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TRANSLATION NO. 2552

DATE: August 1969

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Translation No. T-740-1

Author: Ch. Lombard, Ecole Nationale Veterinaire de Toulouse,
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Title: The cancer resistance of the guinea pig (La cancéro-
résistance du cobaye).

Journal: Bulletin de L'Association Francaise pour L'Etude du
Cancer 47:167-171 (1960).

August 1969

Few authors have attempted to induce tumors in the guinea pig. After Kleinkuhner (1916), Maurey made it the subject of his thesis in 1931. These were followed by the studies of Tamaschke (1955) and by those of Fischer and Kuehl (1958) who reviewed spontaneous tumors in small laboratory animals.

However, there exists no statistics. At the present time, the tendency is to study the guinea pig since the publications concerning the small number of spontaneous tumors observed indicate that this animal is probably one of the least affected mammals.

Is this really the case?

Maury estimated that the number of known tumor cases in this animal is fourteen. He neglected the two cases of mammalian papillary cystadenoma described by Apolant (1906), the ponto-cerebellar teratoma mentioned and described by Fischer in 1910, the mammalian adenocarcinoma of Katase (1912), the pulmonary adenocarcinoma of Goldberg (1920). However, he acknowledged the malignant schwannoma of Babet and Bloch (1934), the renal globocellular sarcoma of Ball and Pagnon (1935), the cortical suprarenal adenomas of Spiegel (1940), the pulmonary adenomas of Norris (1947), of Heston and Deringer, Boniger and Schweisthal (three cases), the undetermined neoplasia of Caranica (1954), the eighteen adenomatous formation and the seventeen pulmonary adenocarcinomas of Fischer (1956), the verifications of the salivary adenomas of Bujard (1957), the fibroblastic sarcomas of Nejedly and Straub (1957), the uterine myxofibroma and the ovarian cystadenoma of Lechner (1958), which makes a total of somewhat over seventeen observations

collected by him as of 1955.

If one disregards the cortical suprarenal adenomas caused by early castration (Spiegel) and also the leukemias belonging to certain types, the observations which are described in the literature can be classified with regard to the organ affected as follows: the lung, 42 (18 adenocarcinomas) a certain number of adenomas not identified; the breast, 7; skin, 2, a certain number of fibroblastic sarcomas; the nervous system, 2; the kidney, 1, the suprarenals, 1; the ovaries, 1; the uterus, 1; the heart, 1; the thyroid, 1; the spleen, 1; the salivary glands, a few cases.

Not one case of a tumor involving the digestive tract, its attached organs or the male genital glands has been described.

As far as the female genital system is concerned, it should be mentioned that Loeb (1905) examined 380 animals and found chorion-epitheliomas in twenty-three of them. These very probably were follicular reactions rather than actual tumors.

The same probably holds true with regards to the frequency of tumors in the region of the lung assuming that it is possible to make such a judgement based on such a small number of cases. This fact is corroborated by the statement of Fischer and the experiments of Grumbach (1926) and of Willis and Britsaert (1928).

In a group of 120 guinea pigs, with interstitial pneumonia, Fischer found not only 18 carriers of pulmonary adenomas and 17 pulmonary adeno carcinomas, as we have mentioned above, but also 15 animals which possessed epithelial, alveolar metaplastic vegetations. He concluded that the proliferation of the alveolar epithelium appears to be related with the inflammatory phenomenon.

Grumbach infected guinea pigs with corynebacteria and found pulmonary adenomatous reactions in those animals which survived for 200 days after infection. Willis and Brutsaert obtained the same results in seven animals in a group of 80 which were exposed to silica dust for 18 to 31 months.

The pulmonary sensitivity, however, is not so great so that it would cause one to doubt the natural cancer resistance that is usually assumed in the case of the guinea pig and which has been supported by the study of experimental cancer resistance with a number of carcinogenic agents.

It is indeed peculiar to state that the accomplishments of grafting or transplantation in these animals are reduced to almost nothing, unless we consider the unusual regions which constitute the anterior chamber of the eye and of the brain, and that chemical agents except estrogen hormones are without effect on them.

Greene (1941-1955) cultivated in the anterior chamber of the eye, a uterine cancer and a mammary cancer from a female rabbit, various cancers of human origin, mouse brain tumors, the avian sarcoma of Rous, and the Brown-Pearce tumor from a rabbit. However, it is known that organic reactions are attenuated in the anterior chamber of the eye and in the brain. Greene noted, however, that the Brown-Pearce tumor grows more slowly in the brain of the guinea pig than in that of a rat or of a mouse, and the avian sarcoma of Rous regresses rapidly if it is 85 % successful.

