GASTRIC NEOPLASIA

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ETIOLOGY

There is no definitive evidence on the etiology of gastric tumors in dogs and cats, and its relative rarity even in countries where there is a high incidence of gastric cancer in humans suggests that these species are not exposed to the same hazards as humans, are not exposed for a long enough period, or have a species-specific resistance. Gastric cancer in humans has been thought to be a consequence of dietary factors such as intake of salt, starch, mycotoxins, and polycyclical hydrocarbons present in smoked meat and fish.[47] Gastric adenocarcinoma has been induced experimentally in dogs fed nitrosamines.[26]

Recently, *Helicobacter* spp. have been involved in the development of proliferative or tumoral lesions in several animal species, including humans beings. Infection with *Helicobacter pylori* has been linked with gastric carcinoma and gastric mucosa–associated lymphoma in human beings.[44] The precise mechanism of carcinogenesis is unclear, but it may involve the induction of nitric oxide synthetase by proinflammatory cytokines with subsequent nitric oxide production and nitrosamine formation.[31] Interestingly, a high prevalence of gastric carcinoma has been observed in *Helicobacter mustelae*–infected ferrets orally treated with N-methyl-N-nitro-N-nitroguanidine, whereas *H mustelae*–free ferrets dosed with N-methyl-N-nitro-N-nitroguanidine did not develop gastric carcinoma.[12] This suggests the participation of *H mustelae* infection in the carcinogenic process. In Mongolian gerbils, long-term infection with

H pylori induces adenocarcinoma.[52] Increased proliferation of gastric epithelia, presumably due to chronic inflammation, has been noted in humans infected with *H pylori*[21] as well as in ferrets infected with *H mustelae,*[57] in rats infected with *Helicobacter heilmannii*–like organisms,[13] and in mice experimentally infected with *Gastrospirillum*-like organisms.[9] This association between bacteria and neoplasia has not been proven in dogs and cats, which frequently harbour different *Helicobacter* spp. in their stomach.[44] A large number of *H heilmannii*–like organisms have been detected in cases of hyperplastic pyloric polyps in young French Bulldogs.[15] Moreover, an intraepithelial *Campylobacter*-like organism similar to the agent of porcine intestinal adenomatosis *(Lawsonia intracellularis)* was detected in a case of canine hyperplastic gastritis.[28]

EPIDEMIOLOGY

Gastric tumors are considered to be uncommon in dogs, accounting for less than 1% of all reported neoplasms.[7, 47]

Carcinoma is the most common gastric neoplasm in the dog.[10, 34, 36, 55] The reported average age for dogs with gastric carcinoma varies from 7.5 to 10.2 years.[10, 21, 25, 41, 46] As is the case in human beings, the prevalence of gastric carcinoma is higher in the male population.[10, 37, 41, 46] Breed predisposition to gastric carcinoma has been reported for the Rough Collie, Staffordshire Terrier,[46] and Belgian Shepherd.[43] An examination of the pedigrees of eight Belgian Shepherds with gastric carcinoma demonstrated that two of these animals were full brothers and that the remaining dogs shared a common ancestor. The mean age of the affected Belgian Shepherds was 9.5 years, with a male-to-female ratio of 2.7:1.0.[43]

Other malignant tumors include leiomyosarcoma and lymphoma. Gastric lymphoma may represent a primary gastric tumor or part of a multicentrical disease.[5, 34] Dogs with a mean age of 7 years are usually affected by gastrointestinal lymphoma, with a higher incidence in male dogs.[5, 39]

Benign tumors are rare and are represented by adenomas and leiomyomas. A mean age of 16 years has been reported for dogs with gastric leiomyomas.[36] Gender bias (male:female ratio) ranges from 1:4[36] to 1.2:1.[39]

From 1985 to 1997, 46 cases of histologically confirmed canine gastric tumors were diagnosed at the Department of Surgery, Faculty of Veterinary Medicine of Milan. The type of tumor, mean age of affected animals, and male-to-female ratio are reported in Table 1. Eighteen of 42 cases of gastric carcinoma were diagnosed in Belgian Shepherds; 4 in Chow-Chows; 3 each in Schnauzers, Cocker Spaniels, and Staffordshire Terriers; 2 each in English Setters and mongrels; and 1 each in other purebreed dogs.

Lymphoma is the most common gastric tumor in the cat.[19, 53, 55] A review of the literature by Weller and Hornof in 1979[53] described eight cases of feline gastric tumor: six were lymphomas, one was an undiffer-

Table 1. HISTOLOGICAL CLASSIFICATION, AGE, AND MALE-TO-FEMALE RATIO IN 46 DOGS WITH GASTRIC TUMORS

Type of Tumor	Number of Cases	Mean Age (y)	Male:Female Ratio
Lymphoma	4	8.0	3:1
Carcinoma (total)*	42	9.5	1.5:1
Tubular adenocarcinoma	4	9.7	1:1
Papillar adenocarcinoma	1	12.0	0:1
Mucinous adenocarcinoma	7	8.5	7:0
Signet-ring cell carcinoma	15	9.3	1.1:1
Undifferentiated carcinoma	15	10.1	0.6.1

*Eighteen of 42 cases of gastric carcinoma were diagnosed in Belgian Shepherds; 4 in Chow-Chows; 3 each in Schnauzers, Cocker Spaniels, and Staffordshire Terriers; 2 each in English Setters and mongrels; and 1 each in other purebreed dogs.

entiated sarcoma, and one was a carcinoma. Lymphocytic-plasmacytic gastroenteritis may constitute a prelymphomatous disorder in cats and dogs.[5] Gastric adenocarcinomas are exceedingly rare in cats; only two cases were diagnosed during a 14-year period at the Washington Animal Disease Diagnostic Laboratory.[48] Cribb[6] reviewed the literature reporting more than 100 adenocarcinomas of the alimentary tract, only 1 of which was located in the stomach. No adenocarcinomas were reported by Priester and McKay[39] in a series of 28 feline gastric tumors.

From 1985 to 1997, four cases of histologically confirmed feline gastric tumor were diagnosed at the Department of Surgery, Faculty of Veterinary Medicine of Milan. All of these cases were histologically diagnosed as lymphoma. There were two male and two female cats affected; three were domestic shorthair cats and one was a Persian cat, and the mean age of these animals was 7 years.

PATHOLOGY

In the dog, most gastric adenocarcinomas are located in the lesser curvature and pylorus[30] and often involve most of the stomach body. Pyloric adenocarcinomas are usually annular and stenosing. The serosal surface of the affected areas shows the presence of prominent lymphatic vessels with a typical arborescent appearance; gastric and duodenal lymph nodes are firm and enlarged up to 2 cm in diameter.[10] The gastric wall is thickened and firm; on cut section, it appears whitish and vitreous and is up to 3 cm thick (Fig. 1). The mucosa lacks the normal rugal folded surface, and a single, large (up to 10 cm) deeply umbilicated ulcer may be present (Fig. 2).

Metastases are common, occurring in 13 of the 15 dogs in which a complete necroscopy was performed.[10, 43] Gastric lymph nodes are most often affected; other affected organs include the liver, spleen, perito-neum, and lung. Mesenteric and omental involvement is commonly
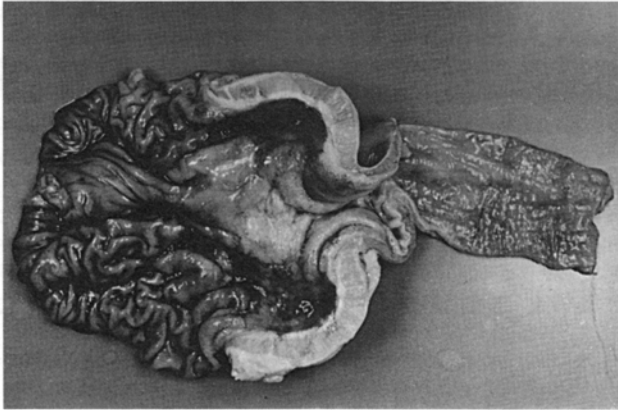
Figure 1. An 8-year-old male Belgian Shepherd Dog with gastric adenocarcinoma. Thickening of the gastric wall involving the fundus and the lesser curvature.

associated with a sclerotic reaction.[40] These metastatic patterns indicate that the tumor cells spread via the lymphatic hematogenous route and by peritoneal exfoliation.

