

PROBLEM-SOLVING EXERCISE: INFLAMMATION & REPAIR PEPTIC ULCER

ANSWER SHEET

Part One

1. *Picture A is a macroscopic view of a portion of the stomach viewed from the mucosal surface.*

Catalogue Number	Small Image	Image Map	Large Image
A_CI_UL_ST_17.jpg	Picture A	Image map	Picture A

2. *Describe the main pathological feature.* Within the centre of the portion of stomach, there is a large oval shaped **peptic ulcer**, with a crisply punched out margin. The base of the ulcer shows necrotic slough, with a central, large, dilated blood vessel.

3. *Pictures B, C, D are microscopic views.*

Catalogue Number	Small Image	Image Map	Large Image
A_CI_UL_ST_18.jpg	Picture B	Image map	Picture B
A_CI_UL_ST_19.jpg	Picture C	Image map	Picture C
A_CI_UL_ST_20.jpg	Picture D	Image map	Picture D

4. *From where would these histological sections be taken in relation to picture A?*

Picture B (low power) is taken from the edge of the ulcer and it shows (on the right of the picture) the mucosal epithelium undergoing **regeneration** (it is this epithelial regenerative component that gives the crisply punched out appearance to the ulcer to the naked eye). To the left of picture B the ulcer base is seen to consist of necrotic slough with underlying inflammation.

Picture C (low power) shows the **zonal pattern** of the ulcer base, with a superficial zone of necrotic slough at the surface, an inflammatory zone in the middle, and at the bottom there is a zone of **repair** with fibrous scarring extending into the muscular layers of the stomach wall. To the left of the picture, there is a dilated, large arterial blood vessel (corresponding to the large blood vessel seen in picture A).

Picture D shows a medium power view of the **zonal pattern** of the ulcer base with **necrotic slough** near the surface with a **fibrinous exudate**. Underneath this, there is a zone of **inflamed granulation tissue**, in which a mixture of capillary blood vessels and fibrous tissue can be discerned. Under that is a zone of **granulation tissue with scarring** (with some chronic inflammation) extending into the muscle wall of the stomach.

5. *Picture E is a high power view of an area of picture D.*

Catalogue Number	Small Image	Image Map	Large Image
A_CI_UL_ST_21.jpg	Picture E	Image map	Picture E

6. *What are the components of this tissue?* Picture E shows a high power view of the zone of inflamed granulation tissue. You can make out the dilated capillary blood vessels, containing red blood cells and occasional marginating neutrophils. In between the capillaries there are spindle shaped fibroblasts laying down collagen (forming fibrous tissue - repair). Within the fibrous tissue there is an infiltrate of inflammatory cells, mostly neutrophils (acute inflammation) with some macrophages and lymphocytes (chronic inflammation). This is **acutely & chronically inflamed granulation tissue** seen within the superficial and middle zone of the ulcer base.

7. *From the above macroscopical and microscopical observations, what do you deduce about the nature of this disease?* There is evidence of persistent or recurrent injury (gastric acid and enzymes) leading to cell death by necrosis at the superficial part of the ulcer. This triggers an acute inflammatory response, leading on to chronic inflammation with granulation tissue, leading to laying down of fibrous tissue and subsequent scarring. This is therefore an example of **acute inflammation, chronic inflammation and repair**.

Part Two

Veterinary surgeons have treated this disease in the following ways: peptic ulceration results from a disturbance in the usual balance between the **mucosal defences** of the stomach wall (a mucus layer on the epithelium) and attack by **gastric acid**.

In some cases this may be due to infection by bacteria of the *Helicobacter* genus, which may induce inflammation of the stomach and directly upset this balance allowing chemical attack of the gastric wall by acid.

Discuss the rationale behind each of these.

1. *Animals with ulcerative gastritis should be given small but frequent meals and non-steroidal anti-inflammatory drugs should be avoided.*

It is important to think about aggravating factors that induce increased production of gastric acid, which then attacks the stomach wall/ulcer base causing persistent or recurrent chemical injury, leading to further cell death and inflammatory responses. Ways of reducing gastric acid production, or neutralising gastric acid once it has been secreted include small but frequent meals in particular those with alkaline foods such as milk. Aspirin, and other non-steroidal anti-inflammatory drugs (NSAIDs), can chemically damage the gastric wall, aggravating peptic ulceration so these should be avoided. Other aggravating factors (that increase acid or reduce defences) include stress (physiological and psychological), which should be avoided if possible.

2. *Dogs with cutaneous mast cell tumours frequently develop gastric ulceration.*

Histamine is released from the cytoplasmic granules of the mast cells within the skin tumours. Systemic circulation of the released histamine, results in binding to, and stimulation of, H₂ receptors on the parietal cells within the gastric glands, resulting in increased gastric HCl production.

