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Reporting OGD Biopsies and Gastric Polyps

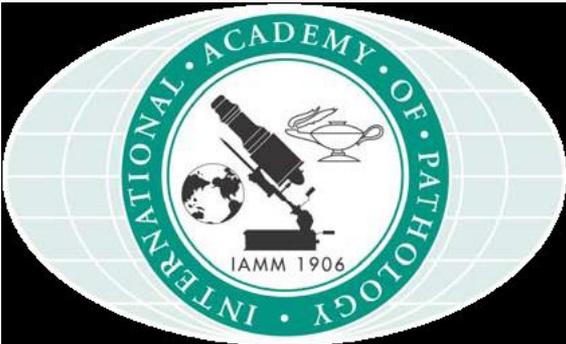
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Sarajevo

November 2016



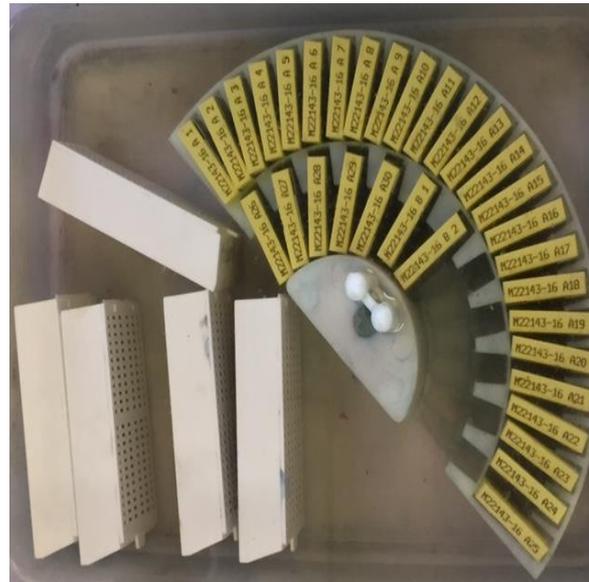
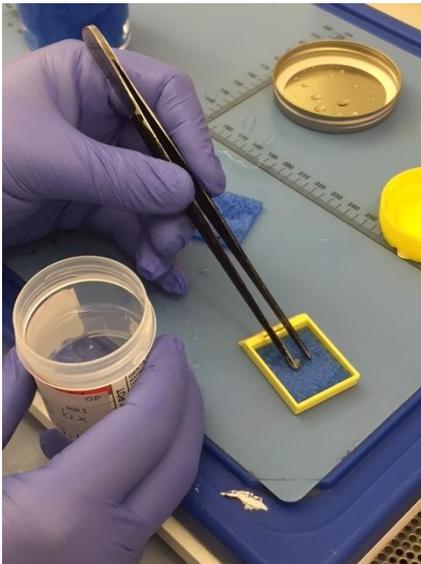
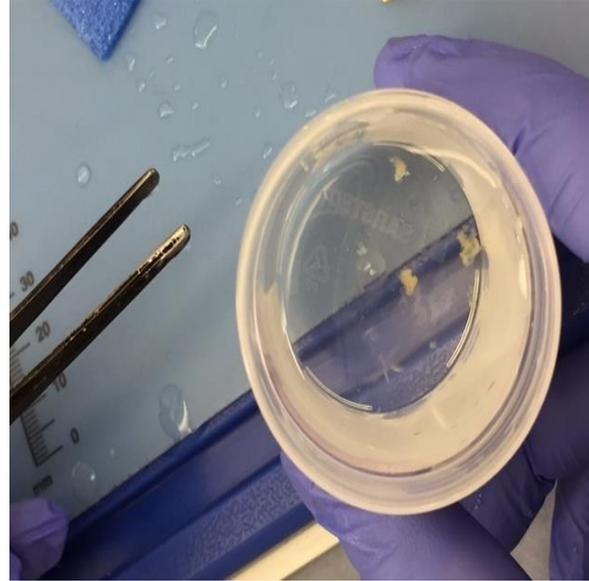
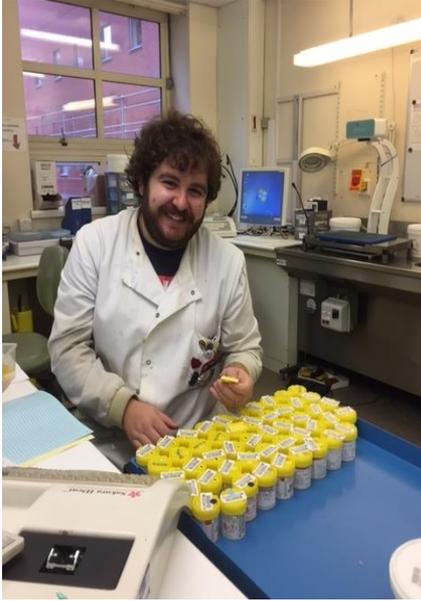
What are the issues?

- Provision of adequate and relevant clinical and endoscopic information
- Appropriate biopsy sampling (site and number of biopsies)
- With thanks to Dr Lucy Foster

Why does it matter?

- Improving chances of reaching the correct diagnosis
- Ensuring the patient is receiving the most appropriate treatment
- Making the best use of resources; in 2015 there were 14705 GI endoscopic biopsy specimens (ie. 14705 pots) processed and reported by the MRI histopathology laboratory and pathologists

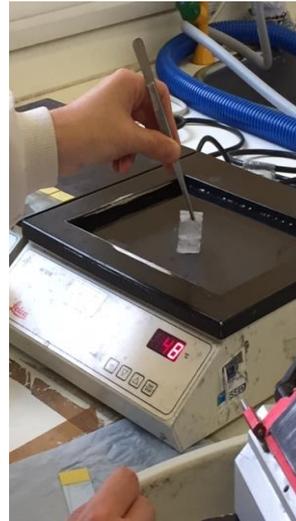
The biopsy's journey from pot to pathologist...



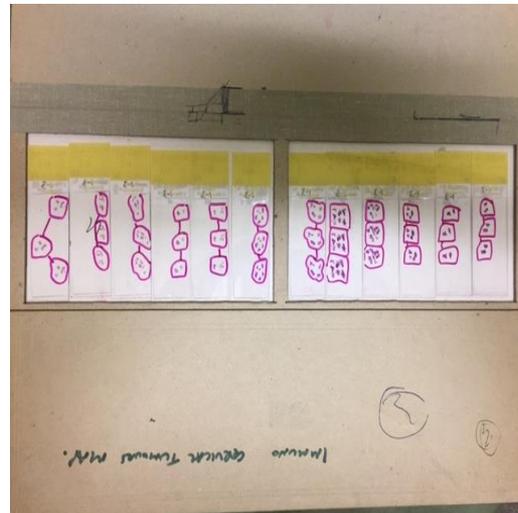
Through wax...



Microtome & Water bath...



Onto glass.



Can we talk about pre-cassetting biopsies in Endoscopy?



Current endoscopy practice

- In Histopathology we notice significant variation in practice across endoscopy practitioners of different grades, from different divisions and from different hospitals
- Standardised protocols?

Guidance for biopsy practice used in endoscopy departments in the Leeds area

Biopsy?	YES	NO
Oesophagus	Diagnosis and surveillance of Barrett's (4 biopsies every 2 cm)	Normal oesophagus
	Any focal lesion or ulceration When the clinical and endoscopic data suggest eosinophilic oesophagitis	Reflux oesophagitis unless ulceration Ultrashort segment Barrett's
Stomach	Any focal lesion	Normal stomach
	Unusual appearance or high suspicion of dysplasia/malignancy (when suspecting malignancy take 8 biopsies from the lesion, avoiding the ulcer base)	Diffuse 'gastritis'—use CLO test to determine <i>Helicobacter pylori</i> status
Duodenum	Diagnose/exclude coeliac disease when clinically indicated (≥3 biopsies in 1 cassette)	'Duodenitis' at endoscopy
Colorectal	Normal colonoscopy in patients with persistent watery diarrhoea (send 2 cassettes—3 biopsies from right side and 3 from left side)	Other normal colonoscopy
	Any polyp/other focal lesion	Ileal biopsy to demonstrate that the ileum has been reached
	Patient with known or genuinely suspected IBD	Random rectal biopsy for rectal bleeding.

Making the most of your endoscopic biopsies, and getting the best out of your histopathologist...