Among the 42 dogs with gastric carcinoma diagnosed at the University of Milan during the period from 1985 to 1998, 15 tumors were located in the lesser curvature, 4 each in the antrum or pylorus, 3 in the fundus, and 2 in the greater curvature. In 14 dogs, the primary tumor was widespread to different gastric sites. Metastases were detected in 29 patients; the most commonly involved organs were the gastric lymph nodes (22 cases), liver (9 cases), spleen (7 cases), omentum (5 cases), lungs (5 cases), and diaphragm (3 cases).
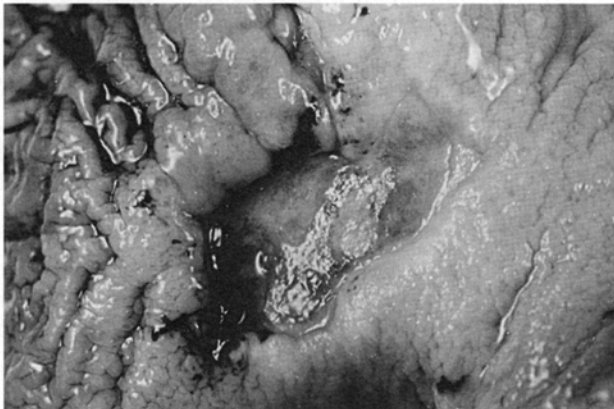

Figure 2. An 11-year-old male Belgian Shepherd Dog with gastric adenocarcinoma. Large and deeply umbilicated ulcer.

Gastric carcinomas show marked variation in histological structure not only between different patients but often between different areas in the same tumor and between the primary tumor and related metastases. Various histological classifications have been proposed for gastric carcinoma in the dog,[18, 36] although no correlation between the histological features, clinical behavior, and prognosis has been demonstrated. The World Health Organization classification[18] includes adenocarcimoma of the tubular, papillary, mucinous, and signet-ring cell types as well as undifferentiated carcinoma. An alternative approach adapted from Lauren's classification for humans has been proposed by Head,[18] and some studies have demonstrated that Lauren's classification can be easily adapted to the dog.[10, 24, 37] Lauren's classification distinguishes two types of gastric carcinoma: the diffuse type and the intestinal type. The diffuse type is characterized by the presence of anaplastic cells which develop poorly defined tubular patterns with highly infiltrative growth. The intestinal type shows well-polarized epithelial cells organized in tubular structures, often with prominent brush borders. The diffuse type is much more prevalent than the intestinal type in the dog.[10, 19, 24, 37, 43] In general, gastric carcinomas are histologically characterized by infiltrative growth from the deeper layer of the mucosa into the submucosa, muscularis, and serosa. In most of the cases, tumor cells are seen to produce a large amount of either extracellular or intracellular mucin (mucinous adenocarcinoma and signet-ring cell carcinoma, respectively). Tumor cells are frequently detectable in the lumen of lymphatic and blood vessels.[10]

Gastric lymphoma may appear as a single tumor mass or as multiple often ulcerated nodules (Fig. 3), or as a diffuse infiltrative lesion.[5] Regional lymph nodes are often involved.
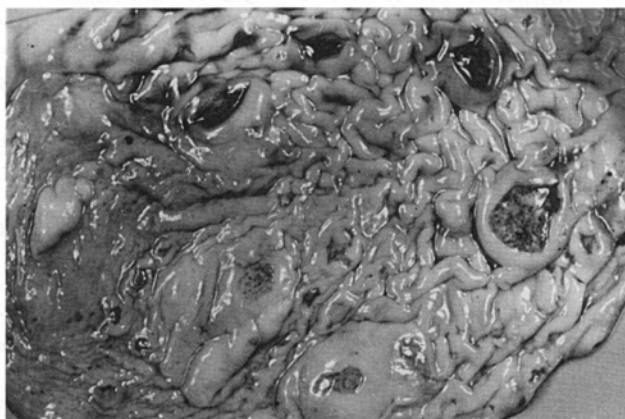

Figure 3. A 5-year-old male German Shepherd Dog with gastric lymphoma. Multiple nodules ulcerated on the mucosal surface.

In three of the four cases of canine gastric lymphoma diagnosed at our institution, the gastric tumor was widespread to different sites, although in the fourth case, the pylorus was affected; in two cases, the gastric lymph nodes were also affected, and in one case, the liver was affected.

Adenomas are flat or polypoid masses composed of moderately atypical glandular epithelium surrounded by lamina propria. Malignant changes have been reported in some adenomatous lesions in the dog.[3, 33] Adenomas share many features with nonneoplastic proliferative lesions[17, 19] such as hypertrophic gastritis (proliferative gastritis, hyperplastic gastritis), which is characterized macroscopically by strongly tortuous folding or nodular or polypoid changes of the mucosa.[51] Hyperplastic gastritis associated with intraepithelial *Campylobacter*-like organisms has been described in a 6-month-old female Beagle.[28] Recently, we have described pyloric polyps causing gastric outflow obstruction in six young French Bulldogs. These lesions were diagnosed histologically as hyperplastic polyps characterized by foveolar hyperplasia.[15] Solitary or multiple polyps from 0.5 to 1.0 cm in diameter are commonly found in the antral mucosa of old dogs; they also have the histological features of hyperplastic polyps.[17]

Leiomyomas can be single or multiple and appear as sessile round polyps protruding into the gastric lumen, which are characterized by a firm consistency and usually covered by a normal mucosa (Fig. 4). They are localized in the gastric body or near the cardia. The term "gastrointestinal stromal tumor" is applied in human pathology to define non-lymphoid mesenchymal tumors arising from the gastric and intestinal walls. Immunohistochemical studies have demonstrated that the majority of canine gastrointestinal stromal tumors are indeed of smooth muscle origin.[27]
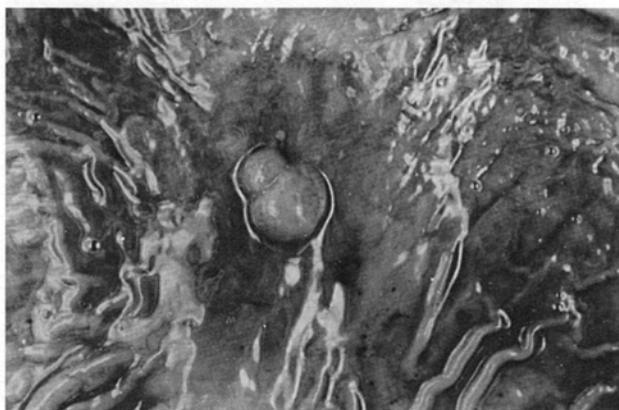

Figure 4. A 12-year-old male mongrel dog with gastric leiomyomas. Two round confluent polyps protrude into the gastric lumen and are covered by a normal mucosa.

Carcinoids are tumors derived from endocrine cells that are scattered throughout the gastrointestinal tract. Gastric carcinoids are rare in dogs[2, 19, 36]; however, endocrine cells were found in each of 5 cases of canine gastric adenoma and in 13 of 22 cases of canine gastric carcinoma.[42] Although the endocrine cells represented a minority of the tumor cell population, this finding indicates that a significant proportion of gastric mucosal tumors of the dog contain a mixture of epithelial and endocrine cells.

DIAGNOSIS

History and Clinical Signs

Clinical signs associated with gastric malignancies are usually mild and vague at the outset and are often chronic, ranging from 2 weeks to 18 months prior to presentation; the median duration is 2 months.[34, 54] In some dogs, however, the signs may be acute and may mimic gastrointestinal obstruction.[4, 49]

Vomiting, weight loss, and anorexia are the most common symptoms.[34, 49, 55] Vomiting is usually persistent and progressive. It is often not related to food intake and may consist of mucus, swallowed saliva, or in the case of bleeding gastric lesions, partially digested blood with the classic "coffee grounds" appearance.[19, 54] Vomiting can vary in both frequency and severity. The authors have not observed a strict relationship between the extent of gastric wall involvement and the severity of vomiting; not infrequently, small and localized gastric lesions have been associated with severe vomiting, although diffuse involvement of the gastric wall has caused a milder symptomatology. The weight loss may be the result of poor digestion, loss of protein and blood from an ulcer, or generalized cachexia.[55] Anemia, diarrhea, and melena are not common but may be seen in cases of tumor ulceration.[49] Vomiting may be accompanied by diarrhea in cases of the diffuse forms of alimentary lymphoma. Perforation of the tumor occurs more frequently with lymphoma than with other malignancies and can cause signs of an acute abdomen with peritonitis.[49]

