In the Hymenoptera, polymorphism finds expression commonly in diploid individuals, rarely in haploid individuals. In many, if not all, polymorphic species, under natural conditions, the production of diploid eggs greatly exceeds that of haploid eggs.

In social species the low incidence of male polymorphism may result either from the mortality of the partially absorbed unfertilized egg, from the fertilization of all the partially absorbed eggs deposited, or from the relatively small nutritional needs of haploid individuals.

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Carcinogenic Substances From Pituitary Glands of Cattle

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The discovery of carcinogenic chemical substances suggested that in certain conditions analogous substances are produced within the organism and thus become responsible for cancerous growth.

Schabad (*12, 14, 15*) obtained a lipid extract from the liver of a patient who died of stomach cancer, and this extract, when injected into white mice, induced malignant tumor growth in some of the animals treated.

In further investigations Schabad, *et al.* (*4, 5*) prepared extracts of human livers from cancerous as well as noncancerous individuals. Of the white mice injected with these extracts about one-third died within the first few months of the experiment. A number of animals which lived to an age of more than 8 months following the first injection developed malignant tumors.

The findings of Schabad were confirmed by other investigators (*1–3, 13, 16–19*).

It must be added that Menke (*10, 11*) injected lipid extracts from human mammary cancers into white mice, and of 36 mice injected, 7 developed sarcomas after 7 to 14 months.

The above experiments indicate that carcinogenic chemical factors of a lipid nature are present in the cancerous as well as in the normal organism. Thus, the question arises as to the origin of these substances.

For investigation of this problem we employed our previous studies, which indicate that the pituitary gland is connected in a hormonal way with the development of cancer (*6, 7*). We therefore examined extracts of the pituitary gland for presence of carcinogenic hormonal factors.

EXPERIMENTAL

In our experiments fresh pituitary glands from cattle were freed from adjacent tissues and the anterior and posterior lobes of the gland carefully separated. One hundred posterior lobes or 50 anterior lobes were used for the preparation of each lipid extract.

The glands were extracted with acetone, ethyl ether, and alcohol, and the brownish oil obtained was suspended in sweet almond oil and injected subcutaneously into white mice of our own breeding. Our purebred strain of mice has a low incidence of spontaneous tumors (two mammary tumors in 1,700 mice).

The amount of extract obtained each time varied from 300 to 800 mg. The animals received 10 to 30 mg. each as a single injection, no difference in the effects being noted with variation of the dose within these limits.

Four extracts were prepared from the anterior pituitary, and 32 white mice were given a single injection of the extracts.

Seven mice died during the first 4 months of the experiment. Of the remaining 25 animals injected with the anterior lobe extracts, 9 developed malignant tumors: 4 females developed breast cancer (after 7, 7, 10, and 14 months), 1 male and 1 female developed carcinoma at the site of injection (after 13 and 6 months), 1 male and 2 females developed liver cancer (after 8, 9, and 8 months).

Of the 16 animals which died without developing tumors, the individuals survived as follows: 3 for 7 months, 3 for 8 months, 2 for 10 months, 1 for 11 months, 2 for 12 months, 3 for 13 months, 1 for 14 months, and 1 for 19 months.

Of the four extracts prepared from the anterior lobe, one caused no malignancy in the animals injected, while another provoked 5 various tumors in 6 injected mice. The remaining two extracts provoked malignancy in 20.6 per cent of the animals injected.

Five extracts were prepared from the posterior lobe of the pituitary gland, and 35 animals were given a single injection of the extracts.

Twelve mice died during the first 4 months of the experiment. Of the remaining 23 animals injected,

9 developed malignant tumors: 3 females developed breast carcinoma (after 5.5, 16, and 19 months), 1 female and 2 males developed lung carcinoma (after 18, 16, and 22 months), 1 male developed liver carcinoma (after 11 months), and 2 males developed sarcoma at the site of injection (one lymphosarcoma after 9 months, and one spindle cell sarcoma after 11 months).

Of the 14 animals injected and dying without developing tumors, the individuals survived as follows: 1 for 9 months, 2 for 11 months, 3 for 13 months, 3 for 15 months, 1 for 16 months, 2 for 17 months, 1 for 19 months, and 1 for 22 months.

Of the five extracts prepared from the posterior lobe, one caused no malignancy in the animals injected, while another provoked 3 breast cancers in 4 mice injected. The remaining three extracts provoked malignancy in 25.4 per cent of the animals injected.

Discussion

In our experiments lipid extracts prepared from the beef pituitary and injected into white mice provoked the growth of malignant tumors in a number of the animals injected. Extracts from the anterior lobe as well as extracts from the posterior lobe of this gland were equally active, provoking malignancy in 26.8 per cent of the animals used in the experiments.

The malignant tumors usually developed in organs at a distance from the site of injection, only 4 animals (of 18) developing cancer at that place.

The malignancy appeared in various histological types including carcinoma as well as sarcoma.

The only difference in the carcinogenic activity noted between the extracts of the anterior lobe and those of the posterior lobe of the gland involves the time of development of tumors after injection. The tumors developed earlier after injection of the anterior lobe extracts than after injection of extracts of the posterior lobe. Of the 9 cancers observed in each of the two experimental series, 8 developed during the first 10 months of the experiment in the series injected with anterior lobe extracts. During that period of time only 2 cancers developed in mice injected with the posterior lobe extracts. The calculated average period of time necessary for the development of the tumor is: for anterior lobe extracts, 9.3 months; for posterior lobe extracts, 14 months.

Assuming that the same chemical agent causes malignancy after injection of the anterior or posterior lobe extracts, an additional factor which accelerates the development of tumors must be present in the extracts prepared from the anterior lobe of the gland. The lipid growth-accelerating hormone isolated by Lustig and Wachtel (*8, 9*) from the anterior pituitary lobe can be considered correlated with the causation of this phenomenon as it markedly increases the growth rate of transplantable mice tumors.

The differences in the degree of the carcinogenic activity observed with different extracts prepared from both lobes of the pituitary gland are still to be explained. Many factors may be operative, e.g. differences in response of animals treated, differences in dosage, or imperfection in the method of extraction. It is also probable that the inactive or feebly active extracts include an unknown factor which renders the carcinogenic component ineffective. If that factor is lost during the extraction, the carcinogenic activities of the extract attain full opportunity for their development. Further experiments for clarification of this subject are in progress.

The histological diagnosis of the tumors was verified by Dr. Francis Carter Wood, to whom we are indebted for his cooperation.

Summary

Lipid extracts from the pituitary gland of cattle were prepared which, when injected into a pure strain of white mice, caused development of malignant tumors in 26.8 per cent of the 67 animals injected, which corresponds with the numerical results obtained by investigators working with human liver extracts. Evidently the carcinogenic power of these lipid extracts is low. The tumors developed chiefly in organs at a distance from the site of injection, exhibiting various histological types including carcinoma as well as sarcoma. The tumors developed at an earlier date after injection of extracts from the anterior lobe as compared with those developing after injection of the posterior lobe extracts, the average period of time necessary for their development being 9.3 months for the anterior lobe extracts and 14 months for posterior lobe extracts.

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