Pathology of the oesophagus and the stomach

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The layers of the GI tract
Some facts about Histopathology and the upper GI tract

- GI biopsies account for 15-25% of the total workload in DGHs
- Half of these are upper GI; the rest are duodenal biopsies, colorectal biopsies, etc.
- Whilst we do see occasional polyps and small resections, in the upper GI tract it is all about biopsies and major resections, the great majority of the latter for adenocarcinomas (of oesophagus and stomach)
To many diagnostic pathologists, the oesophagus is a 24 cms long muscular tube of relative pathological disinterest

Anonymous, 1989
Oesophageal pathology

• Inflammatory
  reflux oesophagitis +/- hiatus hernia
  specific infections: candida
  herpes simplex
  CMV

Reflux oesophagitis – subtle and severe

20% of all upper GI endoscopies - commonest upper GI disease

Reflux oesophagitis

• endoscopic scoring systems are much better than histology at assessing GORD

• specificity of histology 78% but sensitivity is only 30% - histology has no additional value in identifying GERD.
  Nandurkar et al. 2000

• biopsy will be justified only in strictureing disease or when CLO is suspected
Oesophageal pathology

• Inflammatory
  reflux oesophagitis +/- hiatus hernia
  specific infections: candida
  herpes simplex
  CMV

• Metaplastic
  Barrett’s oesophagus (CLO)

Barrett NR.
Chronic peptic ulcer of the oesophagus and "oesophagitis" J. Surg. 1950; 38: 175-182.

1950 congenitally short oesophagus
1970s true glandular metaplasia due to reflux of gastric contents
ACID and OTHER PEPTIC CONTENTS
1990s reflux of duodenal contents
BILE and ALKALI
Barrett’s oesophagus at endoscopy

Epidemiology of Barrett’s oesophagus and its complications

- increasing prevalence of CLO: both real and relative – certainly in the UK
- increasing incidence of adenocarcinoma of oesophagus
- some controversy
- but stated to be the carcinoma increasing the most in the Western World
Problem of oesophageal adenocarcinoma in the UK

Number of new cases and age-specific incidence rate per 100,000 population. Oesophageal cancer: by sex, UK, 2001.


Carcinoma of the oesophagus: SW Cancer Registry, 1983 - 2000

Epidemiology of Barrett's oesophagus and its complications

- Increasing CLO: true prevalence and increasing recognition (in the UK at least)
- Relationship to reflux disease:
  - male
  - middle age
  - white
  - overweight
  - alcohol
  - smoking
  - family history
Relative risk for oesophageal adenocarcinoma
Lagergren et al, 1999

<table>
<thead>
<tr>
<th></th>
<th>Odds ratio</th>
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<tbody>
<tr>
<td>Lean with no reflux symptoms</td>
<td>1.0</td>
</tr>
<tr>
<td>Obese with reflux symptoms</td>
<td>179.2 (34.8 - 922.7)</td>
</tr>
</tbody>
</table>

Barrett’s oesophagus surveillance: UK recommendations

• age and co-morbidity are important: only patients fit for surgery should be surveyed
• cost compares favourably with the treatment of IDDM and with colorectal and breast cancer screening
• all patients should be considered for surveillance regardless of the presence or absence of intestinal metaplasia
• non-dysplastic CLO: survey every 3 years
• LGD: check at 2 months and then 6 monthly
• HGD: repeat at one month and then consider oesophagectomy
• HGD diagnosis to be reviewed & confirmed by two experienced pathologists

Loft, Alderson & Heading, 2005
BSG Barrett’s oesophagus management guidelines

The average long segment CLO surveillance case with Seattle biopsies

40 biopsy pots
352 individual sections
Barrett's surveillance – the battleground

EBM physicians v doing surgeons
pathologists v everyone

Barrett's oesophagus: the future of surveillance

- we will probably have it whether we like it or not
- do we have the necessary endoscopic or pathological workforce and expertise?
- select patients at high risk: dysplasia, longer segments, stricture & ulcer; > males
- improve detection of IM and dysplasia: endoscopic methods, smart endoscopes, molecular markers
- BUT 95% of adenocarcinomas are not currently detected in surveillance programmes
  Brown et al, 1995; Cameron et al 1999; and others

The pathological diagnosis of dysplasia

Surveillance relies on the accurate identification of dysplasia and its appropriate treatment