Benign gastric tumors are often clinically silent and may be observed as incidental findings during endoscopy or necropsy.[49] Animals with leiomyomas are often presented for the investigation of anemia, which may be microcytic or melena. Polyps of the antropyloric region can cause signs of gastric outflow obstruction.[14]

Clinical signs in cats with gastric tumors are similar to those observed in dogs. Vomiting is the most consistent sign and is often accompanied by anorexia and lethargy. Cats with alimentary lymphoma often have a history of protracted and vague clinical signs which progress to anorexia, vomiting, or diarrhea.[4]

The clinical findings in 46 dogs with gastric tumors observed at the University of Milan are listed in Table 2. In dogs with gastric carcinoma,

Table 2. CLINICAL FINDINGS IN 46 DOGS WITH GASTRIC TUMORS

Clinical Findings	Number of Cases
Vomiting	44
Anorexia	18
Weight loss	22
Hematemesis	13
Melena	7
Palpable abdominal mass	16
Anemia	5
Increased liver enzymes	8
Hypoglycemia	3

intermittent and persistent vomiting was the most consistent sign (41/42 dogs) and was usually not related to feeding or to time of day. Most commonly, the vomitus consisted of a yellow or white foamy or fluid material or of partially digested food. Vomitus was often mixed with fresh or clotted blood. The vomitus consisted of only blood clots or "coffee grounds" in a few dogs; anorexia, weight loss, and hematemesis were also common findings, particularly in the late stage of the disease. Six dogs had melena. Dogs affected by gastric lymphoma showed similar clinical signs, except for one dog with gastrointestinal lymphoma that did not vomit but showed weight loss, dehydration, anorexia, and melena.

The above signs were seen from 10 days to 1 year before diagnosis, with a mean time of 3 months. Most dogs had a sudden outset of symptoms, but some cases of chronic and insidious onset were seen.

In four cats with gastric lymphoma, the most consistent sign was vomiting; the vomitus contained food initially but later consisted of a foamy or fluid yellow-white material. One cat vomited clotted and fresh blood before presentation. Anorexia was present in two cats, although two cats had a normal appetite. Signs were seen from 2 to 7 months before admission, with a mean time of 4 months.

Pyloric hyperplastic polyps diagnosed by the authors in six young French Bulldogs caused severe chronic vomiting due to pyloric obstruction. Vomiting usually occurred between 1 and 6 hours after eating and generally consisted of fluids and food from the last meal. In nine dogs of various breeds with hyperplastic (2 dogs), adenomatous (3 dogs), and inflammatory (4 dogs) polyps of the stomach, only two with polyps located at the pylorus vomited, and the others were clinically silent.

Physical Findings

The physical examination of dogs and cats with gastric neoplasia is usually not specific. The animal is often chronically debilitated but can also be in relatively good condition. Many cats with gastric lymphoma are otherwise moderately healthy; in fact, about 70% to 75% of these

cats are feline leukemia virus (FeLV) negative and are not affected by systemic FeLV-induced problems.[50]

Gastric masses are not easily palpated, and abdominal pain is only rarely present. In cases of multifocal lymphoma, other organ masses or mesenteric lymphadenopathy might be palpated.[49] Palpation of a gastric mass may be easier in the cat.

Gastric bleeding may cause pallor and weakness. Signs associated with metastatic involvement of the liver (e.g., ascites, jaundice) or other organs may be recognized.[54]

Benign gastric tumors usually do not cause alterations detectable at the physical examination.

About 50% of dogs with gastric tumors seen at the University of Milan were presented in good general condition, although another 50% showed weight loss, dehydration, and depression. In about one third of these dogs, a mass lesion in the gastric region was palpated, although abdominal pain was rarely elicited.

Among four cats with gastric lymphoma, two showed weight loss and depression, although two had a normal general condition. In three of the four cats, a cranial abdominal mass was palpated.

French Bulldogs with gastric polyps were stunted and underweight but were alert and with good appetites. Palpation was always unremarkable.

Hematological and Biochemical Findings

Hematological and serum biochemical abnormalities in dogs and cats with gastric neoplasia are uncommon and nonspecific.[49] Normocytic normochromic or microcytic hypochromic anemia can occur as a consequence of chronic disease secondary to malignancy or to chronic gastric bleeding (i.e., iron deficiency anemia).[4, 49] Neutrophilic leukocytosis secondary to tumor necrosis can also occur. Hypokalemic or hypochloremic metabolic alkalosis can occur secondary to vomiting or to gastric outflow obstruction. Biochemical abnormalities are usually related to the metastatic extension to other organs.[4, 49]

Hematological and biochemical changes in cases of gastric lymphoma are highly variable and depend on the extension of the disease; anemia, neutrophilic leukocytosis, lymphocytosis, and hypoproteinemia can sometimes be detected.[4] Anemia is uncommon in cats with gastric lymphoma; most of these cats are FeLV negative and lack the direct viral effect of FeLV on the bone marrow cells.[4]

Usually, no changes in the laboratory data are observable in the presence of benign gastric tumors. Most of the 42 dogs with gastric carcinoma observed at the University of Milan did not show severe hematological or biochemical abnormalities (see Table 2). In a few dogs, mild anemia, leukopenia, and increased hepatic enzymes were detected. Hypoglycemia was observed in 3 of these dogs. One dog with gastric

lymphoma showed mild anemia, lymphocytic leukocytosis, and throm-bocytopenia.

Only one of four cats with gastric lymphoma showed severe anemia. One of these cats had an elevated serum creatinine level.

Radiographic Findings

Direct radiographic examination should always be included in the diagnostic procedure for gastric neoplasia. Plain abdominal radiographs might reveal a mass in the gastric region, thickening of the gastric wall, or absence of a normal rugal folding pattern. Abdominal radiographs might also reveal metatastatic involvement of other organs or lymph nodes. Thoracic radiographs are only rarely positive for metastasis but should always be taken.[55]

Usually, barium studies are needed to demonstrate a gastric lesion. Contrast studies may outline intraluminal masses, thickening of the gastric wall, loss or derangement of the rugal folds, ulcers, filling defects, or delayed gastric emptying.[4, 49, 54] Most gastric ulcerations identified radiographically are caused by gastric carcinoma.[16] Gastric polyps and leiomyomas may be radiographically detectable when they attain consid-erable size and cause a mass lesion or delayed gastric emptying of the contrast medium.

Dogs with suspected gastric tumors seen at the University of Milan initially underwent systematical plain and simple contrast radiographic studies of the abdomen and gastrointestinal tract as well as plain radio-graphs of the thorax. Plain abdominal radiographs rarely revealed fea-tures indicative of gastric neoplasia, except for a few cases of thickening or roughening of the gastric wall (Fig. 5). Contrast studies using barium meal were only rarely suggestive of gastric neoplasia, showing delayed or incomplete gastric emptying and filling defects in the pyloric or lesser curvature (Fig. 6). Features highly indicative of metastatic involvement of the lung, liver, or abdominal lymph nodes were only rarely detected on radiographs.

More recently, dogs admitted to our institution in which a gastric neoplasia is strongly suspected undergo upper endoscopy after survey radiographs of the abdomen and thorax. The authors prefer to routinely use endoscopy instead of contrast study of the gastrointestinal tract for the diagnosis of gastric malignancies. Its accuracy for diagnosis has been estimated at greater than 95% in human medicine.[1]

In three cats with gastric lymphoma, plain and contrast radiographs of the gastrointestinal tract were unremarkable, except for one case in which thickening of the gastric wall in the fundic area was evident on direct examination.

