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Diagnostic Endoscopy

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1. Introduction

Gastrointestinal (GI) endoscopy is defined as the direct visualization of the digestive tract, with or without therapy. Endoscopic technology has rapidly advanced over the past 40 years and has become an integral part of clinical gastroenterology. The utilization of endoscopy for both diagnostic evaluation and screening has markedly increased over the last two decades. Many innovations have expanded the indications for endoscopy. Successful endoscopy relies upon the ability to recognize abnormalities and diagnose disease. It is imperative for the endoscopist to detect GI lesions in its early stage to ensure that the patient can receive less invasive treatment and have better prognosis. To make a correct diagnosis of early neoplasm in the GI tract, we first need to detect any lesions with subtle morphologic change.

In this chapter we describe various GI conditions and the role of various endoscopic methods in their diagnosis.

2. Esophagogastroduodenoscopy (EGD)

EGD is performed by passing a flexible scope through mouth to the esophagus, stomach and duodenum. This procedure is the best method to examine upper gastrointestinal mucosa can be performed under conscious sedation in most patients.

The indications for EGD are persistent upper abdominal symptoms despite trial of therapy, upper abdominal symptoms with suspected organic disease (anorexia, weight loss etc.), dysphagia, odynophagia, recurrent or persistent gastroesophageal reflux disease (GERD), persistent vomiting, familial adenomatous polyposis (FAP), GI bleeding, portal hypertension to treat and document esophageal varices, management of achalasia/ esophageal strictures/

stenotic lesions, removal of foreign bodies, placement of feeding tubes, palliative stenting, surveillance of malignancy in Barrett's esophagus, and banding of esophageal varices [1].

Contraindications of EGD are medical instability, patient incooperation and suspected perforation.

Complications of diagnostic EGD are cardiopulmonary events, perforation (0.03%), and bleeding (<0.1%)[2].

2.1. Esophagus

2.1.1. Eosinophilic esophagitis

Eosinophilic esophagitis is a chronic inflammatory disease of the esophagus, usually associated with allergic syndromes. It is increasingly diagnosed in patients presenting with episodic dysphagia and occurs predominantly in males. Endoscopically it is characterized by longitudinal furrows (linear furrowing), widespread white spots, diffuse mucosal nodularity, and multiple rings which fail to disappear with insufflation with air (feline esophagus). Mucosal fragility is frequent. Esophageal mucosa may bleed or become fissured with the scope passage, particularly in the case of a small-caliber or feline esophagus[3,4].

Figure 1. Eosinophilic esophagitis with linear furrowing and rings (pointed by arrows)

2.1.2. Pill-induced esophagitis

Prolonged contact with certain medications can irritate the esophageal mucosa causing esophageal ulcer and esophagitis. Medication-induced esophagitis presents with sudden onset of odynophagia and retrosternal pain. A clinical diagnosis may be made by history without the requirement for confirmatory endoscopy [5](19). The common culprit medications are non-steroidal anti-inflammatory drugs (NSAIDs), tetracyclines, bisphosphonates, potas-

sium chloride, and iron supplements. Endoscopy allows diagnostic confirmation and is a more sensitive procedure than barium swallow [5,6].

Endoscopically, pill-induced esophageal injury presents as a discrete ulcer with relatively normal surrounding mucosa. Exudative inflammation with esophageal thickening and stricture formation are also seen.

The most common sites of injury are the proximal esophagus near the compression from the aortic arch and the distal esophagus in patients with left atrial enlargement. It can also occur in motility disorders which allow prolonged contact of medications with the esophageal wall [5].

2.1.3. Reflux esophagitis and Gastroesophageal reflux disease (GERD)

GERD is defined as the backward passage of stomach contents through the lower esophageal sphincter. The symptoms of GERD include heartburn, chest pain, water brash and odynophagia.

Endoscopy at initial presentation should be considered in patients who have alarm symptoms suggestive of complicated disease or those at risk for Barrett's esophagus. These alarm symptoms are failure to respond to appropriate antisecretory medical therapy, dysphagia, upper GI bleeding, anemia, odynophagia, and weight loss [7].

The severity of esophageal erosions is predictive of a patient's response to therapy and of the likelihood of relapse after therapy. Therefore it is important to grade the severity of erosive reflux esophagitis. Two grading systems which are commonly used are Savary-Miller endoscopic classification and Los-Angeles grading [7].

The Savary-Miller endoscopic classification system is used widely but usage and interpretation are very variable. The "MUSE" (Metaplasia, Ulceration, Stricturing, and Erosions) classification provides clear definitions of the relevant endoscopic features, and it is based on a standardized report form, which allows the endoscopist to make a clear record of esophagitis severity.

Grade I: One or more supravestibular, non-confluent reddish spots, with or without exudates

Grade II: Erosive and exudative lesions in distal esophagus that may be confluent, but not circumferential

Grade III: Circumferential erosions in the distal esophagus, covered by hemorrhagic and pseudomembranous exudates

Grade IV: Chronic complications such as deep ulcers, stenosis, or scarring with Barrett's metaplasia

The "L.A." (Los Angeles) classification describes four grades of esophagitis severity (A to D), based on the extent of esophageal lesions known as "mucosal breaks," but it does not record the presence or severity of other GERD lesions.

Grade A: One or more mucosal breaks each ≤ 5 mm in length

Grade B: At least one mucosal break > 5 mm long, but not continuous between the tops of adjacent mucosal folds.

Grade C: At least one mucosal break that is continuous between the tops of adjacent mucosal folds, but which is not circumferential

Grade D: Mucosal break that involves at least three-fourths of the luminal circumference.

Figure 2. LA grade D esophagitis

Chronic GERD can cause esophageal stricture and Barrett's esophagus (which are described in later sections)

2.1.4. Barrett's Esophagus

Barrett's esophagus is a condition in which metaplastic columnar epithelium that predisposes to cancer development replaces the stratified squamous epithelium that normally lines the distal esophagus. Barrett's esophagus is well recognized as a complication of GERD. Patients with GERD who develop Barrett esophagus tend to have a combination of clinical features, including hiatal hernia, reduced lower esophageal sphincter (LES) pressures or delayed esophageal acid clearance time. The annual incidence of esophageal cancer in a population of patients with Barrett's esophagus is approximately 0.5% per year.

Endoscopically, the typical appearance of Barrett's esophagus is a salmon pink mucosa which extends down and joins the gastric mucosa.

The American Gastroenterologic Association (AGA) suggests endoscopic screening for Barrett's esophagus in patients with multiple risk factors associated with esophageal adenocarcinoma "age 50 years or older, male sex, white race, chronic GERD, hiatal hernia, elevated body mass index, and intra-abdominal distribution of body fat". Once identified, patients with Barrett esophagus should undergo periodic surveillance endoscopy to identify dysplasia. It is recommended that endoscopic evaluation be performed taking 4-quadrant biopsies every 2 cm with biopsy sampling of any mucosal irregularities. Four-quadrant biopsy speci-

biopsies be obtained every 1 cm in patients with known or suspected dysplasia. If there is no dysplasia surveillance endoscopy is recommended every 3-5 years. With low grade dysplasia, 6-12 month surveillance intervals are recommended. High grade dysplasia requires endoscopic biopsy every 3 months if eradication therapy is not performed. The AGA recommends endoscopic eradication therapy with radiofrequency ablation, photodynamic therapy or endoscopic mucosal resection rather than surveillance for treatment of patients with high-grade dysplasia with Barrett's esophagus[8].

