Gastric Intestinal Metaplasia

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Importance

- Gastric cancer
  - 3rd leading cause of cancer mortality globally
  - Leading cause of infection associated cancers
- GIM
  - An intermediate precancerous gastric lesion in the gastric cancer cascade
- Increased risk of gastric cancer in GIM
  - Specific subsets at higher risk of progression

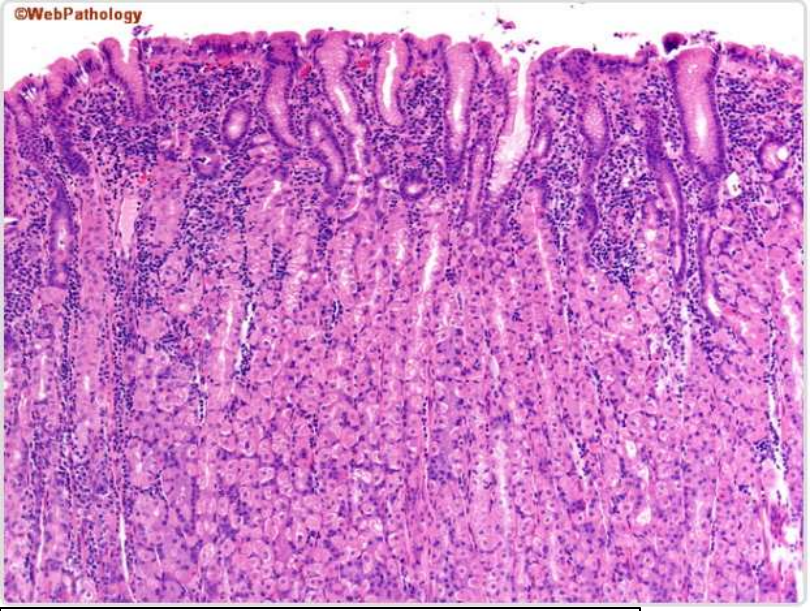
Gastric Intestinal Metaplasia

- An intermediate precancerous lesion in the gastric cancer cascade
  - Chronic gastritis, atrophic gastritis, intestinal metaplasia (IM), dysplasia, and adenocarcinoma

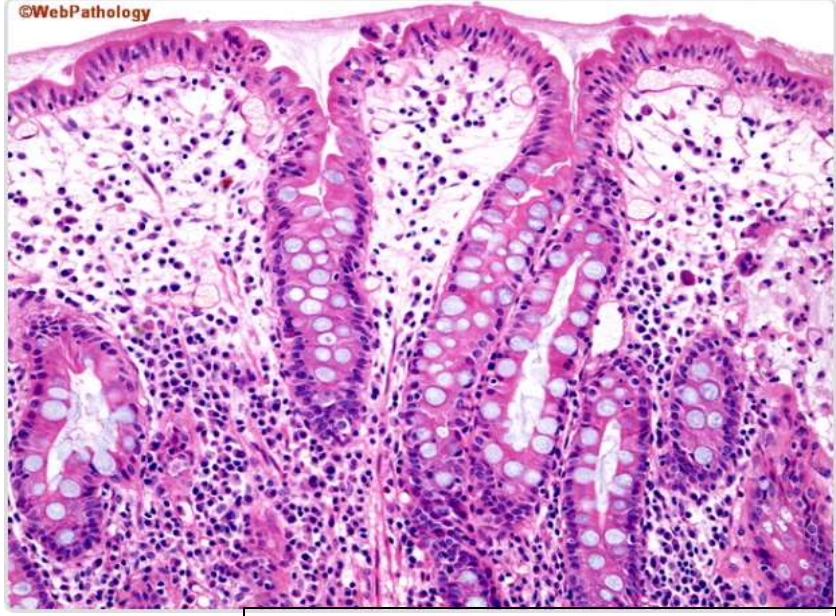
- Definition:
  - Replacement of the surface, foveolar, and glandular epithelium in the oxyntic or antral mucosa by intestinal epithelium

