

# Spontaneous and Induced Tumors of the Guinea Pig

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(Received for publication November 16, 1940)

The occurrence of tumors in the guinea pig is apparently less frequent than in other laboratory animals. Spontaneous tumors are quite rare and only a few transplantable tumors of the guinea pig are available. Jackson (22) in his monograph on the incidence of tumors of domesticated animals made no mention of guinea pig tumors.

One of the best known guinea pig tumors is Murray's (44) transplantable liposarcoma, non-metastasizing, which was primary in the mamma. Migunow (42) reported a non-metastasizing carcinoma of the breast in a male guinea pig. Two papillary cystadenomas of the breast were found by Apolant (3) and an adenocarcinoma of the breast by Sternberg (56) and one by Jones (23). Katase (24) mentioned a sweat gland carcinoma of the breast. A possibly induced, but probably spontaneous, tumor was the mammary adenoma studied by Anderson and Lumbroso (2) in a female guinea pig injected with urine which was being tested for the presence of tubercle bacilli. Blumensaat and Champy (8) found an apparent carcinoma of the right breast in a four year old female guinea pig with ovarian cysts. There were no metastases and grafts were not successful.

Giordano (17) reported a spontaneous teratoma in the ovary of a pregnant guinea pig. The Guérins (20) reported a malignant splenoma. Kröning and Wepler (28) found a spontaneous lipomyxofibroma of the psoas. Leader (30) reported an osteogenic sarcoma of the femur, and Roffo (47) mentioned a transplantable sarcoma. Brunschwig (9) reported a dermoid of the cornea. A teratoma of the pons was described by Lutz (39). Babet and Bloch (5) reported a spontaneous tumor of the abdominal wall which they considered a schwannoma. There were no metastases and they made no attempts to transplant it. Maury's thesis (40) on tumors of the guinea pig is said to have emphasized their rarity, but it is not available to us.

A spindle cell sarcoma of the subcutaneous tissue of the back in a male guinea pig which metastasized to the spleen, and one of the subcutaneous tissue of the chest in a female which metastasized to lymph nodes, liver, spleen, lungs, ovaries, adrenals, and uterus were reported by Lubarsch (37). Both were transplantable. Bender (6) reported a round cell sarcoma of the heart of a guinea pig. Roskin (48) reported a malignant tumor of the adrenal of a guinea pig. Adenomas of the adrenal cortex developed after several years in guinea pigs castrated during the first days of life by Spiegel (53).

Two cases of adenoma of the bronchus were reported by Sternberg (55) and others by Spronck (54).

Loeb (36) reported 23 benign lesions of the ovary resembling chorio-epithelioma among 380 animals.

A probable lymphosarcoma was found by Miguez (41). Leukemia in the guinea pig was studied by Snijders (52).

The biliary tract of the guinea pig appears to be most susceptible to the development of induced malignancy. The earliest report of induced tumors of the guinea pig was that of

Kazama (25). This report is not altogether clear as an unknown number of animals lived for only a short period of time. However, the frequency of development of tumors was very striking. When gall stones or pebbles were placed in the gall bladders of 30 guinea pigs, adenocarcinomas developed in 7 animals and metastases developed in 4. Stones placed in the stomachs of 20 guinea pigs produced no carcinomas. String sutures placed in the gall bladders of 23 guinea pigs produced adenocarcinomas in 6 animals, one of which metastasized; and mucosa placed in the gall bladders of 2 animals produced carcinomas in both, one of which metastasized. "Pityrol" injected into the stomachs of 7 guinea pigs and the urinary bladders of 7 guinea pigs produced no carcinomas, but when injected into the gall bladders of 16 guinea pigs it produced carcinomas in 8 animals. Lanolin injected into the urinary bladders of 3 animals produced no carcinomas, but when injected into the gall bladders of 27 it produced carcinomas in 6 animals. Tar injected into the gall bladders of 2 guinea pigs and into the urinary bladders of 2 others produced no carcinomas. This high percentage of successfully induced tumors has not been achieved by other workers.

In 1924 Kazama (26) reported that various types of irritants in the gall bladders of 244 guinea pigs produced 30 papillomas, 49 heterotopic growths, 60 atypical growths, and 101 adenocarcinomas of which 23 metastasized. Leitch (31) confirmed Kazama's results, producing 8 carcinomas of the gall bladder in 40 guinea pigs by implanting gall stones, pebbles, or pitch pellets. Delbet and Godard (13) produced in 6 guinea pigs, by the implantation of human gall stones within their gall bladders, 1 probable adenocarcinoma and, in a second series of 10 guinea pigs, 3 probable adenocarcinomas. They obtained no metastases and made no transplants. They reported that the injection of tar was without effect. The injection of irradiated ergosterol into the gall bladder by Schmid (50) produced tumors.