Delayed gastric emptying was demonstrated by contrast radiogra-phy in all six French Bulldogs affected by pyloric polyps. In one dog, the contrast medium revealed a suspect irregular mass completely occu-pying the antral canal.
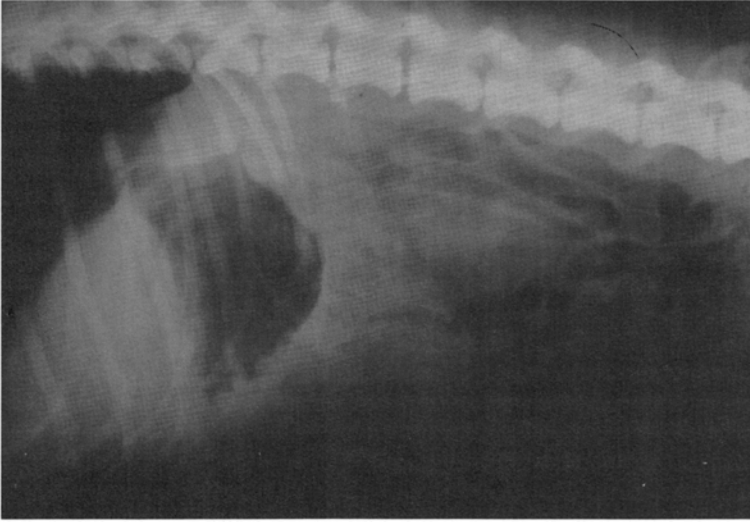
Figure 5. Radiograph of a dog with infiltrative gastric carcinoma: the gastric wall appears diffusely thickened.
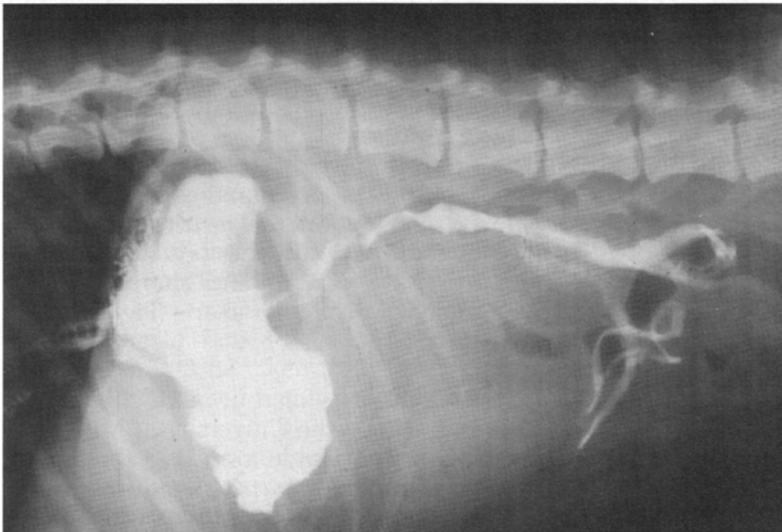

Figure 6. Positive contrast gastrogram of a dog with gastric carcinoma showing filling defects of the gastric wall.

Radiology can be helpful in cases of suspected metastatic diffusion of neoplasia, but unfortunately, many patients have more extensive disease found at laparotomy than may be predicted by preoperative radiographic or ultrasonographic examination.

Endoscopic Findings

Endoscopy is instrumental either to confirm suspected gastric lesions that have been observed by radiography or to visualize lesions not demonstrated on contrast studies. The authors consider endoscopy to be the elective study of choice for diagnosing gastric tumors. The size, location, and morphology of the tumor, including the proximal and distal extent of spread, as well as other mucosal abnormalities are evaluated. Biopsy can be performed at the same time, and the likelihood of a positive yield on multiple endoscopic biopsies is high. The possibility of surgical treatment can also be evaluated by endoscopy.

On endoscopy, gastric malignancies can appear as mass lesions, polypoid lesions, ulcers, or infiltrative lesions.

According to the classification used in the endoscopic examination of humans, gastric carcinomas are typed as polypous, ulcerative, exophytic ulcerative, infiltrative, and advanced unclassifiable tumors.[32] The most common form seen at the University of Milan in dogs affected by gastric carcinoma was the ulcerative type (62%). Less frequently seen were the infiltrative (19%) and the advanced unclassifiable (12%) forms, and the polypous and the exophytic forms were seen only rarely (3% each). In the ulcerative form (Fig. 8), the ulcer was generally large (3–10 cm in diameter), except two cases in which it was quite small (3–5 mm) and characterized by a necrotic base and raised irregular rim. The ulcer was most commonly located on the lesser curvature. The infiltrative form was characterized by a diffuse infiltration of the gastric wall, altering the gastric lumen and shape. The wall consistency was markedly increased, and the gastric plication was uneven and covered by a friable mucosa. In the advanced unclassifiable form, the gastric architecture was severely corrupted, proliferative and ulcerative lesions were mixed and necrotic, and hemorrhagic areas were also present. The polypous form consisted of a proliferative tumor with irregular shape (Fig. 7), although in the exophytic ulcerative form, the tumor was ulcerated with an indistinct edge.

Lymphoma may appear as a mass lesion, but more often, it has an infiltrative pattern. In three dogs seen at the University of Milan, gastric lymphoma was of the advanced unclassifiable form (Fig. 9), although it was infiltrative in one dog. Lymphoma was usually diffuse, and the mucosa appeared white, friable, and easily movable from underlying tissue but severely thickened and firm. On biopsy, a conspicuous amount of tissue was always obtained.

The endoscopic appearance of gastric lymphoma was variable in four cats. One cat had raised and thickened rugal folds of the gastric

fundus, and gastric side of the cardia was covered by superficially eroded mucosa. In three cats, a large ulcer (3–4 cm in diameter) with a thick and irregular rim was observed on the greater curvature, the gastric body, and the small curvature, respectively (Fig. 10).

Infiltrative tumors that have no mass or mucosal involvement are more difficult to identify but might be associated with a lack of distensibility following insufflation with air or with an abnormal rugal folding pattern.[49] The endoscopic aspect of infiltrative tumors should be differentiated from hypertrophic and eosinophylic gastritis. Leiomyomas usually appear as expansile submucosal masses often in the cardia or lesser curvature.

Benign polyps are generally sessile or pedunculated nodules of mucosal proliferation that can be single, multilobated, or grape-like. Rarely, diffuse multiple polyps invade the entire gastric mucosa. Gastric polyps were diagnosed by endoscopy in 15 dogs. Pyloric hyperplastic polyps observed in 6 of 15 French Bulldogs ranged in size from 2 to 4 cm and were sessile, simple, or multilobular and covered by normal to superficially eroded mucosa.[15] The lesion completely obscured and occluded the pyloric orifice. Adenomatous, inflammatory, and hyperplastic polyps observed in the remaining 9 French Bulldogs were usually small (0.5–2.0 cm), sessile, and clinically silent, except when located at the pylorus. In 1 dog, antral inflammatory polyps were multiple and grape-like.

Some nontumoral lesions show endoscopic features similar to those of gastric tumors and should be considered in the differential diagnosis (Figs. 11, 12).

All gastric lesions should be biopsed using endoscopic forceps or cytology brushes. Histological examination of forceps biopsies obtained under endoscopic control is the decisive test to diagnose gastric tumors. In a large survey of the histology of peroral gastric biopsies from 501 dogs, 26 cases of carcinoma, 7 cases of lymphoma, and 1 case of adenomatous polyp were diagnosed.[51] Biopsies should be multiple and deep, because diagnostic accuracy increases with the number of biopsies taken.[49] Biopsies should be taken even in the absence of macroscopically evident lesions to identify infiltrative tumors or early stages of cancer.

Multiple biopsies should be taken for histology, because the presence of necrosis and inflammatory reaction can make it difficult to recognize tumoral tissue.[55] In the presence of an ulcerative lesion, multiple samples should be taken from the edge of the lesion. False-negative results can be obtained in tumors such as leiomyoma and some canine carcinoma characterized by the development of tumor tissue in the submucosa or in the deeper layer of the stomach wall that is not accessible to biopsy forceps (Fig. 13). In gastrointestinal lymphoma, which usually originates in the submucosa, only inflammatory infiltrates can be present in the more superficial mucosa.[5] In patients in which endoscopy is suggestive of gastric tumors but biopsy is negative for the presence of tumoral cells, full-thickness surgical biopsies should be obtained and examined histologically. The authors have successfully

Figure 7. Polypous form of gastric carcinoma of the lesser curvature in a 10-year-old, female, West Highland white terrier. The proliferative tumor has a nodular surface and a friable and bleeding mucosa. The surrounding mucosa appears involved by the neoplastic process.

Figure 8. Ulcerative form of gastric carcinoma of the lesser curvature in an 8-year-old, male, Siberian Husky. Large and deep ulcer with distinct border and nodular whittish base extends from the cardia to the lesser curvature and involves the lateral walls of the stomach.

Figure 9. Advanced unclassifiable form of gastric lymphoma of the lesser curvature and antrum in an 8-year-old, male, Schnauser. The mucosa is severely thickened and firm, appearing as a large mass lesion occupying most of the gastric antrum.

Figure 10. Ulcerative form of gastric lymphoma of the lesser curvature in a 6-year-old, female, domestic shorthair cat. A large ulcer (about 4×4 cm) with distinct border and an even and friable base completely involves the lesser curvature and the lateral walls of the stomach.