- Clinical and Endoscopic information
 - We are not gastroenterologists, we are also not psychic
 - The GI tract, in particular the lower GI tract shows a limited spectrum of histological changes when disease is present
 - Histological findings in GI endoscopic biopsies are often not diagnostic in isolation and clinical information is required to fine tune a differential dx

Making the most of your endoscopic biopsies, and getting the best out of your histopathologist...

- We need the whole picture to work out the most likely cause or to direct us to look for very subtle features which may otherwise not be picked up
- Without knowledge of the nature and duration of symptoms & a good description of the endoscopic appearance and distribution of disease we may only be able to offer a list of differentials
- The more information we have the more likely we are to be able to offer an opinion on what is most likely

What we need to know:

- Clinical History
 - What symptoms does the patient have and why are they having an endoscopy?
 - Duration
 - Any other relevant past medical history
 - Other diseases with GI manifestations
 - Recent surgery (and previous transplant surgery)
 - Medications
 - NSAIDs, Olmesartan, Doxycycline, Iron, Immunosuppression, New agents

What we need to know:

- Endoscopic findings
 - Is it normal?
 - If not why not and what is the distribution?
 - What is your opinion on the likely/possible cause for the appearances?
- We need enough information to be able to work out why the biopsies have been taken and to give us a rough idea of what we're looking for
- Sometimes this will affect how the lab handles the material before the biopsies even get taken out of the pot

Making the most of your endoscopic biopsies, and getting the best out of your histopathologist...

- Why are you taking a biopsy, is it necessary?
- Will the results of histology influence the management of the patient?
- Appropriate site and number of biopsies

Upper Gastrointestinal Tract

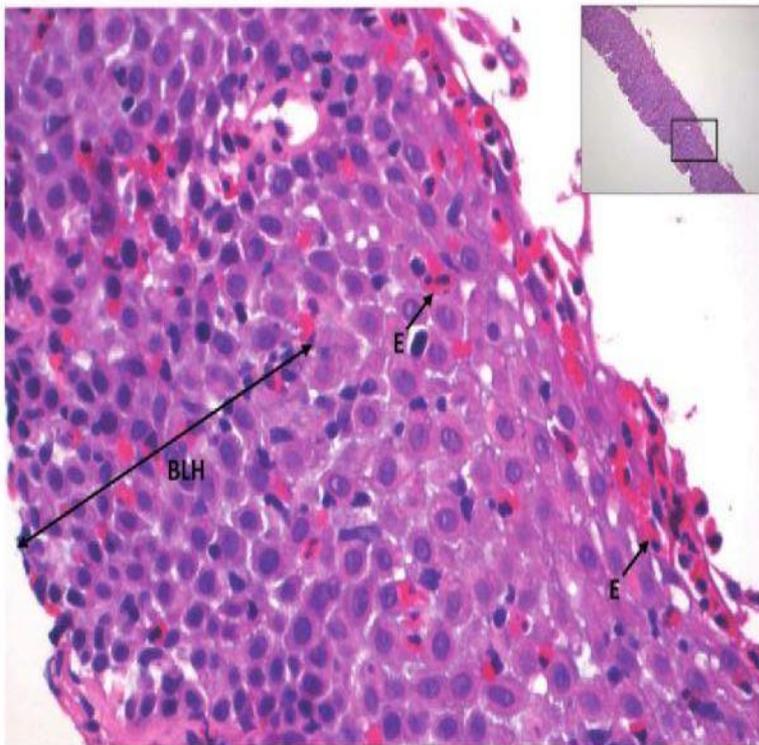
- All sites:
- Any suspicion of neoplasia please biopsy
- With peptic ulcers, the intact mucosa at the edge is more likely to be diagnostic than the centre of the ulcer which often just contains granulation tissue (unless CMV suspected)
- Tell us if the lesion appears submucosal, we often don't get submucosa on endoscopic biopsies but will do deeper levels to try to cut into it if indicated

Oesophagus

- Barrett's Oesophagus
 - Discussed at length in BSG guidelines, I won't discuss this today
- Reflux
 - Biopsies not indicated to confirm endoscopic diagnosis of reflux unless an alternative diagnosis is being considered
- History of dysphagia or food bolus with normal appearing oesophagus
 - If there is clinical (or endoscopic) suspicion of eosinophilic oesophagitis biopsy the oesophagus
 - Helpful to take mid and lower oesophageal biopsies and send separately, at least 3 bx from each site (can be patchy)
 - Overlap in histological features between eosinophilic oesophagitis and reflux, useful to be able to assess whether appearances are worse in the more distal samples

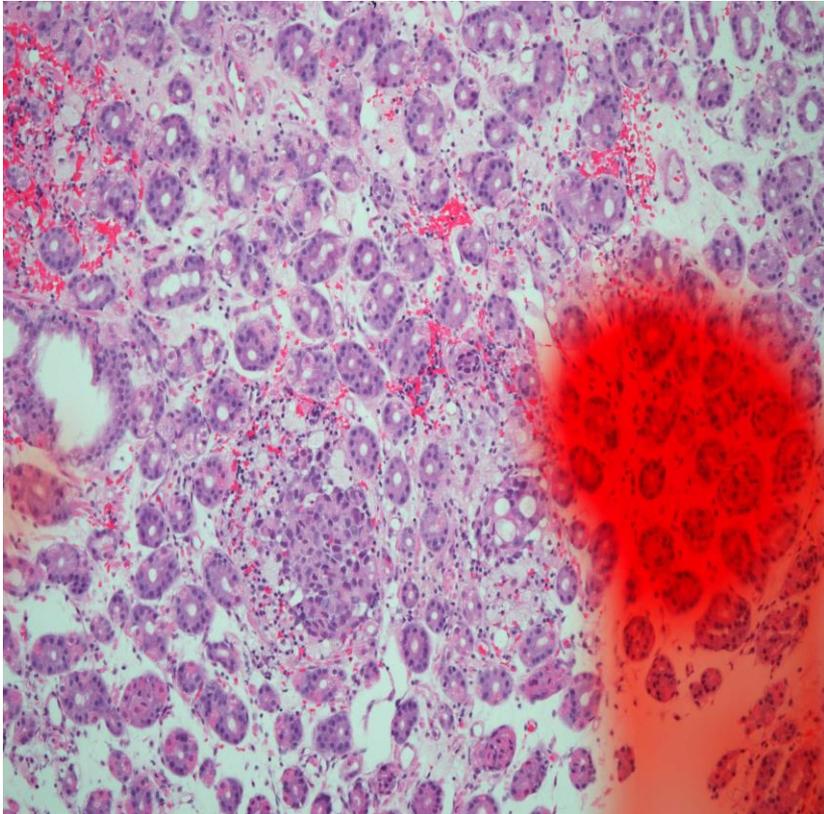
Eosinophilic oesophagitis

Medscape



- Many histological features in common with reflux
- Reflux tends to be worse more distally, this is less likely to be the case with EO
- It may not be possible to distinguish between the two histologically
- If biopsies are being taken because of clinical suspicion for eosinophilic oesophagitis, should other sites be sampled to assess for eosinophilic gastroenteritis?