Figure 3. Long segment Barrett's esophagus

2.1.5. Esophagitis related to infections

Candida

Candida species colonize in 20 % of healthy adults. The risk factors are AIDS, cancer, antibiotic or steroid therapy. The causative organism is almost always *C. albicans*. *Candida* esophagitis usually presents as odynophagia or dysphagia. The diagnosis is based on the endoscopic picture, microscopic examination and culture of the mucosal brushings, and histological examination of the esophageal mucosa. About two-third of patients have signs of oral thrush (thus its absence does not exclude esophageal involvement). EGD with brushings or biopsy is currently the most sensitive and specific method of diagnosis. Endoscopy demonstrates patchy, whitish plaques covering a friable, erythematous mucosa. When the infection is severe, ulceration may be present as well [9]. Confirmatory biopsy shows the presence of yeasts and pseudohyphae invading mucosal cells, and the culture reveals *Candida*.

Figure 4. Pale plaques with erythematous mucosa – esophageal candidiasis

Herpes simplex virus

HSV-1 infection of the esophagus is usually seen in immunocompromised conditions such as organ or bone marrow transplantation. Less commonly in HIV patients and occasionally immunocompetent patients acquire HSV-1 infection. Endoscopically, there are well circumscribed ulcers with raised margins and a punched out appearance, distinguishing them from the ulcers seen in CMV infection. Exudates, plaques, or diffuse erosive esophagitis and vesicles can also be seen. Biopsies should be taken from the edge or margin of the ulcer where viral cytopathic effects are most likely to be present [10].

Cytomegalovirus

The most common cause of esophagitis in patients with advanced AIDS is *Candida*, whereas the most common viral cause is CMV. CMV esophagitis is seen in post-transplantation, long-term renal dialysis, human immunodeficiency virus (HIV) infection, and AIDS and other debilitating diseases. Endoscopically, extensive ulceration of the esophagus is hallmark of CMV esophagitis. It may present as a solitary ulcer or multiple ulcers. Most ulcers are noted in the distal esophagus [11]. The multiple biopsy specimens should be taken from the base of the ulcer.

2.1.6. *Esophageal diverticulum*

The formation of diverticula occurs due to pulsion from increased intraluminal pressure resulting in pushing of esophageal mucosa and submucosa through the focal weakness of mucosal wall. The risk factors are esophageal dysmotility or stricture which contribute to intraluminal pressure [12]. Esophageal diverticula are rare but can occur in any part of the esophagus. If it occurs in the upper esophagus above the upper esophageal sphincter through a weak spot (Killian's triangle) or above the upper esophageal sphincter in the midline posteriorly at the pharyngo-esophageal junction, it is called Zenker's diverticulum. When it oc-

curs in the distal esophagus just above the lower esophageal sphincter, it is called epiphrenic diverticula. Endoscopically appear round with a wide neck.

Endoscopy does not play important role in the diagnosis but the endoscopist should be aware and cautious about their presence as perforation can occur with endoscopy especially when side viewing scopes are used. Esophageal diverticula are well seen on barium x-ray examination, which is the best modality for diagnosis.

2.1.7. Esophageal rings and webs

Esophageal webs are thin membrane like structure containing mucosa and submucosa which can occur anywhere in the esophagus. The patients are asymptomatic or have only intermittent dysphagia. It is frequently discovered incidentally during radiographic studies for other reasons. However, esophageal webs have been described in Plummer-Vinson syndrome which present as iron deficiency anemia, glossitis and koilonychia. Endoscopically, the webs are seen with difficulty due to proximal location. They are covered with squamous mucosa [13,14].

Esophageal rings are thin, fragile structures that partially or completely obstruct the esophageal lumen. They present with dysphagia if the lumen is <13 mm. They are usually seen in the distal esophagus. If the ring occurs at squamocolumnar junction covered with squamous mucosa above and columnar epithelium below, it is called Schatzki ring or Type B ring. If the ring occurs about 1.5 cm proximal to the squamocolumnar junction, it is called Type A ring. Endoscopy is less sensitive than the barium esophagram in detecting esophageal rings [13,14].

Endoscopically, an esophageal ring appears as a thin membrane with a concentric smooth contour that projects into the lumen.

Figure 4. Schatzki ring

Figure 5. Esophageal web

2.1.8. Stricture

The esophageal stricture is narrowing of esophagus which can be benign or malignant. The symptoms of esophageal stricture are usually insidious but progressive with dysphagia to solids followed by dysphagia to liquids. Dysphagia corresponds to the caliber of the stricture; dysphagia to solids is usually present when the esophageal lumen is narrowed to 13 mm or less. The causes of esophageal stricture formation are GERD, long-term use of a nasogastric (NG) tube, complication of sclerotherapy for varices, infectious esophagitis, post surgical resection for esophageal or laryngeal cancer, caustic ingestion, pill esophagitis, and radiation exposure [15].

Endoscopy is helpful as it allows direct visualization, tissue sampling to rule out malignancy, and dilation of the narrowed part of the esophagus.

Figure 6. Esophageal stricture

2.1.9. Hiatus hernia

Hiatus hernia refers to herniation of elements of the abdominal cavity most commonly stomach, into the mediastinum, through the esophageal hiatus of the diaphragm. Endoscopic and radiographic studies have shown a significant relation between GERD and hiatal hernia [16]. The main types of hiatal hernia are sliding type and para-esophageal type.

Sliding hiatal hernia accounts for more than 95 % of cases. It is characterized by widening of the muscular hiatal tunnel and circumferential laxity of the phrenoesophageal membrane, allowing a portion of the gastric cardia to herniate upward. Hiatal hernias that are larger than 2 cm in axial span can be diagnosed easily by barium swallow radiography, endoscopy, or esophageal manometry. Smaller hernias are more difficult to define. Endoscopically, the squamocolumnar junction appears 2-3 cm above the diaphragmatic hiatus. On endoscopic retroflexed view appears as pouch like area just below mucosal junction and above the diaphragm [17].

Figure 7. Sliding hiatal hernia visible in the esophagus

Para-esophageal hernias account for about 5 % of all hiatal hernias. Anatomically, the pouch of stomach herniates into the chest adjacent to the esophagus. Most complications of a para-esophageal hernia are related to mechanical problems caused by the hernia. Para-esophageal hernias are best diagnosed with a barium swallow, although their presence is usually suggested by endoscopy. Endoscopically, they can cause difficulty in locating the main gastric lumen.

Cameron lesions are erosions or ulcers occurring in the sac of a hiatal hernia. They have been described in up to 5.2 % of patients with a hiatal hernia who undergo upper endoscopy. They are usually an incidental finding but rarely cause acute or chronic upper gastrointestinal bleeding and iron deficiency anemia [18].

2.1.10. Motility disorders of the esophagus

Motility disorders in the esophagus present as dysphagia. Evaluation of esophageal motility disorders often begins with endoscopy. The diagnosis can be made with endoscopy alone, however some cases require manometry or barium swallowing study for confirmation.

