

ENDOSCOPIC ASSESSMENT OF GASTRIC CANCER

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BC Cancer Surgery
Network Fall Update

FACULTY/PRESENTER DISCLOSURE

Faculty: Eric Lam

Relationships with commercial interests

- Grants/Research Support: None
- Speakers Bureau/Honoraria: Pendopharm
- Consulting Fees: Olympus Canada
- Other:



MANAGING POTENTIAL BIAS

No mention of proprietary techniques or imaging modalities

Not speaking about any products used in ESD

Relationships do not affect my choices in developing content



OBJECTIVES

Recognize the typical gastric cancer morphologies and precursor lesions

Identify the pathological significance of both benign and malignant histologies

Describe criteria for endoscopic evaluation and critical components of an endoscopic report for gastric cancer

GASTRIC CANCER EPIDEMIOLOGY

Fourth most common incident cancer in the world

Second leading cause of cancer related mortality worldwide

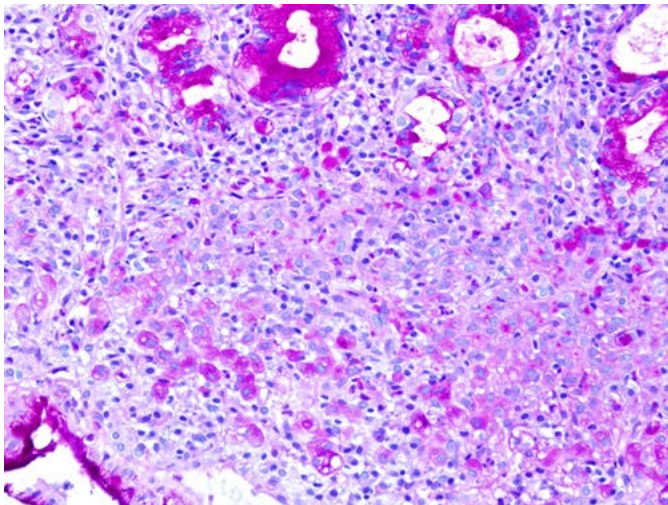
Majority of prevalent cases in east Asia

- 3.5 – 7.8/100,000 US
- 65.9/100,000 Korea

On the decline

- Non Cardia GC – due to declining H. pylori infection

GASTRIC CANCER



Microscopically resemble
intestinal mucosa

Many if not all arise from chronic
gastritis

Oxyntic
atrophy/hypochlorhydria

Distinct differences result in
differences in natural history and
treatment

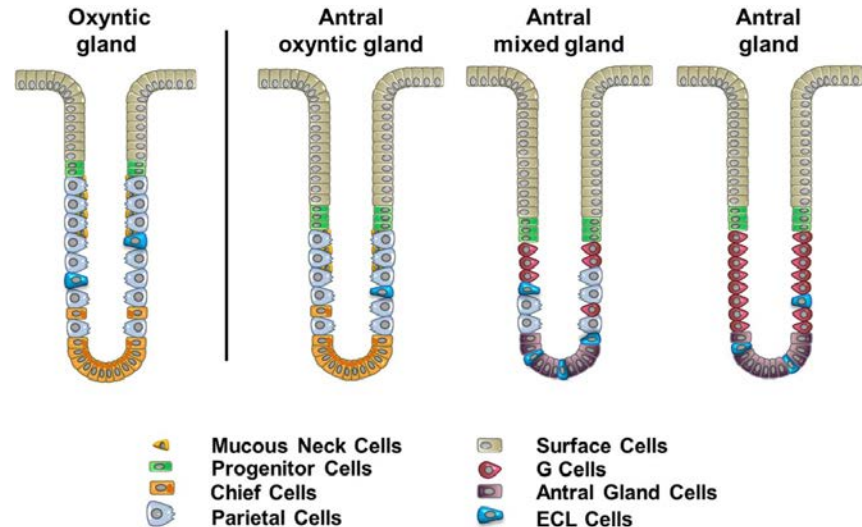
GASTRIC CANCER ORIGIN AND CLASSIFICATION

Complex interaction between

- The etiologic agents of gastritis
- Gastrin effect on ECL cells/histamine release
- Histamine affects on antral cells
- Differentiation differences between antral and oxyntic mucosa

Classification schemes

- Do not explain all forms of gastric carcinoma



GASTRITIS TO HYPERGASTRINEMIA

Etiologic agents of chronic gastritis

- *Helicobacter pylori*
- Other infectious agents (EBV)
- Autoimmune
- Dietary factors

GASTRITIS TO HYPERGASTRINEMIA

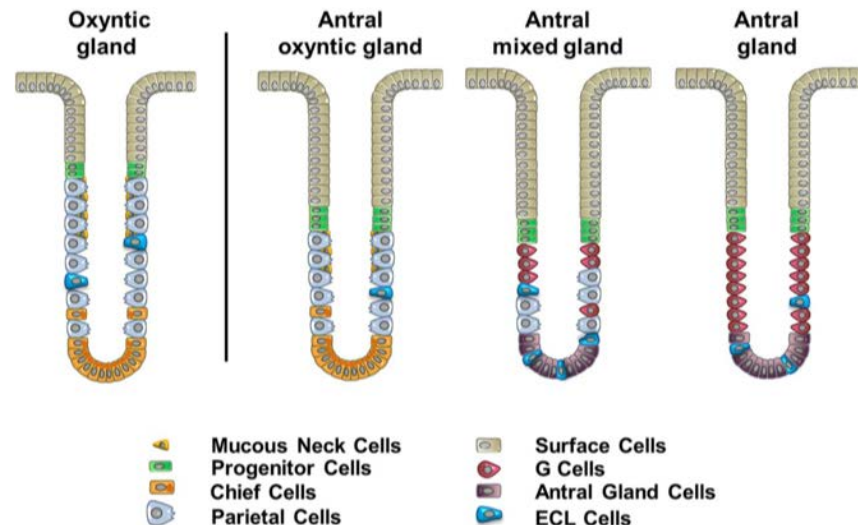
Hypergastrinemia

- Trophic hormone resulting in extrachromaffin cell growth
- Origin of type I gastric carcinoids
- Affects exocrine differentiation
 - Two main growth patterns dependent on which cells involved

LAUREN CLASSIFICATION

Intestinal type (Glandular growth pattern)

- Result of chronic gastritis
- Origins in oxyntic mucosa stem cells in the isthmus of the gastric pit
 - Histamine mediated
- Typically has precursor lesions that can be identified microscopically/endoscopically
 - Chronic active gastritis
 - Atrophic gastritis/pernicious anemia
 - Intestinal metaplasia