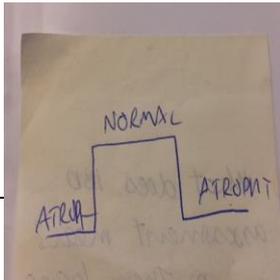
Stomach – suspicion of malignancy



- Any suspicion of malignancy and at least 8 biopsies are recommended
- If a diffuse/linitis type of gastric carcinoma is suspected endoscopically please make this clear on the request card, this can be very subtle histologically and may even look normal on initial levels
- If we know we're looking for something difficult to spot we'll do more levels or mucin stains or immuno

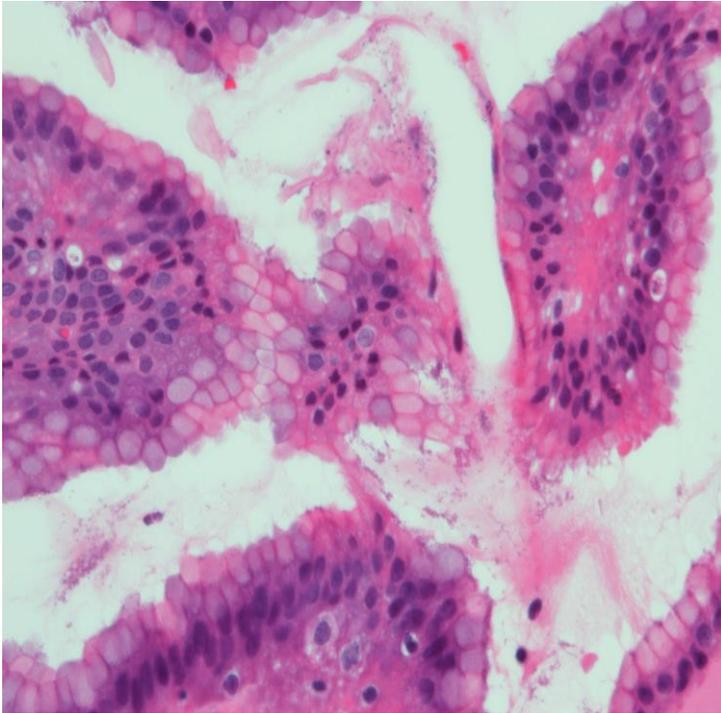
Stomach - polyps

- When biopsying polyps it is useful to send us biopsies of the surrounding mucosa
- Some syndromic type polyps show characteristic histological features in the background mucosa
- The presence of atrophic changes in the background may account for apparently normal appearing mucosa in what endoscopically resembled a polyp:



- Useful to indicate whether the biopsy is from the body or antrum in all cases but in particular where an assessment for atrophy is indicated

Stomach - gastritis



- Will biopsies from an area of gastritis alter management?
- Gastric biopsy for histological assessment should not be considered a diagnostic test for *Helicobacter pylori*
- But if you are going to do it sample from the antrum as a minimum, ideally body as well

GASTRIC BIOPSY: RECOMMENDATIONS

- When reporting biopsies for assessment of gastritis, consideration of the updated Sydney classification is recommended.
- Chronic inflammation, activity, intestinal metaplasia and atrophy can be graded.
- The presence or absence of Helicobacter and dysplasia should be recorded.
- The most common types of gastritis are Helicobacter-associated gastritis and reactive gastritis. As a minimum, a Helicobacter stain is recommended if characteristic inflammation is seen, no Helicobacter are apparent, and no clinical test has been performed.
- An ABPASD stain for mucins may be useful for confirming intestinal metaplasia.
- Routine Helicobacter and/or mucin staining are used in some laboratories, but evidence and support for this approach are inconsistent.

Duodenum – Coeliac disease

- Discussed in detail at a recent Endoscopy Breakfast Meeting
- D1 and D2 biopsies recommended
- Histopathology audit of duodenal biopsies for 2 weeks following the recent breakfast meeting (from 14/09/2016)
- 65 endoscopy cases included duodenal biopsies
- 9 cases described as focal abnormality or duodenitis
- Of 56 remaining cases 18 included D1 + D2 biopsies
- Adequate clinical information essential, serology, reassessment, diet

Villous atrophy in adults

Pathologic findings characteristic but not diagnostic

- Coeliac Disease
- Tropical Sprue
- Adult-onset autoimmune enteropathy
- Hypogammaglobulinemia
- Idiopathic
- AIDS enteropathy

Pathologic findings are non-specific

- Small-bowel bacterial overgrowth
- Infectious enteritis
- Parasitic infestation
- Severe malnutrition
- Small-bowel ischaemia

Pathologic findings could be diagnostic

- Eosinophilic gastroenteritis
- Whipple's disease
- Abetalipoproteinaemia
- Intestinal lymphoma
- Collagenous sprue
- Tuberculosis
- Giardiasis
- Crohn's disease

Serology for coeliac disease

- screen by TTG (check IgA levels)
- if positive, do EMA
- if positive, proceed to duodenal biopsy
- often duodenal biopsy is initial step (or not made aware of the results of serology)
- duodenal biopsy is the gold standard and things may go awry if CD is not so confirmed

Serology for coeliac disease

	sensitivity	specificity	comments
tissue transglutaminase (TTG)	90-95%	50-95% Depends on lab and titre cut-off	IgA Good screen for CD
anti-endomysial antibody (EMA)	90-95%	95%	IgA but really a crude TTG – needs very high titre
anti-gliadin antibody	90% if IgA	80%	Depends on whether IgG or IgA measured

MUCOSAL BIOPSY: RECOMMENDATIONS

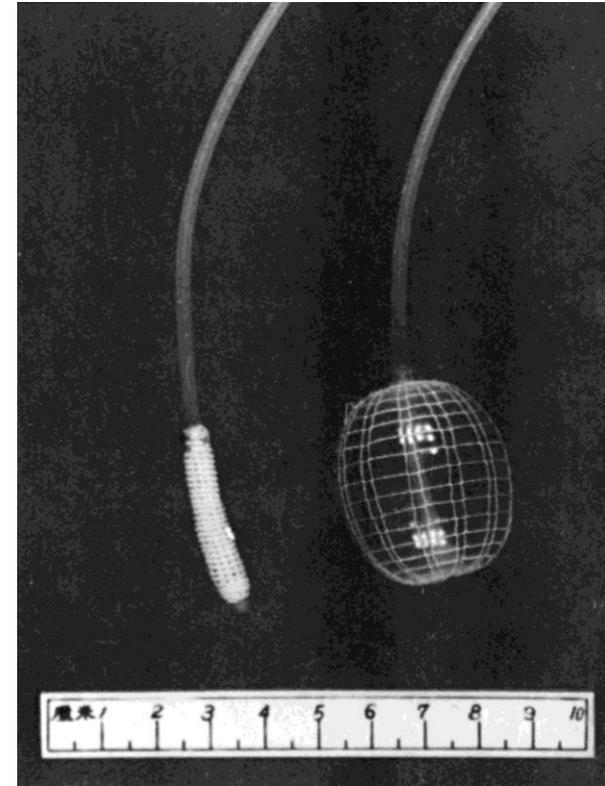
- Adequate clinical details should be provided in all cases.
- Clinicopathological meetings may be useful
- Biopsies from different parts of the GI tract should be submitted in such a way that their site of origin is unequivocal, e.g. multiple pots or multi-well cassettes
- Step sections routinely at two or three levels (e.g. 75 microns apart) are recommended
- Additional levels are often useful

Oesophageal Cancer: Biomarkers

- Ideally should be sensitive, specific, quick, non-invasive, not require specialist intervention
- Endoscopic biopsies are not ideal:
 - Invasive, expensive, time-intensive
 - Inter-observer variability in reporting
 - Sampling problems
- Cytology provides more rapid sampling of greater surface area: contamination with other cells