Endoscopy typically reveals a dilated esophagus in achalasia that often contains residual material. A "popping" effect with difficulty in passing the endoscope through the gastro-esophageal junction may be noted. The esophageal mucosa usually appears normal. Endoscopy is also essential in achalasia to exclude malignancy.

Endoscopic findings in spastic disorders of the esophagus such as nutcracker esophagus and diffuse esophageal spasm are often normal; however, it may reveal sacculations, diverticula, and chaotic contractile activity along the mid or distal esophagus. Endoscopy is usually performed to exclude structural esophageal obstruction.

In scleroderma, endoscopic findings usually relate to a hypotensive lower esophageal sphincter [12].

2.1.11. Other benign lesions of the esophagus

The prevalence of benign esophageal tumors is 0.5%. The majority of these benign tumors are asymptomatic which diagnose incidentally. Dysphagia is the most common presenting symptom in patients with symptomatic benign esophageal tumors which occurs with large sized tumors. Other symptoms include regurgitation, vomiting and retrosternal discomfort [19].

Leiomyomas

Leiomyomas are the most common benign tumors of the esophagus. They arise from smooth muscle cells. Dysphagia can occur only with large sized tumors. Endoscopically, they appear as submucosal masses with smooth margins and normal overlying mucosa.

Esophageal Cyst

Esophageal cysts are second most common benign tumors. Cysts are usually located in the upper esophagus and are lined by ciliated columnar epithelium. Endoscopically, they appear as protruding mass in the lumen. Surgical resection is required as they can cause complication like obstruction or hemorrhage.

Fibrovascular polyps

Fibrovascular polyps are thin, solitary polyps which usually occur in upper esophagus. They present with symptomatic dysphagia. Over 75 % are 7cm or larger. They have large mucosal folds or large pedicles containing blood vessel.

Squamous cell papilloma

Squamous cell papilloma is usually solitary sessile, warty lesion less than 1.5cm occurring most commonly in lower third of the esophagus. Histologically they are finger like projections of hyperplastic squamous tissue. Etiology of these lesions is felt to be due to human papillomavirus (HPV) infection.

Inlet patch

Inlet patch is isolated area in the esophagus resembling gastric mucosa usually found in the proximal esophagus. It can be associated with Barrett's esophagus and esophagitis in about 20% cases. Histologically, oxyntic type gastric mucosa is most commonly seen [20].

Figure 8. Inlet patch in the esophagus

Glycogen acanthosis

Glycogen acanthosis presents as elevated gray-white plaques in the esophagus that range in diameter from 1 to 15 mm. They are seen in 20–40% of endoscopic procedures and are more prominent in the lower third of the esophagus. Histologically, the epithelium is thickened by the proliferation of large squamous cells filled with glycogen. Glycogen acanthosis has been associated with Cowden's syndrome and celiac disease.

2.1.12. Foreign bodies of the esophagus

Ingestion of foreign bodies occurs most commonly among those with psychiatric disorders, mental retardation, prisoners, and alcoholics. The presence of esophageal stricture or ring predispose to impaction of foreign body or food bolus in the esophagus. Fortunately, most pass through the gastrointestinal tract harmlessly. However, 10–20% will require non-operative intervention. Endoscopic extraction is the mainstay of non-operative interventions which usually attempt after radiographic localization. Foreign bodies at the level of the hypopharynx or cricopharyngeus muscle are best treated with rigid laryngoscopy using a grasping clamp. In all other cases esophagoscopy is the method of choice [21].

2.1.13. Esophageal Varices

Varices are dilated veins which develop in the esophagus and stomach due to portal hypertension. Severe upper GI bleeding from varices as a result of portal hypertension develops in

about 30-40% of cirrhotic patients. Mortality of the first variceal bleed is 25-35%. Endoscopic grading of size and stigmata is very important in predicting the risk of hemorrhage. Endoscopic stigmata which are associated with risk of variceal hemorrhage are red wale markings, white nipple sign, cherry red and hematocystic spots and variceal large size [22]. It is recommended that all the patients with cirrhosis have a screening test to determine presence of varices, so that preventive treatments can be recommended to prevent bleeding [23].

Endoscopically, esophageal varices are graded according to their size, as follows [24]:

Small (Grade 1): Small straight varices

Medium (Grade 2): Enlarged tortuous varices occupying less than one third of the lumen

Large (Grade 3): Large coil-shaped varices occupying more than one third of the lumen.

Upper endoscopy plays vital role in diagnosis, management, screening and surveillance of esophageal varices.

Figure 9. Grade 2 esophageal varices

2.1.14. Mallory Weiss Tear

Mallory Weiss tear is a mucosal laceration at the level of gastroesophageal junction or gastric cardia usually caused by forceful emesis or retching. Most tears occur within 2 cm of the cardia side of the gastroesophageal junction on the lesser curvature. The majority of patients present with gastrointestinal bleeding. Endoscopy is the diagnostic test of choice which also helps in allowing visualization of any active bleeding. Usually, a single tear is noted and the most common location is the right posterior aspect of the cardia. Between 2 and 6 O'clock position with patient in left lateral decubitus position. If endoscopy is delayed, a healing tear may be seen with grayish or erythematous granulation tissue [25].

Figure 10. Mallory Weiss Tear at GE junction (pointed by the arrow)

2.1.15. Esophageal neoplasm

Carcinoma of the esophagus presents with dysphagia to solid food usually which progresses gradually to both solids and liquids. There are two main types of esophageal carcinoma: squamous cell type and adenocarcinoma.

Squamous cell carcinoma presents as three typical forms

polypoid mass (most common),

mass with central depressed ulceration, and

diffuse infiltrating form associated with malignant stricture.

Adenocarcinoma usually appears as an infiltrative lesion, with a narrowed lumen with or without associated mass. It often has a nodular appearance with friable and eroded mucosa; stricture may occur.

Endoscopic visualization with multiple biopsies to increase diagnostic yield must be performed to confirm the diagnosis. Chromoendoscopy using Lugol's iodine (discussed later) is helpful to direct the biopsies and identify the disease extent. Endoscopic ultrasound along with PET /CT further defines the extent of the disease.

2.2. Stomach and duodenum

2.2.1. Peptic ulcer disease

Endoscopy is the most accurate diagnostic test for peptic ulcer disease (PUD) which could be benign or malignant ulcers.

Benign Ulcer

Benign ulcers have smooth, regular, rounded edges, with a flat, smooth ulcer base often filled with exudates. The ulcer base is white covered by fibrinous granulation tissue. In the event of recent bleeding, stigmata of recent bleeding can be seen in the ulcer base.

Figure 11. Large cratered clean based gastric ulcer

Malignant ulcer

An ulcerated mass with nodular looking folds and irregular overhanging, nodular margin is suggestive of malignant ulcer. The chance of malignancy is greater in large gastric ulcers. In about 20 % of cases, endoscopic appearance cannot distinguish benign from the malignant ulcer. 4-6 biopsies of the ulcer margin are shown to detect the vast majority of cancers. Multiple endoscopic biopsies of even benign-appearing gastric ulcerations should be performed due to the risk they may harbor malignancy [26].