GIM: Classification

- Topographic Extent
  - Extensive
    - Corpus & antrum/± incisura
  - Limited
    - Antrum or incisura
- Combined PAS staining
- Updated Sydney System
  - OLGA and OLGIM
- Histology
  - Based on H&E staining
    - Complete
      - Small intestinal-type mucosa
    - Incomplete
      - Colonic-type mucosa
  - Mucin Expression
    - I: Sialomucins
    - II: Gastric mucins and intestinal sialomucins
    - III: Sulfomucins

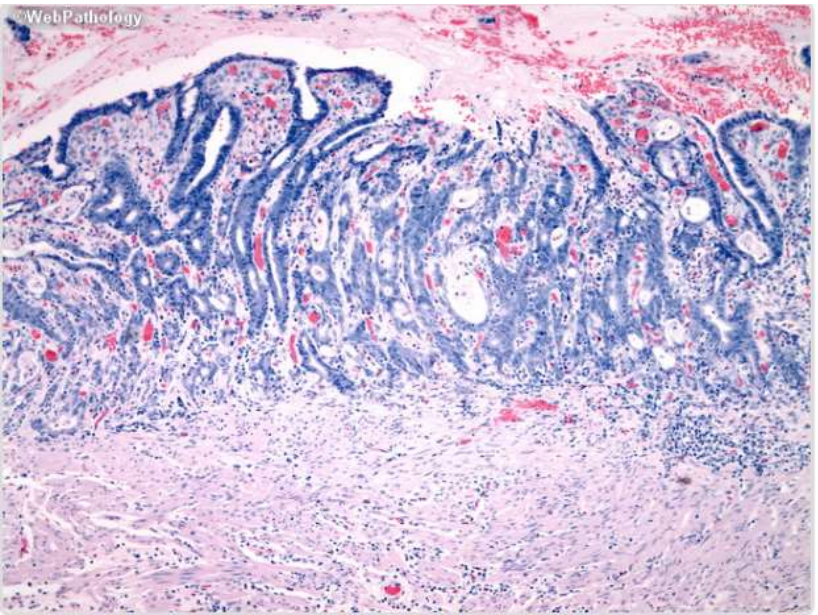


Normal gastric mucosa

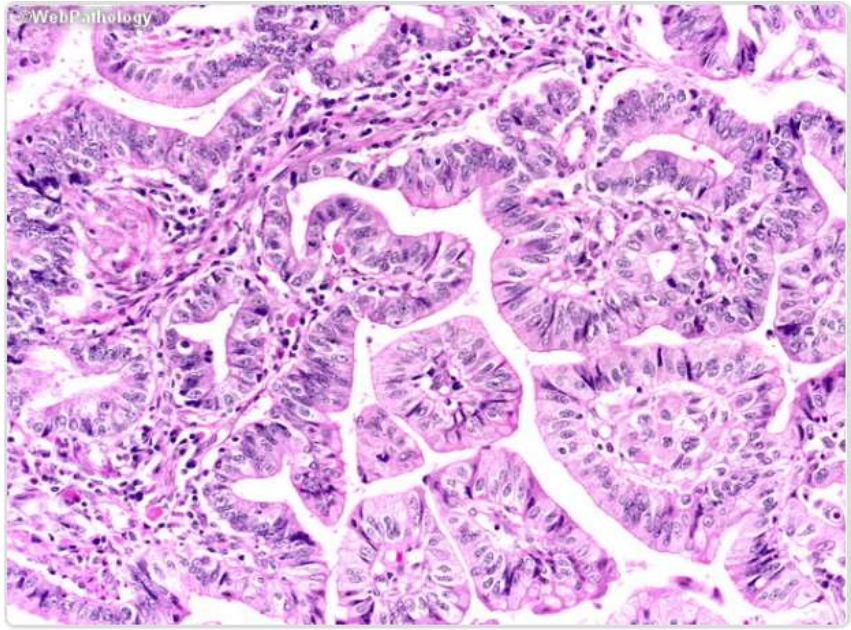


Gastric intestinal metaplasia

