Spontaneous and Induced Tumors of the Guinea Pig

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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. Mignow (42) reported a non-metastasizing carcinoma of the breast in a male guinea pig. Two papillary cystadenomas of the breast were found by Aypdent (3) and an adenocarcinoma of the breast by Sternberg (32) 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. König and Wepler (28) found a spontaneous lipomelphipheroma in the psoas. Leader (36) reported an osteogenic sarcoma of the femur, and Raffo (47) mentioned a transplantable sarcoma. Brunschwigg (9) reported a dermoid of the cornea. A teratoma of the pons was described by Lutz (30). Babbit 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 bronchi were reported by Sternberg (55) and others by Sprock (54).

Loeb (36) reported 23 benign lesions of the ovary resembling chorionic trophoblast among 156 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 (35). 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. Landini 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, 40 adenocarcinomas, 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 back which produced metastatic and could not be transplanted (19). A chondrosarcoma of the tibia was produced by repeated x-ray radiation (38).

Foulds (14) produced both carcinoma and sarcoma in guinea pigs of 134 animals. Each of 50 guinea pigs was injected with a solution of sodium iodide, with or without iron, and with or without lead. The injection of sodium iodide was without effect. The injection of iron alone produced a possible adenocarcinoma in 14 animals. The injection of lead alone produced a possible adenocarcinoma in 14 animals. The injection of sodium iodide and iron produced a possible adenocarcinoma in 14 animals. The injection of sodium iodide and lead produced a possible adenocarcinoma in 14 animals. The injection of iron and lead produced a possible adenocarcinoma in 14 animals. The injection of sodium iodide, iron, and lead produced a possible adenocarcinoma in 14 animals.

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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.

Lipschutz and others (33-35) have produced atypical uterine epithelium in guinea pigs by repeated injections of estradiol. Moricard and Cauchox (43) produced large fibromas in the female guinea pig by injection of a benzole of dihydrofoliculin. Nelson (45) reported in 1937 the production of fibromyomatous nodules in the uterus of guinea pigs by the prolonged administration of estrogentic 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 foliculin.

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 (37). In 1936 Cirio (11) reported that he had painted guinea pigs with tar carcinogenic for mice and had obtained no tumors up to 255 years. Latteri (39) succeeded in producing a sarcoma in the kidney of guinea pigs. Liberti (32) was unable to produce cancer with 1,2-benzpyrene (3,4-benzpyrene) 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-benzpyrene (3,4-benzpyrene) injected subcutaneously by Haagensen and Kreibiel (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-benzpyrene (3,4-benzpyrene) failed to produce tumors (49).

Shear (51), in collaboration with Drs. P. R. Howe and M. Elliott, injected 23 guinea pigs subcutaneously with 5 mgm. of crystalline 3,4-benzpyrene. 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 animals dying of old age without evidence of cancer. (Reimann, S. P. The Biology of the Cancer Cell. Am. J. Roentgenol. 48:275-281. 1940.)

1 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.
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 1: Results of Subcutaneous Injection of Guinea Pigs with 3,4-Benzpyrene Suspended in Glycerine

<table>
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<th>Days after injection still alive</th>
<th>No. of animals</th>
<th>Days after injection tumor found</th>
<th>No. of animals</th>
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<td>341</td>
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<tr>
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<td>53</td>
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### 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.

### References


39. MAURY, A. Thèse Doctorat, Versailles, 1931 [cited by ANDERSON and LUMBROSO (2)].


52. SIDERS, E. P. Over een overentbare leukaemie bij cavia's. Nederl. tijdschr. v. geneesk. 70:1256-1262. 1926.


54. SPRECH, C. H. H. Over Adenoma destruens bi cavia cobaya; een bijdrage tot de erfelijkheid van kanker. Nederl. tijdschr. v. geneesk. 8:103-104. 1907.


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