Refractory ulcers

Refractory ulcers have been defined as those that fail to heal despite 8 to 12 weeks of antisecretory therapy. In patients with refractory PUD, surveillance endoscopy should be considered until healing is documented or until the etiology is defined (eg. NSAID use, high gastrin states, ischemia).

Bleeding ulcers

Endoscopy is an effective tool in the diagnosis, prognostication, and management of ulcer bleeding. Randomized studies have shown early endoscopic interventions (within 24 hours of admission) reduce blood transfusion requirements, shorten intensive care unit and hospital stays, decrease need for surgery, and lower mortality rate [27]. Patients who are hemodynamically stable with endoscopy revealing ulcers without high-risk stigmata may be safely discharged home after endoscopy. Patients with endoscopic stigmata indicating a high risk of rebleeding which includes adherent clots, visible vessels, and active arterial bleeding should all undergo endoscopic therapy to achieve hemostasis and reduce the risk of rebleeding. Recurrent bleeding may occur in as many as 10% of patients despite endoscopic therapy

and the use of high-dose proton pump inhibitors. In patients who rebleed after initial endoscopic therapy, repeat endoscopic therapy is suggested before considering surgical or radiologic intervention [28].

2.2.2. Gastric outlet obstruction

Gastric outlet obstruction may occur as a result of PUD with inflammation and scarring of the pylorus or duodenum. Patients typically present with loss of appetite, epigastric pain, bloating, nausea, vomiting, and weight loss. Endoscopy is important in confirming the diagnosis and differentiating benign from malignant obstruction. Active ulcers may be noted in association with gastric outlet obstruction in as many as one third of patients undergoing endoscopy for this condition [29]. Biopsies to exclude malignancy should be considered.

2.2.3. Gastritis and gastropathy

Gastritis is an inflammatory process while gastropathy demonstrates minimal to no inflammation.

Gastritis

Gastritis is a term that covers entities that induce acute inflammatory changes in the gastric mucosa. The inflammation may involve the entire stomach or a region of the stomach. Acute gastritis is classified as erosive or non-erosive. Erosive gastritis appears as superficial, deep or hemorrhagic erosions. Non erosive gastritis generally caused by *Helicobacter pylori*.

Vascular gastropathy

Vascular gastropathies are abnormalities in the gastric tissue that involve mucosal vessels with or without inflammation. The two most important vascular gastropathies are gastric antral vascular ectasias (GAVE) and portal hypertensive gastropathy (PHG).

GAVE is characterized by longitudinal columns of vascular ectasias that cross the antrum and converge on the pylorus. The columns have the appearance of the outside of a watermelon. Thus, this disorder commonly being referred as "water melon stomach" [30]. Histopathological exam shows minimal inflammation in the lamina propria, but there is prominent fibromuscular hyperplasia with dilated muscular capillaries. It is common in females and is associated collagen vascular disease and liver disease. It can lead to iron deficiency anemia and the patient may become transfusion dependent. GAVE can be treated with endoscopic therapy using argon plasma coagulation.

Portal hypertensive gastropathy (PHG) or (congestive gastropathy) is a rare cause of significant upper GI bleeding in patients with portal hypertension. PHG characteristically appears as a fine white reticular pattern separating areas of pinkish mucosa on endoscopy, giving the gastric mucosa a "snakeskin" appearance. The vascular abnormalities involve deeper submucosal vessels that are dilated, irregular and tortuous. Patients with severe PHG may develop iron deficiency anemia due to active oozing requiring blood transfusions. Since deeper vessels are involved endoscopic treatment is not effective. Treatment is aimed at

1. decreasing portal pressure with beta blockers,

2. portal decompression with transjugular intrahepatic portosystemic shunt (TIPS), or
3. liver transplantation.

Hypertrophic Gastropathy

Gastric mucosal hypertrophy refers to giant gastric folds. Diffuse mucosal hypertrophy may be described as hyperplastic or nonhyperplastic. In hyperplastic gastropathy gastric epithelial cells which compose the oxyntic glands may become hyperplastic and give rise to giant mucosal folds. The conditions include: Ménétrier's disease, hyperplastic hypersecretory gastropathy, and Zollinger-Ellison syndrome. In nonhyperplastic gastropathy - gastric mucosa may contain other cell types which result in enlargement of the gastric folds. These conditions include infiltrative diseases, infections, and malignancy.

Endoscopy with mucosal biopsy is required to distinguish between acute, chronic active and chronic gastritis and gastropathy. All gross abnormalities should be biopsied with multiple biopsies of both the corpus and the antrum to establish the diagnosis of *Helicobacter pylori* or autoimmune gastritis. Biopsies of the duodenum may also be helpful for diagnosing some forms of chronic gastritis such as Crohn's disease in patients with granulomatous gastritis and celiac disease in patients with lymphocytic gastritis [31].

2.2.4. Dieulafoy's lesions

Dieulafoy's lesion is a rare but important cause of upper GI bleeding. Arterial bleeding from an aberrant vessel is visualized without an associated ulcer or mass lesion. The lesion can be easily missed on endoscopy in the absence of active bleeding. It may look like a raised nipple or visible vessel without an associated ulcer. Endoscopy is the diagnostic modality of choice for a Dieulafoy's lesion during acute bleeding [32].

Figure 12. Actively bleeding dieulafoy's lesion

2.2.5. Gastric polyps

Gastric polyps are usually found incidentally when upper GI endoscopy performed for an unrelated indication. They are important since some types of polyps have malignant potential [33]. Adenomatous gastric polyps are at increased risk for malignant transformation and should be resected completely. Hyperplastic polyps have a rare malignant potential. Endoscopic polyp appearance cannot differentiate histologic subtypes, therefore biopsy or polypectomy is recommended when a polyp is encountered. When multiple gastric polyps are encountered, a biopsy of the largest polyps should be performed or they should be excised. Surveillance endoscopy 1 year after removing adenomatous gastric polyps is reasonable to assess recurrence at the prior excision site, new or previously missed polyps, and/or supervening early carcinoma. If the results of this examination are negative, repeat surveillance endoscopy should be repeated no more frequently than at 3- to 5-year intervals. Follow-up after resection of polyps with high-grade dysplasia and early gastric cancer should be individualized. No surveillance endoscopy is necessary after adequate sampling or removal of non-dysplastic gastric polyps [34].

The various types of gastric polyps are briefly described below.

Fundic Gland Polyps

Fundic gland polyps are the most common type of polyps detected by endoscopy. These lesions are typically less than 5 mm in size, sessile and smooth in appearance. They are located in body and fundus. Fundic gland polyps are commonly seen in patients who take proton pump inhibitors (PPIs) on a long-term basis. They have an extremely low malignant potential. The PPI-related lesions may regress in 3 months, once use of the PPI is discontinued. A polyp associated with familial polyposis carries a defined 30% to 50% risk of developing dysplasia. When multiple fundic gland polyps are evident in younger patients, evaluation for familial polyposis should be considered. Biopsy of fundic polyps is done to exclude dysplasia [35].

Hyperplastic polyps

Hyperplastic polyps are caused by an inflamed or atrophic gastric mucosa. They have a smooth, dome-shaped appearance. Hyperplastic polyps can be large in size, and patients may present with chronic blood loss or even gastric obstruction. Elimination of the underlying cause, such as H pylori infection, typically results in polyp regression. The risk of malignancy is higher if polyps exceed 2 cm in size. For this reason, large polyps must be completely excised.