Oesophageal Cancer: Biomarkers

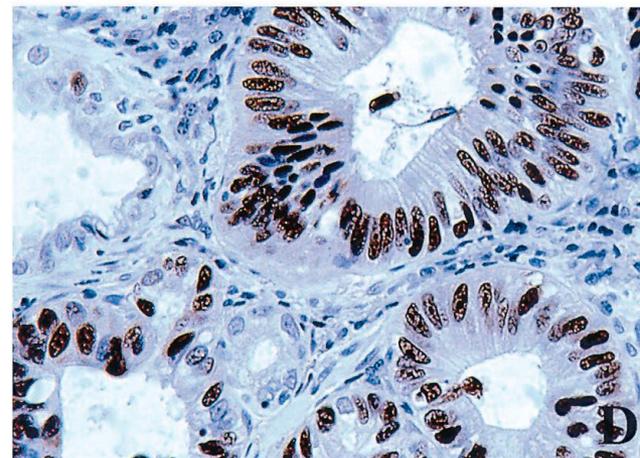
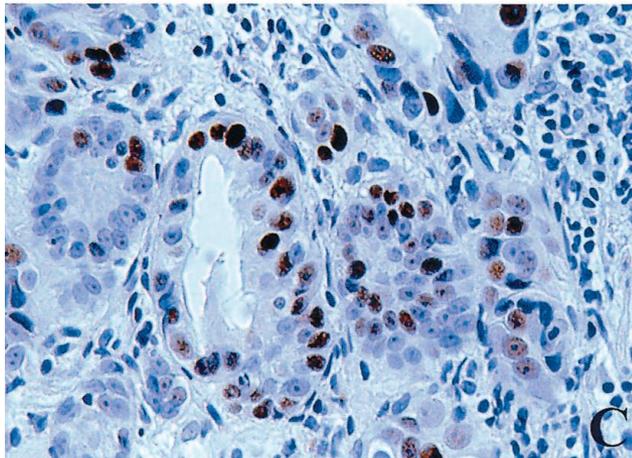
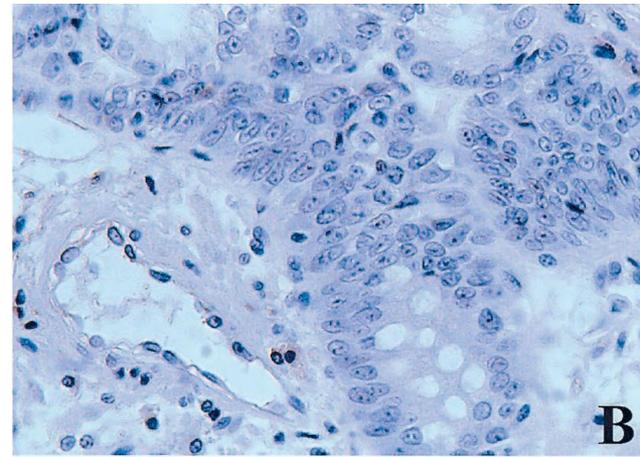
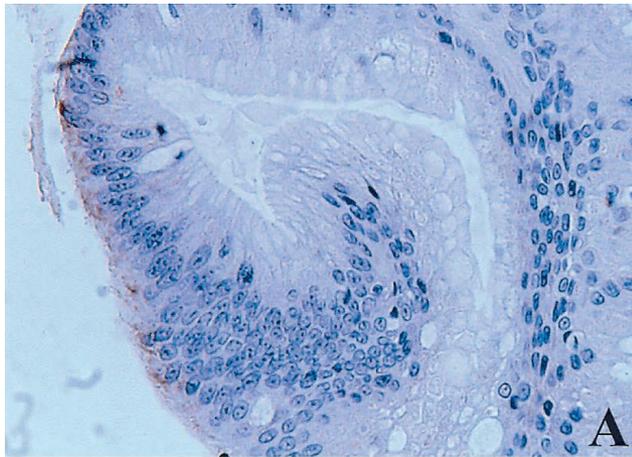
- Cytology used to provide cells for methylated gene studies
- Poor sensitivity and specificity
- Automation possible
- Flow cytometry for ploidy
- FISH for p53/p16, Her-2
- Capsule sponge for Barrett's being evaluated: MCM-2, TFF3
- Toll-like receptor 9 for SCC



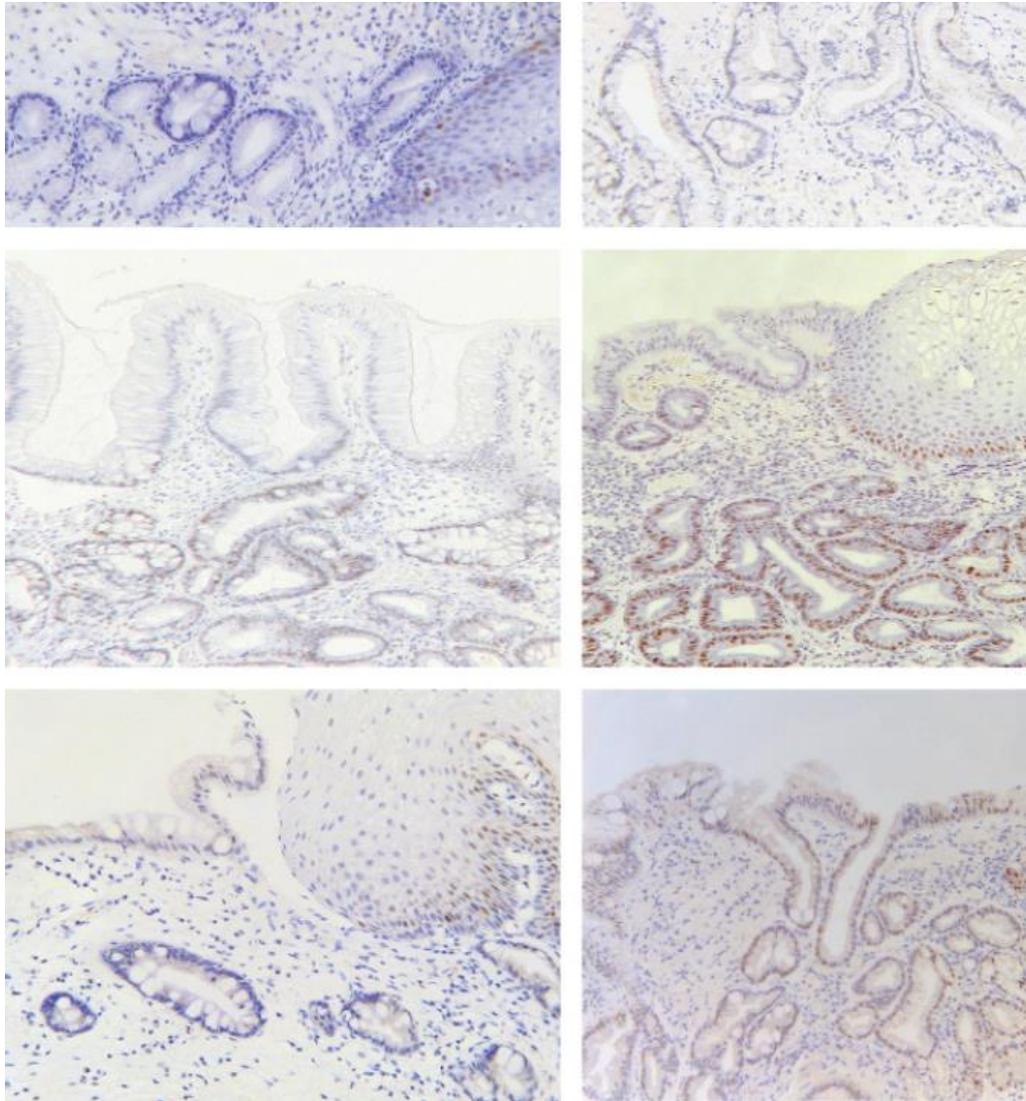
Oesophageal Cancer

Biomarkers in Barrett's mucosa

- High grade dysplasia
- Aneuploidy/LOH (17p, 9p)
- p53 immunohistochemistry
- Mcm2
- Cyclin A
- Methylation



p53 immunohistochemistry from Weston et al
Am J Gastroenterol 2001 96:1355-1362



p53 and cyclin D1 immunohistochemistry from Murray et al
Gut 2006; 55: 1390-1397

<http://www.bsg.org.uk/clinical-guidelines/oesophageal/guidelines-on-the-diagnosis-and-management-of-barrett-s-oesophagus.html>

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Guidelines on the Diagnosis and Management of Barrett's Oesophagus

Fitzgerald RC, di Pietro M, Raganath K *et al.*

Abstract

These guidelines provide a practical and evidence-based resource for the management of patients with Barrett's oesophagus and related early neoplasia. The Appraisal of Guidelines for Research and Evaluation (AGREE II) instrument was followed to provide a methodological strategy for the guideline development. A systematic review of the literature was performed for English language articles published up until December 2012 in order to address controversial issues in Barrett's oesophagus including definition, screening and diagnosis, surveillance, pathological grading for dysplasia, management of dysplasia, and early cancer including training requirements. The rigour and quality of the studies was evaluated using the SIGN checklist system. Recommendations on each topic were scored by each author using a five-tier system (A+, strong agreement, to D+, strongly disagree). Statements that failed to reach substantial agreement among authors, defined as >80% agreement (A or A+), were revisited and modified until substantial agreement (>80%) was reached. In formulating these guidelines, we took into consideration benefits and risks for the population and national health system, as well as patient perspectives. For the first time, we have suggested stratification of patients according to their estimated cancer risk based on clinical and histopathological criteria. In order to improve communication between clinicians, we recommend the use of minimum datasets for reporting endoscopic and pathological findings. We advocate endoscopic therapy for high-grade dysplasia and early cancer, which should be performed in high-volume centres. We hope that these guidelines will standardise and improve management for patients with Barrett's oesophagus and related neoplasia.

