Gastroenterology

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GASTROESOPHAGEAL REFLUX DISEASE

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Introduction 00:00:52

Definition :

Gastroesophageal reflux is defined as the retrograde flow of gastric contents from the stomach to the esophagus.

- When gastroesophageal reflux goes beyond the threshold then the gastro-esophageal reflux disease develops which has symptoms like heartburn and regurgitation.
- in the long term these symptoms can lead to erosive esophagitis which can lead to barret's esophagus.
- Barret's esophagus is the risk factor for esophageal adenocarcinoma.

Prevalence :

- Prevalence around the world is 13%.
- Higher prevalence of GERD : South Asia, European countries.
- Simple GERD/non erosive esophagitis is more common in females.
- Serious type GERD is more common : males.
- Risk of barret's esophagus/adenocarcinoma is high with increasing age.

Etiology :

- Obesity :
  - Mechanical : ↑Abdominal pressure → ↑ intragastric pressure → Decreased LES pressure.
  - Biochemical : Due to cytokine storm → TNF α and IL 6 → modifies LES pressure.
- H. pylori : Produces two types of gastritis :
  - Corpus predominant gastritis : Leads to atrophic gastritis → Decreases H^+ secretion → Protective against GERD.
  - Antrum predominant gastritis : increases acid production → more prone for duodenal ulcer.
- Physical activity :
  - Decreased GER is seen in moderate aerobic exercises.
  - increased GER seen in bending exercises, extreme sports & swimming.
- Nicotine : Associated with esophageal adenocarcinoma & barrets esophagus.

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Pathogenesis

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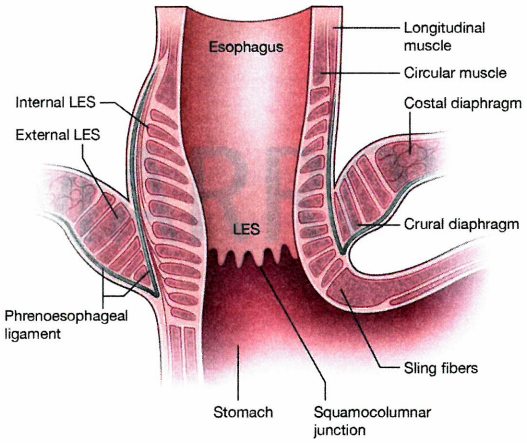
Factors involved in pathogenesis of GERD includes :

- Defensive factors :
  - Anti reflux barriers.
  - Esophageal acid clearance.
  - Tissue resistance.
- Aggressive factors :
  - Gastric acidity.
  - Volume reflux.
  - Duodenal reflux.
  - Hiatus hernia.



Antireflux barrier

Defensive factors :

Anti reflux barriers :

- Lower esophageal sphincter :
  - It is around 2 to4 cms.
  - one half is above the diaphragm and the other half is below the diaphragm.
  - LES maintains tonicity of around 20 to 30 mm Hg.
  - in case of hiatus hernia only the LES will be holding the stomach.
  - LES primarily relaxes after swallowing but the crural diaphragm relaxation is not related to swallowing but to the proximal stomach distension.
- Crura of diaphragm.
- Phrenic ligaments.
- Angle of his.

Esophageal acid clearance :

- Removal of acidic contents in the esophagus by peristaltic waves.
- There are two types of peristaltic waves :
  i. Primary peristaltic wave is related to swallowing.
  ii. Secondary peristaltic wave is related to esophageal distension.
- Salivation has alkaline factor so it mixes with acid in the esophagus and reduces the toxic effect of acid in the stomach.

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Tissue resistance :

- It involves pre epithelial, epithelial and post epithelial protective mechanisms.
  - Pre epithelial : Mucin, prostaglandins.
  - Epithelial : Stratified squamous epithelium.
  - Post epithelial : Esophageal blood supply that clears the toxic metabolites and increases the nutrition.

Aggressive factors :

Gastric acid secretion :

- Normal gastric acid secretion can cause reflux.
- Mechanism : Failure of anti reflux mechanism.
- in Zollinger Ellison syndrome (ZES), due to hypergastrinemia they can also have gastric ulcers and esophageal ulcers too.

Reflux mechanisms :

- Transient lower esophageal sphincter relaxation (tLESRs).
- Low LES pressure.
- Swallow associated LES relaxation.
- Strain and Free reflux.

Transient lower esophageal sphincter relaxation :

- It is associated with inhibition of crural muscles of diaphragm.
- It lasts longer than swallow associated peristalsis (>10 sec).
- Can be physiological/pathological.
- It is pathophysiological cause in 60-70% of GERD.
- Physiological mechanism :
  - Related to distension of the proximal or fundus of the stomach.
  - Pressure in the proximal part of stomach → Afferent vagus is stimulated → Brainstem → Dorsal motor neuron of vagus → Efferent → LES → inhibition of crural muscles of diaphragm and contraction of the longitudinal muscles of esophagus.

Swallow LES relaxation :

- They are shorter (<5 seconds).
- Not associated with crural fibres.
- Swallow → Peristaltic wave → Relaxation of LES.
- It is pathological in 5-10% cases while it is physiological in remaining cases.