Adenomatous Polyps

Adenomatous polyps occur sporadically or in association with familial polyposis. These polyps are circumscribed, pedunculated, or sessile. They are associated with chronic atrophic gastric metaplasia and have a defined cancer risk. Complete removal should be performed.

Polyposis Syndromes

Polyposis syndromes are characterized by multiple polyps. They include juvenile polyposis, Cronkite-Canada syndrome, Peutz-Jeghers syndrome, and Cowden's disease. Hamartomatous polyps may be present in all of these syndromes. Adenomatous polyps may be found in familial polyposis.

Gastrointestinal Stromal Tumor

Gastrointestinal stromal tumors (GISTs) make up 1% to 3 % of gastric neoplasms and occur more frequently in men than in women. GISTs are typically located in the fundus. Biopsy is typically normal. Endoscopic ultrasonography-guided biopsy with fine-needle aspiration provides the best tissue sample for diagnosis. GISTs are categorized as having malignant potential ranging from low risk to high risk on the basis of polyp size and level of mitotic activity. All GISTs should be regarded as having neoplastic potential. Surgical resection is recommended for lesions larger than 2 cm. Endoscopic resection is an option for smaller GISTs [35].

Pancreatic Heterotopia

Pancreatic heterotopia may present as submucosal nodular involvement (single or multiple) at the esophagogastric junction or as a submucosal nodular lesion located in the antrum and prepyloric area. There is a characteristic nodule with a central dimple seen endoscopically. Histological features resemble normal pancreatic tissue. Pancreatic heterotopia is a benign and asymptomatic condition.

2.2.6. Gastric neoplasm

Esophagogastroduodenoscopy has a diagnostic accuracy of 95% in diagnosing gastric cancer. Early gastric cancers may appear as a subtle polypoid protrusion, superficial plaque, mucosal discoloration, depression, or ulcer [33]. Improved detection of abnormal lesions may be possible with chromoendoscopy, narrow band imaging and magnification endoscopy (discussed later). Endoscopy is also the primary method for obtaining a tissue diagnosis of suspected lesions. Biopsy of any ulcerated lesion should include at least 6 specimens taken from around the lesion because of variable malignant transformation. The early use of upper endoscopy in patients presenting with gastrointestinal complaints may be associated with a higher rate of detection of early gastric cancers. During endoscopy, any suspicious-appearing gastric ulceration should be biopsied. The diagnosis of an aggressive form of diffuse-type called "linitis plastica", can be difficult endoscopically. Because these tumors infiltrate the submucosa and muscularis propria, superficial mucosal biopsies may be falsely negative.

In selected cases, endoscopic ultrasound may be helpful in assessing depth of penetration of the tumor in the layers of the stomach or involvement of adjacent structures.

3. Push enteroscopy

The evaluation of small intestine is difficult due to its length, intraperitoneal location and tortuosity. Recent developments of push enteroscopy, balloon assisted endoscopy, and

capsule endoscopy have made endoscopic examination of the entire small bowel examination practical. Methods used to evaluate the small bowel include push enteroscopy, single balloon, double balloon enteroscopy and wireless capsule endoscopy [36].

Push enteroscopy using the enteroscope or pediatric or adult colonoscope allows evaluation of small bowel 70-150 cm beyond ligament of Treitz. The disadvantage is looping of scope resulting in patient discomfort. It helps in diagnosis and therapeutics in small bowel lesions in the proximal small bowel [36].

4. Deep small bowel enteroscopy

Diagnostic indications for deep small bowel enteroscopy include obscure gastrointestinal bleeding, tattooing of suspected small bowel malignancies or abnormal findings on other imaging studies and wireless capsule endoscopy, suspected nonsteroidal anti-inflammatory drug-induced small bowel injury, suspected or established small bowel Crohn's disease, refractory celiac disease, detection of polyps in patients with polyposis syndromes such as familial adenomatous polyposis or Peutz-Jeghers syndrome, examination of the gastric remnant in patients who have undergone Roux-en-Y gastric bypass and removal of foreign bodies like retained wireless capsule [37,38].

Deep small bowel enteroscopy can be performed with balloon-assisted or spiral enteroscopy. Single and double balloon techniques are described. These techniques allow deeper access to the small bowel than push enteroscopy.

Single balloon enteroscopy (SBE) uses the scope's flexible tip to anchor the scope to the bowel and intestinal tract is pleated over the overtube and shortened. On the other hand double balloon uses a second balloon to anchor the bowel instead of the scope tip. The working length of double balloon endoscope (DBE) is about 150-200 cm as a result 150-350 cm of small bowel can be visualized. The success rate of complete inspection of small intestine is 40-80%. Balloon-assisted enteroscopy (ie, DBE and SBE) which can be performed orally or per rectum, whereas spiral enteroscopy can only be performed orally. The complications of double balloon enteroscopy are ileus, pancreatitis, perforation and prolonged duration of procedure [38].

Spiral enteroscopy is a diagnostic and therapeutic intervention of the small bowel. A small enteroscope is used with overtube that has helical spirals on the surface. The overtube slides over the enteroscope. There are no major complications reported. The limitations are increased sedation requirement [36].

5. Wireless capsule endoscopy

Wireless capsule endoscopy is an ambulatory procedure which has become a first line test for visualizing the mucosa of the small intestine. The PillCam is a capsule comprised of a lens

imager, battery and transmitter. The capsule moves from mouth to the anus with peristalsis taking two images per second at 1:8 magnification. The PillCam SB is FDA approved for visualization of the small bowel mucosa in adults and children aged >10 years(4).

The most common indications include evaluation of obscure GI bleeding including iron deficiency anemia, suspected Crohn's Disease, small intestinal tumors and surveillance in patients with polyposis syndromes, refractory malabsorptive syndromes (eg, Celiac disease) [39].

Contraindications suspected GI obstruction, gastroparesis, swallowing disorders, pregnancy, dementia, strictures or fistulas (based on the clinical picture or preprocedure testing), cardiac pacemakers or other implanted electro-medical devices.

5.1. Small intestine

5.1.1. Celiac disease

Celiac disease is a condition in which the immune system responds abnormally to a protein called gluten causing damage to the lining of the small intestine. It affects about 1% of the western population. Patients with celiac disease usually have positive IgA endomysial or transglutaminase antibody. Patients with positive antibodies should undergo endoscopy with small bowel biopsy.

The duodenal mucosa may appear atrophic with loss of folds, contain visible fissures, have a nodular appearance or the folds may be scalloped. Multiple biopsies should be obtained in the second and third portion of the duodenum by upper GI endoscopy. Staining techniques and high resolution magnification endoscopy can also help identify areas of villous atrophy for biopsy (discussed later) [40]. Videocapsule endoscopy shows good sensitivity and excellent specificity for the detection of villous atrophy in patients with suspected celiac disease [41]. The advantages of video capsule endoscopy (VCE) are that it is noninvasive, it images the entire length of the small bowel, and it is able to detect minute mucosal details. For these reasons VCE may be a useful tool for the diagnosis of Celiac disease [42].