 [Download guideline](#) [2.4 Mb]

Guidelines on the Diagnosis and Management of Barrett's Oesophagus - An Update

Tony Tham, Secretary BSG Clinical Services and Standards Committee

This is an update to the management of low grade dysplasia in the recent BSG guidelines on Barrett's oesophagus. The new recommendation is that patients with LGD should have a repeat endoscopy in 6 months time. If LGD is found in any of the follow up OGDs and is confirmed by an expert GI pathologist, the patient should be offered endoscopic ablation therapy after review by the specialist MDT. If ablation is not undertaken, 6-monthly surveillance is recommended. For the full text of the update, please go to the link below:

 [Guidelines on the Diagnosis and Management of Barrett's Oesophagus - 2015 Update](#)

Given the important management implications for a diagnosis of dysplasia, we recommend that **all cases of suspected dysplasia are reviewed by a second GI pathologist**, with review in a cancer centre if intervention is being considered (Recommendation grade C).

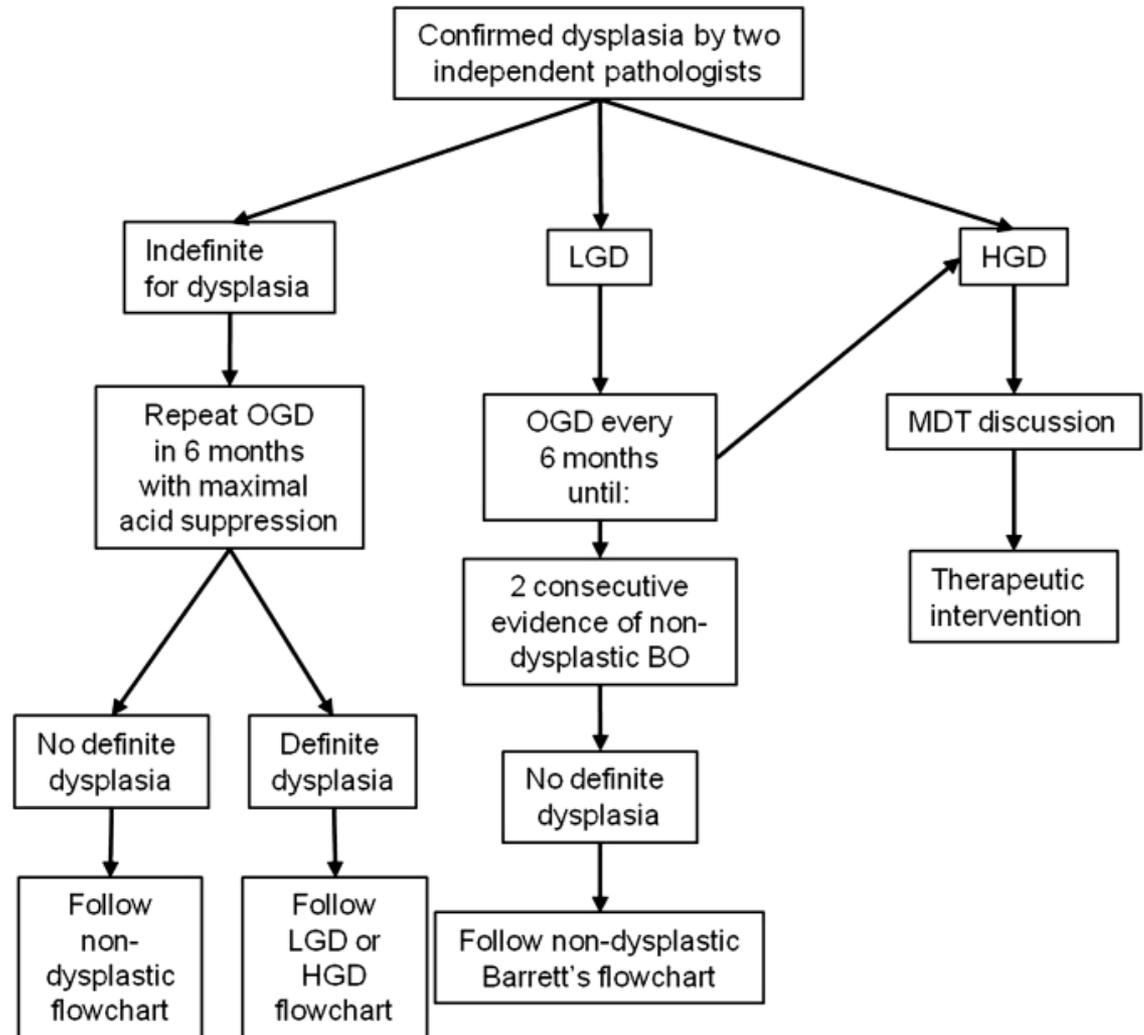
Given the difficulties associated with the management of the **'indefinite for dysplasia'** category, all such cases should also be **reviewed by a second GI pathologist**, and the **reasons** for use of the **'indefinite for dysplasia'** category should be **given** in the histology report in order to aid patient management (Recommendation grade C).

The addition of **p53 immunostaining** to the histopathological assessment **may improve** the diagnostic reproducibility of a diagnosis of dysplasia in Barrett's oesophagus and **should be considered** as an adjunct to routine clinical diagnosis (Recommendation grade C)

If **LGD** is found in any of the follow up OGDs and is **confirmed by an expert GI pathologist**, the patient **should be offered endoscopic ablation therapy** after review by the specialist MDT. If ablation is not undertaken, 6-monthly surveillance is recommended. (Update to Guidance 2015)

Guidelines

Figure 4 Surveillance flow chart for dysplastic Barrett's oesophagus (BO). A pathological finding of indefinite for dysplasia does not exclude the presence of dysplasia, therefore a 6-month follow-up is warranted. Six-monthly surveillance and endoscopic treatment are generally recommended for low-grade and high-grade dysplasia, respectively. MDT, multidisciplinary team; OGD, oesophagogastroduodenoscopy.



OESOPHAGEAL BIOPSY: RECOMMENDATIONS

- ABPASD staining may be useful. Routine ABPASD staining may be appropriate for some laboratories, but evidence and support for this approach are inconsistent
- Diagnosis of intestinal metaplasia requires the presence of goblet cells.
- When reporting biopsies for assessment of Barrett's oesophagus, the approach based on British Society of Gastroenterology guidelines is recommended.
- Histological distinction of eosinophilic oesophagitis from reflux oesophagitis can be difficult. Correlation with clinical findings is advisable.

Classification of gastric polyps

Epithelial Polyps

Fundic gland polyp

Hyperplastic polyp

Adenomatous polyp

Hamartomatous polyps

- Juvenile polyp

- Peutz Jeghers syndrome

- Cowden's syndrome

Polyposis syndromes (non-hamartomatous)

