Veterinary Bioscience: Digestive System

LECTURE 19
PATHOLOGY OF THE STOMACH AND ABOMASUM

LECTURER

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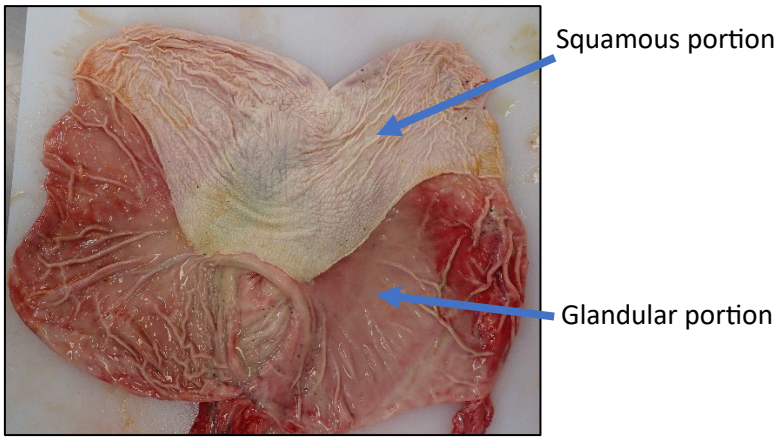
The stomach was long thought to be a sterile organ because of its high acidity. More recently there has been a greater understanding of the role of the gastric microbiome in disease and neoplasia in humans. While there has not been a clear link described in animals, it is likely the microbiome plays a role in normal homeostasis and the development of disease. In humans it is also widely accepted that gastric neoplasia does arise from a background of chronic inflammation.

Variations in anatomy are important to consider. A squamous portion of the stomach is present in horses and pigs (as well as some wildlife) and can have difference susceptibility to insult.



Undiluted gastric secretion in the dog and cat should be pH <3.0 and abomasal content should be pH <3.5-4.0.

The gastric mucosal barrier prevents acid-back diffusion and autodigestion. The integrity relies on the intact surface layer of epithelial cells with tight junctions and the production of the mucus, bicarbonate and hydrophobic phospholipid surface layer. Prostaglandins are important in the protection of the gastric mucosa through functions including mucous and bicarbonate secretion, inhibition of histamine-stimulated acid secretion by parietal cells and inducing proliferation of the foveolar mucous epithelium.

Response of the gastric mucosa to injury

Restitution

Following acute surface damage (erosion or trauma) there is a rapid (minutes) immigration of adjacent surface mucosa to cover the defect. This occurs before an inflammatory response has been generated. A thick layer of gastric mucus mixed with fibrin and exfoliated cells overlying gastric ulcerations forms a protective barrier and encourages restitution.

Atrophy of specialised cell types (parietal cells)

This typically is associated with chronic disease and is seen as replacement of parietal cells with more primitive cells. This condition is not noticeable grossly but is seen microscopically with a change in the cell types present. A condition called achlorhydria can result, due to loss of acidic secretions which leads to maldigestion in the lower gastrointestinal tract.

Mucous metaplasia and hyperplasia

Develops as a consequence of chronic irritation/inflammation which stimulates proliferation of mucus neck cells with an accompanying loss of parietal cells. The mucosa becomes thickened and often nodular. The change can be localised or diffuse depending on the cause. Similar to above, achlorhydria can develop followed by disruption to the microbiome. One classic example is ostertagiosis in ruminants (see below).

Pyloric Stenosis

This is a functional or anatomic lesion which can be congenital or acquired. Clinically it is associated with delayed gastric emptying. Physical causes can include ulceration, granulation and stricture, polyps, tumours or foreign bodies.

In dogs there is a condition that has mucosal hypertrophy, smooth muscle hypertrophy or a combination of the two that is known as *chronic hypertrophic pyloric gastropathy*. Mucosal hypertrophy alone is most common. This condition is most commonly seen in small-breed dogs. The pathogenesis is poorly understood. Grossly this appears as enlarged mucosal folds surrounding and obstructing the pyloric canal. This condition requires full thickness (not endoscopic pinch) biopsies for diagnosis.