3. *Animals with ulcerative gastritis can be treated with either a histamine H₂ receptor antagonist or a proton pump inhibitor.*

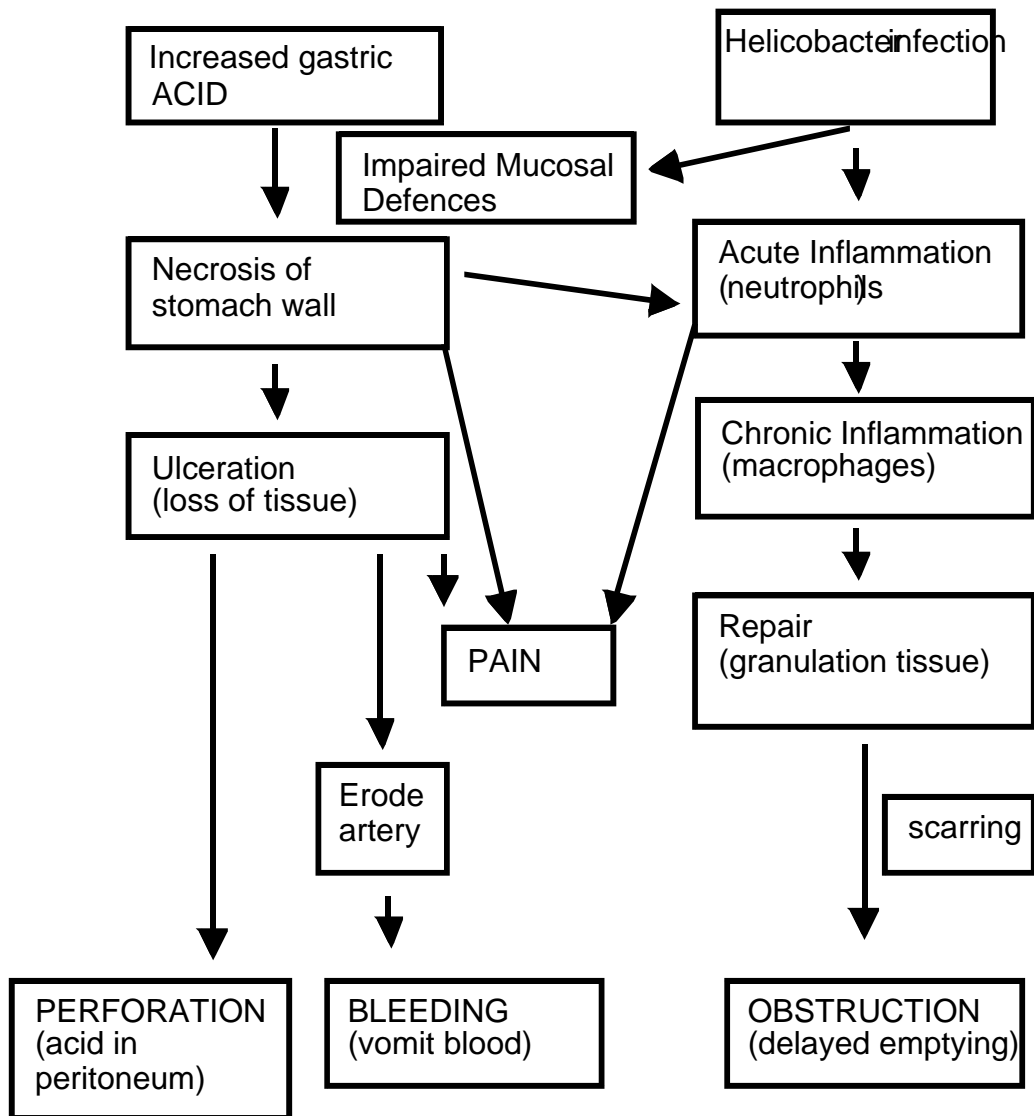
One of the main influences on gastric acid secretion is the stimulatory effect of histamine on the H₂ receptor on the acid-producing parietal cells. Drugs are available to block this interaction between the ligand (histamine) and its receptor (the H₂ receptor), such as cimetidine. Other drugs are also available that can inhibit the proton pump in the parietal cells responsible for the secretion of acid, such as omeprazole.

4. *Sometimes antibiotics can be used to treat animals with ulcerative gastritis.*

One of the key initiating factors causing gastritis in small animals (cats, dogs, ferrets) is gastric mucosal infection by *Helicobacter* spp. Treatment with antibiotics, such as amoxicillin or metronidazole, to eradicate these bacteria is therefore sensible. Sucralfate has the effect of increasing the viscosity of the gastric mucus and helps to form a physical barrier over the ulcerated site, further protecting it from the effects of the luminal gastric HCl.

Part Three

Sketch out a flow diagram, linking the aetiology and pathogenesis of this disease to its presentation, the subjective symptoms the animal might have felt and the physical signs of disease it might have exhibited.



Part Four

What other disease of the stomach could have a similar appearance? A cancer (an unregulated growth of cells) in the wall of the stomach could also ulcerate giving a similar appearance to the naked eye (or looking at the internal lining of the stomach in the patient with a fibre-optic instrument – endoscope).

How would you distinguish between them? A biopsy (a small fragment of tissue taken with a “grabbing” instrument using an endoscope) could be taken from the stomach of the patient, fixed and processed to make a slide of a section stained with haematoxylin & eosin. Microscopic examination of the slide would allow you to see if there were cancer cells present or whether there was acute and chronic inflammation with repair.