

# Multiple Primary Tumors in Dogs

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(Received for publication April 13, 1944)

From the point of view of comparative oncology the subject of multiple tumors has always been of great interest, particularly with regard to human neoplasms. Since a high incidence of spontaneous tumors is found in dogs, the cases of multiple canine tumors recorded in the literature have been surveyed in order to determine the age, sex, and breed of the dogs afflicted and the types and sites of the neoplasms encountered.

Any discussion of multiple tumors in dogs may be properly prefaced by an analysis of the papers by Goodpasture and Wislocki (8), by Goodpasture (7), by Cohrs (3), and by Pallaske (14) since they were the only thoroughgoing investigations of all the organs of old dogs at routine necropsy found in the literature. In the first paper were described 15 old dogs, which were included with 35 other old dogs discussed in the second paper. The 50 dogs studied were 37 males and 13 females, which were chosen because of such evidences of old age as decay and loss of teeth, grayness of hair, and presence of senile cataract. The average age range was about 9 to 14 years. Projecting above the surface of the adrenals in 41 dogs multiple, small, nodular tumors of the fascicular cells of the cortex were found. In 39 the spleen was involved by 1 to 6 smooth, tense, round, deep purple tumors projecting above the surface and composed of densely packed masses of lymphocytes with large proliferating centers. Myelopoiesis was seen near these growths. Most of the spleens were affected by hemosiderosis. In 39 dogs the liver was the site of 3 to 20 small nodular tumors of liver cells. The prostates of 22 males were affected by benign enlargement. Situated in the testes were 17 benign growths including multiple interstitial cell tumors and adenomas of the tubules. In 11 dogs the thyroid was the seat of multiple tumors including cylindromatous, fetal-adenomatous, and massed cellular arrangements. Pancreatic adenomas of acinar origin were discovered in 5 dogs. In addition, 13 malignant neoplasms and a variety of benign tumors were observed. The high incidence of small, nodular tumors of the fascicular cells of the adrenal cortex; of the smooth, tense, round, deep purple tumors of lymphatic tissue in the spleen; of the small nodular tumors of liver cells; of benign hypertrophy of the prostate; of the interstitial cell tumors and tubular adenomas in the testes; and of

the nodular tumors of varying architecture in the thyroid would indicate that these proliferations could be more properly designated nodular hyperplasias of these organs rather than true tumors. The growths of acinar origin in the pancreas might also be thought to belong among the nodular hyperplasias of parenchymatous viscera, particularly in the light of the statistics of Cohrs (3) and of Pallaske (14).

In the necropsy findings on 29 dogs examined by Cohrs (15 males, 13 females, and 1 of unmentioned sex, in 27 of which the ages ranged between 10 and 22 years), nodular hyperplasia of the adrenal cortex was present in 17; of the splenic follicles, in 15; of the liver cells, in 13; of the pancreas, in 13; and of the thyroid, in 5. Cohrs (3) called the nodules in the adrenal cortex "hypernephromas"; the tumors of the liver cells, "adenomas"; and the nodules in the thyroid, "strumas."

In his necropsy investigation of interstitial cell tumors ("*Zwischenzellentumoren*") of the testis Pallaske studied 107 male dogs, of which 17 were 5 years of age or younger; 37, 6 to 9 years old; and 53, 10 to 20 years old. Of these 107 dogs, the 31 with so-called interstitial cell tumors of the testis were 6 to 20 years of age; 23 of the 31 were 10 to 20 years old. Seventy-one dogs, 6 to 20 years old, revealed nodular hyperplasia of one or more of 5 organs; namely, liver, adrenals, spleen, pancreas, and thyroid. Of these 71, 28 animals, 6 to 16 years old, also had so-called interstitial cell growths of the testes. From the evidence presented in these 4 papers the presence of one or more nodular "tumors" of the fascicular cells of the adrenal cortex, of the lymphatic tissue of the spleen, of the liver cells, of the acini of the pancreas, of the interstitial cells of the testes, and of the thyroid parenchyma may be suitably termed "nodular hyperplasias" rather than true neoplasms. Such cellular proliferations (including benign prostatic hypertrophy) found in dogs at routine necropsy should be accepted as internal evidences of senility of the animals just as surely as decay and loss of teeth, grayness of hair, and senile cataract are external evidences of canine old age. This is especially true if one recalls that such changes are preponderant in dogs 10 years of age or older, and rare in dogs under the age of 6 years.

## A REVIEW OF THE LITERATURE

In the following summary from the literature of multiple tumors in dogs nodular hyperplasias as defined will be omitted when they have been found in the protocols of cases reviewed. This procedure has resulted in the rejection of some of the cases described by Cohrs as instances of multiple tumors.

