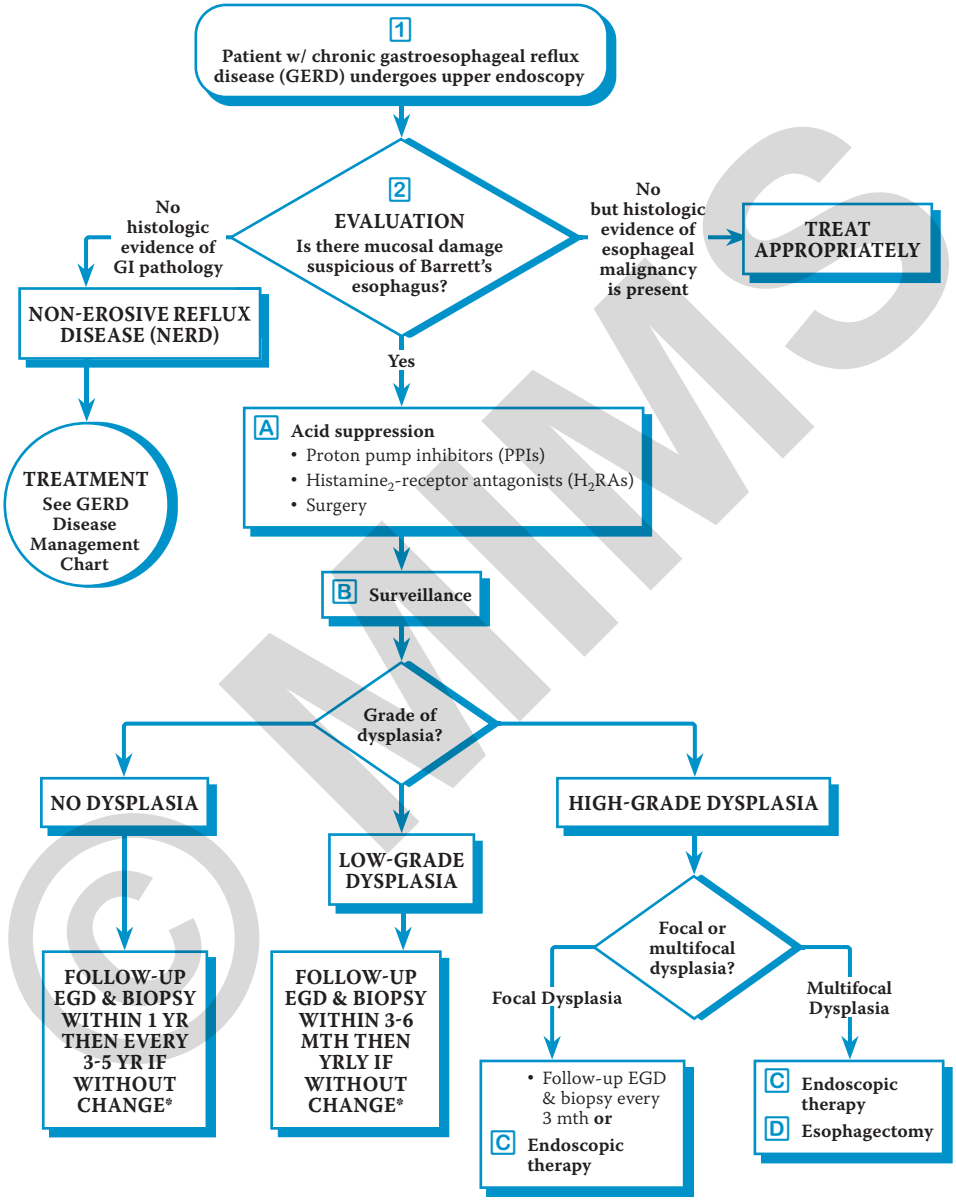
Barrett's Esophagus (1 of 5)



EGD: Esophagogastroduodenoscopy
*If w/ dysplasia, treat appropriately

1 RECOMMENDATIONS REGARDING ENDOSCOPY IN CHRONIC GERD PATIENTS

- The main reason to evaluate patients w/ chronic GERD symptoms is to identify Barrett's esophagus
  - Patients w/ chronic GERD are the most at risk to develop Barrett's esophagus & should undergo upper endoscopy
  - Endoscopy to screen for Barrett's esophagus is recommended in patients w/ >5 years of GERD symptoms
  - Routine screening of GERD patients may not be appropriate in the Asian population because of the low prevalence of Barrett's metaplasia in Asia
- Patients w/ alarm symptoms or high risk should be immediately referred for endoscopy to screen for malignancy or Barrett's esophagus
  - Alarm symptoms: Dysphagia, odynophagia, bleeding, weight loss
- Those who have had GERD symptoms of >3x/week for >20 years have 40-fold increased risk of developing adenocarcinoma
- Many patients who develop Barrett's esophagus are asymptomatic
  - 40% of patients w/ esophageal adenocarcinoma have no history of GERD
- Decision to screen should be individualized