Radiation has produced tumors. One of 20 guinea pigs, 15 months after x-ray radiation, developed a polymorphocellular sarcoma of the back which did not metastasize and could not be transplanted (19). A chondrosarcoma of the tibia was produced by repeated x-ray radiation (38).

Another method of production of tumors by radiation was developed by Daels and Biltris (12). These experiments were broadened by Biltris (7) who produced, by the implantation of small amounts of radium element in collodion, a spindle cell sarcoma of the kidney, a spindle cell sarcoma of the meninges, and an intra-abdominal spindle cell sarcoma arising from the abdominal wall which was successfully transmitted by grafting; 6 carcinomas of the biliary tract, 1 of which produced metastases; and 2 tumors of the spleen. Gavrilov, Demoor, and Fester (15) found that no tumors could be produced by the injection of guinea pigs with the filtrate of the Daels-Biltris sarcoma and that repeated injection of the animals with embryonic guinea pig juice increased the number of induced tumors from 75 per cent to 90 per cent. Gavrilov and Silberfeld (16) reported that 11 of 74 guinea pigs injected with the Daels-Biltris tumor developed metastases.

Foulds (14) produced both carcinoma and sarcoma in guinea

pigs by injections of thorotrast. These tumors were transplantable and developed in 4 out of 9 guinea pigs given small injections of thorotrast in the breast tissue. Tumors comprised a carcinoma, 2 sarcomas, and a fibrosarcoma, of which only the first 3 were transplantable.

Petrov and Krotkina (46) placed radioactive glass in the gall bladders of 12 guinea pigs and produced metastasizing carcinoma in 2. They also placed glass without radioactivity in the gall bladders of 7 guinea pigs and produced metastasizing carcinoma in 2.

Lipschütz and others (33-35) have produced atypical uterine epithelium in guinea pigs by repeated injections of estradiol. Moricard and Cauchoix (43) produced large fibromas in the female guinea pig by injection of a benzoate of dihydrofolliculin. Nelson (45) reported in 1937 the production of fibromatous nodules in the uterus of guinea pigs by the prolonged administration of estrogenic hormones. While extreme growth of the cervical epithelium with metaplasia may be produced by administration of estrogens to the female guinea pig, Allen (1) found no instance of cervical carcinoma. Champy (10) produced adenomas and cysts in the ovaries of guinea pigs injected with folliculin.

The production of tumors in guinea pigs by injection of bacteria cultured from human carcinoma has been reported by Glover, and his views in this highly controversial field have been recently put forth (18).

Carcinogenic hydrocarbons have rarely been effective in producing tumors in guinea pigs. Instillation of tar into the bronchial tree produced adenocarcinoma of the bronchial epithelium (27). In 1936 Cirio (11) reported that he had painted guinea pigs with tar carcinogenic for mice and had obtained no tumors up to 2½ years. Latteri (29) succeeded in producing a tar cancer in the kidney of guinea pigs. Liberti (32) was unable to produce cancer with 1,2-benzopyrene (3,4-benzopyrene) in guinea pigs although it was carcinogenic for white mice and rats. A sarcoma of the heart, probably spontaneous, developed in 1 of 33 guinea pigs injected with methylcholanthrene (4). Liposarcomas were produced in 4 guinea pigs by 1,2-benzopyrene (3,4-benzopyrene) injected subcutaneously by Haagensen and Krehbiel (21), who also mentioned that only 2 spontaneous tumors of guinea pigs had been observed in 23 years at the Institute of Cancer Research of Columbia University. Painting the skin of guinea pigs with 1,2-benzopyrene (3,4-benzopyrene) failed to produce tumors (49).<sup>1</sup>

Shear (51), in collaboration with Drs. P. R. Howe and M. Elliott, injected 23 guinea pigs subcutaneously with 5 mgm. of crystalline 3,4-benzopyrene. Nineteen lived for 20 months, 1 developing a tumor during the 14th month which killed the animal in the 23rd month, and 1 developing a tumor at 20 months.