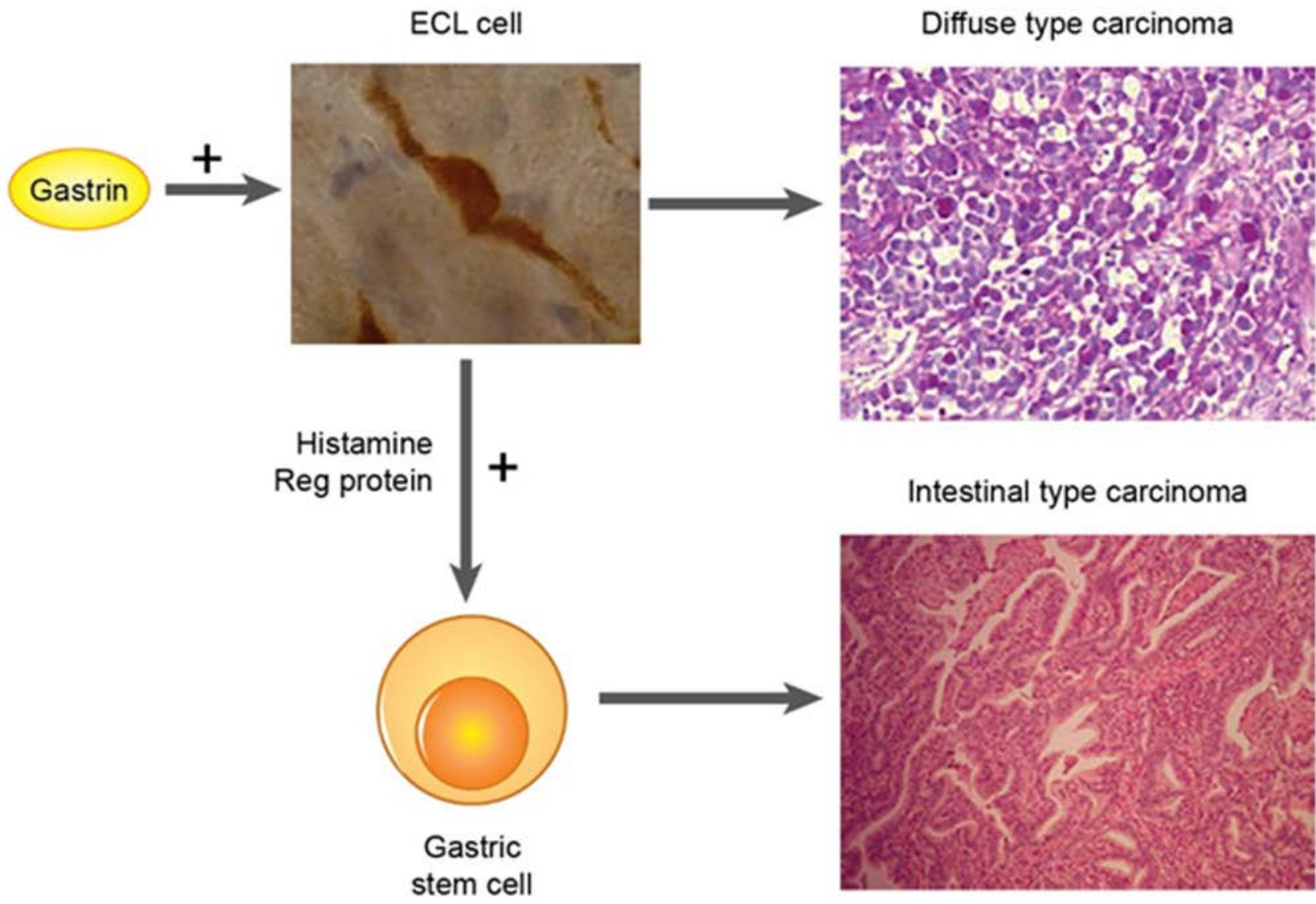
LAUREN CLASSIFICATION

Diffuse type (Infiltrative growth pattern)

- Origins in ECL cells
- Paracrine effects the antral mucosa cells
- Epithelial cell adhesion (E cadherin)
 - Hereditary CDH1 Gene mutation
 - Somatic mutations leading to E cadherin loss

All gastric cancers have neuroendocrine testing

- Synaptophysin and chromogranin A



MACROSCOPIC DISTRIBUTION

GE Junctional tumours

- Arising from specific cell type vs metaplasia?

Tumours distal to the cardia

- Oxymtic origins (glandular growth pattern)
- Antral origins (infiltrative growth pattern)

Distribution of antral and oxymtic cells less demarcated than once thought

LAUREN CLASSIFICATION

Does not account for about 15% of gastric carcinomas

- GE Junctional tumours
- Microsatellite unstable tumors in Lynch syndrome
- Gastric carcinoma with lymphoid stroma (Medullary carcinomas)

WHAT IS THE ENDOSCOPIC PRESENTATION OF THE SUBTYPES OF GASTRIC CANCER?

Polypoid

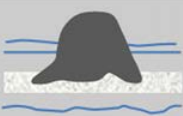


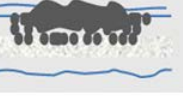
Fungating

Ulcerating

Infiltrating

- Linitis plastica

Table 2
The Borrmann classification of advanced gastric cancer

Type I		Polypoid tumors
Type II		Fungating carcinomas
Type III		Ulcerated carcinomas
Type IV		Infiltrating carcinomas

BIOPSYING GASTRIC CANCER

Multiple biopsies necessary for diagnosis and IHC

- Eight biopsies minimum to get $> 90\%$ probability of enough tissue for HER-2 testing

Biopsying on the edge of an ulcer

- Scirrhus cancers might have marked fibrosis
- Need to follow gastric ulcer to resolution

EUS assisted biopsies

WHO CLASSIFICATION

More related to microscopic morphology

- Tubular
- Papillary
 - >50% of the involved area contains papillary structures
 - Higher lymphovascular invasion
- Mucinous
- Signet ring cell

Loose association with the Lauren classification

JAPANESE CLASSIFICATION

Classification into differentiated and undifferentiated

Differentiated

- Well or moderately differentiated
- Tubular or papillary subtype

Undifferentiated

- Poorly or signet ring differentiation
- Mucinous adenocarcinoma

JAPANESE CLASSIFICATION

Mixed type

- Refers to mixed differentiation
- Differentiated mixed with undifferentiated component
 - Behaves like differentiated
- Undifferentiated type predominant
 - Behaves like undifferentiated
- Is associated with higher LNM or LVI than pure type gastric cancer

INVESTIGATION OF SYMPTOMS VS SCREENING

Symptoms that warrant investigation

- New onset dyspepsia
- Anemia
- Weight loss

Screening

- Not approved but done for a variety of reasons
 - Family history of gastric cancer
 - Patient from high prevalence area
 - Chronic dyspepsia

EXPANDED SCREENING

BSG gastric cancer guidelines 2019

Intent to screen and survey high risk patients

- Family history
- Known intestinal metaplasia proximal to antrum
- Prior history of gastric dysplasia
- Known atrophic gastritis/pernicious anemia

Might increase the chances of picking up early gastric cancer

GASTRIC POLYPS

Usually found incidentally on upper endoscopy

Rarely symptomatic

Seen in about 6% of upper endoscopic procedures

Classification and management depends on cellular type



GASTRIC POLYPS

Fundic gland polyps

Hyperplastic polyps

Gastric adenomas

Gastric neuroendocrine tumors (carcinoids)

