Tumors Characteristic for Certain Animal Species

A Review*

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The tumors of man may originate in virtually every organ or tissue, as witness the hundreds of morphologically distinct neoplasms that have been identified. Among the domestic and common laboratory animals, a large variety of tumors has also been reported. This observation has tended to obscure the fact that in each species some tumors occur much more frequently than others and may be regarded as a species characteristic (Table 1). These tumors merit consideration in any truly comprehensive study on the natural history of the species.

It is the aim of this paper to review these neoplasms and to interest biologists, who examine large numbers of animals not commonly studied by oncologists, in collecting and recording the tumors encountered (24). The information so obtained will contribute to our knowledge of comparative oncology, and may provide data on the interaction of genetic and environmental factors in the etiology of neoplasia.

ZOLOGICAL DISTRIBUTION

Fishes.—Tumors have been reported in over 120 species of fishes (75). Although isolated instances have been described in which one or another viscus was affected, neoplasms of the skin and subcutaneous tissue are by far the most common. The low incidence of tumors of the gastrointestinal and genitourinary tracts is probably real and not solely due to the lesser accessibility of these organs for inspection. In several of the more common food fishes such as herring (Clupeidae), cod (Gadidae), and mackerel (Scombridae), which are caught in vast numbers, the reported cases of neoplasia are few, are of connective tissue origin, and without apparent species specificity.

These fishes may be contrasted with members of the snapper family (Lutianidae), in which single or multiple nerve sheath tumors are of frequent occurrence. In 2 months Lucké (52) was able to collect 76 specimens that had single or multiple neurilemomas. He estimated that they occur in 0.5–1 per cent of snappers seen in the Tortugas waters, where the commercial fishermen of Key West call them "cancer fish." No other tumors have been seen in these fish, nor were similar tumors observed in other species found in those waters.

Among goldfish, Carassius auratus, neurilemomas also appear to be characteristic of the species. Approximately 10 per cent of the goldfish in a large urban lagoon in Cleveland exhibit nerve sheath tumors (71). They usually appear as multiple neoplasms of the skin but may occur singly in the abdominal cavity. Some are invasive and show cytological changes characteristic of malignancy. The writer has also collected goldfish with similar tumors from ponds in Atlantic City, N.J., and Columbus, Ohio. The difficulty in determining the histogenesis of the less well differentiated tumors is considerable, and it is very probable that most of the instances of fibrosarcoma reported in goldfish are, in fact, cases of neurilemoma. De-
spite careful dissection of many hundreds of adult goldfish from various parts of the United States, tumors other than the neurilemoma were encountered only twice. One was a cutaneous papilloma, the other an osteochondroma arising from the basisphenoid bone of the skull.

Papillary epithelial tumors of the lips have been reported as common in several species of fishes; in each instance the affected animals were limited to a restricted area of the geographic range of the species. Small papillary tumors were found on the lips of barbels, *Barbus fluviatilis*, caught in the Mosel River, Germany, by Keysselitz (43). In the neoplastic epithelial cells he described intranuclear inclusions surrounded by an achromatic halo and readily distinguishable from nucleoli.