We have encountered only 1 spontaneous tumor in a guinea pig. The animal was received from a dealer in 1935 and proved to have a fibrosarcoma, probably of neurogenic origin, which had developed over the angle of the right jaw and which was ulcerated and partly necrotic. Attached to the maxilla and infiltrating the soft parts, it extended downward and mesially. X-ray of the bone was negative. The tumor, on removal, had a total volume of 4.5 cc. Centrally it was

<sup>1</sup> Reimann states he has rubbed with dibenzanthracene the skins of a number of guinea pigs three times a week for 5 years, the animals dying of old age without evidence of cancer. (Reimann, S. P. *The Biology of the Cancer Cell*. Am. J. Roentgenol. 43:275-281. 1940.)

necrotic. On section, the viable portion was pale pink, fibrous, firm, and infiltrating the adjacent muscle. Transplants were made subcutaneously in the flank of 20 stock guinea pigs. Local tumors were obtained in 6 of the 20 animals. Transplants from one of these gave a subsequent tumor in 1 of 6 animals, and from another in 1 of 5 animals. Further transplants were unsuccessful. No metastases appeared in any animal.

We have found it difficult to induce tumors by carcinogenic hydrocarbons. In a series of 30 guinea pigs on a scorbutic diet (Howe-Wolbach), given just sufficient orange juice from time to time to prevent death from scurvy, 1 small nodule of actively proliferating granulomatous tissue appeared at the end of 142 days as a result of repeated injections subcutaneously of 1,2,5,6-dibenzanthracene (Eastman) dissolved in lard oil. This nodule we did not consider to be neoplastic. The other animals gave a completely negative reaction, as did the 6 similarly injected control animals on the same diet given an adequate amount of orange juice daily. Since in this series of experiments only a few of the animals lived beyond 100 days, the results were of little value.

No tumors developed in 12 normal guinea pigs which were followed for 15 months after subcutaneous injection with 5 mgm. of 1,2,5,6-dibenzanthracene in cholesterol pellets.

In a subsequent series of 44 normal guinea pigs woolen yarn which had been saturated with a benzene solution of 1,2,5,6-dibenzanthracene and allowed to dry was implanted subcutaneously. The dose was approximately 1 mgm. per animal. The animals were killed at intervals up to 4 months. No histologic evidence of tumor was obtained although there was marked focal necrosis and fibroblastic proliferation immediately surrounding the dibenzanthracene.

In a third series of experiments in which 5 mgm. of 3,4-benzopyrene (Hoffman-LaRoche, m. p. 178-179° C) suspended in 0.5 cc. of glycerine were given in a single injection subcutaneously, 53 guinea pigs lived over 196 days after inoculation (Table I), and 24 lived over 500 days.

Four tumors were obtained: a liposarcoma at 340 days, a fibrosarcoma at 454 days, a fibrosarcoma at 561 days, and a malignant mesenchymal tumor, probably a liposarcoma, at 579 days. This last tumor was noted when about 1 cm. in diameter, and killed the animal 53 days later, reaching a size of 4x5x5 cm. In none of the animals did metastasis occur. Death was apparently due to cachexia in all cases, probably secondary to the large size of the tumor and absorption from necrotic portions. Transplants were attempted from only 1 tumor, as the other 3 animals with tumor were found dead. From that tumor, a fibrosarcoma, no takes were obtained in 8 animals. Grafts of any tumor

of the guinea pig rarely take as well as do those of transplantable tumors in mice, rats, or rabbits. Possibly better results would be obtained if guinea pigs of pure strain were used. These experiments were carried out on heterozygous animals.

TABLE I: RESULTS OF SUBCUTANEOUS INJECTION OF GUINEA PIGS WITH 3,4-BENZOPYRENE SUSPENDED IN GLYCERINE

No tumor		Tumor		
Days after injection still alive	No. of animals	Days after injection tumor found	No. of animals	Type
196	11			
230	3			
289	1			
330	6			
367	1	340	1	Liposarcoma
371	1			
373	1			
395	1			
405	1			
425	1			
454	1	454	1	Fibrosarcoma
472	1			
519	3			
		561	1	Fibrosarcoma
		579	1	Liposarcoma (?)
589	6			
646	1			
654	9			
779	5			
	—			
	53		4	

SUMMARY

1. Cases of development of tumors, both spontaneous and induced, in guinea pigs have been collected.
2. One spontaneous and 4 induced tumors are reported.
3. The guinea pig appears to be resistant to the development of spontaneous tumors; to transplantation, at least in heterozygous animals, of tumors spontaneous and induced; and to the production of induced tumors other than of the gall bladder.
4. Carcinogenic hydrocarbons are much less potent in guinea pigs than in mice.

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