

[Chronic gastritis ABC]

- A – autoimmune
- B – bacterial (*helicobacter*)
- C - chemical

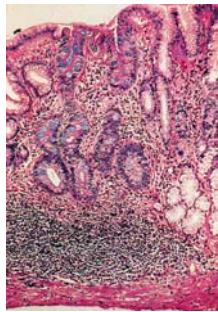
[Autoimmune chronic gastritis]

- Autoantibodies to gastric parietal cells
- Hypochlorhydria/achlorhydria
- Loss of gastric intrinsic factor leads to malabsorption of vitamin B12 with macrocytic, megaloblastic anaemia

[Morphology of chronic gastritis]

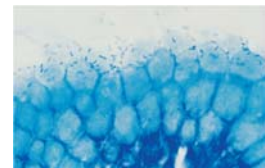
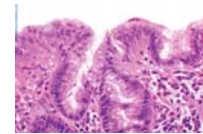
- Chronic inflammatory cell infiltration
- Mucosal atrophy
- Intestinal (goblet cell) metaplasia

Seen in *Helicobacter* and autoimmune gastritis (not chemical)



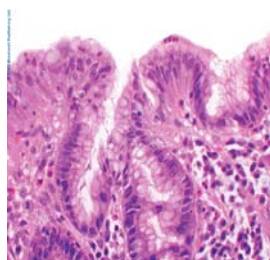
[*Helicobacter pylori*]

- Adapted to live in association with surface epithelium beneath mucus barrier
- Causes cell damage and inflammatory cell infiltration
- In most countries the majority of adults are infected



[*Helicobacter* gastritis]

- Acute inflammation mediated by complement and cytokines
- Polymorphisms infiltrate epithelium and may be partly responsible for its destruction
- An immune response is also initiated (antibodies may be detected in serum)

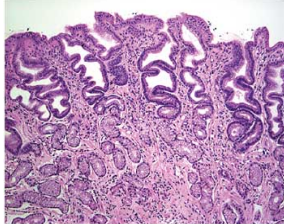


[*Helicobacter* gastritis]

- 2 patterns of infection
 - Diffuse involvement of body and antrum ("pan gastritis" associated with diminishing acid output)
 - Infection confined to antrum (antral gastritis, associate with *increased* acid output)

Chemical gastritis

- Commonly seen with bile reflux (toxic to cells)
- Prominent hyperplastic response (inflammatory cells scanty)
- With time – intestinal metaplasia



Consequences of gastritis

- Peptic ulcer disease (*Helicobacter*)
 - Adenocarcinoma (all types)
- The “African enigma” – are complications of *H.pylori* infection less frequent in Africans?
- Case not yet resolved

Peptic ulcer disease

- A surface breach of mucosal lining of GI tract occurring as a result of *acid and pepsin* attack
- Sites:
 - Duodenum (DU)
 - Stomach (GU)
 - Oesophagus
 - Gastro-enterostomy stoma
 - Related to ectopic gastric mucosa (e.g. in Meckel's diverticulum)

Acute peptic ulcer

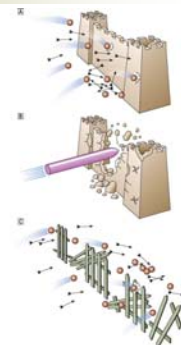
- Like acute erosion but breaching muscularis mucosae
- Specific examples
 - Curling's ulcer (following severe burns)
 - Cushing's ulcer (following head injury)

Chronic peptic ulcer

- Complex epidemiology
 - DU most common in Europe, GU in Japan
 - Incidence of DU declining, GU stable

Pathogenesis

- In normal acid/pepsin attack is balanced by mucosal defences
- Increased attack by hyperacidity
- Weakened mucosal defence – the major factor (*H. pylori* related)



Acid production

- Tends to be high in DU patients. Antral gastritis causes increased gastrin production and acid secretion
- Acid stimulates development of gastric metaplasia in the duodenum
- *Helicobacter* organisms colonise the metaplastic epithelium and cause inflammatory damage leading to ulceration

Acid in GU

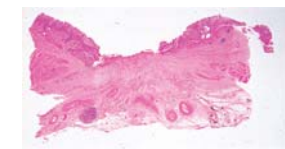
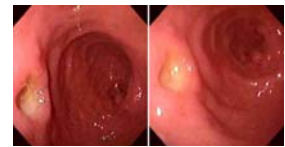
- Pan gastritis diminishes acid secretion
- Ongoing gastritis and epithelial damage is the main causal factor for ulceration