Gastric impaction

Impaction can occur in horses and cattle. Causes include:

- Feeding low quality roughage, low water intake or poor mastication (dental disease)
- Pyloric obstruction e.g. due to hairballs (trychobezoars similar to those that occur in the rumen) and other foreign material also cause impaction
- Vagal nerve damage (due to pneumonia, pleuritis or lymphoma) → abnormal gastric motility and emptying (so called vagal indigestion)

In dogs and cats foreign body obstruction is more common (hairballs in cats)

On post mortem examination the condition is typically characterised by distended, abnormally packed stomach containing dry ingesta.

Gastric dilation and rupture in horses

Gastric dilation can occur as primary or secondary disease.

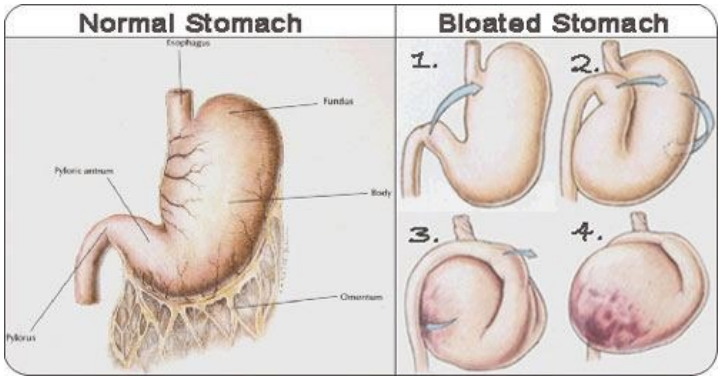
Secondary disease is mostly seen associated with physical obstruction of the stomach or intestine or colic with ileus.

Primary disease occurs most commonly in horses fed with rapidly fermentable carbohydrates (analogous to grain overload in ruminants), lush pasture, or excessive water intake. The ingesta swells due to increased gastric secretion and saliva. Bacterial fermentation of the carbohydrates produces gas and lactic acid which leads to increased osmotic pressure and thus an influx of water.

Consequently there is further distension and systemic dehydration which can result in **shock** and death. Animals that do survive can develop laminitis.
Gastric rupture can occur in primary or secondary disease or in some cases can be idiopathic. Peritonitis develops rapidly due to release of gastric content into the abdominal cavity and usually results in death. On post mortem examination, free ingesta is found in the abdominal cavity and the gastric wall is lacerated. Gastric rupture can also occur post mortem. It is important to distinguish post mortem from ante mortem rupture. In true ruptures the borders are hyperaemic and haemorrhagic.

Gastric dilatation and volvulus (GDV) in dogs

This condition is a relatively common emergency presentation in dogs particularly in large, deep-chested breeds such as Great Danes, St Bernards, wolfhounds etc. Predisposing factors are controversial but are thought to include laxity of the hepatosplenic ligament, prior splenectomy, diet of small food particles, recent kennelling and infection with nasal mites inducing 'reverse sneezing'. The condition is associated with overeating or eating large meals once daily. Distension of the stomach by food and fluid is compounded by gas accumulation, possibly from aerophagia. In simple dilation, the oesophagus is not occluded, and the duodenum is slightly displaced. Whilst the pathogenesis of volvulus is poorly understood it is thought that with multiple episodes of gastric dilation there is stretching and relaxation of the gastrohepatic ligament. Recurrent dilation, combined with overfeeding, postprandial exercise and perhaps hereditary predisposition can result in gastric volvulus.
Gastric volvulus results as the stomach rotates clockwise. The stomach is usually rotated clockwise on a ventrodorsal axis when viewed from the ventral abdominal surface. Rotation is usually 180-360 degrees. The spleen follows the gastrosplenic ligament and ends up in a right ventral position, bent into a "V" shape.