Other Risk Factors Linked to Barrett's Esophagus

- White or Hispanic race
- Male sex
- Advancing age (>50 years, reaching a plateau in the 60's) - reported as a significant risk factor in various Asian studies
- Hiatal hernia
- Smoking
- Central obesity (intra-abdominal body fat distribution)
- Alcohol (as shown in an Asian study)

2 EVALUATION

Barrett's Esophagus

- Defined as the endoscopic finding in the distal esophagus of proximal-appearing columnar-lined esophagus of at least 1-cm length that is confirmed by histology
- Considered a premalignant metaplastic condition that usually involves the distal esophagus
  - It is postulated that exposure of the esophageal epithelium to acid damages the lining resulting in chronic esophagitis & its healing involves metaplastic process
- The incidence of progressing to adenocarcinoma is approximately 0.27-0.59% of Barrett's esophagus patients per year
  - Intestinal metaplasia is not required for diagnosis, though risk of progression to carcinoma is higher in its presence
- Diagnosed by endoscopy & histological examination

Physical Exam

- Clinicians must examine the patient & look for any sign of extraesophageal disease, complications of advanced disease or any underlying disease that may manifest as GERD

Endoscopy

- Each upper endoscopy should record the squamocolumnar junction, the gastroesophageal junction (GEJ), presence of a hiatal hernia & the location of the diaphragmatic hiatus in patients suspected of Barrett's esophagus
  - The Asia-Pacific consensus defines the GEJ as the proximal limits of gastric folds
- Use Prague criteria in documenting extent of suspected Barrett's esophagus on endoscopy
- Consider endoscopic screening in patients w/ or without history of reflux symptoms & w/ a family history of >2 first-degree relatives w/ Barrett's esophagus or esophageal adenocarcinoma
- If initial endoscopy is negative, it is not recommended to repeat it; however, in patients w/ suspected Barrett's esophagus & negative histology, endoscopy may be repeated in 1-2 years

A ACID SUPPRESSION

Therapeutic Principles

- Patients w/ Barrett's esophagus have greater esophageal acid exposure than other GERD patients
- Treatment of Barrett's esophagus aims to diminish the reflux of acid into the esophagus which includes acid suppression to control the signs & symptoms of GERD & maintain a healed mucosa
  - Acid suppression therapy is important for healing & squamous regeneration during & after endoscopic therapy
- Aggressive medical treatment w/ PPIs & H_2RAs to produce near-complete achlorhydria has been recommended
  - However, relief of symptoms does not correlate well w/ complete acid control
- There is no anti-reflux treatment that has been proven to decrease the risk of esophageal adenocarcinoma

A ACID SUPPRESSION (CONT'D)

Proton Pump Inhibitors (PPIs)
- Commonly used as 1st-line therapy especially in severe esophagitis
- Given to patients w/ Barrett's esophagus w/ or without GERD symptoms or signs of reflux esophagitis on endoscopy
- If once-daily dosing of PPIs does not control symptoms, increasing the dose to twice daily is appropriate

Histamine$_2$-Receptor Antagonists (H_2RAs)
- May be sufficient for patients w/ short-segment disease & only mild esophagitis

Surgery
- Appropriate surgical candidates may consider fundoplication to control reflux symptoms
- Surgical intervention to prevent adenocarcinoma remains unproven

B SURVEILLANCE

Principles of Endoscopic Surveillance
- Surveillance aims to detect dysplasia & early cancer
  - Dysplasia is described as cellular & architectural changes & represents the final step of neoplasia
- Endoscopy w/ random sampling for dysplasia remains the clinical standard for managing Barrett's esophagus
  - Perform endoscopy w/ high-definition white light & preferably optical chromoendoscopy & do a 4-quadrant biopsy every 2 cm for surveillance & every 1 cm in patients in whom dysplasia is documented or suspected
  - Visibly raised or depressed lesions should be biopsied & endoscopically resected
- Patients w/ documented Barrett's esophagus should undergo surveillance endoscopy & the interval is determined by the grade of dysplasia
- Dysplasia is considered as the best current indicator of cancer risk
  - A meta-analysis of multiple studies showed a 6-7% risk of progression from high-grade dysplasia to cancer per patient per year
  - Biomarkers, though promising, cannot be used for confirmation of the diagnosis of Barrett's dysplasia or as a way of stratifying risk for progression in patients w/ Barrett's esophagus at the current time
- Endoscopic surveillance should also be continued after a successful endoscopic therapy & complete removal of intestinal metaplasia to detect recurrence
  - Inspect the neosquamous mucosa & the gastric cardia (retroflexed) using high-definition white light & preferably optical chromoendoscopy & do 4-quadrant biopsies