Helicobacter factors in pathogenesis

- Some strains are more pathogenic than others. The Cag A (cytotoxic) antigen is one important virulence factor
- Human variability also plays a part (e.g. individuals who produce high levels of IL-1 β in inflammation get pan gastritis and GU, lower levels associated with antral gastritis and DU)

Morphology of peptic ulcers

- Clean, non-elevated edge
- Granulation tissue base (floor)
- Underlying fibrosis



© Elsevier Ltd. Underwood: General and Systemic Pathology www.studentconsult.com

Complications of peptic ulcer

- *Perforation* leading to peritonitis
- *Haemorrhage* by erosion of vessel in base
- *Penetration* of surrounding organ (liver/pancreas)
- *Obstruction* (by scarring) – pyloric stenosis
- (Cancer – rare event in true peptic ulcer)

Gastric neoplasms

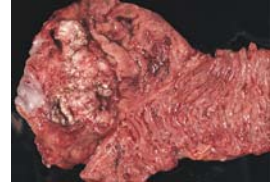
- Polyps are common but usually not neoplastic (hyperplastic polyps. Hamartomas, ectopic pancreas)
- Adenomas occur but are rare

Carcinoma of the stomach

- The second most common *fatal* malignancy in the world
- (after lung cancer)
- Commonest in Far East (Japan)
- Incidence declining
- High mortality unless disease detected early

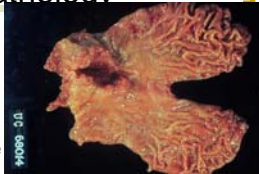
Pathology

- Vast majority are adenocarcinomas
- Arise on background of chronic gastritis, intestinal metaplasia, dysplasia
- Most cases advanced at presentation



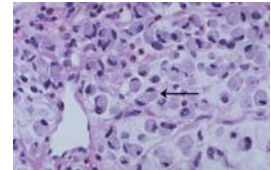
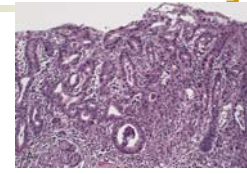
Macroscopic Pathology

- Gross types
 - Polypoid
 - Ulcerative
 - Infiltrative (extreme is *linitis plastica* – “leather bottle stomach”)



Microscopy

- Intestinal type (forms glands – like cancers of colon and oesophagus)
- Diffuse type – dissociated tumour cells often containing a mucinous “blob” – signet ring cells



Spread of gastric carcinoma

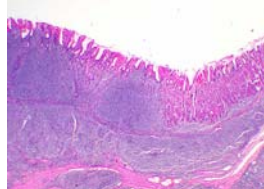
- Local infiltration (through wall of stomach to peritoneum, pancreas etc)
- Lymphatic – local and regional lymph nodes
- Blood – liver, lungs
- Transcoelomic (across peritoneal cavity). Often involves ovaries (esp. signet ring cancer) – Krukenberg tumour.

Less common gastric neoplasms

- Lymphoma
- Gastrointestinal stromal tumour (GIST)
- Neuroendocrine (carcinoid) tumours

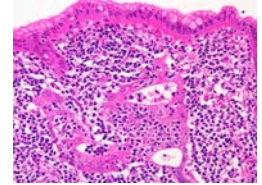
Gastric lymphoma

- Malignant neoplasm of mucosa associated lymphoid tissue (MALT)
- A (usually) low grade B-cell (marginal cell) lymphoma



Gastric lymphoma (maltoma)

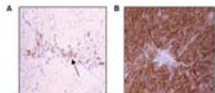
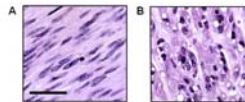
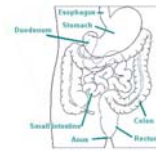
- Neoplastic cells infiltrate the epithelium (lymphoepithelial lesions)
- Strongly associated with *H. pylori* and can be cured by eliminating infection.



Gastrointestinal stromal tumours (GIST)

- Mesenchymal neoplasms
- Derived from interstitial cells of Cajal (pacemaker cells controlling peristalsis)
- Overexpress *c-kit* oncogene
 - Used as diagnostic aid on tissue
 - A target for therapy with tyrosine kinase inhibitor imatinib (also used in CML)

GIST-spindle cell neoplasm of GI tract



GIST

- Larger tumours with high mitotic rate tend to behave malignantly
- Stomach is commonest site

Neuroendocrine tumours

- Carcinoids are tumours of resident neuroendocrine cells in gastric glands
- Usually seen in context of chronic atrophic gastritis (driven by gastrin)
- Clinical behaviour variable