Virchow (19) described a bitch with: (a) a large ossifying enchondroma of the breast with ossifying metastases of fibrous hyaline cartilage in the lungs, pleura, and mediastinum; and (b) a large, centrally cystic tumor of the omentum.

van Gieson (18) reported the case of a female adult dog afflicted by: (a) intracanalicular fibromas of the right penultimate and hindermost mammae, (b) a telangiectatic sarcoma of mesenteric lymph nodes, (c) 2 myomas of the stomach, (d) a fibroma of the uterus, and (e) a follicular cyst of the left ovary.

Petit (15) recorded the case of a female dog with: (a) mammary carcinoma with generalized metastases, (b) multiple fibromas of the vagina, and (c) ovarian cysts.

Case 4 of Ortschild (13) was an 8 year old Gordon setter bitch in which were found: (a) an adenocarcinomatous mixed tumor of the right hindermost mamma, and (b) a lipoma of the left pectoral region.

In a male St. Bernard dog 12 years old Cullen (4) discovered: (a) a recurrent squamous cell carcinoma of the skin of the back, and (b) an adenocarcinoma of the prostate.

Heny and Wooldridge (9) discussed the case of an aged female dachshund with: (a) a lipoma of the perineum, and (b) a fibroma of the right penultimate mamma.

Winokuroff (20) described a 22 year old dog afflicted by: (a) a spindle cell sarcoma of the retroperitoneal connective tissue in the neighborhood of the left inferior costal arch, and (b) primary multiple cystadenomas of the liver.

Stephan (17) reported the case of a 10 year old female terrier with: (a) a mammary carcinoma with pulmonary metastases, and (b) a cavernous hemangioma of the liver.

Wooldridge (21) recorded the case of a male fox terrier 14 years old with: (a) adenoma of the prostate, and (b) adenocarcinoma of the liver.

Bartlett (2) reviewed the subject of multiple primary malignant tumors and included 2 cases occurring in dogs. The first dog was an old male afflicted with: (a) an adenocarcinoma of the thyroid with metastases to the lungs, mediastinum, and pineal region; (b) bilateral primary adrenal mesotheliomas showing early malignancy; (c) bilateral congenital multicystic kidneys; and (d) a cavernous hemangioma of the liver. The second dog was an old female with: (a) an

adenocarcinoma of the thyroid with metastases to the cervical lymph nodes and lungs, and (b) a mixed tumor (chondrosarco-endothelioma) of the right caudal mamma.

Ball (1) described a 9 year old male poodle with: (a) a metatypic glandular epithelioma of the pancreas; and (b) a large round cell sarcoma of the duodenum with metastases to the oriental lymph nodes, lungs, spleen, and kidneys.

Mettam (12) reported the case of a male pointer 17 years old with: (a) an adenocarcinoma of the anal sebaceous glands with metastases in the right lung, and (b) a spindle cell sarcoma of the ileocecal mesentery.

In an old male setter Goodpasture (7) found: (a) chronic lymphatic leukemia with the primary focus in the 2,730 gm. spleen; secondary foci in the thymus, mediastinum, and pelvis; and metastases in the brain, heart, and testis; and (b) 2 large carcinomas of the lung.

Joest (11) reported the case of a female St. Bernard dog 12 years old with (a) a polymorphous chondroblastic sarcoma of the pubic bone with metastases in the lungs, and (b) multiple fibrosarcomas of the vagina.

Scheunert (16) recorded the case of a dog 11 years old with: (a) a primary spindle cell sarcoma of the subcutis without metastases, and (b) a primary spindle cell sarcoma of the omentum with metastases.

Holtmann (10) described an old female dog with: (a) a primary sarcoma of the liver with metastases, and (b) a primary carcinoma of the breast.

Cohrs (3) reported several cases of multiple primary tumors in dogs. Summaries of the acceptable cases are as follows:

*Case 1.*—Male dachshund, 14 years old; (a) cutaneous melanoma with transformation to spindle cell sarcoma adjacent to the left eye, (b) 4 hard cutaneous papillomas of the neck and trunk; (c) an ulcerated, cornified, squamous cell carcinoma of the lumbar skin; (d) 3 lumbar sebaceous gland adenomas, (e) 2 adenomas of the circumanal glands; and (f) a papillary adenoma (originating from bronchial glands) of the right lung.

*Case 2.*—Male poodle, 12 years old; (a) adenoma of the circumanal glands, (b) subcutaneous hemangioma of the left hind leg, and (c) ulcerated leiomyoma of the ileum.