Figure 11. Differential diagnosis: pyloric antrum of a dog affected by eosinophilic gastritis in a 3-year-old, male, German Shepherd. The mucosa is diffusely thickened, firm, and uneven, organized in rough longitudinal rugal folds; the endoscopic appearance may mimic an infiltrative form of gastric lymphoma.

Figure 12. Differential diagnosis: pyloric hyperplastic polyposis in a 10-year-old, female, Siberian Husky. The endoscopic appearance may mimic a proliferative form of gastric carcinoma.
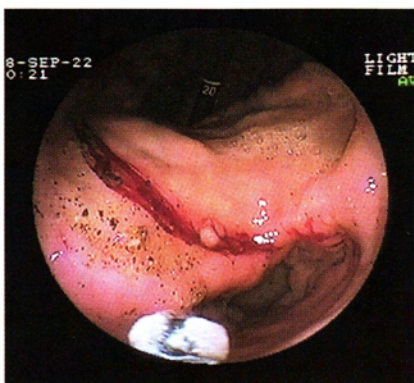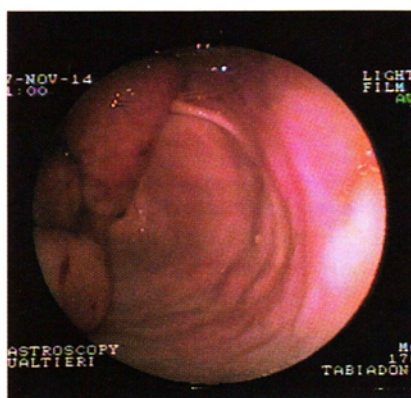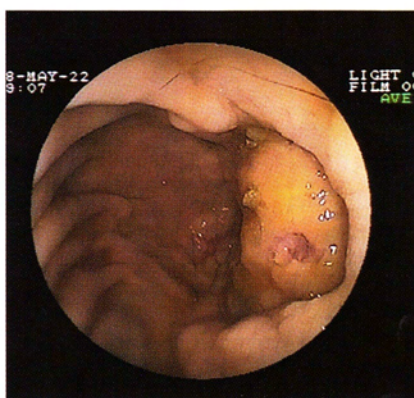
Figure 7.

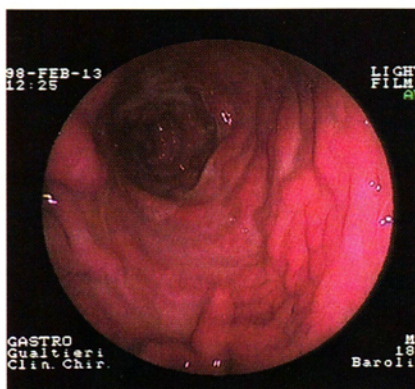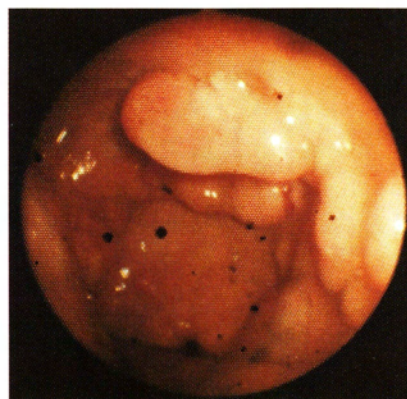
Figure 8.

Figure 9.

Figure 10

Figure 11.

Figure 12.

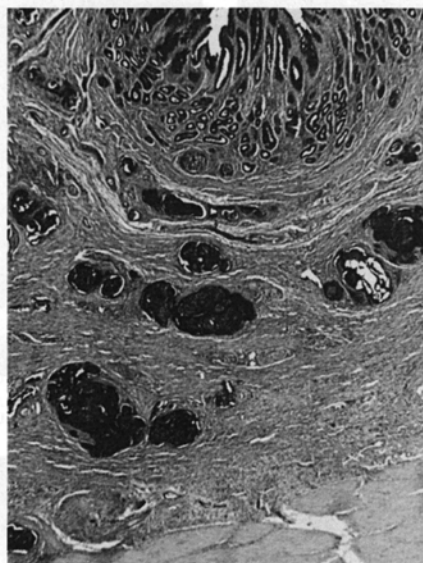*Color reproduction courtesy of* Waltham/Dolma s.p.a. Italy.

Figure 13. A 10-year-old female Belgian Shepherd Dog with gastric adenocarcinoma. The submucosa and muscular layer are infiltrated by groups of tumor cells selectively stained for mucins (in black). The overlaying mucosa is unaffected (periodic acid-Schiff and alcian blue, original magnification ×50).

employed an endoscopic tru-cut biopsy forceps, which allows deeper sampling than the traditional forceps, to diagnose gastric neoplasia.

Fiberoptic procedures allow also direct gastric sampling for cytological examination by brushing or lavage.[23] In cytological specimens, commonly observed gastric epithelial cells in both normal and abnormal conditions are seen as cohesive clusters of columnar cells. The nucleus is small and round, with a finely granular chromatin pattern. In humans, parietal cells are described as large, pale, triangular cells with granular cytoplasm. Ciliated respiratory cells, squamous cells of oral and esophageal origin often carrying bacteria, and food particles may contaminate the specimen. Gastric tumors can be classified by cytology as epithelial, spindle-cell (mostly mesenchymal), and round-cell tumors. Cytology can help to distinguish between the intestinal type and diffuse type of gastric carcinoma, with the latter being characterized by the presence of signet-ring cells in which a large, cytoplasmic, mucus-containing vacuole forces the nucleus to the periphery of the cell. Nonepithelial gastric tumors develop beneath the gastric epithelium and have to ulcerate to be diagnosed by brush cytology or lavage. Cytology allows a diagnosis of gastric lymphoma (Fig. 14). The cytological diagnosis of gastric lymphoma can be difficult in cases of well-differentiated lymphocytic lymphoma, however, as the presence of mature lymphocytes is a common finding in chronic gastritis. A false-positive diagnosis of neoplasia must
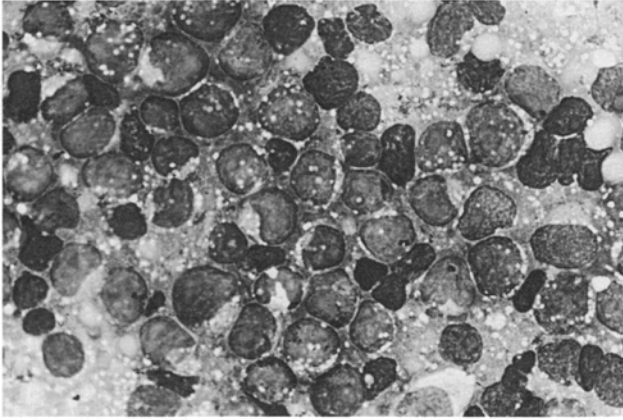
Figure 14. A 7-year-old male domestic shorthair cat with gastric lymphoma. Cytological smear from a gastric brushing showing an homogeneous population of immature, medium- to large-sized lymphoid cells (May-Grünwald Giemsa, original magnification ×600).

be avoided when employing cytology; therefore, extreme caution should be used in making a cytological diagnosis of neoplasia in cases of ulcers, where the surrounding tissues may show chronic inflammation and reactive fibrosis and the epithelium undergoes hyperplasia and regeneration. These cases can be extremely difficult to assess, and a histological sample should always be taken.

Ultrasonographic Findings

Transabdominal ultrasonography has been reported to be valuable in the diagnostic work-up of animals suspected of having gastric tumors.[22, 38] The features to be looked for in an ultrasonographic examination are thickening of the gastric wall, disruption of the gastric wall layers, enlargement of abdominal lymph nodes, and hypoechoic lesions in other organs such as the liver or spleen.[22, 38] Solitary or multiple sites of alimentary lymphoma can be identified by ultrasonography.