**TABLE 1**

<table>
<thead>
<tr>
<th>Species</th>
<th>Organ</th>
<th>Tumor</th>
<th>Reference</th>
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<tr>
<td><strong>FISHES:</strong></td>
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<tr>
<td>Eel</td>
<td>Lips</td>
<td>Papilloma</td>
<td>Schaeperclaus (70)</td>
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<td>Anguilla anguilla</td>
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<td>Catfish</td>
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<td>Ameiurus nebulosus</td>
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<td>Red tai</td>
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<td>Northern pike</td>
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<td><em>Esox lucius</em></td>
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<td>Muskelunge</td>
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<tr>
<td><em>Esox masquinongy</em></td>
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<td>Snapper</td>
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<tr>
<td><em>Lutianus Sp.</em></td>
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<td>Goldfish</td>
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<tr>
<td><em>Carassius auratus</em></td>
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<td>Killifish hybrid</td>
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<td>X. helleri x P. maculatus</td>
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<td><strong>AMPHIBIANS:</strong></td>
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<tr>
<td>Axolotl</td>
<td>Skin</td>
<td>Melanoma</td>
<td>Brust (78)</td>
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<td>Siren don mexicanum</td>
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<tr>
<td>Leopard frog</td>
<td>Kidney</td>
<td>Adenocarcinoma</td>
<td>Lucké (50)</td>
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<tr>
<td><em>Rana pipiens</em></td>
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<td><strong>REPTILES:</strong></td>
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<tr>
<td>Green turtle</td>
<td>Skin</td>
<td>Papilloma</td>
<td>Smith &amp; Costes (82)</td>
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<tr>
<td><em>Chelonia mydas</em></td>
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<td><strong>BIRDS:</strong></td>
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<tr>
<td>Chicken</td>
<td>Lymphoid tissue</td>
<td>Lymphomatosis</td>
<td>Olson &amp; Bullis (63)</td>
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<tr>
<td>Gallus domesticus</td>
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<tr>
<td>Duck (Campbell breed)</td>
<td>Liver</td>
<td>Malignant hepatoma</td>
<td>Campbell (11)</td>
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<td>Anser platyrhynchos domest.</td>
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<tr>
<td>Parakeet</td>
<td>Kidney</td>
<td>Adenocarcinoma</td>
<td>Schlumberger (unpubl.)</td>
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<tr>
<td><em>Melopsittacus undulatus</em></td>
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<td><strong>MAMMALS:</strong></td>
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<tr>
<td>Horse</td>
<td>Nasal sinuses</td>
<td>Carcinoma</td>
<td>Karnbach (42)</td>
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<tr>
<td>Equus caballus</td>
<td>Skin</td>
<td>Melanoma</td>
<td>McFadyean (55)</td>
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<tr>
<td>Cattle</td>
<td>Eye</td>
<td>Carcinoma</td>
<td>Russell et al. (69)</td>
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<tr>
<td>Bos taurus</td>
<td>Liver</td>
<td>Adenoma &amp; carcinoma</td>
<td>Tamaschke (87)</td>
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<td>Sheep</td>
<td>Lung</td>
<td>Adenoma &amp; carcinoma</td>
<td>&quot; (87)</td>
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<tr>
<td>Ovis aries</td>
<td>Kidney</td>
<td>Nephroblastoma</td>
<td>Monlux et al. (56)</td>
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<td>Swine</td>
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<tr>
<td>Sus scrofa</td>
<td>Breast</td>
<td>Mixed tumor</td>
<td>Mulligan (50)</td>
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<td></td>
<td>Skin</td>
<td>Mastocytoma</td>
<td>&quot; (58)</td>
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<tr>
<td>Dog</td>
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<tr>
<td>Canis familiaris</td>
<td>Uterus</td>
<td>Adenoma &amp; carcinoma</td>
<td>Green &amp; Saxton (54)</td>
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<tr>
<td></td>
<td>Skin</td>
<td>Fibroma &amp; papilloma</td>
<td>Shope (78, 90)</td>
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<td>Rabbit</td>
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<tr>
<td>Oryctolagus cuniculus</td>
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<td>Adenoma &amp; carcinoma</td>
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<td></td>
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<td>Fibroma &amp; papilloma</td>
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<tr>
<td>Mouse</td>
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<tr>
<td>Mus musculus</td>
<td>Breast</td>
<td>Adenocarcinoma</td>
<td>Horn &amp; Stewart (40)</td>
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<tr>
<td>Rat</td>
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<tr>
<td>Rattus rattus</td>
<td>Breast</td>
<td>Fibroadenoma</td>
<td>Bullock &amp; Curtis (8)</td>
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<tr>
<td></td>
<td>Liver</td>
<td>Fibrosarcoma</td>
<td>&quot; (7)</td>
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<tr>
<td>Deer</td>
<td>Liver</td>
<td>Hepatoma</td>
<td>Krause (48)</td>
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<td>Capreolus capraea</td>
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* Other examples on which data are still incomplete are given in the text. In identifying tumors as species-characteristic, due regard must be given to the age of the animals collected, the care with which they were examined, and the number available for study.
Among the stilt, Osmerus eperlanus, from an inlet of the Baltic Sea, Breslauer (5) in 1916 found 37 specimens with cauliflower-like growths that occasionally were as large as the head of the affected fish. Histologically, they were papillomas with occasional intracytoplasmic inclusions. It is of interest that recently Schaeperclaus (70) observed similar tumors in eels, Anguilla anguilla, also caught in the Baltic Sea. Although previously rarely observed, the lesions began to attract the attention of fishermen in 1948 and by 1950 approximately 5 per cent of the catch was affected. Since then, the incidence has gradually declined. In addition to eels, codfish, Gaeus sp., were occasionally affected.