Inflammatory fibroid polyps

FUNDIC GLAND POLYPS

Very common finding in the West

- Most FGP are sporadic
- Associated with PPI usage
- *H. pylori* rarely seen in association with FGP
- Almost all asymptomatic and range from 1-8mm in size

PPI induced FGP will regress with discontinuation of PPI



SYNDROMIC FUNDIC GLAND POLYPS

Familial Adenomatous Polyposis

- 20 – 100% will have FGP
- 30-50% will show dysplasia typically low grade and rarely progress to gastric cancer
 - Carpeting FGP
 - Polyps > 10mm to rule out malignancy
 - Ulcerated FGP

Bianchi LK, et al. Clin Gastroenterol Hepatol 2008;6(2):180
Mankaney G, et al. Fam Cancer 2017 16(3):371-376

HYPERPLASTIC POLYPS

Hyper-regenerative epithelium in response to chronic inflammatory stimulus

- Atrophic gastritis
- H. pylori
- Sites adjacent to gastroenterostomy
- Adjacent to chronic ulcer/erosion

Most are asymptomatic

- Some cause bleeding
- Intermittent pyloric obstruction
- Typically small 5 – 15mm in the antrum



MALIGNANT POTENTIAL OF HYPERPLASTIC POLYPS

Follows hyperplasia-dysplasia-carcinoma sequence

Transformation to dysplasia 2-19%

Higher risk

- Pedunculated lesions
- Size >10mm

Biopsies should be taken around the polyp to look for dysplasia in adjacent mucosa

Han AR, et al. Gut Liver 2009;3(4):271-5
Terada T. Med Oncol 2011;28(4):941-4.

GASTRIC ADENOMA

Seen in both chronic inflammatory states and familial clustering

Can occur anywhere in the stomach

Risk of malignant transformation increases

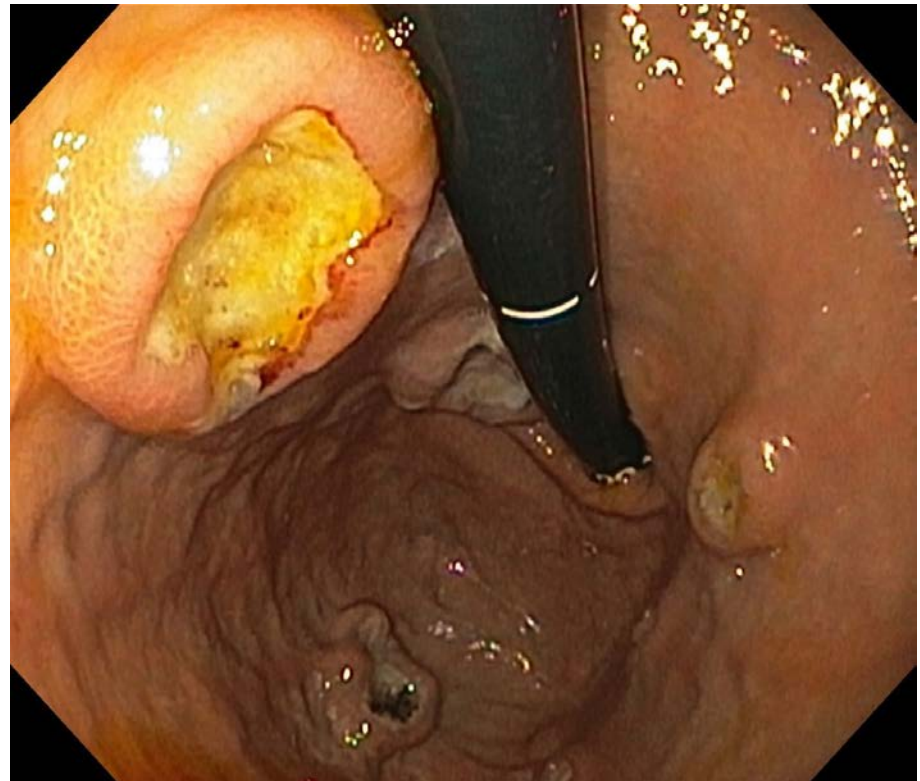
- With increased size of lesion $> 2\text{cm}$
- Presence of severe dysplasia
- Annual incidence 0.6% for mild/moderate dysplasia to 6% for severe dysplasia

Best removed by ESD for lesions $> 10\text{mm}$

ADDITIONAL MALIGNANT HISTOLOGIES

Metastatic disease

- Breast adenocarcinoma
- Melanoma



WHAT GOES IN A GOOD ENDOSCOPY REPORT

Concise, accurate and descriptive

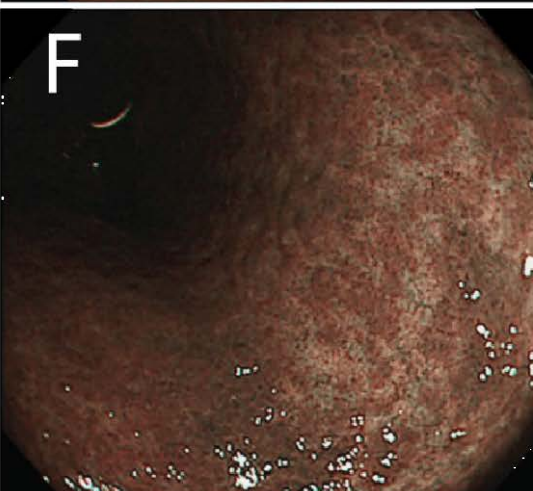
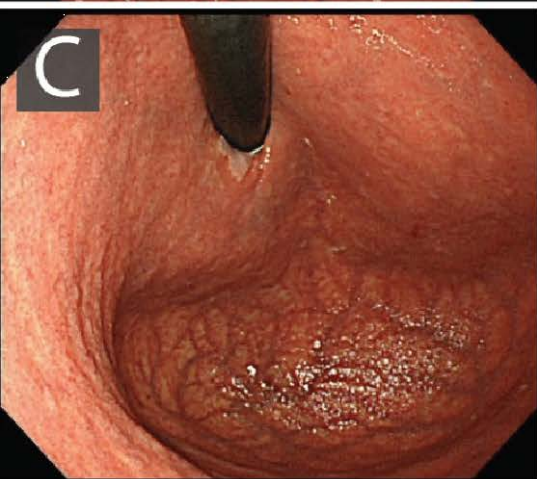
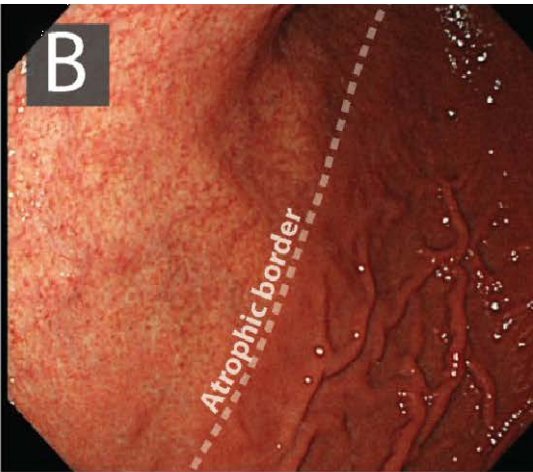
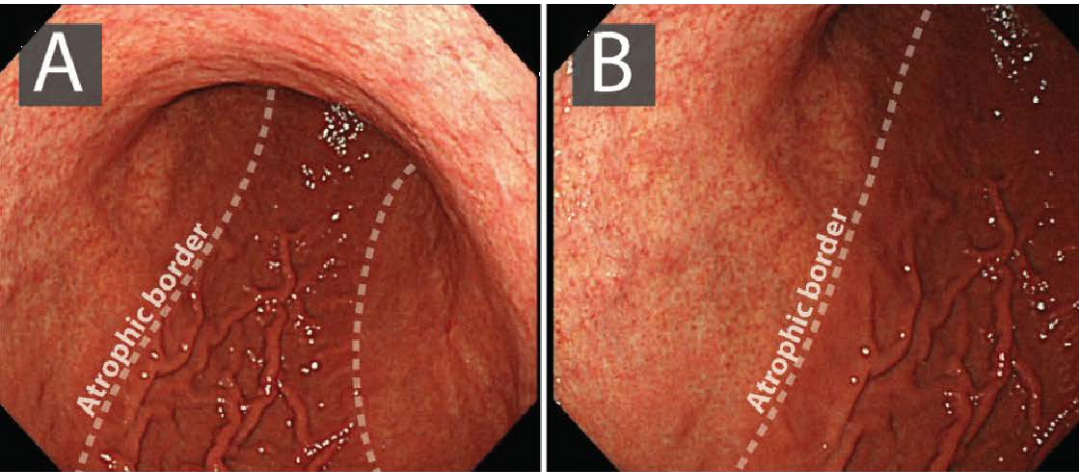
More description better for all physicians involved with patient care