5.1.2. Crohn's disease

Crohn's disease is characterized by transmural inflammation of the gastrointestinal tract. Crohn's disease may involve the entire gastrointestinal tract from mouth to the perianal area. It mostly affects distal small bowel and right colon and 20-30% have disease limited to the small bowel only. Thus colonoscopy with ileoscopy and biopsy is a very important test in the diagnosis of Crohn's disease. It can be diagnosed by upper endoscopy, enteroscopy, wireless capsule endoscopy or colonoscopy with terminal ileum intubation based on the location of GI tract involvement. Capsule endoscopy and double balloon enteroscopy have comparable yield. Therefore, capsule endoscopy may be part of an initial evaluation followed by double balloon enteroscopy if biopsy or intervention is needed [43]. Capsule retention is the main and only complication which is indefinite presence of capsule which occurs most commonly in patients of known Crohn's disease [39]. This can be avoided by the use of patency capsule (disintegration time-controlled capsule) in patients with high risk of capsule retention [44].

Figure 13. Crohn's disease ulcer in the colon (pointed with an arrow)

On enteroscopy, the findings in Crohn's Disease are linear ulcers, aphthous ulcers, round or irregular ulcers, pseudopolyps, cobblestoning, stricture or stenosis.

5.1.3. Tumors of small bowel

Tumors of the small bowel are relatively uncommon and account for approximately 3% of gastrointestinal neoplasms. As the symptoms are vague and conventional diagnostic tests are unsatisfactory. These tumors often present a clinical, radiological, and endoscopic challenge. Endoscopy is very accurate in diagnosing and identifying small bowel lesions[45]. Capsule endoscopy is helpful in the diagnosis of small bowel tumors[46]. Double balloon endoscopy is shown to have good diagnostic capabilities due to its ability to take biopsies[47]. However, isolated mass lesions can be missed on incomplete balloon endoscopy or capsule endoscopy[48]. The clinical conditions that predispose to small bowel neoplasms are Familial adenomatous polyposis, hereditary non-polyposis colorectal cancer (HNPCC), Peutz-Jeghers syndrome, celiac disease, and Crohn's disease[45].

Adenocarcinomas are the most common type of primary malignant small bowel tumors mostly occurring in duodenum. They appear as circumscribed, polypoid usually large and circumferentially involving the bowel wall.

Carcinoids mostly occur in the terminal ileum, less than 1 meter from IC valve. They are usually small and found incidentally.

GISTs appear as dome shaped submucosal with central ulceration, commonly seen in jejunum.

6. Colonoscopy

Colonoscopy is endoscopic visualization of colonic mucosa. A complete exam is possible in 95-99% of patients. The main indications to colonoscopy are screening and surveillance for

colon polyps, pathological bowel wall thickening noted on imaging procedures, diarrhea, malabsorption, rectal bleeding, unexplained iron deficiency anemia, positive fecal occult blood test, suspected short strictures of the colon, rectal foreign bodies, weight loss and abdominal pain [49]. The contraindications of colonoscopy are peritonitis, perforation, fulminant colitis and recent surgical anastomosis.

Complications of colonoscopy are perforation (0.2% with diagnostic colonoscopy and 0.32% with polypectomy), hemorrhage (0.09% with diagnostic colonoscopy and 1.7% with polypectomy) and postpolypectomy coagulation syndrome (electrocoagulation injury inducing transmural burn in 0.5-1.2%, occurs 1-5 days of polypectomy, requires no surgical intervention) and sedation related complications [50]. Thus, polypectomy is the single greatest risk factor for complications of colonoscopy.

6.1. Colon

6.1.1. Screening colonoscopy

Screening for colorectal cancer with colonoscopy is the most common procedure performed by gastroenterologists in the US. Identification of premalignant polyps is primary goal. Some polyps are only hyperplastic with minimal malignant potential. Polyps of concern are called adenomas which are premalignant. Guidelines recommend colonoscopy every 10 years beginning at age 50 years. The follow up colonoscopy should be based on number, size and pathologic findings of the adenomatous polyps removed. Patients with 1-2 small (<1cm) tubular adenomas with only low grade dysplasia should get follow up after 5 years, whereas patients with 3 or more or advanced adenomatous lesions should get repeat colonoscopy in 3 years or before if colonoscopy was incomplete, preparation was poor or >10 polyps are removed. If surveillance colonoscopy is normal, follow up colonoscopy is recommended after 5 years. Patients with large, sessile adenomatous lesions which are removed in piecemeal should have repeat examination within 2-6 months to exclude and remove remnant polypoid tissue [51].

6.1.2. Colonic polyps

Colonic polyps are benign neoplasms that arise from the epithelial cells lining the colon. Colonic polyps are divided into 3 groups: hyperplastic polyps, adenomas, and polyposis syndromes [52].

Hyperplastic polyps

Hyperplastic polyps comprise about 90% of all polyps. They are rounded and sessile measuring few millimeters in size and cannot be distinguished from adenomas. Hyperplastic polyps most commonly occur in the rectosigmoid region. They lack malignant potential especially if they are located in the rectosigmoid area and if the size is few mm. Malignant potential is present only in the setting of very large polyps.

Polyps with architecture similar to hyperplastic polyps but the cytology is different with surface mitotic activity, higher nuclear /cytoplasmic ratio and serrated glandular pattern as a result they are termed as "serrated adenomas" [52].

Figure 14. Stalked colon polyp

Adenomas

Adenomas can be seen throughout the colon. Most (70%) found in the left colon and are <1 cm. Three histological subtypes are described: tubular, villous and tubulovillous. Tubular adenomas are the most common and can be found anywhere in the colon. Villous adenomas most commonly occur in the rectal area, larger than the other two types, and tend to be non-pedunculated, velvety, or cauliflower-like in appearance. They are more likely to harbor carcinoma in situ or invasive carcinoma compared to other adenomas. The risk of progression to carcinoma is related to both the size and the histology of the adenoma. Adenomas that are greater than 1 cm with villous component carry an increased cancer risk.

The shape or gross structure of the polyp is also clinically significant. Polyps with a stalk are called pedunculated. Those polyps without a stalk are called sessile. Sessile polyps are more concerning than large pedunculated polyps for two reasons. First, the pathway for migration of invasive cells from the tumor into submucosal and more distant structures is shorter. Second, complete endoscopic removal is more challenging and more difficult to accomplish. Premalignant flat lesions are now more readily detected by new endoscopic imaging methods, such as narrow-band imaging or mucosal staining (described later). The colon polyps are removed with snare cautery, cold biopsy, hot biopsy or cold snaring [53].

6.1.3. Inherited syndromes

Familial adenomatous polyposis (FAP) is an autosomal dominant condition in which at least 100 adenomatous polyps in the colon, most numerous in the distal colon. When left untreated these polyps develop into colon cancer by third to fifth decade [52].

Hereditary non-polyposis colorectal cancer (HNPCC)/Lynch syndrome is a misnomer as these patients have adenomas similar to general population. However, the adenomas appear at younger age and presents with early onset of colorectal cancer before the age 40, mostly in the right colon. There can be metachronous or synchronous colorectal malignancies, associated with tumors of other organs especially endometrium, ovary and stomach.