Catfish, Ameiurus nebulosus, found in streams near Philadelphia commonly bear epithelial tumors that appear as solitary or multiple red fleshy masses on the lips or dental plates, where they may interfere with closure of the mouth (58). Histologically, the tumor has the structure of a rather solid papilloma with a delicate vascular connective tissue stroma. The growths may invade adjacent structures, but metastases were never observed. During a 2-year period 168 tumor-bearing catfish were examined in addition to several hundred apparently healthy fish. Except for a microscopic renal adenoma, no other tumors were encountered.

Bony lesions, provisionally identified as osteomas, are common on the ventral spinous processes of the sixth to eighth caudal vertebrae of a Japanese food fish, the red tai, Pagrosomus major. Takahashi (86) examined over 100 fish with this growth; the high incidence of the osteomas is also indicated by the fact that among three P. major selected at random from the collection in the National Museum in Washington, one bore the characteristic tumors (75). The earliest lesions are fusiform; as they increase in size, they become nearly spherical, reaching a diameter of 1–2 cm. Histologically, the growths are composed of cancellous bone and may represent a species-characteristic excess callus rather than a true tumor. The great variety of genetically controlled bony overgrowths of fishes and their possible significance for the problem of neoplasia has been discussed by Breder (4).

Lymphosarcoma is the most common tumor in two species of the genus Esox, viz., the northern pike, E. lucius (= E. estor), and the muskellunge, E. masquinongy. Nigrelli (60) studied twelve northern pike ranging in age from 2 to 6 years that were kept in the same tank and died at intervals over a period of 1 year. The primary tumor, composed of large lymphoblasts, apparently arose in the lymphoid tissue normally present in the kidney. Smaller growths were found in the liver, spleen, and retroperitoneal tissue. The writer has found a similar tumor in another fish of this species, and Haddow and Blake (36) have also reported a case.

For several years Ritchie has been conducting an extensive investigation of lymphosarcoma in the muskellunge, a large relative of the northern pike.1 About 10 per cent of these fish taken from Lake Scugog in the neighborhood of Toronto, Ontario, bear the tumor. The lesions differ from those of the pike, described by Nigrelli, in that the tumors apparently arise in the subcutaneous tissue from where they invade the trunk musculature. Later the kidney, spleen, and liver become diffusely enlarged, the result of a lymphoblastic infiltration, accompanied by lymphatic leukemia. Occasionally, the skin lesions heal, and the fish recovers; but the cells appear to be definitely neoplastic, and in most cases the tumors progress until the fish succumbs. Initial studies by Ritchie indicate that the tumor can be transplanted and that it is contagious to muskellunge living in the same water with fish bearing the growth. No other varieties of tumors were found in any of the affected normal fish.

The platyfish, Platypoecilus maculatus, and swordtail, Xiphophorus helleri, do not hybridize in their native rivers of Mexico, but do so readily in aquaria. Among the hybrids, the black or spotted fish often develop melanomas, whereas the nonspotted siblings are free of tumors. The genetics of this neoplasm has been extensively investigated by Gordon (32). It is the species-specific tumor of these hybrids.

Amphibia.—Tumors are not frequently observed in amphibians. Among urodeles, with the exception of the axolotl, only a few reports describing single cases are on record (75). A renal adenocarcinoma in Necturus maculosus was recently studied in this laboratory; but this specimen, contributed by Professor W. J. Leach, is the only one with a tumor of any kind observed by him over a period of many years in several hundred of these animals dissected by students.