Based on preliminary data, it appears that a gastric malignancy should be strongly suspected when a thickened gastric wall associated with loss of gastric wall layering and enlargement of regional lymph nodes are observed.[22] Ultrasound-guided fine-needle aspiration biopsy and core-automated biopsy have been used successfully for the diagnosis of gastrointestinal diseases in small animals,[8] but there are few data on the outcome of transabdominal gastric tumor biopsy. A fine-needle aspiration of lymphomatous masses or lymph nodes usually yields sufficient material to obtain a cytological diagnosis.[4]

Endoscopic ultrasonography is a new imaging technique that uses a high-frequency transducer at the end of an endoscope. It allows highly

accurate staging of the depth of invasion of the primary tumor (tumor stage) and evaluation of locoregional lymph node status.[1]

Ultrasonography is sometimes used for the evaluation of metastasis in dogs at the University of Milan. Hepatic and lymph node involvement is more frequently detected by means of ultrasonography. Cats with single or multiple abdominal masses sometimes undergo ultrasonography and fine-needle aspiration of masses.

Exploratory Laparotomy

Surgery is the most invasive but also the best diagnostic method for evaluating gastric neoplasia in the dog and cat.[49] It allows palpation of the stomach for evaluating mass lesions or thickening of the gastric wall. Metastatic involvement of other organs or lymph nodes can also be evaluated. As previously mentioned, many patients have more extensive disease found at laparotomy than was predicted by preoperative radiographic or ultrasonographic examination.

The surgeon can perform a full-thickness gastric biopsy, thus minimizing false-negative results. The real extent of the lesion can be fully appreciated in order to plan a correct therapeutical approach (surgery vs chemotherapy) and to formulate a prognosis.

The authors generally proceed to exploratory laparotomy only in dogs in which surgical treatment is considered. If indicated, gastrectomy is performed at the same time.

STAGING

The clinical stage for gastric adenocarcinoma in dogs and cats can be obtained by applying the tumor, lymph node, and metastasis (TNM) classification proposed by Owen.[35] The minimal requirements for assessing tumor category are clinical and surgical examination (laparotomy or laparoscopy, endoscopy); for lymph node category, surgical examination (laparotomy or laparoscopy) is required; and for metastasis category, clinical and surgical examination and radiography of thorax are necessary. In the TNM classification, the deepest layer of the gastric wall reached by the tumor, the involvement of the regional lymph nodes, and the presence of distant metastases are schematically recorded according to the following indications:

Tumor categories: 0, no evidence of tumor; 1, tumor not invading serosa; 2, tumor invading serosa; 3, tumor invading the neighboring structures (m is added for multiple tumors).

Lymph node categories: 0, no evidence of regional (gastrosplenic) lymph node involvement; 1, evidence of regional lymph node involvement; 2, distant lymph nodes involved.

Metastasis categories: 0, no evidence of distant metastasis; 1, distant metastasis detected (specify site[s]).

The TNM data collected in a study of 11 cases of canine gastric carcinoma indicate that the diagnosis is frequently made in the late stage of the disease.[43]

In human pathology, the term "early gastric cancer" is applied to a carcinoma limited to the mucosa or mucosa/submucosa, regardless of the presence of lymph node metastases.[20] Patients with early gastric cancer have a much more favorable prognosis than patients with advanced carcinoma.[20]

The TNM system cannot be used for lymphoma. A clinical staging classification of lymphoma in domestic animals has been proposed.[35] The extent of the disease is assessed on clinical, radiographic, and hematological examination and is described as being with or without systemic signs. This classification includes:

Stage I: involvement limited to a single node or lymphoid tissue in a single organ.
Stage II: involvement of many lymph nodes in a regional area.
Stage III: generalized lymph node involvement.
Stage IV: liver or spleen involvement.
Stage V: involvement of blood and bone marrow or other organs.

Each stage is subclassified into a (without systemic signs) and b (with systemic signs) parts.

TREATMENT

Surgery is the only potentially curative modality for localized gastric carcinoma. At the time of surgery, a careful evaluation of liver and regional lymph nodes should be made to stage the cancer correctly.[55] All abdominal lymph nodes (the gastric and hepatic lymph nodes in particular) and the liver and spleen should be evaluated for metastatic involvement. The authors have also frequently found metastatic involvement of the omentum, spleen, and diaphragm. Less frequently, the parietal peritoneum was involved.

The extent of the lesion is then evaluated by palpation of the stomach, which complements endoscopic evaluation. We do not recommend making a gastrotomy incision, as this may cause dissemination of tumor cells or contamination of the abdominal cavity.

Malignancies of the stomach should be removed by wide local resection with margins that include greater than 1 to 2 cm of apparently normal tissue around the tumor. Segmental resection and partial gastrectomy are usually indicated. In many cases, such dissections are precluded by the extent and location of the lesion. Tumors involving the antro-pyloric area can be managed by antropylorectomy followed by gastroduodenal anastomosis (Billroth I procedure) or gastrojejunostomy

(Billroth II procedure). The Billroth II procedure is considered to be associated with increased morbidity.[54, 55] Lesions requiring extensive surgery (complete gastrectomy) are generally too advanced to make these procedures worthwhile in terms of survival,[55] and in the authors' opinion, they are probably not ethically acceptable in domestic animals. Palliative surgery with the aim of improving the clinical signs in case of inoperable or metastatic obstructive lesions may justifiably increase survival times by some months.[49]

Gastric surgery for removal of malignancies should carefully follow the principles of oncological surgery to minimize the risk of tumor cells seeding in the abdominal cavity or other areas. A wide exposure is provided at the surgery site, thus ensuring easy access to the tumor and potential metastasis and aiding minimal manipulation of and trauma to neoplastic tissue.[29, 56] The laparotomy margins of the incision are protected with laparotomy pads or adhesive tissue. Minimal gentle handling of neoplastic tissue is imperative, as excessive surgical trauma may cause exfoliation of tumor cells into the body cavity or embolization in the systemic circulation.[29, 56] Early vascular ligation (especially venous) should be attempted to diminish the release of tumor emboli into the systemic circulation.[56] The need for sterile lavage of the residual surgery site and abdominal cavity is controversial, although it is generally advisable.[45]

Removal of regional lymph nodes draining the primary tumor site is controversial as well. Removal is indicated for lymph nodes involved by the neoplastic process, but this is not always easily established. Features of lymph node metastasis are node enlargement, immobility, and adhesions to surrounding tissue. In man, the ability to correctly diagnose metastatic involvement by intraoperative macroscopic examination has been reported to be low. It has also been shown that 30% of all metastases to lymph nodes occur in small nodes.[1] Conversely, a hyperplastic or reactive lymph node can represent a first line of immune defense of the organism. The routine application of lymphadenectomy for potentially curative gastric cancer is currently being evaluated in several trials.

Patient stabilization is generally needed before surgery. Fluid and electrolyte imbalances should be corrected. Blood is transfused in case of severe anemia (packed cell volume < 20%).

Enterostomy tube placement can be considered postoperatively to provide nutrients directly to the small intestine. Alternatively, 24 to 48 hours of fasting and fluid therapy should be provided after gastrectomy. Nutrition can be gradually replenished with small amounts of bland food. Total parenteral nutrition may be beneficial in some cases. The extraordinarily rich blood supply, rapidly regenerating epithelium, and defense mechanism provided by the omentum allow gastric incisions to heal quickly.[11] Electrolytes (especially potassium) should be monitored postoperatively.[11] Radiation therapy is rarely used, because surrounding organs poorly tolerate it.[55]

Although combination chemotherapy, including 5-fluorouracil de-

rivatives and mitomycin C, has improved the 5-year survival rate in humans with gastric carcinoma, it has reportedly been of little or no benefit in dogs.[4] Results of various combinations of chemotherapy for canine gastric carcinoma have been discouraging.[4, 34]

Treatment of gastric lymphoma can be either surgical or chemotherapeutical or both. Localized lymphoma can be excised. The need for postoperative chemotherapy after "complete" resection of localized lymphoma is unknown. If metastases have not been detected in other sites and if the margins of resection are free of tumor, chemotherapy may not be necessary.[55] Nevertheless, the real extension of lymphomatous involvement can be difficult to assess; thus, adjunctive chemotherapy is often advisable. Chemotherapy alone is indicated for inoperable, diffuse, and metastatic lymphoma. Various combination protocols have been described for gastrointestinal lymphoma in dogs and cats. Gastrointestinal lymphoma appears to be more resistant to chemotherapy than other forms of lymphoma. The currently suggested protocol for treatment of gastrointestinal lymphoma in the dog is cyclophosphamide vincristine cytosine arabinoside prednisone (COAP) chemotherapy followed by the chlorambucil prednisone methotrexate (LMP) protocol for mainteinance.[4] For adjuvant chemotherapy, either the COAP or LMP protocol can be used, although remission and survival times appear to be longer when using the former.[4]

Eleven dogs affected by gastric carcinoma have been treated at the University of Milan (Table 3). The remaining 31 dogs with gastric carcinoma have been euthanatized due to tumor inoperability (extension to > 70% all of the stomach), distant metastatic involvement, or owner request. Preoperative care included rehydration, correction of fluid and electrolyte imbalances, and blood transfusion when necessary.