Early gastric cancer



Gastric adenocarcinoma – intestinal type



Clinical Scenario

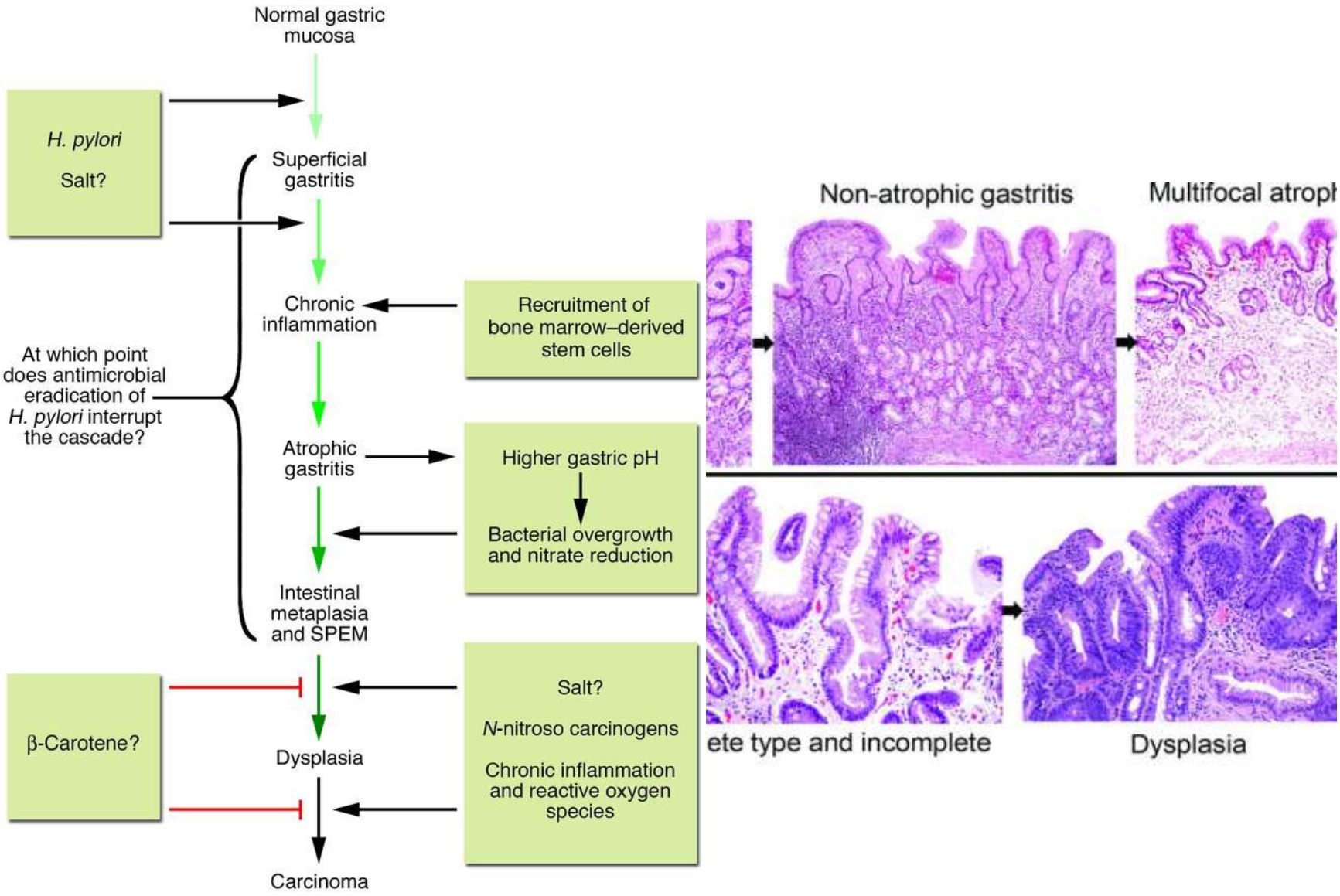
- Prevalence based on gastric cancer incidence
  - 4% (low prevalence) to 20% (high prevalence)
  - Increases with age, smoking, H.pylori infection
- Non specific symptoms
- On endoscopic evaluation for dyspepsia
- Symptoms of gastric hypochlorhydria
- Features of SIBO
  - Bloating, abdominal discomfort, diarrhoea

Correa Cascade

- Gastric cancer multistage model (intestinal subtype)
  - Host/genetic factors
  - H.pylori genomics
  - Dietary/environmental factors