In view of this dearth of material, the occasional occurrence of melanomas in the skin of axolotls, Siredon mexicanum, is of particular interest. First reported in a single specimen by Krontovky (46), a similar tumor in each of a pair of grey axolotls and in another unrelated female was studied by the Brunts (78). Among the offspring of the pair, as well as in subsequent gen-

1 Personal communication dated April 3, 1957, from Dr. R. C. Ritchie, Department of Pathology, Banting Institute, University of Toronto, Toronto, Ontario.
erations, slow-growing transplantable melanomas appeared on the skin. Another report is that of Finkelstein (27), who stated that during the decade 1920–1930 there were in the aquarium of the Kiev Roentgenological Institute axolots with a hereditary tendency to melanoma.

With one outstanding exception, tumors are as uncommon among frogs and toads as they are in the urodèles (75). The exception is the renal adenocarcinoma of the leopard frog, *Rana pipiens*, first adequately described by Lucké (50) in a report based on 158 cases. Since then over 1500 cases have been examined by Lucké and the writer, while many more have been seen by other investigators. Nearly all are found in frogs caught in their natural habitat, New England, particularly Vermont. In large shipments of these animals the incidence is usually about 1–2 per cent but may be as high as 5 per cent. The neoplasms arise in the renal tubular epithelium, are often multicentric, metastasize, and have been carried in serial transplantation through many passages (76). Intranuclear inclusions first suggested a possible virus etiology for the tumor, a view supported by Finkelstein (27), who stated that during the decade 1920–1930 there were in the aquarium of the Kiev Roentgenological Institute axolots with a hereditary tendency to melanoma.

During the past 4 years the problem of neoplasia in the shell parakeet has been under investigation in our laboratory. Among cage and captive wild birds, sporadic cases of tumor-bearing individuals have been reported (30, 37). However, in 1933 Ratcliffe (66) noted that, of 6898 birds autopsied at the Philadelphia Zoo, 81 were found to have a tumor, and, of these, 42 were birds belonging to the order Psitaciformes that comprised only 17 per cent of all birds examined. A single species, the shell parakeet, *Melopsittacus undulatus*, with 177 autopsied specimens, made up 28 of the 42 cases. This incidence of 15.8 per cent was unequaled by any other species of bird or mammal exhibited in the Zoo. A similar high incidence of tumors in this species was later reported from the Moscow Zoological Park (21).

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finding was that tumors of the pituitary are relatively common in the shell parakeet (72); this organ was the site of a primary adenoma or carcinoma in 156 instances. The tumors often produce blindness by pressure on the optic nerves and are frequently associated with polydypsia, hyperglycemia, and obesity. The metabolic disturbances are also found in birds with subcutaneous transplants of the tumor (74). Although it is apparent from the figures cited that both renal carcinoma and the pituitary tumor are characteristic of *Melopsittacus undulatus*, the species-specificity of the pituitary tumor is made more striking by the infrequent occurrence of pituitary growths in other animals.

**Mammals.**—In contrast to the other vertebrate classes where data on neoplasia are meager, the descriptive literature about tumors in mammals is enormous. Nevertheless, of the more than 10,000 mammalian species only about ten are represented by more than a few reports of isolated cases. The species on which adequate information is available are the domesticated and the common laboratory animals. In most of these there is definite evidence for a species-specificity of certain tumors.

During the past several decades the horse population of Western Europe and the United States has declined rapidly. For this reason most of the surveys on large numbers of animals were reported during the first 30 years of this century (84). Tumors of the nose and accessory sinuses are more common in horses than in any other species. Kärnbach (42) found 100 instances of neoplasia at this site; and in a series of 1447 equine tumors collected from the literature by Tamaschke (87), 304 were primary in the nose or sinuses; of these, 70 were carcinomas, 50 sarcomas, and the rest benign. In the same series other frequent sites of cancer were the gastrointestinal tract with 95 cases, the testis with 88, and the penis with 81. However, the most striking incidence of a tumor in these animals is that of the melanoma in grey horses. The site of the primary growth is usually the skin about the anus and genitalia. Although rare in horses of other coat colors, it is virtually unknown in animals under 6 years, rises to 36 per cent at 8–10 years, and 61 per cent at 10–12 years of age.