Peutz-Jeghers syndrome is characterized by the presence of hamartomatous polyps occurring more frequently in the small bowel and colon. Melanin spots may be seen on lips and buccal mucosa. These polyps are not precancerous but patients are prone for tumors of breast, lung, ovary and pancreas.

Juvenile polyposis is a condition presenting with hamartomatous polyps in the colon, stomach and small bowel. These polyps may be precancerous and require close endoscopic surveillance.

6.1.4. Ischemic Colitis

Ischemic colitis is the most frequent form of mesenteric ischemia, presenting with sudden onset of abdominal pain followed by bloody diarrhea. Colonoscopy or sigmoidoscopy is often required to establish the diagnosis of ischemic colitis. The examination usually performed without bowel preparation (to avoid reducing blood flow from dehydrating cathartics), and with minimization of air insufflation (to avoid distention and perforation). Colonoscopy is more sensitive in detecting mucosal lesions allows biopsies, and does not interfere with subsequent angiography.

Colonoscopic findings in the acute setting frequently include pale mucosa with petechial bleeding with bluish hemorrhagic nodules may be seen representing submucosal bleeding [54]. Cyanotic mucosa and hemorrhagic ulcerations are seen later in the course [55]. Segmental distribution, abrupt transition between injured and non-injured mucosa and rectal sparing favor the diagnosis of ischemic colitis [54].

Figure 15. Ischemic colitis

6.1.5. Pseudomembranous colitis

Pseudomembranes are pathognomonic of pseudomembranous colitis (*Clostridium difficile* associated colitis) but are not found in all cases. *Clostridium difficile* toxins cause cytoskeleton disruption causing shallow ulcerations which exude serum proteins and inflammatory cells forming pseudomembranes. Endoscopic findings include raised yellow or off-white plaques up to 2 cm in diameter scattered over the colorectal mucosa which cannot be removed by lavage. These lesions are discrete but may become confluent plaques in more advanced cases. The other colonic findings are edema, erythema, and inflammation with or without pseudomembranes [56].

Figure 16. Pseudomembranous colitis- pseudomembranes(pointed by arrows)

6.1.6. Diverticular disease of colon

Diverticula are outpouching of mucosa through the muscle wall of the colon. Colonic diverticula are most frequent source of hematochezia followed by angiodysplasia and inflammatory bowel disease (IBD) [55]. Approximately 95% diverticulosis is noted in descending and sigmoid colon. The prevalence increases with age, from less than 5 % at age nearly two-third by age 80. The diverticular bleed presents as painless, acute hematochezia which is arterial in origin occurring at dome or neck of the diverticulum. About 60 % of diverticular bleeds occurs in left colon, however angiography study recognizes diverticular bleeding more often in the right colon. Bleeding stops spontaneously in 80% cases [55].

Figure 17. Diverticulosis of colon (pointed by the arrows)

6.1.7. Arteriovenous malformations or Angiodysplasia

Angiodysplasia are detected in about 3-12% cases of lower GI bleeding. Most patients are asymptomatic and overt bleeding occurs in presence of coagulopathy or platelet dysfunction. They are mainly found as multiple lesions in the right colon, appearing as red, circumferential lesions measuring from one millimeter to a few centimeter. The incidence increases with age.

Multiple telangiectasias in pale mucosa can also be seen in case of radiation induced proctopathy which occurs following radiation therapy for prostatic carcinoma [55].

6.1.8. Inflammatory bowel disease

Endoscopic findings in ulcerative colitis (UC) are mucosal erythema and edema with loss vascular pattern. Granularity of mucosa with friability, spontaneous bleeding and ulcers are also seen. Some of patients of UC have focal inflammation around the appendiceal orifice that is not contiguous with disease elsewhere in the colon which is known as "cecal patch". It is important to obtain adequate mucosal biopsies to help distinguish Crohn's ileocolitis from pan-ulcerative colitis with backwash ileitis (UC with distal ileum involvement).

Figure 18. Ulcerative colitis- friable colon mucosa

Endoscopy in Crohn's disease reveals aphthous ulcers, cobble stoning or skip lesions. A normal rectum supports the diagnosis of Crohn's disease, since UC always involves the rectum. The presence of normal vasculature adjacent to affected tissue is seen in Crohn's disease, while loss of vascularity and friability is more typical of UC [57].

6.1.9. Hemorrhoids

Hemorrhoids are clusters of veins, smooth muscle and connective tissue lined by the normal epithelium of the anal canal. They are categorized into internal and external hemorrhoids. These categories are anatomically separated by the dentate (pectinate) line. External hemorrhoids are hemorrhoids covered by squamous epithelium below the dentate line, whereas internal hemorrhoids are lined with colonic columnar epithelium proximal to dentate line. Internal hemorrhoids are not supplied by somatic sensory nerves and therefore cannot cause pain. Internal hemorrhoids are classified in 4 degrees by the Goligher classification (Table 1). They are best viewed on retroflexed view on flexible endoscopy [58].

First degree	Bleeds but donot prolapse
Second degree	Prolapse but spontaneously reduce
Third degree	Prolapse but require manual reduction
Fourth degree	Unable to reduce

Table 1. Stains used in chromoendoscopy

Figure 19. Internal hemorrhoids on retroflexed view

External hemorrhoidal veins are found circumferentially under the anoderm and are innervated by cutaneous nerves that supply the perianal area. Symptoms may occur anywhere around the circumference of the anus [58].

6.1.10. *Melanositis coli*

Deposition of pigment in the intestinal mucosa is commonly observed on endoscopy, especially within the colon. Electron microscopy has shown that this pigment is not melanin at all, but lipofuscin deposition in macrophages of colon mucosa. Herbal remedies or anthraquinone containing laxatives are often implicated. The pigment intensity is not uniform, being more intense in the cecum and proximal colon compared to the distal colon. Colorectal adenomas do not contain the melanin-like pigmentation. The association of adenomas with melanositis coli can be explained by the ease of detection of even tiny polyps as white spots within a dark-colored colonic mucosa [59]. The condition is benign requiring no treatment.

Figure 20. Melanositis coli – colon polyp noted (pointed by an arrow)

6.1.11. Solitary rectal ulcer syndrome

Solitary rectal ulcer syndrome (SRUS) is a rare disorder of defecation presenting as bleeding per rectum. The term SRUS is a misnomer, as 34% of the endoscopic findings are multiple lesions. Endoscopic findings include mucosal ulcerations, polypoid lesions or simply erythema. It is a rare and poorly understood disorder that occurs in people with chronic constipation [60]. Treatments for solitary rectal ulcer syndrome range from changing diet and fluid intake to surgery.

6.1.12. Stercoral ulcer

Stercoral ulceration is the loss of bowel integrity from the pressure effects of inspissated feces. It usually occurs in constipated and bedridden patients. Because of associated diseases in the population at risk, perforation and hemorrhage are the principal complications resulting in a mortality exceeding 50%. Endoscopically, it appears as an isolated lesion in the rectosigmoid area [61].

6.1.13. Colorectal cancer

Colorectal cancer presents commonly as abdominal pain, hematochezia, change of bowel habits, anemia, or weight loss. Early diagnosis depends on routine screening. Colonoscopy is the single best diagnostic test in symptomatic individuals, since it can localize and biopsy lesions throughout the large bowel, detect synchronous neoplasms, and remove polyps. Air contrast barium enema (BE), supplemented with flexible sigmoidoscopy, is also used to evaluate symptomatic patients.