- Juvenile polyposis

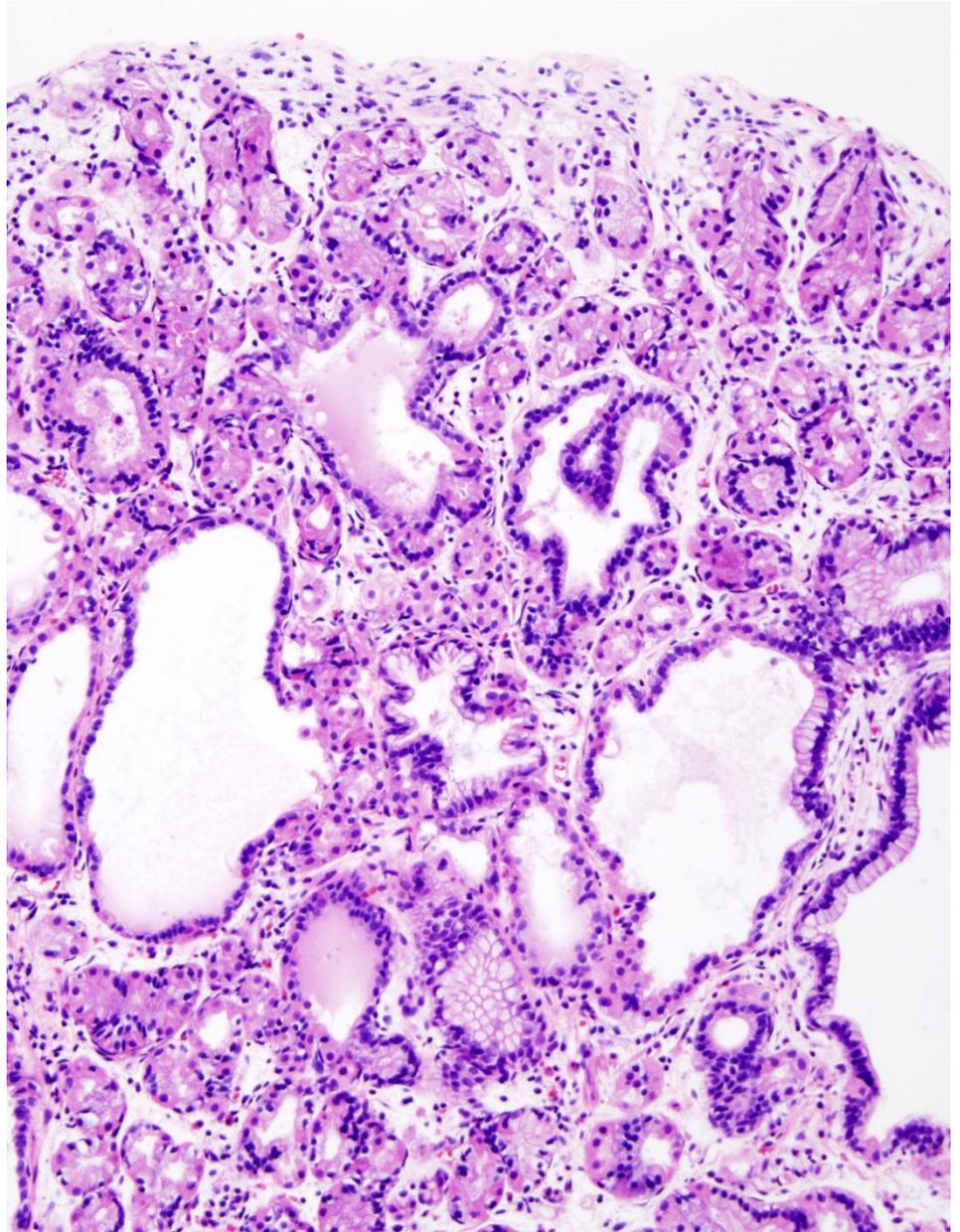
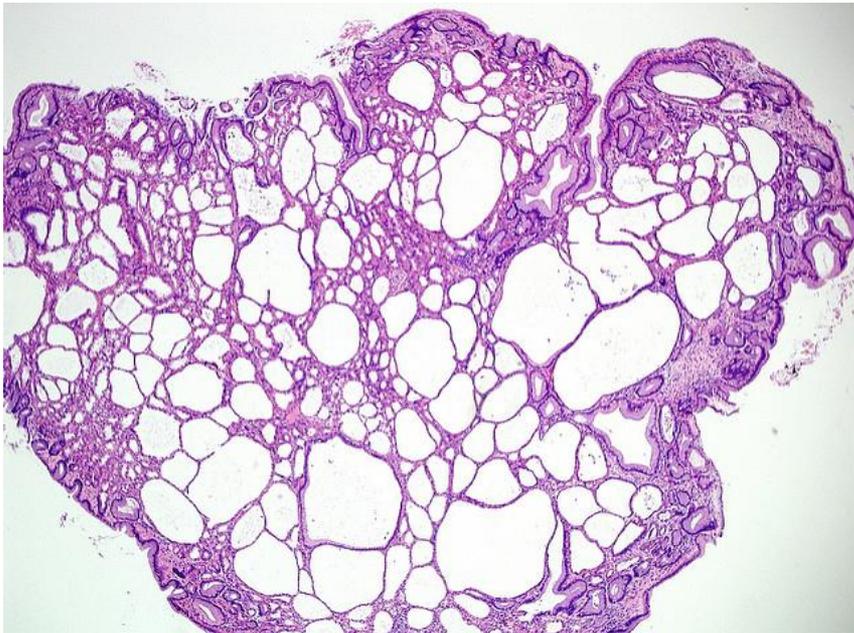
- Familial adenomatous polyposis

Fundic gland polyps (FGPs)

- constitute 16-51% of BEGPs
- may be observed in 0.8-23% of endoscopies
- usually multiple transparent sessile polyps
- 1-5mm in diameter
- located in the body and fundus.
- microscopy shows cystically dilated glands lined by gastric body type mucosa
- most sporadic but some associated with chronic PPI use or FAP

Cystic Fundic Gland Polyp

microscopy shows cystically dilated glands lined by gastric body type mucosa



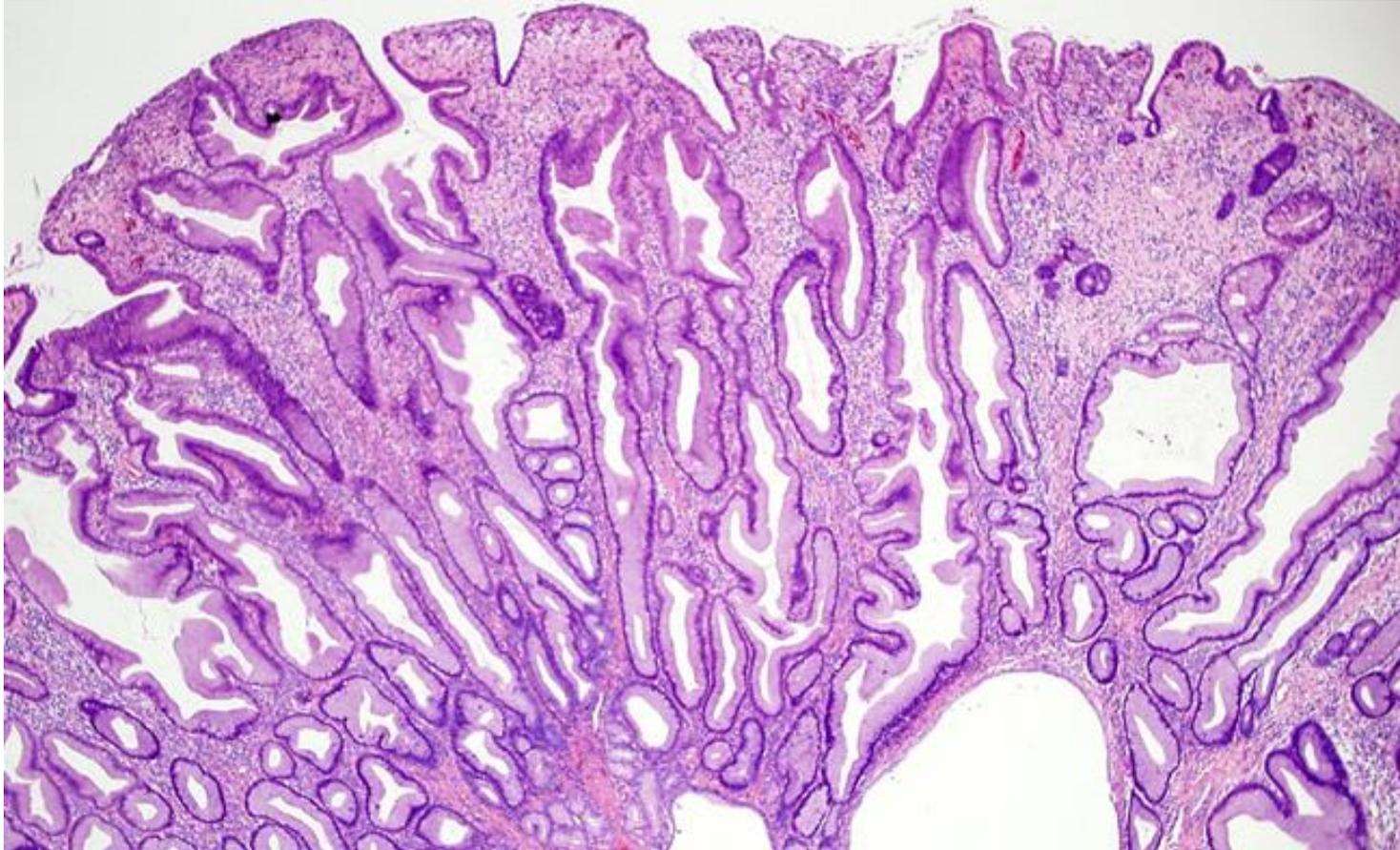
Recommendations for the management of FGPs

- Polypectomy not required for sporadic FGPs.
- Biopsy of probable FGPs recommended to exclude dysplasia, adenocarcinoma (and possible FAP) and to exclude the need for polypectomy as required for other types of polyp.
- In patients with multiple (>20) FGP <40 years of age, not on PPI, or dysplasia on bx, consider colonoscopy to exclude FAP

Hyperplastic polyps

- Constitute 30-93% of all BEGPs
- Sessile or pedunculated polyps <2 cm in diameter.
- Single polyps usually in the antrum or as multiple polyps throughout the stomach.
- Multiple hyperplastic polyps are also found in Menetrier's disease.
- Histologically, proliferation of surface foveolar cells lining elongated, distorted pits that extend deep into the lamina propria.
- May contain pyloric glands, chief cells, and parietal cells.
- Overlap with hamartomas and inflammatory conditions.