Among the treated dogs, 10 underwent surgical treatment and 1 received photochemotherapy. Surgery consisted of partial distal gastrectomy followed by gastroduodenal anastomosis (Billroth I procedure).

Table 3. TREATMENT AND SURVIVAL TIMES OF DOGS AFFECTED BY GASTRIC CARCINOMA SEEN AT THE UNIVERSITY OF MILAN

Case	Treatment	Survival Time
1	PG	3 years (dead due to UP)
2	PCT	45 days (euth due to PD)
3	PG	55 days (euth due to PD)
4	PG	30 days (euth due to PD)
5	PG	38 days (dead due to PD)
6	PG	40 days (dead due to PD)
7	PG	4 years (dead due to UP)
8	PG	3 days (dead due to UP)
9	PG	20 months (euth due to PD)
10	PG	3 months (euth due to PD)
11	PG	5 months (alive)

PG = partial gastrectomy; PCT = photochemotherapy; UP = unrelated problem; euth = euthanasia; PD = progressive disease.

When possible, a margin of 1 to 3 cm of apparently normal tissue around the tumor was removed with the neoplasm. Gastrectomy involved a portion of the organ not greater than 70%. When the tumor was localized to the pylorus, a modified Billroth I procedure (von Haberer procedure) was performed. Locoregional lymph nodes were always removed even if not enlarged. At the request of one owner, gastrectomy was performed in a dog with two hepatic metastases.

Photochemotherapy consisted of a combined treatment of dihematoporphyrin ether (2.5 mg/kg), a photosensitizer drug, and a dye laser as a light source transmitted by an endoscope-guided optic fiber.

Postoperative care included 48 to 72 hours of fasting and fluid therapy (electrolyte solutions), antibiotics for 10 days (cephalosporins), H$_2$ blockers (ranitidine) or omeprazole for 20 days, and promotility agents for 7 days (clebopride). Feeding was started 2 or 3 days after surgery with a high-energy diet (Waltham Concentration Instant Diet, Masterfood Austria-Bruck/Leitha) administered in small amounts six to eight times a day. Feeding was then gradually normalized.

Complications of surgery were limited in a few cases to postprandial discomfort, vomiting, and diarrhea of 10 to 15 days duration, probably due to lack of the normal storage function of the stomach and to consequent passage of undigested food directly into the small intestine ("dumping" syndrome).

Survival times of treated dogs are summarized in Table 3 and Fig. 15. Except for 3 of 11 dogs, death was generally due to tumor-related problems. Four dogs affected by gastric lymphoma were euthanatized at the owners' request.

Of four cats with gastric lymphoma, one was euthanatized at exploratory laparotomy due to extensive metastatic involvement and bad gen-
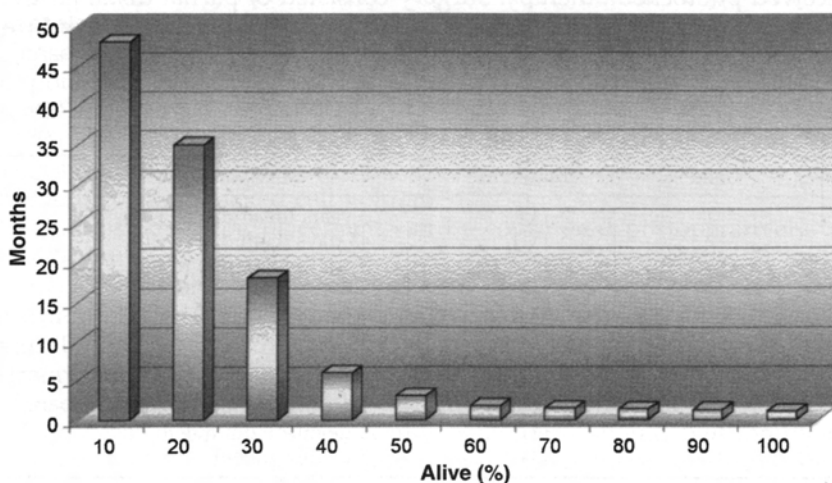

Figure 15. Survival of 10 dogs with gastric carcinoma treated at University of Milan.

eral condition. Three cats underwent partial gastrectomy, and one also received adjuvant chemotherapy (doxorubicin + chlorambucil predni-sone methotrexate [A + LMP] protocol).

All French Bulldogs with pyloric hyperplastic polyps were surgi-cally treated using different techniques, including the Billroth I proce-dure (1 dog), pyloroplasty (1 dog), and partial (1 dog) or total (3 dogs) pyloric submucosal resection.

PROGNOSIS

Gastric carcinoma has a poor prognosis reflecting the advanced clinical stage of the tumor at the time of diagnosis, the high metastatic rate, and the difficulties in achieving wide surgical margins. In spite of the existence of several reports of long survival times in individual animals after tumor resection, there are few long-term survival studies. Palliative surgical resection might prolong survival for several months.[49] Surgical excision of solitary lymphoma can result in 2- to 3-month survival times, and adjuvant chemotherapy appears to improve the length of survival.[49]

Cats with localized gastric lymphoma treated with combination chemotherapy seem to have a better prognosis than those with other forms of gastrointestinal lymphoma. The results of treatment of diffuse gastrointestinal lymphoma are discouraging.[4]

The prognosis for benign gastric tumors is good, and cure is possible after complete surgical excision.

Results of surgery in 10 dogs with gastric carcinoma treated at the University of Milan are summarized in Table 3. Morbidity after gastrectomy was low. Three dogs had extended survival times: 2 lived for 3 years and 4 years, respectively, and died due to causes not related to the gastric tumor; 1 lived for 20 months and was then euthanatized due to progressive disease. The median survival time of dogs treated by surgery is 72 days.

Of three treated cats with gastric lymphoma, one died 48 hours after surgery for probable complications of surgery. One cat lived for 2 months and did not receive chemotherapy on the request of its owner. The cat that received chemotherapy lived 12 months and died due to progressive disease.

Surgically treated French Bulldogs had an excellent prognosis, with complete remission of symptoms and absence of relapse.

SUMMARY

Gastric tumors are rare in dogs and cats but should always be considered, particularly in older dogs with chronic vomiting.

The most common gastric tumor in dogs is carcinoma, although lymphoma is rare. Breeds that seem to be predisposed to gastric carci-

noma are the Rough Collie, Staffordshire Terrier, and Belgian Shepherd. Lymphoma is the most common gastric malignancy in cats.

Contrast radiographic examination and endoscopy are the elective procedures of choice for the diagnosis of these conditions. Biopsy is essential to confirm the diagnosis.

Surgery is the only potentially curative modality for localized gastric carcinoma. Chemotherapy alone or following surgery is the elective treatment of choice for gastric lymphoma in dogs and cats.

The prognosis is poor for both types of tumor, but prolonged survival times in individual animals are possible.