- Endoscopic pictures extremely valuable
- Video recordings even better

Conditions that aid in situations where procedures need to be repeated

Documentation of complications and adverse events

Plan of action



Chronic Atrophic Gastritis

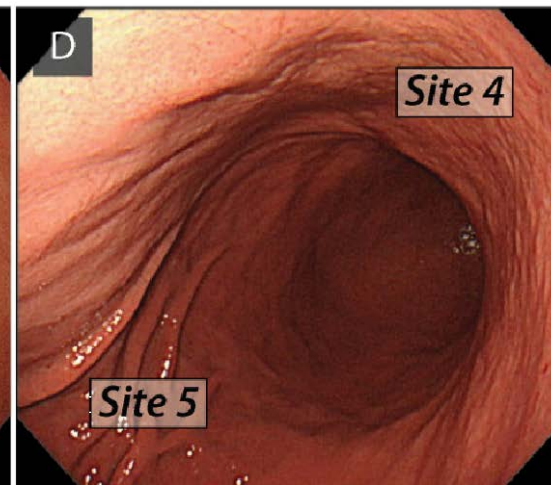
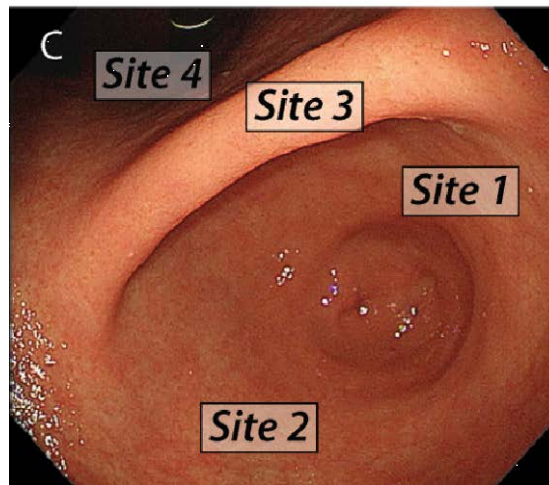
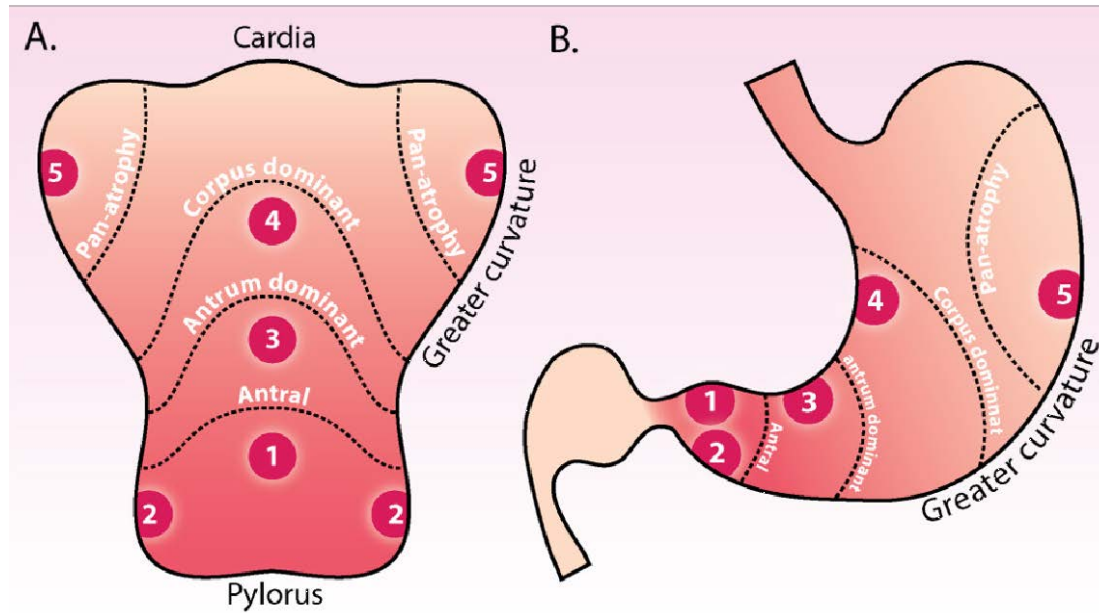
- A. Palor
- B. Loss of gastric folds
- C. Prominence of the vessels
- D. Atrophic border