Pathological overcalling seems to be a big problem

- inflammation causing reactive epithelial hyperplasia
- juxtaposition in patchwork mucosa
- reactive changes akin to reactive gastritis
- surface squamous re-epithelialisation
Juxtaposition in patchwork mucosa: intestinal-type mucosa adjacent to cardiac and/or fundic-type mucosa

Diagnosis of dysplasia in CLO

- **HGD** associated with co-existent adenocarcinoma in 25-55% of cases (now probably lower - 25% quoted in 2003)
- is an indication for oesophagectomy in Management guidelines in Europe & North America
- inter-observer agreement good (amongst experts) for HGD (kappa 0.65) but LGD and indefinite - lower levels of I-O agreement
  - Reid et al 1988, Montgomery, 2002
- HGD diagnosis to be reviewed & confirmed by two experienced pathologists
  - Loft & Alderson 2005
- Management of dysplasia should always be discussed in Upper GI MDT
  - Warren & Manek 2005

Oesophageal tumours

- **Benign**
  - rare
  - squamous papilloma
  - connective tissue tumours

- **Malignant**
  - Squamous cell carcinoma 20% M:F = 3:1
    - lower > upper > middle
    - China, Japan, Iran, South Africa
    - prognosis poor: DXR = surgery
  - Adenocarcinoma 80%
    - increasing + +
    - @ Barrett’s ? surveillance
    - prognosis good only if early

Oesophageal cancer is now the 6th commonest cancer killer in males in the UK
Worldwide incidence of oesophageal carcinoma

Oesophageal resections

• it's all in the RCPath dataset and reporting proforma!
  • circumferential margin assessment
  • lymph node harvests and sites of lymph node involvement
  • serosal involvement

Involved lymph nodes in oesophageal cancer – common and not necessarily where you expect them

• 141 patients with oesophageal carcinoma resections
  - 47 with intramural disease
  - 21% thoracic nodal metastases
  - 11% cervical nodal metastases
  - 23% ‘jumping’ metastases to extra-mediastinal nodes
  
  Nishimaki et al, 1994

• 110 patients with pT1 SCC of the oesophagus
  - 43 (39%) had lymph node metastases
  - 51% involved deep cervical nodes
  - 33% involved perigastric nodes
  - only 8% had metastases in intrathoracic nodes
  
  Matsubara et al, 1999
Gastric histology

cardiac mucosa  body/fundic mucosa  antral mucosa
Normal gastric histology?

Why biopsy the stomach?
- diagnosis
- suspected neoplasia
- surveillance or screening
- to assess effects of treatment
- research
- because it’s there
- to be able to send a ‘full’ report to the GP
- endoscopic ignorance

The ABC classification of gastritis
Wyatt & Dixon 1988

<table>
<thead>
<tr>
<th>Type</th>
<th>Cause</th>
<th>Synonyms</th>
<th>Pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>auto-immune (or atrophic)</td>
<td>Auto-immune</td>
<td>Chronic atrophic gastritis, Chronic atrophic gastritis with IM</td>
</tr>
<tr>
<td>B</td>
<td>bacterial</td>
<td>Chronic superficial gastritis</td>
<td>Chronic active gastritis</td>
</tr>
<tr>
<td>C</td>
<td>Chemical, bile reflux, drugs</td>
<td>Reflux gastritis, reactive gastritis</td>
<td>Foveolar hyperplasia, oedema, telangiectasia and lack of inflammatory cells</td>
</tr>
</tbody>
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The Sydney classification - histological division

* Price et al, 1990; Dixon et al, 1996

Helicobacter-associated chronic active gastritis

Chronic gastritis - some facts

- endoscopic features and histology correlate poorly
  * Khakoo et al 1994

- chronic gastritis is essentially a histological diagnosis

- the classification of chronic gastritis has changed dramatically over the years because of changes in our understanding of the causes

- there have also been dramatic changes in the epidemiology of gastric diseases which have altered the spectrum of gastritis that we see
Helicobacter pylori and the evolution of upper GI disease in the West: Blaser 1999