Surveillance Recommendations
- Prior to endoscopy, patients should be treated w/ empiric therapy since it facilitates identification of Barrett's esophagus by reducing any tissue inflammation
- Routine surveillance w/ other advanced imaging methods except for electronic chromoendoscopy is not recommended in patients w/ Barrett's esophagus at the current time

No Dysplasia
- In patients without dysplasia, a follow-up esophagogastroduodenoscopy (EGD) w/ biopsy is performed within 1 year & repeated every 3-5 years if without change
- If w/ findings of dysplasia, follow appropriate treatment protocol

Low-Grade Dysplasia
- A follow-up EGD w/ biopsy is performed within 3-6 months & repeated annually if without change
  - If results are negative for 2 consecutive years, follow surveillance protocol for patients without dysplasia
  - An expert/experienced GI pathologist should confirm the reading
- If w/ findings of dysplasia, follow appropriate treatment protocol
- After complete endoscopic & histologic eradication of intestinal metaplasia w/ endoscopic therapy, perform surveillance endoscopy w/ biopsies at 1 & 3 years

High-Grade Dysplasia
- Finding of high-grade dysplasia requires a repeat thorough biopsy protocol ideally w/ therapeutic endoscopic & large-capacity biopsy forceps
  - An expert/experienced GI pathologist should confirm the reading of high-grade dysplasia
- Focal high-grade dysplasia (<5 crypts) may be followed w/ surveillance endoscopy every 3 months
- After complete endoscopic & histologic eradication of intestinal metaplasia w/ endoscopic therapy, perform surveillance endoscopy w/ biopsies at 3, 6 & 12 months then yearly thereafter
- The routine use of endoscopic ultrasound to differentiate between mucosal & submucosal disease is not recommended in patients w/ high-grade dysplasia or early esophageal adenocarcinoma

B SURVEILLANCE (CONT'D)

Surveillance Recommendations (Cont'd)

Indefinite for Dysplasia

- Biopsy changes that cannot be described as reactive or neoplastic
- Endoscopy is repeated after acid suppressive therapy for 3-6 months
  - If the finding is indefinite for dysplasia, a 12-month interval for surveillance is recommended

C ENDOSCOPIC THERAPY

- Goals of therapy include eradication of dysplasia &/or cancer, prevention of progression to invasive cancer & reduction of mortality from esophageal adenocarcinoma
- Visible lesions are resected then the mucosa is ablated to achieve complete eradication of intestinal metaplasia
  - Eliminates Barrett's epithelium by removing the tissue (eg endoscopic mucosal resection or endoscopic submucosal dissection) &/or ablating the tissue (eg radiofrequency ablation, hybrid argon plasma coagulation or cryotherapy)
  - Mucosal ablation should only be done w/ flat Barrett's esophagus without inflammation & visible abnormalities
- Most common complications include formation of stricture, bleeding & perforation
- Recurrent disease is treated similarly as that of the initial disease
- Counsel patients regarding cancer risk in the absence of or after endoscopic therapy

Low-Grade Dysplasia

- If endoscopy shows a visible focal lesion, complete resection of the lesion should be performed; if focal lesions are absent, may consider radiofrequency ablation
- Patients w/ documented & persistent low-grade dysplasia may be managed w/ both endoscopic therapy & continued surveillance

High-Grade Dysplasia

- Preferred treatment over esophagectomy
- For patients w/ confirmed multifocal high-grade dysplasia, intervention should be considered (eg endoscopic mucosal resection, radiofrequency ablation or ablation using cryotherapy, photodynamic therapy, esophagectomy)
  - Complete endoscopic & histologic eradication of the Barrett's esophagus segment along w/ other dysplastic lesions is the goal of endoscopic treatment in patients w/ Barrett's esophagus-associated neoplasia
  - Any visible raised or suspicious lesions should undergo diagnostic endoscopic resection in patients w/ dysplastic Barrett's esophagus or early esophageal adenocarcinoma
  - Radiofrequency ablation is the preferred endoscopic ablative therapy for patients w/ flat-type dysplastic Barrett's esophagus non-nodular disease; undetected synchronous lesions can be treated & development of metachronous lesions can be prevented
    - Mucosal ablation should be applied circumferentially using focal/targeted therapy to the GEJ/gastric cardia as this is an area that is difficult to treat & a common site for recurrent neoplasia
- As synchronous cancer can occur w/ high-grade dysplasia, intervention (eg endoscopic resection) instead of continued surveillance may be done
  - Endoscopic resection may be performed if the lesion can be localized endoscopically