The regularly transplantable tumors in the guinea pig are derived from the guinea pig itself. They will revert back to

the cortico-suprarenaloma of Roskin, which kills the stock in three to four weeks, to the mammary carcinoma of Jones which has allows for a somewhat longer survival, to the liposarcoma of Murray, whose evolution is so slow that the transplantable tumor would easily attain a considerable volume if it were not for the leukemia which is easily transmissable as noted in the works of Miguez (1918), Fischer and Kantor (1919), Snijders (1924), Tio Tjwan Gie (1927), and Nadel (1957). In 1919, Lubarsch was able to transmit a sarcoma of the nucha (the nape of the neck) for six generations and a sarcoma of the neck for three generations.

The experiments aimed at producing tumors by introducing foreign materials into the gall bladder: small stones (Kasamia, 1922; Leitch, 1924); human gall stones (Leitch, 1924; Delbet and Godard, 1928); crystals (Gioja, 1929) gave way to numerous critics. Greighton (1924) contested the cancerous nature of the lesions observed by Leitch in animals which survived for more than four months. In the case of Gioja's study, the fibrous epitheliomic lesions that were achieved were not the result of foreign objects but were rather due to the length of the survival. They may lead to papilliferic adenomas but not to infiltrating cancers. Very definitely, the malignancy of the lesions produced is questionable.

Limited success with radiation. Gerard (1925) applied X-rays to the backs of twenty guinea pigs and noted on one of them 18½ months after the first application, the appearance of a sarcoma with found cells growing prolifically. Daels and Biltris (1931) implanted radium in between the meninges and the cranial wall, into the peritoneum, in the liver, and the kidney, and obtained two

sarcoma in the first case (fifty experimental animals) three epitheliomas of the intrahepatic biliary tracts in the second and third cases together (52 experimental animals), two sarcomas of the kidney (22 experimental animals). The total number of experimental animals was 124 of which only seven developed cancers. As one can see, these results are very disproportionate. The works of Lorenz and his co-workers (1946), who also used radium and determined formation of pulmonary tumors, obtained almost similar results.

Complete failure of chemical substances to induce cancer with the exception of estrogene hormones. The guinea pig is not sensitive to the action of tar and carcinogenic hydrocarbons, 2-acetylaminofluorine, p-dimethylazobenzine. On the hand, treatment with estrogens induce a desired reaction.

The estrogene hormones cause in the uterus of the animal experimental fibromatosis. This has instigated numerous investigations including those of Nelson (1937), Moricard and Cauchoix (1938), Lipschutz and his co-workers (1938-1939), and Cauchoix (1939). After 4 months of treatment by weekly injections of 1 mg of estradiole benzoate, the appearance of uterine fibromas and extra-uterine fibromas almost always occurs. In addition to those in the uterus, fibrous tumors are likely to develop in the abdominal cavity, on the lateral walls, the spleen, the mesentery, and the diaphragm, and the epiploon. In exceptional cases, they can be found on the pleura and the pericardium. In male animals, they can develop in the prostate and in the vas deferens (Lipschutz, Yanine, Schwartz, Bruzzone, Acuan, and Silberman, 1945). These are limited to the uterine area, but a tumor causing an affect on the entire system, a real fibromatosis, a diffuse and extrusive fibrosis of the conjunctive stroma was observed by Bimes (1945).

The initiation of tumors is more constant, more rapid, and more severe in the altered female. Perloff and Kurzkrok (1914) observed the initiation of a fibrous tumor as a result of a compressed tablet introduced into the myometrium.

In order of decreasing activity, the estrogens tested are: hexestrol (Lipschutz, Vargas, Eyana and Bruzone, 1941) stilbestrol (Lipschutz and Vargas, 1940) and the stradiol. Playing a preventive role against the fibromatosis of the guinea pig are progesterone, testosterone propionate, desoxycorticosterone, and progesterone being the most active agent. (Lipschutz and co-workers, 1939, 1941, 1948).

When treated in this manner with estrogens, the guinea pig produces conjunctive tumors, manifold genital and extragenital tumors, and essentially fibrous tumors easier and more rapidly than other animals. However, these tumors do not become malignant even after 30 months of treatment. The guinea pig inhibits the carcinomatous evolution. The tumor regress as soon as estrogen treatment is stopped.

One can conclude that in the mammalian scale, the guinea pig manifests itself as a cancer-resistant animal. This fact is quite remarkable considering the fact that the guinea pig is a rodent. Its behavior with regards to tumors, however, is quite different from those of other rodents such as the rabbit, the hamster, and the rat. It is, therefore, a question of species.

SUMMARY

The author studying the spontaneous tumors of the guinea pig as well as the experimental attempts to induce cancers concluded that this animal is resistant to cancer. The fact is more significant

when one considers that this animal, although it belongs to the rodent class, reacts differently from the hamster the mouse, and the rat.

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