https://criticalcaredvm.com/wp-content/uploads/2015/02/52152_orig.jpg

Following torsion, there is constriction of venous outflow and infarction occurs. Grossly the stomach wall is oedematous and dark red to black. The mucosa becomes necrotic and, in some cases, the stomach may rupture. The combination of the obstructed veins from the volvulus and pressure from the distended stomach on the portal vein and vena cava results in decreased venous return to the heart, reduced cardiac output and circulatory shock. In addition, the increase in intrabdominal pressure can impinge on the diaphragm and compromise respiration. The gastric volvulus also initiates a variety of acid-base and electrolyte abnormalities which add to the clinical compromise and sometimes disseminated intravascular coagulation.
Decreased portal vein flow can also cause pancreatic ischemia and, with myocardial necrosis, can cause release of *myocardial depressant factor* which can trigger cardiac arrythmias.

Adult sows can develop gastric volvulus. This is associated with excitement prior to feeding especially in animals fed at long intervals.

Abomasal displacement in ruminants

This condition most commonly develops in high producing, intensively managed dairy cows but can be present in pasture fed animals. Normally the abomasum lies over the xyphoid process at the abdominal ventral midline (transverse along ventral body wall). Displacement leads to partial disruption of abomasal outflow. The sequestration of chloride in the abomasum and subsequent metabolic alkalosis is part of the associated clinical syndrome.

Left-sided abomasal displacement (LDA) is most common and is a generally non- fatal entity of high-producing dairy cattle during the 6 weeks following parturition. The abomasum shifts ventrally and to the left of the rumen. In the post-calving period, abomasal atony can occur as a result of heavy grain feeding and hypocalcaemia. Many affected animals have concurrent problems, including ketosis, hypocalcemia, metritis, and retained placenta.

Right-sided displacement (RDA) is less common (15% of cases) and can occur in post- parturient dairy cows and calves. Approximately 20% of these cases can progress to abomasal torsion which is clinically more serious. Similar to GDV in dogs, cattle with abomasal torsion can develop significant electrolyte disturbances (mostly metabolic alkalosis) and progress to ischemic necrosis and rupture.

Gastric inflammation (gastritis, abomasitis)

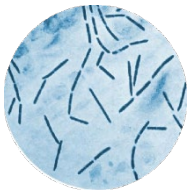
Gastritis is a term used broadly both clinically and in pathology that reflects a wide variety of insults on the stomach. Disease can be acute or chronic.

Acute gastritis can be seen grossly as mucosal sloughing, ulceration, oedema, haemorrhage, hyperaemia, excess mucus and sometimes with the presence of parasites or foreign bodies. Clinical signs that accompany acute gastritis = vomiting, anterior abdominal pain, salivation, +/- diarrhoea.

Chronic gastritis can be seen as knobby, irregular and thickened rugal folds +/- abscesses or granulomas. Chronic gastritis results in changes to mucosa such as atrophy of specialized cells, including parietal and chief cells, and mucous cell hyperplasia and achlorhydria can develop. In dogs, horses and pigs, chronic gastritis may lead to a condition known as *hypertrophic gastritis*. Causes include gastric parasitism, lymphocytic-plasmacytic gastritis and food allergy.

Causes of gastritis

Infectious causes of gastritis are relatively uncommon in dogs and cats. Chronic inflammation is much more common and is associated with food allergies or is considered idiopathic (ie. part of idiopathic inflammatory bowel disease). Bacterial, fungal and viral infections do occur in ruminants however are often part of a systemic disease process (viral) or secondary to other underlying disease (fungal).



Braxy

- *Clostridium septicum* infection (gram-positive bacilli)
- Acute abomasitis in sheep and less commonly cattle
- The cause is poorly understood but the disease generally occurs in cold weather and is thought to arise associated with mechanical trauma to the abomasal mucosa
- There is bacterial exotoxin production and death due to toxaemia. The toxins cause severe tissue damage, increase capillary permeability and tissue necrosis which facilitates spread of the infection
- Grossly there is mucosal and submucosal oedema and haemorrhage. There can also be significant gas formation by the bacteria (fermentation) giving rise to submucosal emphysema

Viral abomasitis

- Abomasitis is rarely the sole lesion, more commonly it is just one of many lesions associated with the infection
- Examples include: infectious bovine rhinotracheitis in calves and, rarely, older animals, herpesviral infections of small ruminants, bovine viral diarrhea, malignant catarrhal fever, and bluetongue.