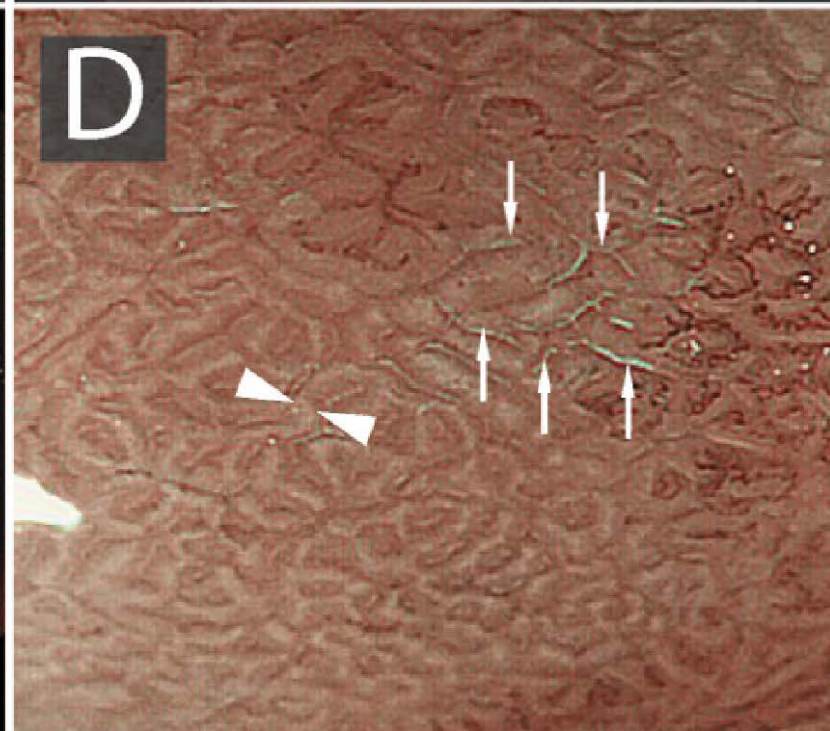
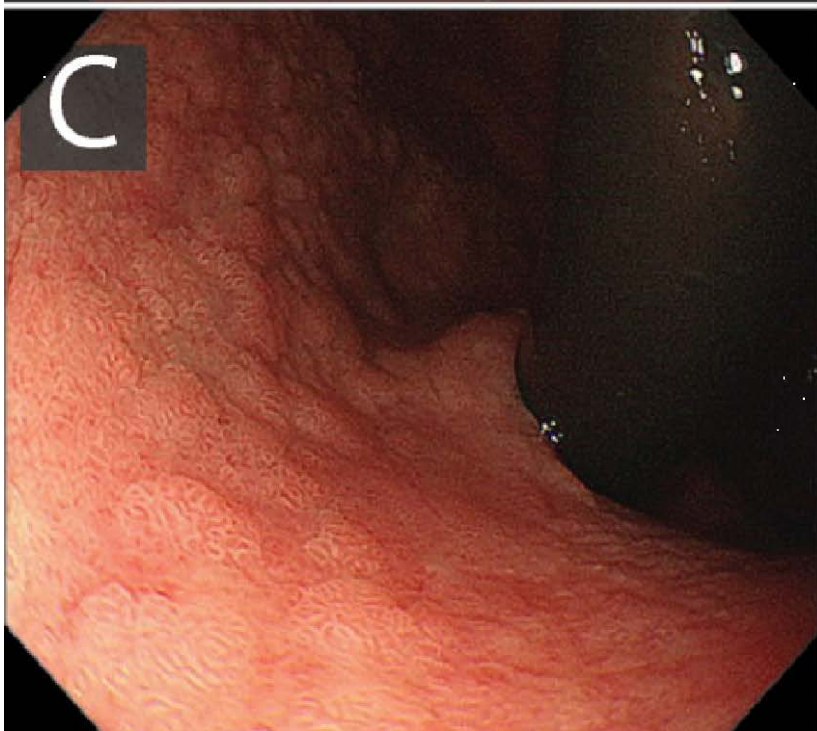
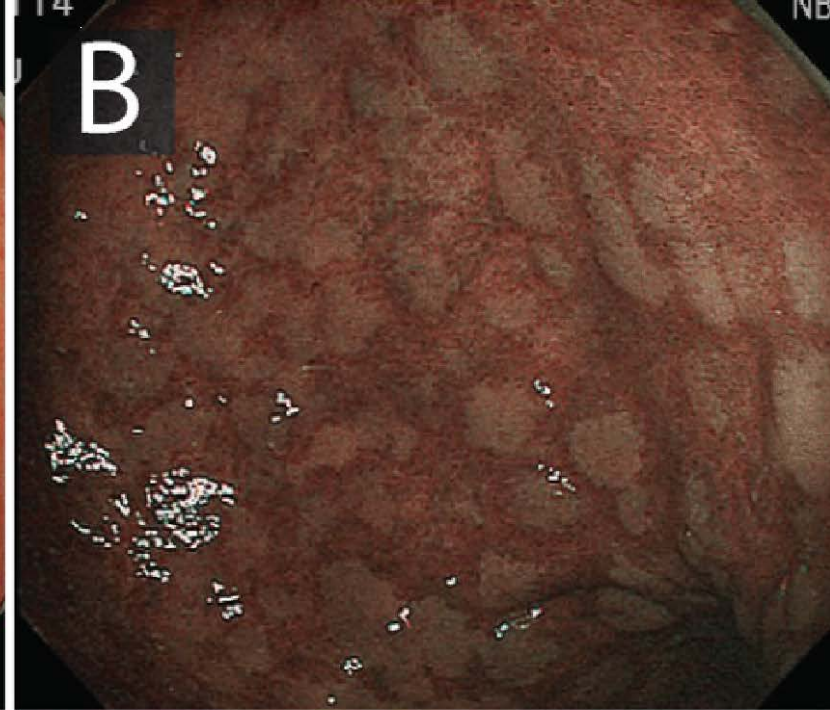
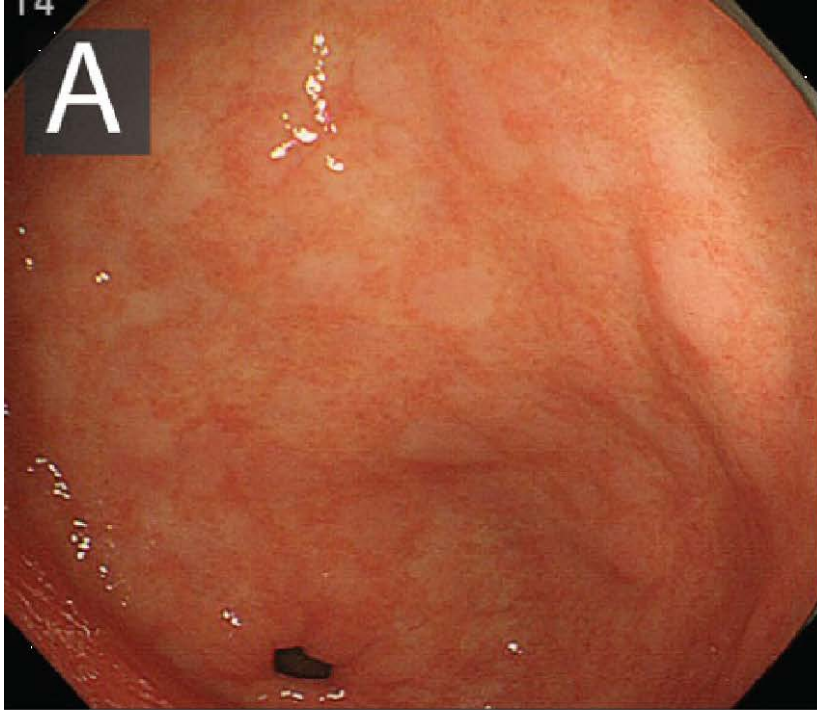
BIOPSY PROTOCOL IN SUSPECTED INTESTINAL METAPLASIA