Figure 21. Colon cancer (pointed by an arrow)

Most colon cancers are adenocarcinomas which can be detected on colonoscopy and is undoubtedly the single best diagnostic test in symptomatic individuals since it can localize and biopsy lesions throughout the large bowel, detect synchronous neoplasms, and remove pol-

yps.Endoscopically,lesions may appear as circular proliferating,exophytic or stenosing lesions and uncommonly as plaque like, flat discoid mass with slight depression or ulcer [52]. The likelihood of detection of colorectal cancer can be enhanced by novel methods like chromoendoscopy, narrow band imaging, confocal laser endomicroscopy and high resolution and high magnification endoscopy (described later).

7. Novel and adjunct methods with endoscopy

It is shown that certain flat adenomaswith subtle dysplastic and early neoplastic changes are missed with white light endoscopy as they as they are too small,flat or depressed to be detected. This has led to the development of techniques that compliment conventional endoscopic methods and help in detection of subtle GI lesions by enhancing the image by high magnification or high definition. Image enhanced endoscopy technology can either be dye based (Chromoendoscopy), equipment based (Narrow band imaging), or electronic based [62].

7.1. Chromoendoscopy

Chromoendoscopy involves the topical application of various stains or pigments to subtle GI lesions to improve tissue localization and characterization resulting in targeted biopsies of those lesions. The mucosa is pretreated with a mucolytic agent to remove excess mucus from the mucosal surface. Most commonly 10 % N-acetylcysteine is used. Targeted spraying via a spray catheter is performed for colon polyps and entire surface is stained inthe evaluation Barrett’s esophagus. Glucagon is administered just before spraying to decrease contractions and uneven spraying.It is considered to be a safe and nontoxic procedure [63]. The table below describes various stains used in various conditions with their side effects (Table 2).

Stains	Conditions	Side effects
Methylene Blue	Esophagus: Barrett’s mucosa/Post ablation to find Barrett’s mucosa. Gastric: Intestinal metaplasia Colon:Chronic ulcerative colitis	Harmless , transient blue green discoloration of urine and feces
Toluidine blue	Esophagus: Squamous cell cancer	None reported
Lugol’s solution	Esophagus: Squamous dysplasia and early squamous cell carcinoma,	Retrosternal burning and nausea which can be treated with application of 5% sodium thiosulfate which can neutralize residual iodine. Avoided in patients with Iodine hypersensitivity and hyperthyroidism
Indigo carmine	Colon : Colorectal neoplasia,chronic ulcerative colitis	None reported

Table 2. Stains used in chromoendoscopy

Chromoendoscopy has been shown to detect higher number of lesions per patient compared with narrow band imaging (NBI), autofluorescence, or white light colonoscopy [64]. It is an inexpensive, safe and relatively easy to perform but it is not standardized and is subject to observer interpretation.

7.2. Narrow band imaging

Conventional white light endoscopy uses full visible wavelength (red-green-blue) to produce an image. On the other hand narrow band imaging uses special filters which increase relative intensity of the blue band thus enhancing the image quality. NBI used along with magnifying endoscopy allows the analysis of the surface architecture of the epithelium (pit pattern) and the analysis of the vascular network resulting in better characterization of distinct types of gastrointestinal epithelia (e.g. intestinal metaplasia in Barrett's esophagus), as well as the disorganization of the vascular pattern in inflammatory disorders and the irregular pit pattern in early neoplastic lesions of the esophagus, stomach and large bowel [65].

The NBI generates a darker field of view than white light and allows adequate inspection of the mucosal surface. The tip of the endoscope needs to be closer to the mucosa. The presence of bile and blood strongly absorb narrow band light thus obscuring the view under NBI. The NBI images are not yet standardized. There are no reported complications with NBI [66].

7.3. Confocal Laser Endomicroscopy

Confocal Laser Endomicroscopy (CLE) is a new imaging modality of GI endoscopy which allows in vivo imaging of the mucosal layer at cellular and subcellular resolution making in vivo histology possible during endoscopy. CLE is based on the principle of illuminating a tissue with a low-power laser and then detecting fluorescent light reflected from the tissue. To illuminate the tissue, an exogenous agent is applied topically or systemically. Most commonly used agent is intravenous fluorescein sodium which highlights the extracellular matrix enabling confocal imaging. The laser is focused at a specific depth and only light reflected back from that plane is refocused and able to pass through the pinhole confocal aperture. As a result, scattered light from above and below the plane of interest is not detected, increasing spatial resolution. The area being examined is scanned in the horizontal and vertical planes and an image is reconstructed. In this manner, microscopic imaging of biological tissue in vivo is possible due to the high lateral resolution of confocal imaging. It helps in differentiation of neoplastic from non-neoplastic polyps, for example, neoplastic lesion in patients with Barrett's esophagus [67], or ulcerative colitis, differentiation of benign from malignant biliary strictures.

Currently, there are two CLE systems used, probe based (confocal probe passes through the accessory channel of a standard video-endoscope) and integrated endoscopy (CLE integrated in the distal tip of endoscope).

More data is needed to support these modalities. In future, CLE will develop multicolor analysis of several layers with 3-dimensional reconstruction allowing deeper penetration depth [68].

7.4. High resolution and high magnification endoscopy

High-resolution imaging improves the ability to discriminate detail while magnification enlarges the image. Magnification endoscopy often utilizes a movable lens controlled by the endoscopist to vary the degree of magnification (100X as compared with 30X in standard endoscopy). Both high magnification and high-resolution endoscopes were designed to be used in conjunction with chromoendoscopy. High-resolution and high-magnification endoscopy may enhance the diagnosis and characterization of some mucosal lesions and may detect changes in vascular architecture of patients with early esophageal cancer. Magnification chromoendoscopy has been used to characterize Barrett's esophagus, early gastric cancer and villous atrophy [69]. The magnification endoscopy is simple, inexpensive, requiring no special light processors. The disadvantages are lack of standardization and prolongation of procedure time [70]. Whether high-resolution or high-magnification endoscopy will decrease the need for endoscopic biopsy or increase the diagnostic yield of endoscopic procedures has not yet been determined [71,72].

7.5. Autofluorescence imaging

Autofluorescence imaging utilizes changes in concentrations of endogenous fluorophores, for example flavin adenine dinucleotide, collagen and nicotinamide adenine dinucleotide. The video-endoscopy adds green and red reflectance improving the image quality. The dysplastic tissue there is lack of fluorescence due to lack of collagen resulting in increased red and decreased green fluorescence. It has been shown useful in detection of dysplasia in Barrett's esophagus and early esophageal cancer but there is insufficient data to support its routine clinical use [62].

7.6. Endocytoscopy

Endocytoscopy is a new imaging method which provides combination which combines chromoendoscopy with ultra-high magnification catheter which is passed through the working channel of the endoscope [73]. Unlike confocal endomicroscopy, it provides images in color but is limited to superficial layer. It has been shown to give accurate results which are almost comparable with histological results. The diagnosis based on endocytoscopic imaging is subject to interpretation, and there is no validated criteria regarding tissue diagnosis and differentiation for various GI conditions.

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