Mycotic gastritis/abomasitis

- Generally occurs as a secondary disease where there is already underlying achlorhydria, atrophy, necrosis or ulceration
- There may also be compromised resistance with endotoxemia, septicemia, endogenous or exogenous steroids, neoplasia, viral disease, and altered gastrointestinal flora caused by antibiotic therapy
- Most commonly infection is with the zygomycetes (phycomycetes) such as Rhizopus, Absidia, or Mucor; rarely, Aspergillus
- Fungal hyphae infiltrate the submucosa typically invade venules and arterioles, causing thrombosis and hemorrhagic infarction
- Grossly lesions are of mucosal necrosis with surface haemorrhage and haemorrhage and oedema in the submucosa

Chemical injury

- Causes acute gastritis
- Grossly seen as diffuse gastric congestion, haemorrhage, necrosis, ulceration, oedema.
- Causes include arsenic, phosphatic fertilizers, various plants, heavy metals, dishwashing powder, metaldehyde, and blister beetles/cantharidin toxicity(horses)

Non-steroidal inflammatory drugs (NSAIDS)

- NSAIDs inhibit prostaglandin production thus removes their protective effects of the gastric mucosa
- There is reduced bicarbonate and mucus production leading to mucosal erosion and ulceration

Lymphoplasmacytic gastritis/gastroenteritis

This is a common diagnosis in dogs and cats which is believed to arise as an idiopathic reaction to a range of intraluminal antigens with food and/or bacterial allergens often being implicated. There is currently no direct association with infection by *Helicobacter* spp. in domestic animals other than in the ferret (see further comments below).

Uraemia

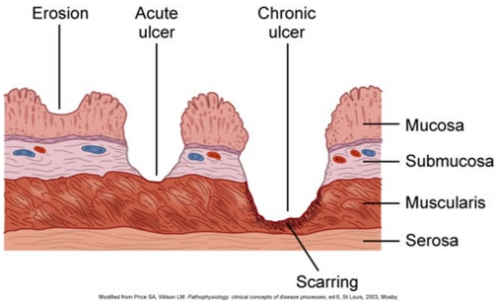
- Occasionally seen in dogs, cats and horses due to renal failure
- Grossly there is red-black discolouration of the mucosa due to severe congestion, with associated haematemesis and melena. Mineral deposition may be seen if it is severe enough
- Histologically there is mineral deposition in the basement membranes of vessels, glands and degenerative smooth muscle
- Mineral deposition is associated with calcium imbalance. Uraemic toxins also cause vascular endothelial damage leading to oedema, thrombosis and mucosal ischemic damage.

Helicobacter-associated gastritis

Helicobacter spp. are a spirochete bacteria and are the most common cause of gastritis and ulceration in humans (*Helicobacter pylori*). Furthermore, infection with *H. pylori* in humans is considered a risk factor for the development of gastric neoplasia. In dogs and cats, identified *Helicobacter* spp include: *H. heilmannii*, *H. cania* and *H. felis*.
The role *Helicobacter* spp. in gastric disease in domestic animals is not proven. Described pathology associated with Helicobacter infections ranges from the presence of organisms in the absence of noticeable mucosal injury to severe gastric disease characterised by mixed mucosal inflammation, erosions and ulcerations. Such differences in gastric pathology may be influenced by the Helicobacter species and strain and the mammalian host or may indicate a lack of causation of *Helicobacter* in gastric ulceration of domestic animals. One exception amongst the domestic species is the ferret where *H. mustelae* has been shown to be causal of lymphoplasmacytic gastritis. Gastritis in cheetah has been associated with Helicobacter infection.