Extent of intestinal metaplasia confers risk of intestinal type of adenocarcinoma

Although IM can be detected endoscopically, more difficult with non magnifying scopes

SYDNEY PROTOCOL





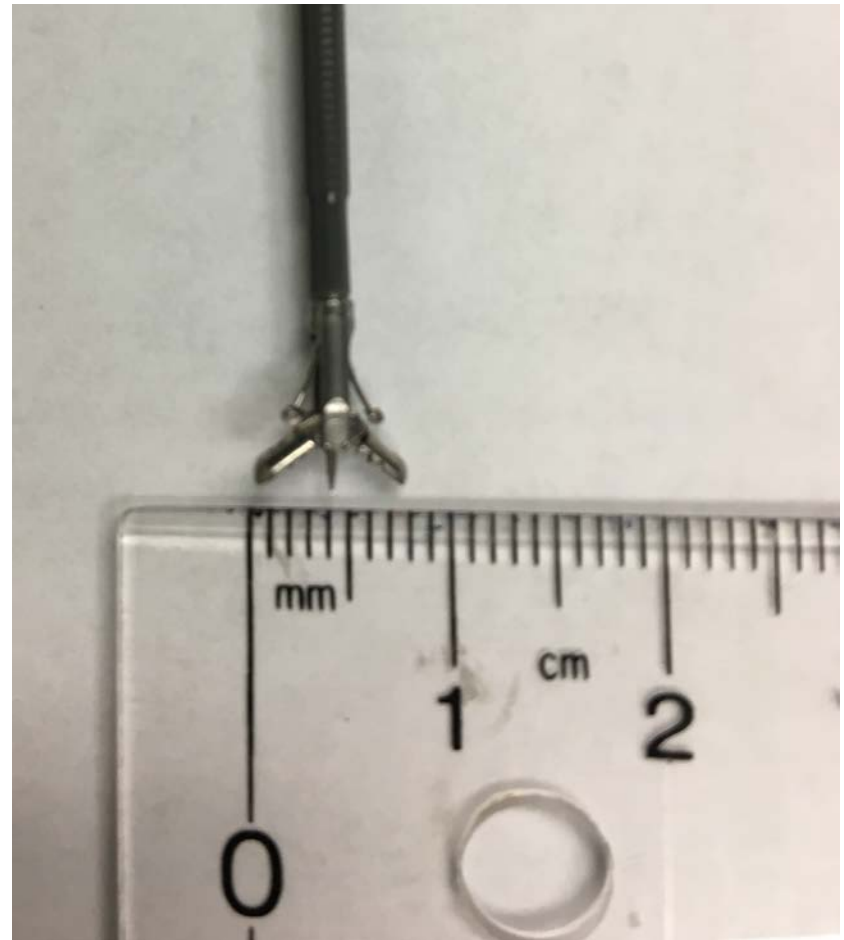
DESCRIPTION OF THE LESION

Location

- Distance from GE junction to the proximal extent
- Anatomical location of the lesion in the stomach
- Which wall of the stomach

Size of the lesion

- Open forceps 8mm
- Estimation of lesion relative to the circumference of the stomach



DESCRIPTION

Relevant common anatomical variations

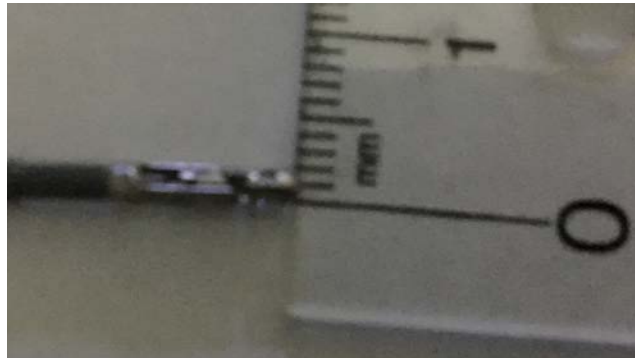
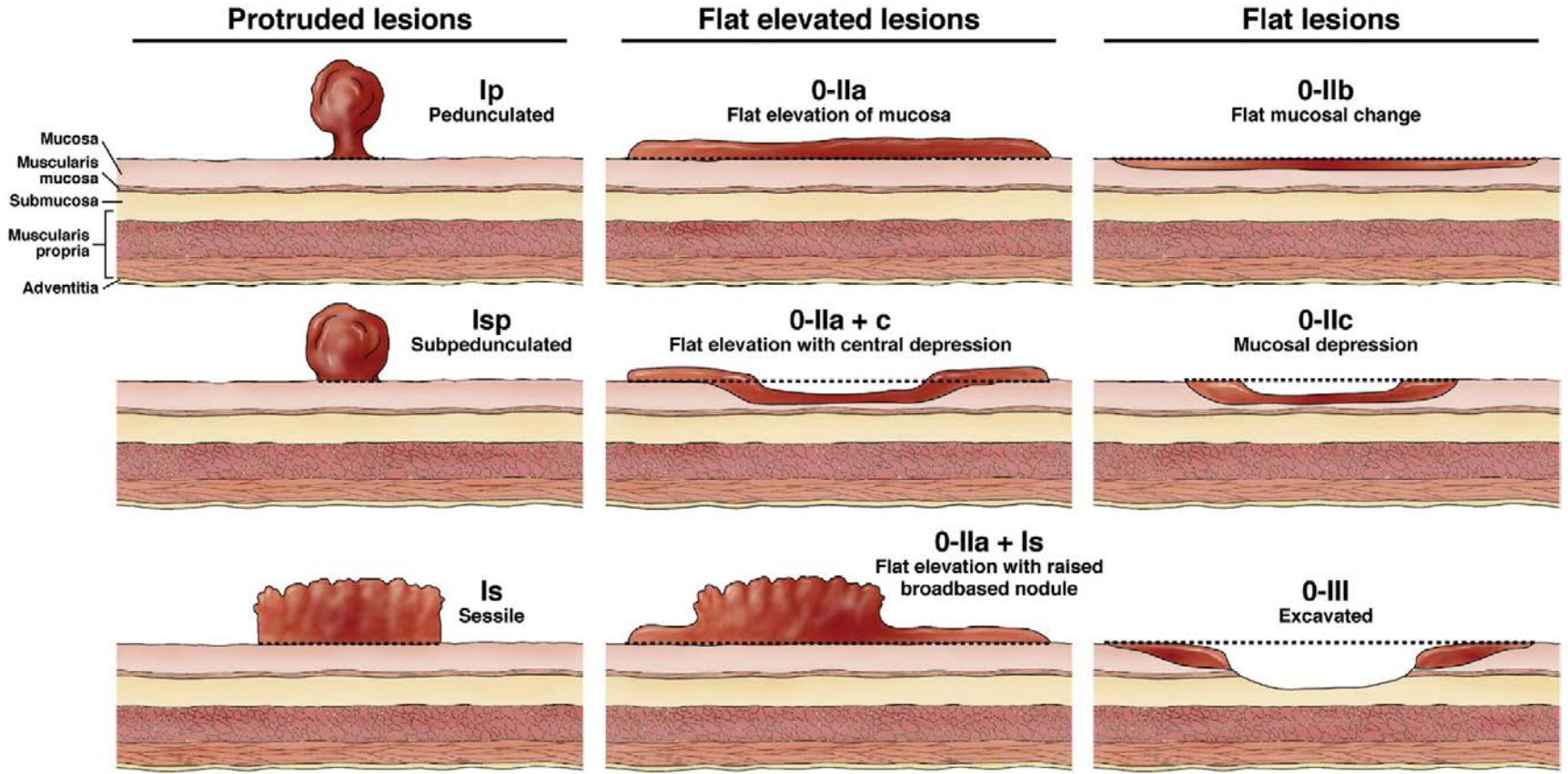
- Presence of hiatus hernia/Schatzki ring
- Presence/type of previous surgery