In cattle the high incidence of epithelial tumors arising on the cornea or conjunctiva has long been recognized as characteristic for these animals (26). In 1900 Loeb noted that ocular cancer appeared to be endemic on a ranch in Wyoming (49). At a meat inspection center in Denver 908 tumors were found in slaughtered cattle during the 2 years 1953 and 1954. Of the total, 722 were ocular tumors collected during only a part of 1 year, permitting a conservative estimate of 1400 eye tumors for the 2-year period, to contrast with 186 tumors from all other sites (56). In reports of the Meat Inspection Branch for the years 1950–54, 82 per cent of condemnations for neoplasms in cattle were for cases of ocular squamous carcinoma (69). Among 2003 bovine neoplasms in India, 42 per cent were diagnosed as carcinoma of the eye (12). Russell et al. (89) have estimated the overall incidence of ocular epithelioma among cattle in the United States at 0.8–1.6 per cent. They observed that 75 per cent of the tumors arise on the cornea or limbus.

In sheep most reported series of tumors are quite small and show considerable variation in relative organ incidence. In two of the largest collections (56, 87), benign and malignant tumors of the liver comprise 12 and 30 per cent, respectively, of all neoplasms. Although infrequent in the United States, Tamaschke (87) found tumors of the lung to be as common as the hepatic neoplasms; of 32 cases, 26 were listed as adenomas. Tumors of the adrenal cortex or medulla are also relatively frequent in sheep; however, there is no tumor that can be considered characteristic of these animals in the manner of melanoma in horses and ocular carcinoma in cattle.

Among swine, the kidney is the site of 30–50 per cent of all neoplasms reported (27, 56, 87). By far the greatest number are embryonal nephromas, comparable to the Wilms' tumor in children. Histologically, they are composed of both epithelial and mesenchymal elements; hence, the descriptive term “adenosarcoma.” The young age at which swine are slaughtered may in part account for the relative frequency of this tumor which in other animals and man is characterized by a high incidence in young individuals.

Dogs, many of which reach an old age as pets, are subject to a wide variety of tumors. Most common are benign and malignant lesions of the skin, comprising about 35 per cent of the total (16, 59). Another 20 per cent are neoplasms of the mamma, in which over half are mixed tumors composed of epithelium, connective tissue, and other mesenchymal elements. This high incidence of mixed tumors is peculiar to the canine mammary gland. Thyroid carcinoma, now uncommon in the U. S. where iodized salt is widely used, is still frequent in parts of Europe. Dobberstein (17) has recently reported from Germany that it rep-
rarely become carcinomas, but when the virus is transmitted to the domesticated rabbit the recent papillomas usually undergo malignant transformation.

Many thousands of guinea pigs are annually sacrificed in laboratories throughout the world, but few tumors are on record. In part this may be attributable to the youth of most of the animals when killed. Although less than 30 tumors had been reported by 1940, in that year Papanicolaou and Olcott stated they had found about 100 neoplasms among 7000 guinea pigs, most of which were senile. In a preliminary survey it appeared that the commonest tumor was a fibromyoma of the lower segment of the uterus. These investigators have described nine tumors in detail: four leiomyomas and one lipoma of the stomach, two neurilemmomas and one liposarcoma of the intestine, and a chondrosarcoma of the iliac bone. Another tumor of bone, an osteogenic sarcoma of the femur, was reported by Leader, who listed nineteen additional tumors described in the literature: eight sarcomas of various sites, eight adenocarcinomas of the mammary gland (three were in males), an adenocarcinoma of the kidney, an adenoma of the adrenal, and an embryoma of the ovary. A recent report by Congdon and Lorenz suggests that leukemia is of relatively frequent occurrence, in one inbred strain attaining an incidence of 6.7 per cent. No valid conclusion concerning species-characteristic tumors can be reached from the data now available.