- Stages
  - Pan Gastritis
  - Gastric atrophy
  - Intestinal Metaplasia ➔ Point of no-return
  - Dysplasia
  - Adenocarcinoma

Correa Cascade



Pathogenesis

- Metastatic foci
  - Initially at antrum-corpus junction then involving incisura angularis
  - Later foci enlarge and coalesce
  - Extending to antrum and corpus
- Original glands
  - Replaced by atrophic glands
- Decrease in the normal gastric secretions

Finally leading to

- Hypochlorhydria
- Low pepsin
- High gastrin

Cancer Risk

- Rates of gastric cancer in Europe, Asia and US
  - Vary between 1.1 and 2.0 per 1000 person-years
  - Up to 3 per 1000 person-years (high-grade dysplasia)

- Risk higher with
  - Incomplete vs complete type
  - Extensive vs limited type
  - Family h/o gastric cancer in a first degree relative
  - Immigrant population from a high risk to low risk zone

Diagnosis

- UGIE biopsy
- Gastric topographic biopsy mapping
- Magnification chromoendoscopy
- Confocal endomicroscopy
- Biomarkers

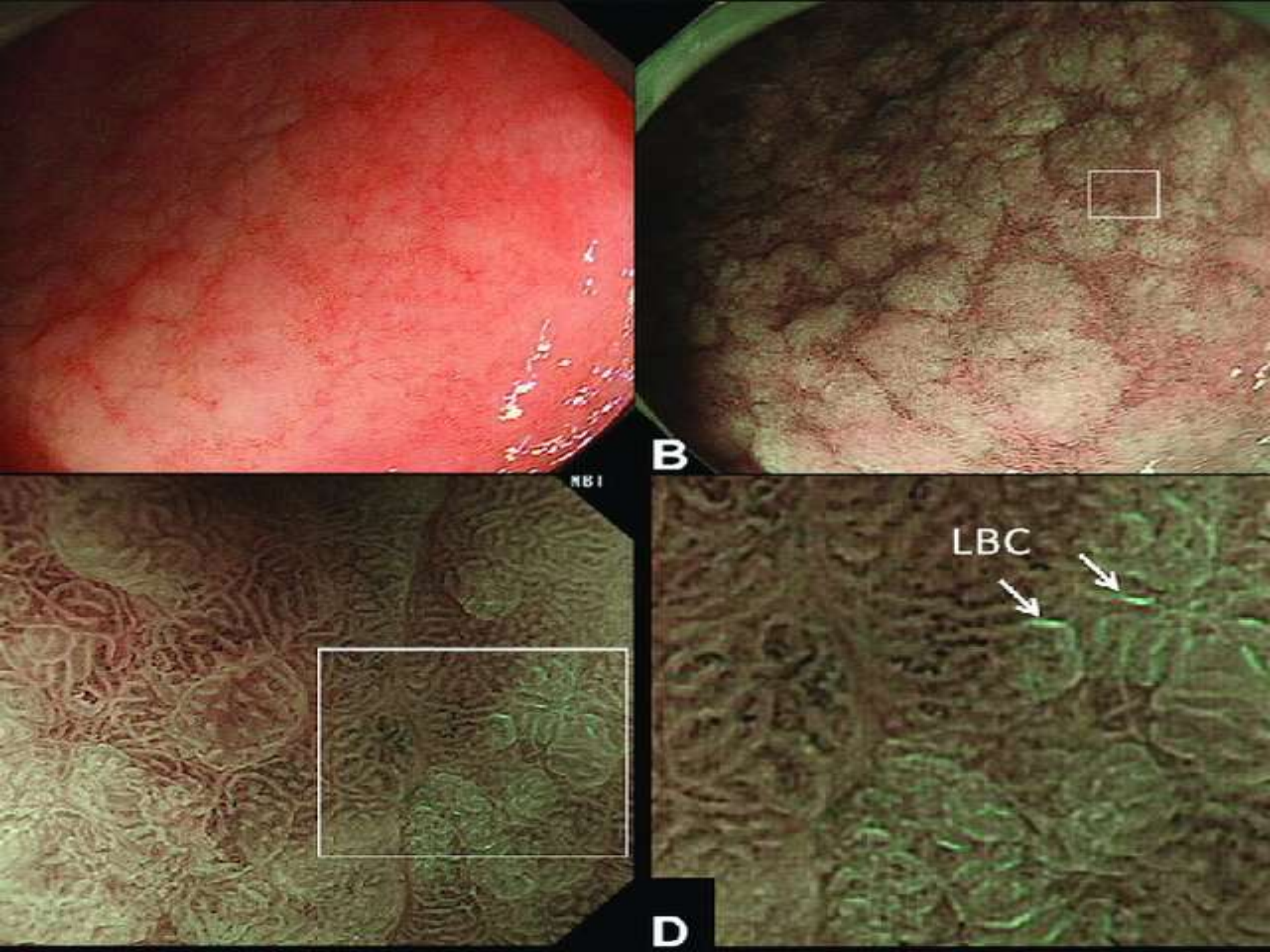
Endoscopic Evaluation

- Appearance
  - Small grey-white slightly elevated plaques
    - Surrounded by mixed patchy pink areas of mucosa (irregular, uneven surface)
  - Mottled patchy erythema

- Protocol
  - Adequate examination time (7minutes I to E)
  - Mucosal cleaning
  - Air insufflation for better mucosal visualisation

- White-light endoscopy – low sensitivity for GIM

- NBI with Magnification endoscopy
  - 89% sensitivity, 93% specificity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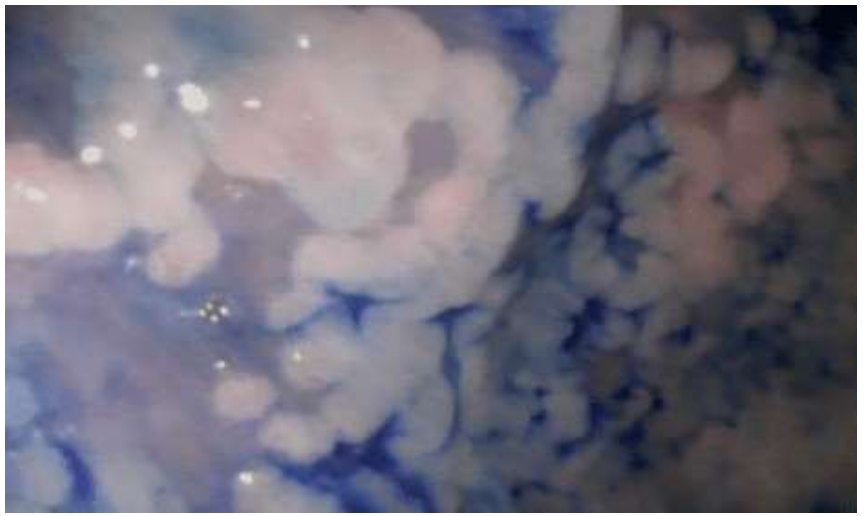
Gastric Topographic Biopsy Mapping

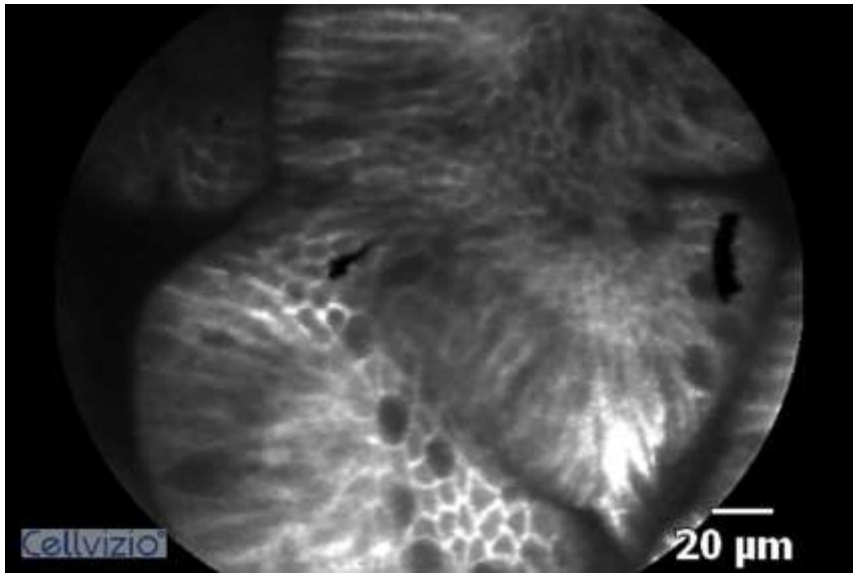
- Diagnostic findings
  - Replacement of the surface, foveolar, and glandular epithelium in the oxyntic and/or antral mucosa by metaplastic epithelium
- Non-targeted biopsy sites (at least 5)
  - Lesser and greater curvatures of both the antrum and corpus and incisura angularis
- Targeted biopsies
  - From irregular areas of mucosa to rule out dysplasia