DESCRIPTION: MORPHOLOGY AND THE PARIS CLASSIFICATION

Paris classification helps to describe the endoscopic morphology of the lesion

Used for all lesions in the GI tract

Can confer a degree of lesion severity

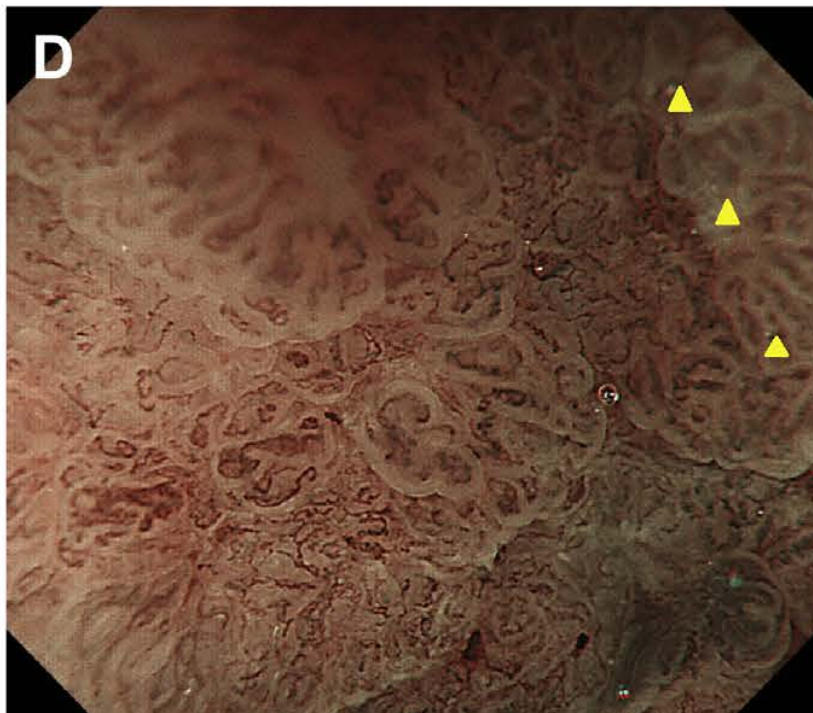
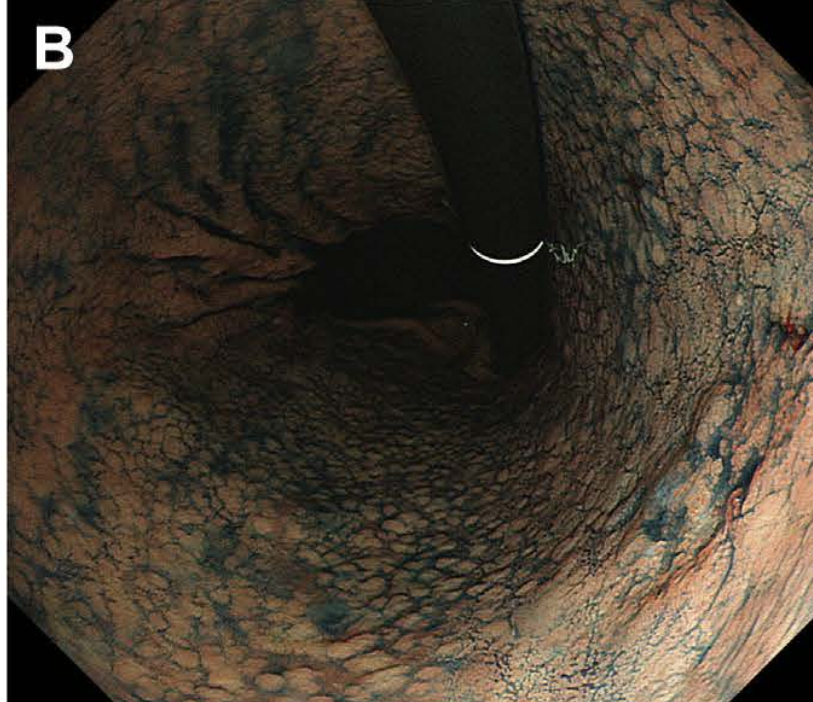
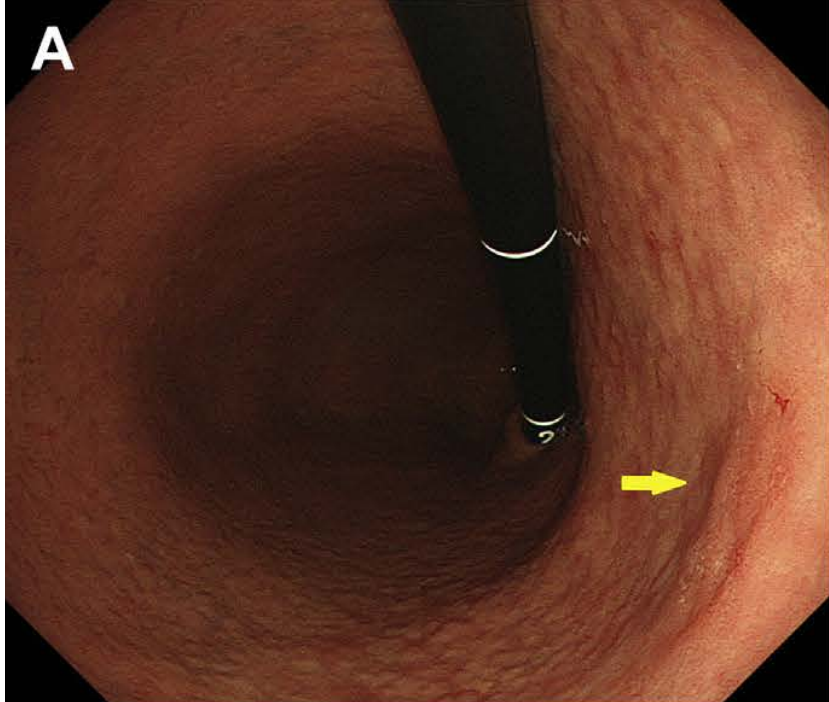


JAPANESE ENDOSCOPIC CRITERIA FOR EARLY GASTRIC CANCER

Dependent on

- Size of lesion
- Presence of demarcation line
- Presence of microvascular distortion or microsurface distortion