The common laboratory mammals used in cancer research are all rodents, with the exception of the rabbit which is usually grouped with the Lagomorpha, a closely related order of gnawing animals. Relatively few instances of neoplasia in the rabbit are described in the literature; in 1927, Polson collected 96 cases, of which 29 were adenomas or adenocarcinomas of the uterus. In a colony of 500 female rabbits observed over a period of 4 years, Greene found 83 cases of benign or malignant epithelial uterine tumors. The animals belonged to nine different breeds; each had borne two to sixteen litters over a 12- to 14-month period, suggesting that pregnancy is significant for the induction of these tumors. Although the most common tumor in domesticated rabbits is the uterine adenoma or adenocarcinoma, its frequency among wild rabbits is unknown. Because of the short average life span of the latter in their natural environment, the incidence of all tumors is probably lower. An exception to this are two virus-induced skin tumors of the wild cottontail rabbit, *Sylvilagus floridanus*. These are a fibroma, first described by Shope in 1932, and a wartlike papilloma reported by the same author in the following year. In some regions of Kansas 25 per cent of the cottontail rabbits may bear papillomas. In the natural host these rarely become carcinomas, but when the virus is transmitted to the domesticated rabbit the result is a fibroma, first described by Shope in 1932 (79), in those too are the most common tumor in domesticated rabbits. Relatively few instances of neoplasia in the rodent are reported, with the exception of the common laboratory mammals used in cancer research, and the rat is the animal in which the problem of neoplasia has been studied most intensively. The literature is almost endless, and the variety of neoplasms reported approaches that in man. Many of the tumors are transplantable (18), and some have a very high incidence among inbred strains of mice (19). In the C58 strain approximately 85 per cent of the animals develop leukemia after they are 6 months old, and there is evidence that a viral agent is transmitted from mother to offspring during gestation (35). However, among noninbred mice, which compare more closely with the individuals of a species occurring in nature, breast cancer is by far the most common malignant tumor (40). The breast lesion may be considered the species-specific neoplasm of the mouse (29, 57).

The organ incidence of tumors in the rat is directly dependent on the degree to which the colony is infested by larvae of the cat tapeworm, *Taenia crassicolis* (*taeniaeformis*). The larvae lodge in the liver and lead to changes in the connective tissue that terminate in fibrosarcoma (7). In a colony of 500 female rabbits observed over a period of 4 years, Greene found 83 cases of benign or malignant epithelial uterine tumors. The animals belonged to nine different breeds; each had borne two to sixteen litters over a 12- to 14-month period, suggesting that pregnancy is significant for the induction of these tumors. Although the most common tumor in domesticated rabbits is the uterine adenoma or adenocarcinoma, its frequency among wild rabbits is unknown. Because of the short average life span of the latter in their natural environment, the incidence of all tumors is probably lower. An exception to this are two virus-induced skin tumors of the wild cottontail rabbit, *Sylvilagus floridanus*. These are a fibroma, first described by Shope in 1932, and a wartlike papilloma reported by the same author in the following year. In some regions of Kansas 25 per cent of the cottontail rabbits may bear papillomas. In the natural host these rarely become carcinomas, but when the virus is transmitted to the domesticated rabbit the result is a fibroma, first described by Shope in 1932 (79), in those too are the most common tumor in domesticated rabbits. Relatively few instances of neoplasia in the rodent are reported, with the exception of the common laboratory mammals used in cancer research, and the rat is the animal in which the problem of neoplasia has been studied most intensively. The literature is almost endless, and the variety of neoplasms reported approaches that in man. Many of the tumors are transplantable (18), and some have a very high incidence among inbred strains of mice (19). In the C58 strain approximately 85 per cent of the animals develop leukemia after they are 6 months old, and there is evidence that a viral agent is transmitted from mother to offspring during gestation (35). However, among noninbred mice, which compare more closely with the individuals of a species occurring in nature, breast cancer is by far the most common malignant tumor (40). The breast lesion may be considered the species-specific neoplasm of the mouse (29, 57).