ACKNOWLEDGMENT

References

1. Alexander HR, Kelsen DP, Tepper JE: Cancer of the stomach. *In* De Vita VT, Hellman S, Rosenberg SA (eds): Cancer Principles and Practice of Oncology, ed 4. Philadelphia, JB Lippincott, 1993, p 818
2. Barker IK, Van Dreumel AA, Palmer N: The alimentary system. *In* Jubb KVF, Kennedy PC, Palmer N (eds): Pathology of Domestic Animals, vol 2, ed 4. San Diego, Academic Press, 1993, p 72
3. Conroy SD: Multiple gastric adenomatous polyps in a dog. J Comp Pathol 79:465, 1969
4. Couto CG: Gastrointestinal neoplasia in dogs and cats. *In* Proceedings of the 17th Waltham/Ohio State University Symposium, 1993, p 13
5. Couto CG, Rutgers C, Sherding RG: Gastrointestinal lymphoma in 20 dogs: A retrospective study. J Vet Intern Med 3:73, 1989
6. Cribb AE: Feline gastrointestinal adenocarcinoma: A review and retrospective study. Can Vet J 29:709, 1988
7. Crow SE: Tumors of the alimentary tract. Vet Clin North Am Small Anim Pract 15:577, 1985
8. Crystal MA, Penninck DG, Matz ME, et al: Use of ultrasound-guided fine-needle aspiration biopsy and automated core biopsy for the diagnosis of gastrointestinal diseases in small animals. Vet Radiol Ultrasound 34:438, 1993
9. Eaton KA, Radin MJ, Krakowka S: An animal model of gastric ulcer due to bacterial gastritis in mice. Vet Pathol 32:489, 1995
10. Fonda D, Gualtieri M, Scanziani E: Gastric carcinoma in the dog: A clinicopathological study of 11 cases. J Small Anim Pract 30:353, 1989
11. Fossum TW: Surgery of the stomach. Gastric neoplasia and infiltrative diseases. *In* Fossum TW (ed): Small Animal Surgery. St. Louis, Mosby-Year Book, 1997, p 289
12. Fox JG, Dandler CA, Sager W, et al: *Helicobacter mustelae*-associated gastric adenocarcinoma in ferrets *(mustela putorius furo)*. Vet Pathol 34:225, 1997
13. Giusti AM, Crippa L, Bellini O, et al: Gastric spiral bacteria in wild rats from Italy. J Wildl Dis 34:168, 1998
14. Gualtieri M, Monzeglio MG: Gastrointestinal polyps in small animals. Eur J Comp Gastroenterol 1:5, 1996
15. Gualtieri M, Monzeglio MG, Scanziani E, et al: Pyloric hyperplastic polyps in the French Bulldog. Eur J Small Anim Pract VI:51, 1996
16. Guilford WG, Strombeck DR: Neoplasms of the gastrointestinal tract, APUD tumors, endocrinopathies and the gastrointestinal tract. *In* Strombeck DR (ed): Strombeck's Small Animal Gastroenterology, ed 3. Philadelphia, WB Saunders, 1996, p 519

17. Hayden DW, Nielsen SW: Canine alimentary neoplasia. Zentralbl Veterinarmed [A] 20:1, 1973
18. Head KW: Tumours of the lower alimentary tract. Bull World Health Organ 53:167, 1976
19. Head KW: Tumors of the alimentary tract. *In* Moulton JE (ed): Tumors in Domestic Animals, ed 3. Berkeley, University of California Press, 1990, p 347
20. Johansen AA: Early gastric cancer. Curr Top Pathol 63:1, 1976
21. Jones NL, Shannon PT, Cutz E, et al: Increase in proliferation and apoptosis of gastric epithelial cells early in the natural history of *Helicobacter pylori* infection. Am J Pathol 151:1695, 1997
22. Kaser-Hotz B, Hauser B, Arnold P: Ultrasonographic findings in canine gastric neoplasia in 13 patients. Vet Radiol Ultrasound 37:51, 1996
23. Koss LG: The gastrointestinal tract. *In* Diagnostic Cytology and Its Histopathologic Bases, vol 2, ed 4. Philadelphia, JB Lippincott, 1992, p 1018
24. Krauser K: Neoplasien des magens beim Hund. Berl Munch Tierarztl Wochenschr 98:48, 1985
25. Krook L: On gastrointestinal carcinoma in the dog. Acta Pathologica Microbiologica Scandinavica 38:47, 1956
26. Kurihara M, Shirakabe H, Murakami T, et al: A new method for producing adenocarcinomas in the stomach of dogs with N-ethyl-N-nitro-N-nitrosoguanidine. Gann-Japanese Journal of Cancer Research 65:163, 1974
27. LaRock G, Ginn PE: Immunohistochemical staining characteristics of canine gastrointestinal stromal tumors. Vet Pathol 34:303, 1997
28. Leblanc B, Fox JG, Le Net JL, et al: Hyperplastic gastritis with intraepithelial *Campylobacter*-like organisms in a Beagle dog. Vet Pathol 30:391, 1993
29. Levine SH: Surgical therapy. *In* Slatter D (ed): Textbook of Small Animal Surgery, ed 2. Philadelphia, WB Saunders, 1993, p 2048
30. Lingeman CH, Garner FM, Taylor DON: Spontaneous gastric adenocarcinomas of dogs: A review. J Natl Cancer Inst 47:137, 1971
31. Mannick EE, Bravo LE, Zarama G, et al: Inducible nitric oxide synthetase, nitrotyrosine, and apoptosia in *Helicobacter pylori* gastritis: Effects of antibiotics and antioxidants. Cancer Res 56:3238, 1996
32. Maratka Z: Terminology, definitions and diagnostic criteria in digestive endoscopy. Scand J Gastroenterol 19:34, 1986
33. Murray M, Robinson PB, McKeating FJ, et al: Primary gastric neoplasia in the dog: A clinicopathological study. Vet Rec 91:474, 1972
34. Ogilvie GK, Moore AS: Gastrointestinal tumors. *In* Managing the Veterinary Cancer Patient: A Practice Manual. Trenton, Veterinary Learning System, 1995, p 351
35. Owen LN: TNM Classification of Tumours in Domestic Animals. Geneva, World Health Organization, 1980, p 26
36. Patnaik AK, Hurvitz AI, Johnson GF: Canine gastrointestinal neoplasms. Vet Pathol 14:547, 1977
37. Patnaik AK, Hurvitz AI, Johnson GF: Canine gastric adenocarcinoma. Vet Pathol 15:600, 1978
38. Penninck DG, Nyland TG, Kerr LY, et al: Ultrasonic evaluation of gastrointestinal diseases in small animals. Vet Radiol 31:134, 1990
39. Priester WA, McKay FW: The Occurrence of Tumors in Domestic Animals. Bethesda, National Cancer Institute Monograph. 1980, p 38
40. Roth L, King JM: Mesenteric and omental sclerosis associated with metastases from gastrointestinal neoplasia in the dog. J Small Anim Pract 31:28, 1990
41. Sautter HJ, Hanlon GF: Gastric neoplasms in the dog: A report of 20 cases. JAVMA 166:691, 1975
42. Scanziani E, Crippa L, Giusti AM, et al: Argyrophil cells in gastrointestinal epithelial tumours of the dog. J Comp Pathol 108:405, 1993
43. Scanziani E, Giusti AM, Gualtieri M, et al: Gastric carcinoma in the Belgian Shepherd dog. J Small Anim Pract 32:465, 1991
44. Skirrow MB: Disease due to *Campylobacter*, *Helicobacter* and related bacteria. J Comp Pathol 111:113, 1994

45. Soderstrome MJ, Gilson SD: Principles of surgical oncology. Vet Clin North Am Small Anim Pract 25:97, 1990
46. Sullivan M, Fisher EW, Nash AS, et al: A study of 31 cases of gastric carcinoma in dogs. Vet Rec 120:79, 1987
47. Theilen GH, Madewell BR: Tumors of the digestive tract. *In* Veterinary Cancer Medicine, ed 2. Philadelphia, Lea & Febiger, 1987, p 499
48. Turk MAM, Gallina AM, Russel TS: Nonhematopoietic gastrointestinal neoplasia in cats: A retrospective study of 44 cases. Vet Pathol 18:614, 1981
49. Twedt DC: Gastric neoplasia. *In* Anderson NV (ed): Veterinary Gastroenterology, ed 2. Philadelphia, Lea & Febiger, 1992, p 359
50. Twedt DC: Gastric neoplasia. *In* Sherding RG (ed): The Cat: Diseases and Clinical Management, ed 2. Philadelphia, WB Saunders, 1994, p 1204
51. Van der Gaag I: The histological appearance of peroral gastric biopsies in clinically healthy and vomiting dogs. Can J Vet Res 52:67, 1988
52. Watanabe T, Tada M, Nagai H, et al: *Helicobacter pylori* infection induces gastric cancer in Mongolian gerbils. Gastroenterology 115:642, 1988
53. Weller RE, Hornof WJ: Gastric malignant lymphoma in two cats. Mod Vet Pract 60:701, 1979
54. White RAS: The alimentary system. *In* Manual of Small Animal Oncology. London, British Small Animal Veterinary Association, 1991, p 237
55. Withrow SJ: Gastric cancer. *In* Withrow SJ, MacEwen EG (eds): Clinical Veterinary Oncology. Philadelphia, JB Lippincott, 1989, p 58
56. Withrow SJ: Surgical oncology. *In* Withrow SJ, MacEwen EG (eds): Clinical Veterinary Oncology. Philadelphia, JB Lippincott, 1989, p 193
57. Yu J, Russell RM, Salomon RN, et al: Effect of *Helicobacter mustelae* infection on ferret gastric epithelial cell proliferation. Carcinogenesis 16:1927, 1995

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