Gastric and abomasal ulcers

An ulcer is a mucosal defect in which the entire mucosal thickness, down to or through the basement membrane, has been lost. Penetration through the remaining tissue layers to the peritoneal cavity is termed **perforating ulcer**. In comparison an e**rosion** results in partial-thickness mucosal damage.



Ulcers can be acute or chronic. Acute ulcers have associated hyperaemia (redness). Chronic ulcers lack this redness and have a thickened, firm rim of fibrosis around the periphery. Gastric ulcers occur in dogs, cats, horses, cattle and pigs.
The pathogenesis of gastroduodenal ulcers in animals is incompletely understood. Stress is believed to play a role.

Pathogenesis of gastric ulcers

The primary underlying mechanism is likely to be impairment of mucosal integrity in the face of normal acid secretion. This imbalance is a result of the following:

- Local disturbance or trauma to the epithelium
    - Back flush of bile acids from duodenum
    - Mechanical trauma (foreign bodies etc)
- High gastric acidity
    - Gastrinomas (Zollinger-Ellsion syndrome) or mast cell tumours (histamine release) can lead to gastric acid hypersecretion
- Local disturbances in blood flow resulting in ischemia
    - Stress
- NSAIDS or endogenous or exogenous steroids
    - Inhibition of prostaglandin leading to vasoconstriction and reduced mucous production
    - NSAIDS can also promote gastric hypermotility which alters vascular blood flow and decreased mucosal response to injury
    - Phenylbutazone may also have a direct toxic effect on vascular endothelium in the mucosa

Perforation of gastric ulcers results in massive abdominal haemorrhage and/or release of gastric contents into the abdomen and a fatal peritonitis.

Equine gastric ulceration

Due to its complicated and multifactorial nature, the term equine gastric ulcer syndrome (EGUS) has been used to describe this disease. There are two main disease subsets:

Foals most commonly have ulceration in the squamous portion of the stomach but can develop in the glandular portion if NSAIDs have been administered.

Adult horses commonly have ulceration in the squamous portion of the stomach. Gastric ulcers occur in 40% to 90% of competitive and performance horses, especially thoroughbreds. The most severe ulcers occur in those animals that are worked the hardest.

Proposed causes of ulceration of the non-glandular mucosa include:

- fasting
    - hay and saliva protect the gastric mucosa
- intense exercise
    - increased abdominal pressure leads to prolonged exposure of the non- glandular mucosa to acid
    - exercise can have inhibitory effect on gastric emptying

Gastric ulcers in the glandular mucosa of adult horses are mainly associated with NSAIDS administration.

Porcine gastric ulceration

Ulceration is common in the stomach of pigs and usually restricted to pars oesophagea.

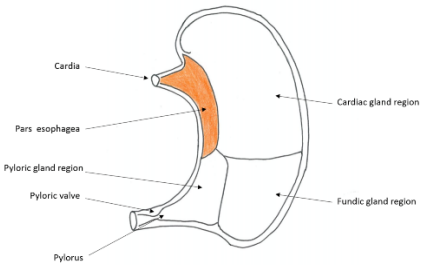
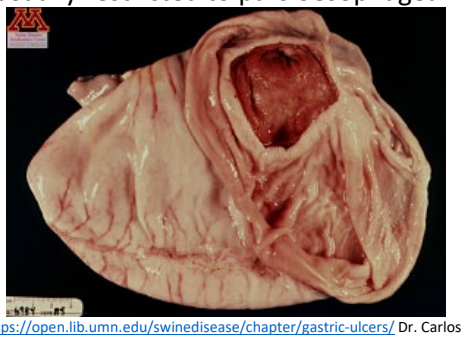


Figure 1- Anatomy of the pig stomach



https://open.lib.umn.edu/swinedisease/chapter/gastric-ulcers/ Dr. Carlos Pijoan

Weaners and growers are more susceptible to gastric ulcers and the disease is associated with stress and diet formulation (finely ground grain). Other associations include slatted flooring and high carbohydrate foods. In pigs, the typical preceding lesion in the gastric mucosa is hyperkeratosis of the pars oesophagea, which then erodes and an ulcer develops. Acute hemorrhage can result in severe acute blood loss and death. These pale, anaemic pigs are sometimes described as 'porcelain pigs'.