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large rat colony used in the study of the hepatic sarcomas, Bullock and Curtis found 2450 animals with the specific liver tumor, as well as 489 rats with other neoplasms that were independent of the parasites (8). Of these, the largest number—94—were in the breast and, except for two carcinomas and two carcinosarcomas, were represented by benign fibroepithelial tumors. In 506 inbred laboratory rats of the Sherman-Mendel strain, Olcott (61) found ten tumors; all but one, a nephroblastoma, were of nonepithelial tissues. Two groups of investigators (54, 92) examined a total of 123,000 wild rats, Rattus norvegicus, and found 125 tumor-bearing animals, an incidence of approximately 1 per thousand. Forty tumors were primary in the breast; of these, 36 were adenomas or adenofibromas, and only four were classified as adenocarcinomas. Tumors of the liver totaled 25 cases, of which 21 were sarcomas, nearly all associated with the tapeworm larvae. From these data it is apparent that in the rat, barring the infested liver, the breast is the most common site of neoplasia, but in the rat, unlike the mouse, the great majority of these are benign tumors of fibroepithelial origin. Also characteristic of the rat is the greater frequency of sarcoma as compared with carcinoma, whether the site be the skin, liver, or other organ.

The reported cases of neoplasia in species of wild animals living in their native habitat or in captivity are generally too few in number to permit conclusions on species specificity. Among the best sources of data are the annual reports of the prospector to the Zoological Society of London in the Society’s Proceedings, the recent bibliography of diseases in wild mammals and birds by Halloran (37), and the surveys of tumor incidence among animals at the Philadelphia Zoo by Fox (30) and Ratcliffe (66).

In captive and wild deer, at least eighteen instances of adenoma or carcinoma of the liver have been reported (58, 91). Krause studied seven cases and collected eight additional ones from the literature (45). Most of his material was from the roe deer, Capreolus capreolus, of Germany. The majority of tumors were liver cell carcinomas; only an occasional one had its origin in bile duct epithelium. The sex distribution was about equal, and most of the animals were over 5 years old. Within recent years a fibroma of the skin has been frequently observed in wild deer from widely scattered regions of the United States. The tumors are multiple and range in size from 0.5 to 10 cm. in diameter; Shope (81) has been able to transmit them using cell-free filtrates.

Goiter and thyroid carcinoma are of relatively frequent occurrence in captive wild mammals (78). Carcinoma affects a wide variety of animals but particularly the Canidae (foxes, wolves) and the Procyonidae (raccoons). The high incidence among the Canidae is of interest in view of the frequent occurrence of thyroid cancer in dogs reported by Dobberstein in Germany (17).

Evidence of the growing interest among pathologists in the comparative study of neoplasia may be found in the recent reports of tumors in whales. At least nineteen neoplasms have been described; the greatest number were fibromas, of which Stolk (85) found seven on the skin or tongue. Rewell and Willis (67) collected four ovarian tumors: a mucinous cystadenoma in a blue whale, and three granulosa-cell tumors in another blue whale and two fin whales.

**ETIOLOGY**

The term “species characteristic” carries an implication of constitutional susceptibility. However, the susceptibility need not be to neoplastic growth per se, but rather to a particular environmental factor or even a behavior pattern that, in turn, initiates the tumor. An example of the indirect direction of heredity is seen in the development of intramandibular carcinoma in nearly 1 per cent of old mice of the 020 Amsterdam strain (90). In many strains of mice hair of cage mates is occasionally found cleaving the gingival and enamel-forming epithelium to produce cysts in which carcinoma may arise. The high incidence of the tumors in the 020 Amsterdam strain is linked in part to the more frequent occurrence of the cysts, attributed to the inheritance in these mice of a greater disposition to gnaw the hair of cage mates.

The relative importance of heredity and environment varies with the particular tumor and with the species affected. Pigment-cell tumors of killifish hybrids, axolots, and horses appear to be independent of environmental factors. It is noteworthy that, in both the axolotl and in the horse lightly pigmented (grey) individuals are particularly affected. The genetic mechanism of melanoma has been most clearly elucidated in the killifish hybrids (platyfish X swordtail). Gordon (32) observed that the swordtails, Xiphophorus hellerii, possess only micromelanophores, or no melanophores at all; platyfish, Platypoecilus maculatus, bear both micro- and macromelanophores. In the platyfish the gene Sp controls the growth of the micromelanophores; if the hybrid receives the Sp gene but not some of the modifiers normally present in either parent, there is an accelerated proliferation of the macromelanophores. This leads
to melanosis, often followed by the development of a melanoma.