Difficult to determine without magnifying endoscopy



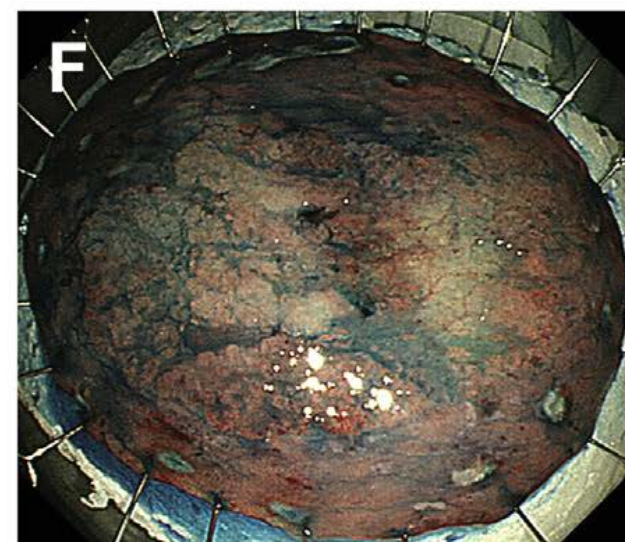
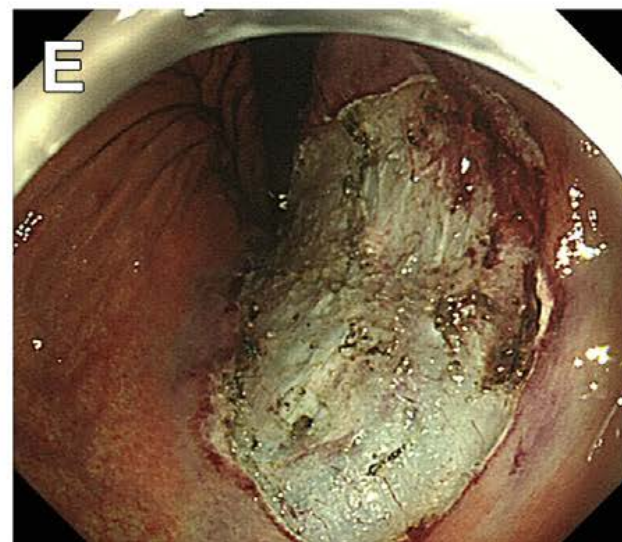
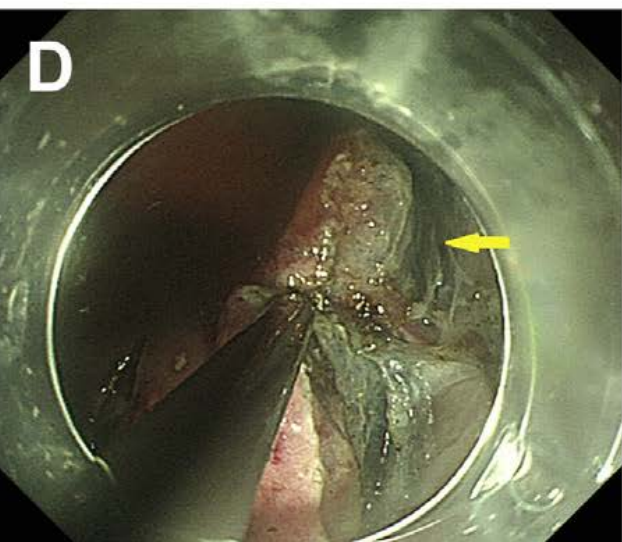
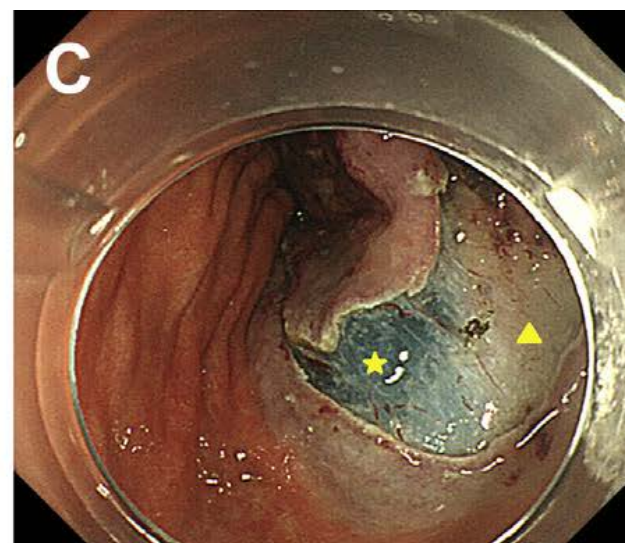
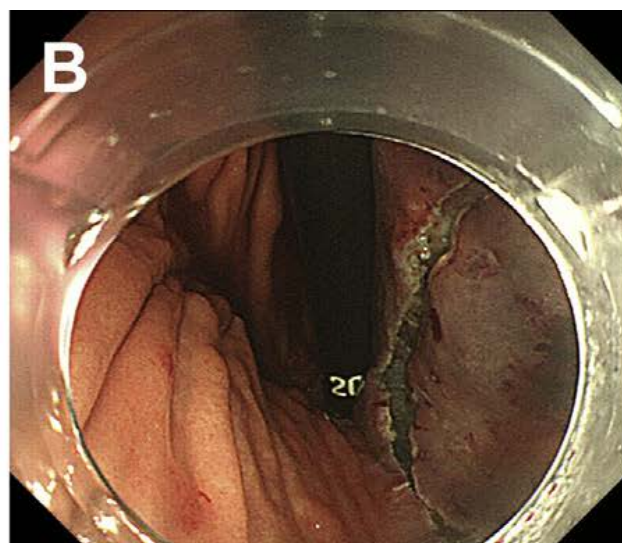
ENDOSCOPIC SUBMUCOSAL DISSECTION

En bloc removal of gastric lesions >10mm

Beneficial for those lesions with superficial dysplasia

Dissection is down to muscle layer

- Can assess submucosal invasion



JAPANESE EXTENDED CRITERIA FOR ESD

Table 1
Indication of endoscopic submucosal dissection for early gastric cancer

Abnormality	Mucosal			
	Ulcer (–)		Ulcer (+)	
	≤2 cm	>2 cm	≤3 cm	>3 cm
Differentiated type ^a	A	E	E	X
Undifferentiated type ^b	E	X	X	X

A – absolute indication for ESD

E – extended criteria of ESD

X – ESD not recommended

WHAT TO DO TO DETECT PREMALIGNANT LESIONS

Use Paris classification

Accurately report size and location

High index of suspicion for small lesions in the setting of

- Chronic gastritis
- Atrophic gastritis
- Intestinal metaplasia

Biopsy any suspicious areas

CONCLUSION

Gastric cancer classification remains incomplete general categories well established

Precursor lesions can be identified as potential risks for development of adenocarcinoma

A standardized report with photos/videos is essential for subsequent management