Bovine abomasal ulceration

Abomasal ulcers are common in cattle while duodenal ulcers are rare.

In calves, ulcers are associated with:

- dietary changes and mechanical irritation of the abomasum with roughage
- stress also is a contributing factor

In adult dairy cattle ulcers are associated with:

- heavy grain feeding (lactic acidosis) at the time of parturition
- displacement of the abomasum
- viral infection (BVD (pestivirus), malignant catarrhal fever (herpesvirus))
- impaction

Grossly, they present as linear brown, black haemorrhagic areas along margins of the rugae, primarily in pyloris and can measure up to 15 cm in diameter. Ulcers should be considered where there is anaemia and/or melena, and perforation suspected where there are signs of septic peritonitis.

Canine gastric ulceration

Gastric ulceration is clinically associated with variable appetite, abdominal pain, vomition, melena and anaemia. Ulcers are usually found in the pyloric antrum and proximal duodenum.
Causes include:

- Dermal mast cell tumours
  - release histamine into the blood stream which binds to receptors on parietal cells increasing HCl secretion.
- Gastrinomas (pancreas or duodenum)
  - secretion of gastrin increases secretion of HCl (so called Zollinger- Ellison syndrome).
- NSAIDS
  - Inhibition of prostaglandins leads to vasoconstriction and reduced mucus production thus reduced integrity of the mucosal barrier
- Trauma
  - Physical loss of the epithelium
- Uraemia
  - Damage to endothelial cells leading to vascular compromise + increased ammonia secretion and caustic injury = necrosis

Parasitic diseases of the stomach

Gastric parasitic infections are an uncommon cause of gastritis in dogs and cats. In contrast they are the cause of significant disease in ruminants.

Cattle, sheep and goats

Haemonchus contortus/*H. placei*

- Large, abomasal blood-sucking nematode parasites capable of causing severe anaemia and hypoproteinaemia
- Egg hatch in pasture and moult 3 times to L3 larvae which is infectious when eaten. Larvae survive for some time on pasture particularly in cool conditions
- The parasites have high fecundity, a short life cycle and high degree of genetic variation which means that they can make rapid adaptive changes and potentially rapidly develop resistance to drenches
- In cold weather larvae undergo hypobiosis (arrested development) and resume developing once conditions are warmer. This important in “spring rise” disease onset where ewes are more susceptible under the stress of late pregnancy and parturition
- Engorged females have a ‘barbers pole’ appearance with the red blood in their intestinal tract wrapping around their white genital tract
- Gross lesions are of severe oedema (bottle jaw) and pallor from anaemia

Ostertagia spp

- Cattle: *Ostertagia ostertagi* and *O. lyrate*
- Sheep and goats: *Teladorsagia circumcincta*
- Very important cause of diarrhoea, ill thrift and death in grazing ruminants in temperate regions.
- Causes protein loss with diarrhoea
- Has a Direct lifecycle.
    - 3rd stage larva (L3) ingested and invade abomasal glands

  Type I ostertagiasis → direct development to L5 leading to disease
  Type II ostertagiasis → hypobiosis of L4 in glands
    - The larvae damage mucosa leading to inflammation and mucous neck cell hyperplasia and metaplasia
- Adults live on the mucosal surface
- Gross changes are of a markedly thickened mucosa which is inflamed with raised, pale nodular lesions, often with a slightly depressed centre (= larval stages in glands).
    - The merging nodules are described as "Morocco leather" pattern or cobblestone pattern to the irregularly thickened mucosa.

