table 1. They show that in the experiments of series I the mean latent period of development of papillomas in the males was 2.4 weeks shorter ( $P < 0.001$ ) and of malignant tumors 1.6 weeks shorter ( $P < 0.001$ ); the mean number of papillomas per mouse was greater by 1 ( $P < 0.01$ ).

In series II in the experiments to study cocarcinogenesis there was a tendency for papilloma development in the males to be more rapid, and the difference in the mean number of papillomas per mouse was significant ( $P < 0.01$ ).

In series III the mean latent period of development of papillomas also was shorter by 4 weeks in the males ( $P < 0.001$ ), for carcinomas it was 1.7 weeks shorter ( $P < 0.001$ ), and the mean number of papillomas per mouse was higher by 2.4 ( $P < 0.001$ ); the number of mice with carcinomas was 37% higher than the number of females ( $P < 0.001$ ). The results thus point to the existence of sex differences in the development of skin tumors induced by PAH in mice: In this case also males proved to be more susceptible to the induction of skin tumors by chemical carcinogens.

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