<table>
<thead>
<tr>
<th>Era</th>
<th>Time of acquisition of HP</th>
<th>Pathological effect</th>
<th>Prevalent disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ancient</td>
<td>Infant</td>
<td>Long term body-predominant gastritis &amp; IM</td>
<td>Gastric cancer</td>
</tr>
<tr>
<td>Pre-modern</td>
<td>Early childhood</td>
<td>Pan gastritis</td>
<td>Gastric peptic ulcer</td>
</tr>
<tr>
<td>Modern</td>
<td>Late childhood/early adulthood</td>
<td>Antral gastritis, high acid, duodenal GM</td>
<td>Duodenal peptic ulcer</td>
</tr>
<tr>
<td>Post-modern</td>
<td>Never</td>
<td>High (normal) acid with other factors of GOR</td>
<td>GORD, GLO and oesophageal cancer</td>
</tr>
</tbody>
</table>

Stages in the development of gastric carcinoma (after Correa)

- Normal gastric mucosa
- H pylori
- Superficial gastritis
- Atrophic gastritis
- Intestinal metaplasia
- Dysplasia
- Carcinoma

Risk of developing cancer in different gastric regions in H pylori infected individuals

- 0.3
- 3.8
- 5.9
- 4.2
- 24.0

Hansen et al 1999
Phenotypes resulting from *H. pylori* infection

- mild pan-gastritis
- corpus-predominant
- antrum-predominant

- gastritis
- atrophy
- intestinal metaplasia
- hypochlorhydria
- hyperchlorhydria
- DU phenotype
- gastric cancer phenotype
- no significant disease

HP and gastric neoplasia

- worldwide
  - *H. pylori* is the commonest bacterial infection
  - gastric carcinoma is the 2nd leading cause of cancer-related deaths

- pathogenesis of gastric carcinoma is complex and multifactorial but key pathophysiological events are triggered by *H. pylori* infection, which is now regarded as a class 1 carcinogen

- host genetic factors, bacterial virulence factors and the environment all play an important role

Utility of histology in the diagnosis of HP gastritis

- Not cost effective to use histopathology to detect *H. pylori*
  - Urease 50p: 2 hour sensitivity 80%, 24 hour sensitivity 95%
  - Pronto £2.00: 1 hour sensitivity 95%
  - Histology with special stain £35.00: 2 week sensitivity 95%

- No good evidence base that the grade of gastritis, associated IM, etc materially affect outcome

- Don’t let them take antral biopsies for the routine diagnosis of HP gastritis
Reactive gastritis

- more frequently recognised
- now the commonest form of chronic gastritis
- bile reflux (Dixon, 1986)
- drugs - aspirin, other non-steroidal anti-inflammatory drugs (NSAIDs)
- alcohol

HP gastritis and reactive gastritis - change in 15 years in GRH
Reactive gastritis – mild, moderate and severe

Gastric Tumours

Adenocarcinoma
- M:F = 3:1
- Still 4th commonest cancer killer in UK
- Japan, China
- Diet - salt, low dairy products
- @ helicobacter
- @ intestinal metaplasia
- poor prognosis if advanced (<20%)
- good prognosis if EGC (90%)

Lymphoma
- increasing
- @ helicobacter / chronic gastritis
- good prognosis if localised and responds to antibiotics

GISTs (gastro-intestinal stromal tumours)
- benign v malignant difficult
- lots of interest because of effective treatment (glivec: imatinib) for advanced disease

Adenocarcinoma of the stomach

- intestinal-type 50%
- diffuse-type 35%
- mixed, others 15%

Lauren 1965

* prognosis
  - type
  - stage - locally advanced
  - early gastric cancer
Gastric resections

- it's all in the ROPath dataset and reporting proforma
- local spread - pT
- lymph node harvests and sites of lymph node involvement
- serosal involvement
Junctional cancers

Junctional tumours: the Siewert classification

- Type I adenocarcinoma of the distal third of the oesophagus (1-5cm above cardio) oesophageal rules
- Type II adenocarcinoma straddling the gastro-oesophageal junction (1cm above to 2 cm below cardio) gastric rules
- Type III subcardial gastric adenocarcinoma that grow proximally to involve the GOJ (2-5 cm below cardio) gastric rules

Siewert RJ et al, 2000

- remains controversial but at least it gives us a guideline

Upper GI pathology

- it's fascinating!
- it's mainly about biopsies (especially looking for neoplasia) and resections for adenocarcinoma
- the importance of the macroscopic assessment and dissection of resection specimens cannot be overemphasised
- GISTs, lymphomas and other rarities add a bit of spice
- can't see why you would consider an interest in any speciality other than GI!!
And now for the lower GI tract