Hyperplastic polyps



Hyperplastic polyps

Associated with

- chronic gastritis
- *Helicobacter* associated gastritis
- pernicious anaemia
- reactive or chemical gastritis
- adjacent to ulcer erosions
- gastroenterostomy stomas

Hyperplastic polyps

- Dysplasia rare
- Reported 1.9% to 19%
- Adenocarcinoma 0.6-2.1%
- Controversy on biopsy versus polypectomy
- Single polyps >1cm should be removed
- Smaller polyps biopsied and surveilled
- Consider *H pylori* eradication

Adenomatous polyps

True neoplasms, precursors of gastric cancer

Histological classified into tubular, villous and tubulovillous types

Constitute 3-26% of BEGP, frequently solitary, found anywhere in the stomach, commonly antrum

Background atrophic gastritis and intestinal metaplasia, no proven association with *H. pylori* infection

Neoplastic progression is greater with polyps larger than 2 cm in diameter

Occurs in 28.5-40% of villous adenomas and 5% of tubular adenomas

Adenomatous polyps

Recommendations for management

- Complete removal of the adenoma
- Biopsy of the surrounding mucosa to determine the clinicopathological context of the adenoma
- Endoscopic follow up is required
- The time interval can be guided by the degree of dysplasia or completeness of polyp resection.

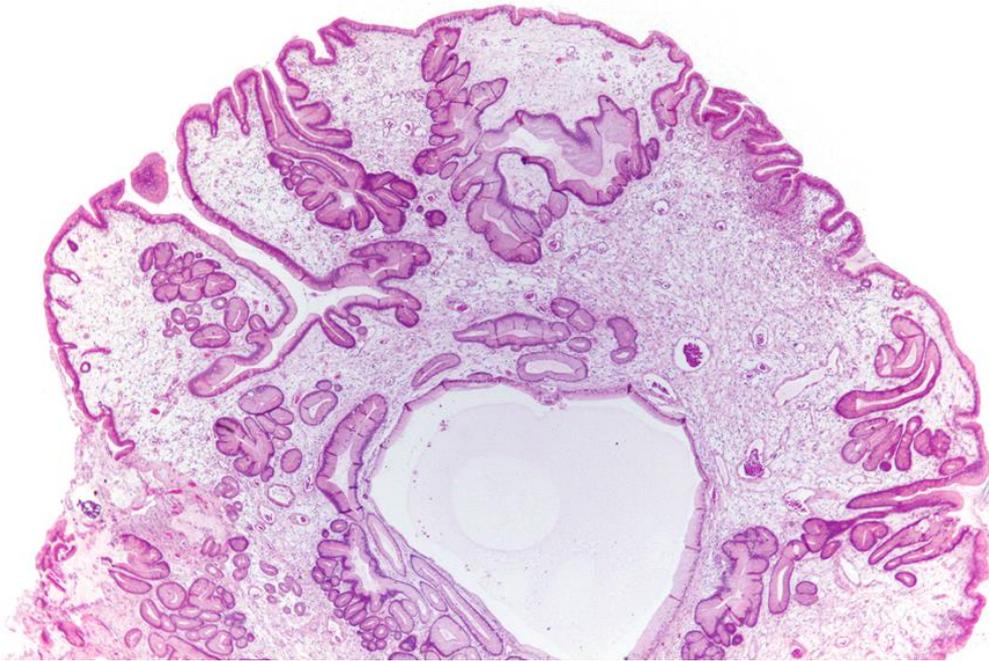
Hamartomatous polyps

Juvenile polyps

- Mainly antral
- Solitary polyps: hamartomatous or inflammatory components; no neoplastic potential.
- Histologically
- irregular cysts lined by normal gastric epithelium;
- possible stromal haemorrhage, surface ulceration and chronic inflammation due to torsion.
- Multiple polyps are associated with juvenile polyposis.

Hamartomatous polyps

Juvenile polyps



irregular cysts lined by normal gastric epithelium
stromal haemorrhage and oedema,
surface ulceration and chronic
inflammation due to torsion

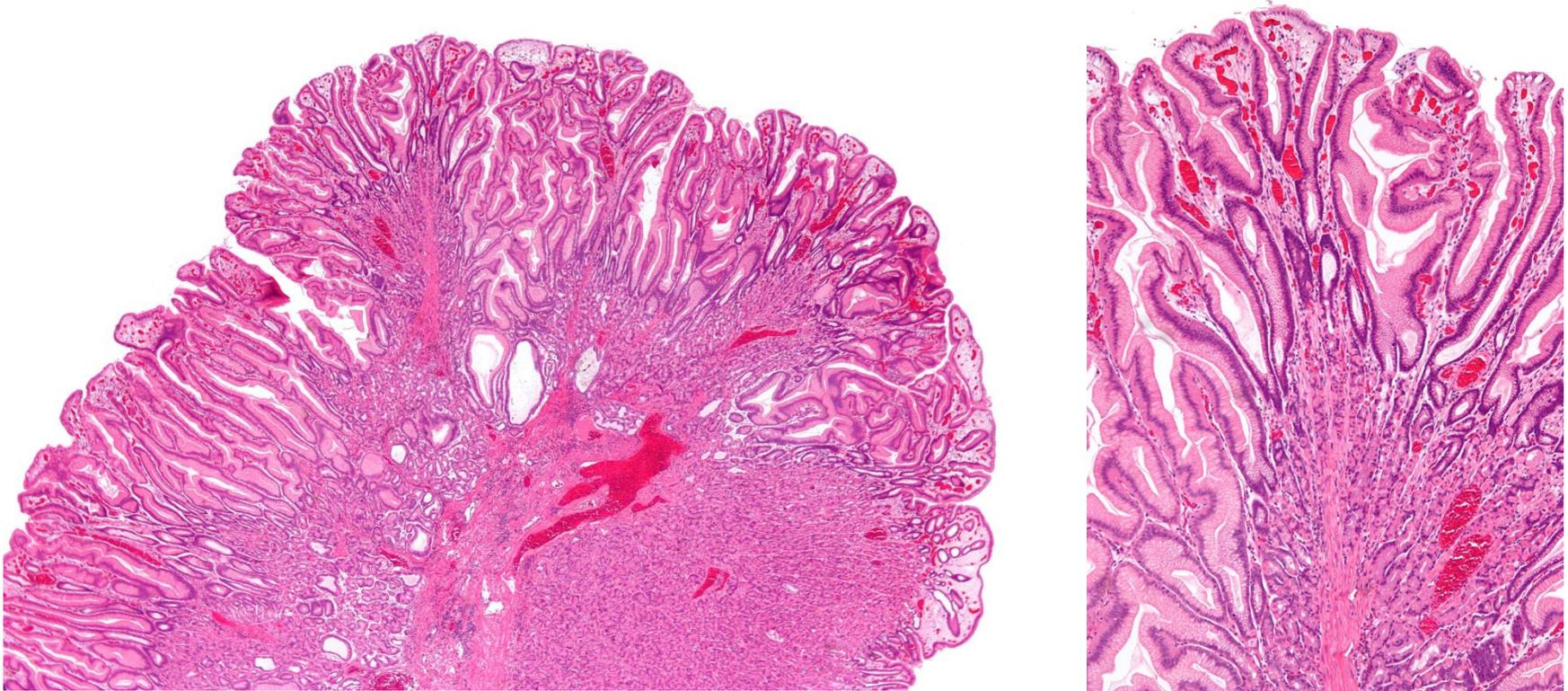
Hamartomatous polyps

Polyps of Peutz Jeghers syndrome (PJS)