*Case 3.*—Male pinscher, 20 years old; (a) multiple leiomyomas of the stomach, and (b) 3 cystadenomas of the testes.

*Case 5.*—Male mongrel dachshund, 15 years old; (a) adenocarcinoma of the circumanal glands with pulmonary metastases, (b) leiomyoma of the spleen, and (c) medullary carcinoma of the right testis.

*Case 6.*—Female Doberman, 16 years old; (a) teratoid mixed tumor of the left hindermost mamma with chondrosarcomatous metastases to the regional lymph nodes and lungs, (b) teratoid mixed tumor of the right hindermost mamma, and (c) fibroma of the spleen.

*Case 7.*—Female boxer, 11 years old; (a) 2 subcutaneous fibrolipomas, (b) 2 subcutaneous lipomas, (c) a subcutaneous fibroma, and (d) teratoid mixed tumors of both third mammae and of the right fifth mamma.

*Case 8.*—Female French bulldog, 13 years old; (a) medullary carcinoma of the right lobe of the liver with metastases to other liver lobes, the gall bladder, the portal lymph nodes, the diaphragm, and the lungs; (b) an epulis adjacent to the left upper canine tooth; (c) a leiomyoma of the stomach; and (d) 5 leiomyomas of the urinary bladder.

*Case 9.*—Female dachshund, 14 years old; (a) fibrosarcoma of the lower jaw, and (b) adenocarcinoma of the left hindermost mamma.

*Case 11.*—Female fox terrier, 14 years old; (a) teratoid mixed tumor of the right first mamma, and (b) carcinoma of the thyroid gland with pulmonary metastases.

*Case 12.*—Male pinscher, 14 years old; (a) multiple hard cutaneous papillomas, and (b) solid carcinoma of the liver with hepatic metastases.

*Case 13.*—Female sheep hound, 12 years old; (a) recurrent mixed cell sarcoma of the third left mamma, (b) teratoid mixed tumor of a right mamma, and (c) adenocarcinoma of the liver with pulmonary metastases.

*Case 14.*—Male pinscher, 5 years old; (a) periosteal mixed cell sarcoma of the left foreleg with pulmonary metastases of large round cell sarcoma, and (b) a medullary carcinoma of the left testis.

*Case 17.*—Male German sheep hound, 14 years old; (a) 2 leiomyomas of the stomach, and (b) a leiomyoma of the gall bladder.

*Case 18.*—Female pinscher, 15 years old; (a) sebaceous adenoma of the left hind leg, (b) 5 mammary adenomas, (c) an adenocarcinoma of the liver with metastases in the liver and portal lymph nodes.

*Case 19.*—Female fox terrier, 14 years old; (a) a sebaceous adenoma of the left hind leg, and (b) a papillary adenoma (originating from bronchial glands) of the left lung.

*Case 21.*—Male Rehpinscher, 16 years old; (a) leiomyoma of the gall bladder, (b) a medullary carcinoma in each testis, and (c) a medullary carcinoma of the thyroid gland.

*Case 22.*—Female pinscher, 11 years old; (a) subcutaneous hemangioma of the right thoracic wall, (b) a hard papilloma of the vulva, and (c) an adeno-

carcinoma of the right third mamma with metastases in the neighboring axillary lymph nodes.

*Case 23.*—Female fox terrier, 17 years old; (a) adenomas of the last left and the right third mammae; (b) a subcutaneous, large, round cell sarcoma of the right thoracic wall; (c) 5 subcutaneous lipomas of the trunk; (d) a polypoid fibroma of the internal os of the uterus.

*Case 24.*—Female mongrel Doberman pinscher, about 14 years old; (a) leiomyoma of the pylorus, and (b) 7 spindle cell sarcomas of the vagina.

*Case 25.*—Male fox terrier, 16 years old; (a) an adenoma of the circumanal glands, (b) a carcinoma of the liver with hepatic metastases, and (c) a lipoma of the spleen.

*Case 26.*—Female pug dog, 13 years old; (a) multiple pigmented cutaneous nevi, (b) subcutaneous lipoma of the right thoracic wall, (c) adenoma of the circumanal glands, (d) leiomyoma of the esophagus, and (e) a polypoid fibroma of the vagina.

*Case 27.*—Male hunting dog, 16 years old; (a) ulcerated, cornified, squamous cell carcinoma of the right cervical region; (b) adenocarcinoma of the left lung; and (c) squamous cell carcinoma of the urinary bladder.

*Case 28.*—Old dachshund of unmentioned sex; (a) ossifying, periosteal, round cell sarcoma of the left foreleg, and (b) carcinoma of the thyroid with metastases to the lungs.