Other genetically controlled neoplasms that may be independent of environmental factors are the liver tumors in the Campbell breed of ducks and some tumors of inbred strains of mice. In recent years the possible effects of geophysical and geochemical factors on the development and geographic distribution of cancer have come under investigation (83, 88). Physical agents as ubiquitous as sunlight may act in conjunction with a hereditary trait to induce neoplasia. The nonpigmented conjunctiva and periocular tissue of the white-faced Hereford cattle are believed by some investigators to be particularly susceptible to the carcinogenic effect of ultraviolet rays in sunlight.

A similar relation has been suggested to account for the higher incidence of skin cancer in the white than in the colored races of man. Except for a case of osteogenic sarcoma in a muskrat (47), ionizing radiations have not yet been implicated in the production of cancer among wild animals. The muskrat, Ondatra zibethica, was caught near Oak Ridge National Laboratory in Tennessee. Analysis showed that the animal's tissues were receiving at least 40 rep per day, largely from radiostrontium stored in the skeleton. The food plants in the area contained relatively large amounts of radioactive elements.

Chemicals in the water may account for some of the lip tumors in fishes. This is particularly true of the epitheliomas on the lips of catfish from streams heavily polluted by chemical wastes (59). Recently, Russell and Kotin have suggested a similar etiology for the lip papillomas of white croakers, Gengonemus lineatus, taken in Santa Monica Bay, California (68). The association of a genetic factor is likely, for in both instances other species of fish caught at the same time and place were free of tumors. However, the importance of the environment is indicated by the absence of similar tumors among the same species of catfish and croakers caught elsewhere.

Occasionally the absence of a trace element may be responsible for the initiation of cellular overgrowth. The classic example of this is the occurrence of goiter and thyroid carcinoma in animals receiving an inadequate amount of iodine (73). The importance of the animal's hereditary constitution is manifested by the difference in the amounts of iodine required to prevent goiters in various species; e.g., under similar environmental conditions goiter is common in trout, rare in carp; frequent in dogs, rare in cats.

Viruses have proved to be the causative agents of several species-characteristic tumors, including neoplasms of the hematopoietic tissue in chickens (2, 9, 23) and mice (35); of the connective tissue tumors of fowl (28), rabbits (79), squirrels (44), and deer (81). Other virus-induced tumors are the kidney carcinoma of frogs (51), some breast tumors of mice (3), and the epidermal papillomas and carcinomas of rabbits (80). There is evidence that the lip tumors of the barbel, stink, and eel, as well as the lymphosarcomas of the pike and muskellunge (Table 1), are initiated by a virus, but none of these tumors has yet been transmitted experimentally. A few of the viruses, such as those of the rabbit papilloma, squirrel fibroma, and chicken sarcoma, will induce neoplasms in related species under experimental conditions, but many are species- and even strain-specific.

Among tumors that occur with a sufficiently high incidence to be regarded as species-specific, only the fibrosarcoma in the liver of rats has been clearly linked to a metazoan parasite (7). The carcinogenic effect of cat tapeworm larvae is not limited solely to the rat, for it has been observed in mice and even in the muskrat (81). Nevertheless, in the mice as well as in other rodents that harbor the parasite, liver sarcomas are rare. This provides another illustration of the importance of the particular genetic constitution in the production of neoplasia by an environmental factor.

**SUMMARY**

There is great variety in the nature and incidence of tumors found among different animals; but when sufficient data are available, a certain neoplasm often proves characteristic for a particular species. Although these species-specific tumors have a genetic basis, evocation of the neoplastic growth is often dependent upon infectious agents or physical and chemical factors in the environment.

**REFERENCES**


7. BULLOCK, F. D., and CURTIS, M. R. A Study of the Reactions of the Tissues of the Rat’s Liver to the Larvae of


GROSS, L. V. 1956.


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Cancer Research

Tumors Characteristic for Certain Animal Species: A Review

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Cancer Res 1957;17:823-832.

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