- rare autosomal dominant inherited condition
- hamartomatous gastrointestinal polyps
- mucocutaneous pigmentation of the lips, buccal mucosa and digits
- PJS increases the risk of gastrointestinal cancer through the hamartoma-adenoma-carcinoma sequence and de novo malignant change

Hamartomatous polyps

Polyps of Peutz Jeghers syndrome (PJS)



Microscopically

hyperplastic glands lined by foveolar epithelium and broad bands of smooth muscle fibres

Management of gastric polyps associated with polyposis syndromes

Syndrome	Lifetime risk of malignancy	Surveillance recommendation
FAP	100% (colon)	OGD every 2 years after age 18 Biopsy >5 polyps Remove polyps >1cm Surveillance also required for duodenal polyps
PJS	>50% (extra-GI)	OGD every 2 years after age 18 Biopsy >5 polyps Remove polyps >1cm
Juvenile Polyposis	>50%	OGD every 3 years after age 18
Cowden's	Rare	Eradicate <i>H. pylori</i> No further OGD needed

Gastric polyp characteristics and malignant potential

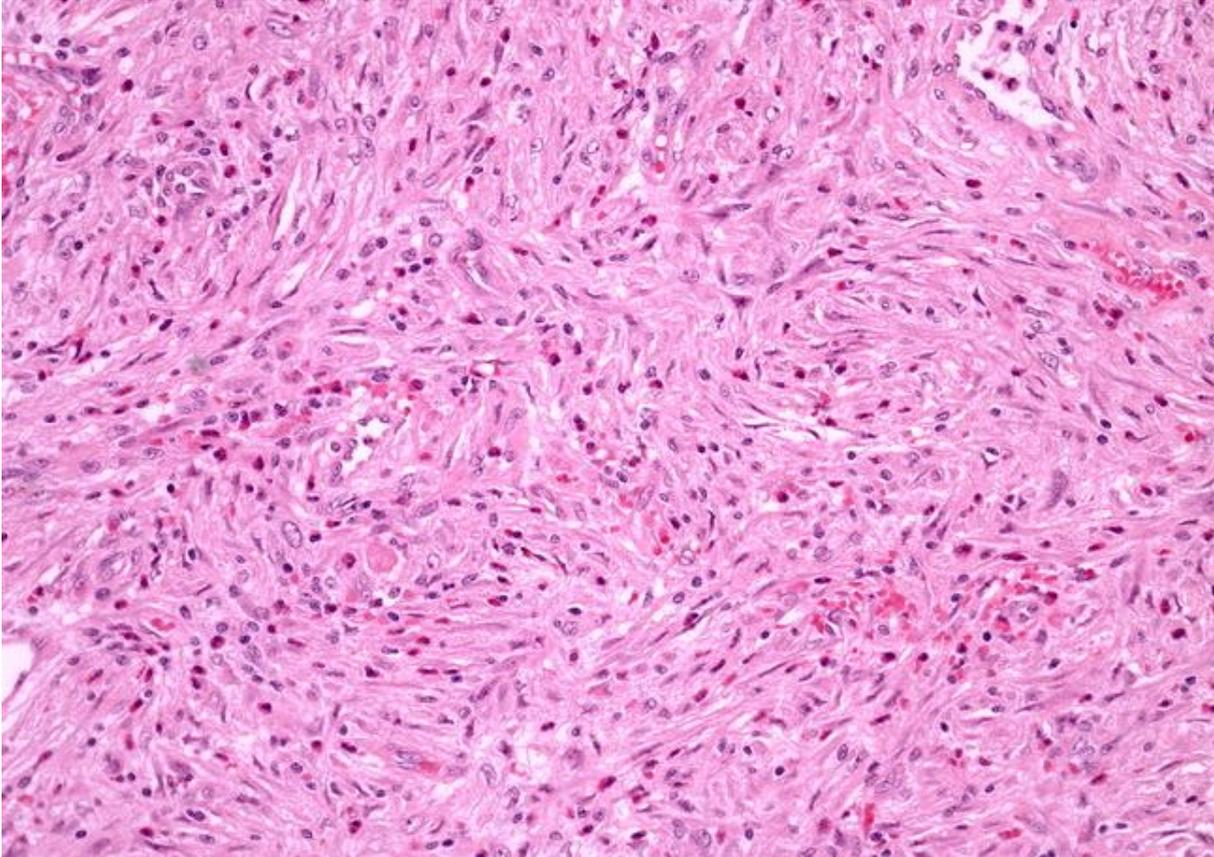
Polyp type	Usual number and size	Usual site	Malignant potential of polyp	Malignant potential of background mucosa	Management
Sporadic Fundic Gland Polyp	Multiple 1-5mm	Upper and lower body	Very low	Very low	Biopsy to confirm nature of polyp No follow-up needed
FAP associated Fundic Gland Polyp	Multiple 'carpet' <1cm	Upper and lower body	Low	Low	Biopsy to confirm nature of polyp Repeat OGD every 2 years
Hyperplastic	Single 1-2cm	Antrum	Low but significant	Low	Remove polyp Eradicate <i>H pylori</i> Repeat OGD 1 year
	Multiple <1cm	Lower body	Low but significant	Low	Eradicate <i>H pylori</i> Repeat OGD 1 year
Adenoma	Single 1-2cm	Antrum	High	Significant	Remove polyp Sample rest of gastric mucosa Repeat OGD at 1 year and 2 yearly thereafter
Inflammatory Fibroid Polyp	Single 1-5cm	Antrum	Very low	Very low	Biopsy to confirm nature of polyp Remove if causing obstruction No follow-up

Classification of gastric polyps

Non-mucosal Intramural Polyps

- Gastrointestinal stromal tumour
- Leiomyoma
- Inflammatory fibroid polyp
- Fibroma and fibromyoma
- Lipoma
- Ectopic pancreas
- Neurogenic and vascular tumours
- Neuroendocrine tumours (carcinoids)

Inflammatory Fibroid Polyp



Histologically
blood vessels
spindle cells (CD 34 and fascin positive)
chronic inflammatory cells
predominantly eosinophils
occasional multinucleated giant cells

Polyp type	Prevalence (frequency relative to other polyps)	Gastric location	Size	Endoscopic appearance	Pathological features of background gastric mucosa	Comments
Fundic gland	13–77%	Fundus and upper body	<1 cm	Smooth, glassy, transparent; usually multiple polyps are found	<i>Helicobacter pylori</i> -associated gastritis is rare	Associated with PPI use; may regress; dysplasia found in patients with FAP
Hyperplastic	18–70%	Random, adjacent to ulcers or stoma sites, or in the cardia if related to acid reflux	Generally <1 cm	Small polyps have a smooth dome; large polyps are lobulated, and erosions are common	Atrophic gastritis with intestinal metaplasia; <i>Helicobacter pylori</i> -associated gastritis (25%)	Found in patients with gastritis; dysplasia is rare (<3%) and found in polyps <2 cm
Adenoma	0.50–3.75% (in Western hemisphere)	<i>Incisura angularis</i> , found more in the antrum than fundus	<2 cm	Velvety, lobular surface; exophytic, sessile or pedunculated; usually solitary (82%)	Atrophic gastritis with intestinal metaplasia	May be accompanied by coexistent carcinoma
Inflammatory fibroid	0.1–3.0%	Submucosal, found near the pyloric sphincter	Median 1.5 cm; generally <3 cm	Single, firm, sessile, well-circumscribed, ulceration is common	Pernicious anemia commonly found; atrophic gastritis	Etiology is believed to be reactive, but genetic mutations are common
Peutz–Jeghers	Rare	Random	<1 cm	Pedunculated with a velvety or papillary surface	Normal	Risk of adenocarcinoma, but rare in gastric polyps
Juvenile	Rare	Found more in the body than in the antrum	Variable	More rounded than hyperplastic polyps; superficial erosions; multiple polyps are usually found	Normal	Polyps may exclusively involve stomach; risk of adenocarcinoma but rare in gastric polyps

Abbreviations: FAP, familial adenomatous polyposis; MEN, multiple endocrine neoplasia; ZES, Zollinger–Ellison syndrome.

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