D ESOPHAGECTOMY

- Some clinicians recommend esophagectomy for healthy patients w/ high-grade dysplasia or patients w/ invasion of the submucosa, lymph node metastasis or failed endoscopic therapy
- The natural history of high-grade dysplasia is variable & therefore, the decision to perform esophagectomy should be carefully considered
- Associated w/ higher morbidity & mortality at low-volume institutions
- Esophagectomy at a high-volume institution may be considered in patients who are fit for surgery w/ recurrent, diffuse, high-grade dysplasia that is confirmed by an expert/experienced GI pathologist

Dosage Guidelines

HISTAMINE$_2$-RECEPTOR ANTAGONISTS (H_2RAs)

Drug	Dosage	Remarks
Cimetidine	200-400 mg PO 6 hrly **or** 800 mg PO 24 hrly **or** 400 mg PO 12 hrly	**Adverse Reactions** • CNS effects (headache, dizziness, somnolence, insomnia, agitation); GI effects (diarrhea, N/V); Other effects (rashes, myalgia, arthralgia) • Altered LFTs, reversible confusion in the elderly & those w/ renal failure have occasionally occurred • Rarely reported effects: Hepatotoxicity, hypersensitivity reactions, CV effects (tachycardia, bradycardia, hypotension), Hematologic effects (leukopenia, thrombocytopenia, agranulocytosis), acute pancreatitis • Cimetidine has weak anti-androgenic effects; impotence & gynecomastia have occurred & are usually reversible **Special Instructions** • Use w/ caution in patients w/ hepatic & renal impairment; dose adjustment recommended • Cimetidine may reduce hepatic metabolism of some drugs through inhibition of cytochrome P450 isoenzymes; closely monitor those on oral anticoagulants, Lidocaine, Phenytoin or Theophylline; dose reduction may be necessary
Famotidine	20-40 mg PO 12 hrly	
Nizatidine	150-300 mg PO 12 hrly	
Ranitidine	150 mg PO 12 hrly **or** 300 mg PO at bedtime	

PROTON PUMP INHIBITORS (PPIs)

Drug	Dosage	Remarks
Dexlansoprazole	30-60 mg PO 24 hrly	**Adverse Reactions** • Generally well tolerated; most commonly reported: Headache, diarrhea, rash • Less common: GI effects (constipation, flatulence, abdominal pain, N/V, dry mouth); Dermatologic effects (pruritus, urticaria); Musculoskeletal effects (arthralgia, myalgia); Hematologic effects (eosinophilia, leukopenia, thrombocytopenia); Other effects (dizziness, fatigue, insomnia, cough, upper resp tract infection) • Hypersensitivity reactions, elevated liver enzymes, & isolated cases of photosensitivity & hepatotoxicity have been reported **Special Instructions** • Use w/ caution in patients w/ hepatic impairment; dose adjustment recommended • Concomitant use w/ Atazanavir or Nelfinavir is not recommended (PPIs reduce exposure to these drugs) • Exclude possibility of gastric malignancy prior to treatment • Bone fracture: Several published observational studies suggest that PPI therapy may be associated w/ an increased risk for osteoporosis-related fractures of the hip, wrist or spine. Patients should use the lowest dose & shortest duration of PPI therapy appropriate to the condition being treated
Esomeprazole	20-40 mg PO 24 hrly	
Lansoprazole	15-30 mg PO 24 hrly	
Omeprazole	10-40 mg PO 24 hrly	
Pantoprazole	20-40 mg PO 24 hrly	
Rabeprazole	10-20 mg PO 24 hrly	

All dosage recommendations are for non-pregnant & non-breastfeeding women, & non-elderly adults w/ normal renal & hepatic function unless otherwise stated.
Not all products are available or approved for above use in all countries.
Products listed above may not be mentioned in the disease management chart but have been placed here based on indications stated in locally approved product monographs.

Specific prescribing information may also be found in the latest copy of MIMS.

Please see the end of this section for the reference list.