Bovine abomasal ostertagiasis

https://wellcomecollection.org/works/zvr2gpx9

- Pathogenesis:
  Parietal cells replaced by mucous neck cells (mucous cell metaplasia) → decreased HCl secretion (**achlorhydria**) →increased abomasal pH (up to 7 or more) → Pepsinogen not converted to pepsin (due to incr. pH) → decreased protein digestion (**hypoproteinemia**) → bacterial overgrowth in intestine → diarrhea
  Blood gastrin increases as body tries to stimulate acid secretion (**hypergastrinemia**) → central effect on satiety center and decreased GI motility → decreased appetite
  Gastritis → increased vascular permeability → leaky junctions between hyperplastic mucous cells → protein loss into abomasum
- Clinically: loss of appetite; diarrhea; wasting
- Clinical pathology: hypoproteinaemia; achlorhydria; increased plasma pepsinogen

Trichostrongylus axei

- Occurs in ruminant and horses
- It has a direct lifecycle
- The parasites live in intra-epithelial tunnels in mucosa which leads to mucous metaplasia and hyperplasia of glands with subsequent protein loss and achlorhydria.
- Grossly the stomach is thickened with nodules or folds of mucosa + erosions and it is covered in thick mucus.

Horses

Draschia megastoma

- Burrows into submucosa along margo plicatus forming large nodules or pouches of granulomatous inflammation containing worms

Habronema majus, H. muscae

- Parasites on mucosal surface

Gasterophilus spp (Fly larvae or bots)

- Very common!
- Life Cycle: flies lay eggs on hairs which are licked by the horse and they hatch and develop as larvae in stomach
- The parasites may cause small erosions and ulcers, but infection is generally asymptomatic

Trichostrongylus axei – see above

Pigs

Hyostrongylus rubidus

- Clinical signs are usually absent in light infections but heavy infections can lead to decreased appetite, weight loss, and anemia
- Infections are primarily confined to animals reared outdoors
- Larval hypobiosis can occur

Gastric neoplasia

Gastric neoplasia is relatively rare in dogs and cats. The stomach is the most common site for gastrointestinal neoplasia in horses.

Adenocarcinoma

This tumour is most common in dogs ~ 10 years of age. They are considered rare in other species. Adenomas are also uncommon. Over 50% of adenocarcinomas occur in the pyloric region. Grossly they are variable in appearance; some are proliferative and protrude into the lumen, others a large, ulcerated crater while others are localised, plaque-like thickenings. Most incite a scirrhous reaction which is a firm fibrous tissue component. Canine gastric adenocarcinomas also have high metastatic potential, with nodal metastases reported in around 70% of dogs at diagnosis. Distant metastases are observed in 15–70% of dogs at diagnosis, with metastases most common in the liver, spleen, lung, and adrenal glands.

Squamous cell carcinomas

These tumours most commonly occur in middle-aged horses in the squamous portion of the stomach. Grossly these tumours appear as cauliflower-like masses projecting from the mucosal surface. Equine gastric SCCs can cause hypercalcemia and hypophosphatemia, most likely due to paraneoplastic production of PTH-rp. If they extend through to the serosal surface they can 'seed' throughout the peritoneal cavity. The tumour can also spread directly to liver, spleen and diaphragm and can metastasis to the liver or lung.

Lymphoma

Gastric lymphoma occurs most commonly in cats, cattle and dogs. In cattle the abomasum is a common site for lymphoma associated with enzootic bovine leukosis. Grossly the neoplastic cell infiltrates can develop as a diffuse thickening however some cases appear more nodule. Both T and B lymphocyte variants occur.

Spindle cell tumours
Spindle cell tumours can arise from the wall of the stomach. They can be either leiomyomas/sarcomas or gastrointestinal stromal tumours (GISTs) which arise from the interstitial cells of Cajal. These tumour types can only be differentiated on immunohistochemistry. These appear as firm, pale masses within the wall of the stomach. Both gastric leiomyosarcomas and GISTs have been reported to metastasize.

Neuroendocrine tumours (Gastric carcinoid)
These tumours are derived from enteroendocrine cells. They are relatively rare and are more likely to develop in proximal parts of the stomach. While function tumours exist in humans, none have been described in domestic animals. While some of these tumors are well differentiated and locally expansile, metastasis has been described in domestic animals.

Additional Reading

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