*Case 29.*—Male fox terrier, 10 to 15 years old; (a) subcutaneous lipoma of the left thoracic wall, (b) a carcinoma simplex of the left testis, and (c) a papillary adenoma of the left lung.

*Case 30 (surgical).*—Female dog, 3 years old; (a) a subcutaneous lipoma in the neck, and (b) a fibroma of the vagina.

*Case 31 (surgical).*—Male spaniel, 9 years old; (a) squamous cell carcinoma of the foot, and (b) adenoma of the circumanal glands.

Feldman (6) described a male shepherd dog 13 years old with: (a) a squamous cell carcinoma of the gum over the left side of the mandible, with metastases to a left submaxillary lymph node; (b) multiple cavernous hemangiomas of the liver; (c) a leiomyosarcoma of the cecum; and (d) a papillary cystadenoma of the prostate.

In their investigation of the canine prostate in relation to normal and abnormal testicular changes, Zuckerman and McKeown (22) studied the prostates and testes of 243 dogs, among which was a fox terrier (Case 225) 6 years old that had: (a) an adenocarcinoma of the testis, and (b) a carcinoma of the prostate.

Curth and Slanetz (5) described acanthosis nigricans in a female, part collie, German shepherd dog, 14

years old, that also had: (a) a carcinoma of the liver, and (b) a subcutaneous lipoma.

TABLE I: BREEDS OF 37 DOGS

Pinscher (various types)	8
Fox terrier	7
Dachshund	5
Setter	2
St. Bernard	2
Poodle	2
Sheep hound	2
Shepherd	2
Pointer	1
Doberman	1
Boxer	1
Bulldog	1
Hunting dog	1
Spaniel	1
Terrier	1
<b>TOTAL</b>	<b>37</b>

TABLE II: TYPES OF NEOPLASMS

Carcinoma	36
Sarcoma	21
Adenoma	14
Leiomyoma	11
Fibroma	9
Lipoma	9
Hemangioma	5
Mixed tumor	4
Cyst	4
Papilloma	3
Cystadenoma	3
Mesothelioma	1
Epulis	1
Melanoma	1
Fibrolipoma	1
<b>TOTAL</b>	<b>123</b>

In an analysis of the 46 cases of multiple primary tumors in dogs found in the literature, the following statements may be made concerning age and sex. The ages were known in 36; 2 were under 6 years, 4 were 6 to 9 years, 29 were 10 to 20 years, and 1 was over 20 years old. Of the 43 animals in which sex was mentioned, 23 were females and 20 were males. In

TABLE III: PRIMARY SITES OF 123 NEOPLASMS

Primary site	Total tumors	Malignant tumors	Benign tumors
Breast	18	10	8
Subcutaneous tissue	14	2	12
Skin	12	5	7
Liver	12	8	4
Circumanal glands	7	2	5
Testes	6	5	1
Thyroid	5	5	0
Stomach	5	0	5
Vagina	5	2	3
Lungs	5	2	3
Prostate	4	2	2
Spleen	4	1	3
Bone	3	3	0
Buccal cavity	3	2	1
Omentum	2	1	1
Uterus	2	0	2
Ovaries	2	0	2
Small intestine	2	1	1
Urinary bladder	2	1	1
Gall bladder	2	0	2
Adrenals	1	1	0
Kidneys	1	0	1
Pancreas	1	1	0
Large intestine	1	1	0
Mesentery	1	1	0
Esophagus	1	0	1
Lymph nodes	1	1	0
Retroperitoneum	1	1	0
<b>TOTAL</b>	<b>123</b>	<b>58</b>	<b>65</b>

TABLE IV: COMBINATIONS OF MALIGNANT AND BENIGN NEOPLASMS

1 malignant, 1 benign	11
1 " , 2 "	7
1 " , 3 "	2
1 " , 4 "	1
2 " , 1 benign	11
2 " , 2 "	3
2 " , 4 "	2
3 " , 1 benign	1
2 benign	5
4 " , 1 benign	1
5 " , 1 benign	1
<b>Total</b>	<b>46</b>

Table I are listed the breeds of the 37 dogs in which the breed was stated. The 123 tumors found in the 46 cases included 58 malignant and 65 benign neoplasms. In Table II are summarized the various types of tumors represented. In Table III the primary sites of these 123 neoplasms are tabulated. Table IV contains the various combinations of malignant and benign neoplasms encountered in the 46 cases.

SUMMARY

The cases of multiple canine tumors recorded in the literature have been surveyed in order to determine the age, sex, and breed of dogs afflicted and the types and sites of the neoplasms encountered. The various combinations of malignant and benign neoplasms encountered in the 46 cases have been tabulated also.

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