Other Endoscopic Modalities

- Magnification chromoendoscopy
  - Involves topical application of stains/pigments to improve tissue localisation
  - Indigo carmine (methylene blue, acetic acid)



- Confocal endomicroscopy
  - Illuminating a tissue with a low-power laser
  - Then detecting fluorescent light reflected from the tissue



Bio-Markers

- Serum pepsinogen I and pepsinogen I/II ratio
- H.pylori serology
- Gastrin 17 Assay

Post-Diagnostic Evaluation

- High risk of gastric cancer
  - Family history of gastric cancer in a first-degree relative
  - Incomplete GIM, Extensive or corpus GIM
  - Racial/ethnic minorities and/or immigrants from high-incidence areas

- Hereditary gastric cancer syndrome suspected in
  - Gastric cancer in one family member before age 40
  - Gastric cancer in two $1^{st}/2^{nd}$ degree relatives before age 50
  - Gastric cancer in three $1^{st}/2^{nd}$ degree relatives independent of age

- Screening for H.pylori infection

Management

- General measures
  - Smoking cessation
  - Moderation of alcohol intake
  - Eradication of *H. pylori*

- Endoscopic surveillance
  - Family h/o gastric cancer in a first-degree relative
  - Incomplete GIM
  - Extensive or corpus GIM
  - Racial/ethnic minorities
    - Non-Caucasian race/ethnicity, African Americans, Hispanics, Asians
  - First-generation immigrants from high-incidence areas
    - Eastern Asians, Latin Americans

Conclusions

- GIM
  - Replacement of the surface, foveolar, and glandular epithelium in the oxyntic or antral mucosa by intestinal epithelium
  - An important premalignant stage in the gastric cancer cascade through a series of well-defined and recognizable precursors
- CORREA Cascade-Gastric adenocarcinoma multistage model
  - A combination of host genetic factors and responses, H.pylori genomics, with modulation by dietary & environmental factors
  - Predisposing to early pan-gastric mucosal inflammation, resulting in gastric atrophy, IM, dysplasia, and adenocarcinoma

Conclusions

- Increased risk for gastric cancer
  - In areas of low gastric cancer incidence (2.5/1000 person-yrs)
  - In individuals with extensive and incomplete IM
  - Family history of gastric cancer in a first-degree relative
  - Racial/ethnic minorities
  - First-generation immigrants from high-incidence areas

- Clinical scenario
  - Non-specific symptoms
  - Diagnosed incidentally
    - In patients undergoing UGIE for dyspepsia
  - Associated with gastric hypochlorhydria and SIBO

Conclusions

- UGIE in patients with GIM
  - Nonspecific appearance
  - Involved mucosa has a rough or villous appearance
    - May be seen as thin, white mucosal deposits
  - Suspected based on endoscopic findings, but established by histology
    - High-quality endoscopy is needed to improve detection
    - UGIE with narrow band imaging (NBI) and biopsy mapping
- Determining the type and extent of GIM requires gastric topographic mapping
  - Targeted and non-targeted biopsy sites

Conclusions

- General measures to decrease the risk of GIM progression to gastric cancer
  - Smoking cessation
  - Moderation of alcohol intake
  - Eradication of H. pylori

- In individuals with high-risk GIM
  - Surveillance upper endoscopy at three-year interval
    - Detailed visual inspection with high-resolution endoscopes
    - NBI if there is local expertise
    - Gastric biopsy mapping

Thank You!!!