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Strain induced reflux :

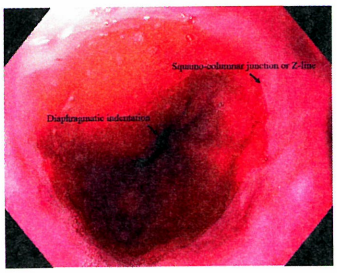
- Hypotensive LES.
- intra abdominal pressure >30 mm Hg → Slightly hypotensive LES → Reflux from stomach gastric to the esophagus.

Free reflux :

- When LES pressure is <5 mm Hg even in normal cases there is reflux of gastric contents.
- It is seen in :
  - Post POEM (Per oral esophageal myotomy).
  - Heller's myotomy.
  - Progressive systemic sclerosis.

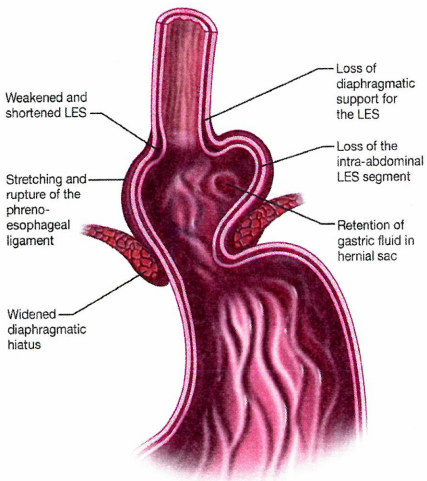
Hiatus hernia :

- Herniation of superior part of the stomach into the intarathoracic cavity.
- Acid pockets are formed in the stomach from where the reflux occurs.
- 2 hit hypothesis : When both LES and crural diaphragm are affected gastroesophageal reflux happens.



Z line

Hiatus Hernia



Acid pocket :

- In the fasting state the stomach is very much acidic (pH is 2).
- After food intake the food acts as a buffer with acid and increase the pH.
- Paradoxically in the post prandial phase GERD develops.
- Acid pocket : Proximal part of the fundus of the stomach that has very less contact with food and escapes the buffering act of food is more acidic.

Clinical features

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Symptoms :

- Heartburn (most common).
- Regurgitation (20-30%) : Feel of food flowing back to oesophagus.
- Dysphagia (Alarming symptom) causes :
  - Esophagitis.
  - Peptic esophageal stricture.
  - Adenocarcinoma.
- Waterbrash : Reflux in upper esophagus → Stumlates salivary gland → Excessive saliva secretion to wash acid → Salty (Alkaline) feel in the mouth.

Extraesophageal manifestations :

- Chest pain.
- Asthma : 1/3 rd patients have GERD (Some ILDs → Complication of GERD).
- Chronic cough.
- ENT : Laryngopharyngeal reflux → Posterior part of vocal cords are affected → Laryngitis → may present as decreased quality of sound.
- Dental erosions.
- Sleep disorders : Obstructive sleep apnea .

Associated conditions :

- Pregnancy : Estrogen/progesterone decreases the tone of LES and pressure from gravid uterus can cause reflux.
- Scleroderma : 30% of the patients will have severe esophagitis.
- Zollinger Ellison syndrome.
- Post POEM.
- Ryle's tube.

Diagnosis

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investigations :

- Empirical acid suppression : PPI are given for a month with OD dose → If there is no suppression of acid → Endoscopy is done.
- Endoscopy.
- Biopsy.
- pH monitoring.
- Esophageal manometry.

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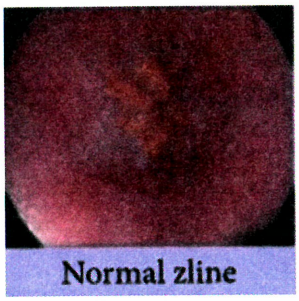
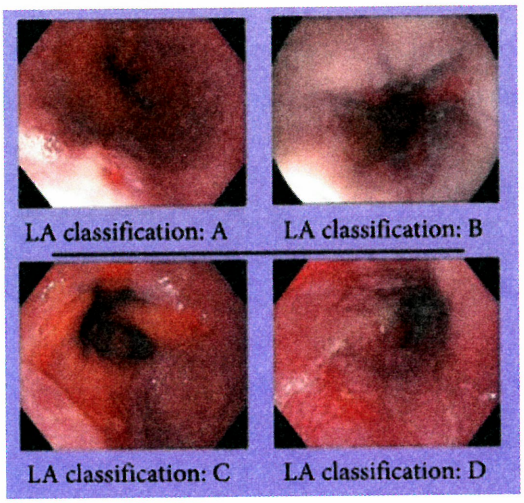
Endoscopy :

Los Angeles classification :

- Grade A : one or multiple small erosions of <5mm.
- Grade B : more than 5 mm erosions, no connection.
- Grade C : multiple erosions with connections but no circumferential involvement of esophagus.
- Grade D : multiple erosions with connections with circumferential involvement of esophagus.



Normal zline



Biopsy :

- Patient with dysphagia and GERD :
  - Biopsy should be done to look for eosinophilic infiltration to rule out eosinophilic esophagitis.
  - >15 eosinophils/HPF : Diagnostic of eosinophilic esophagitis.
- Biopsy is done to rule out Barret's esophagus.

pH monitoring :

- pH testing is done in two conditions :
  i. Normal endoscopy but with severe symptoms.
  ii. No improvement in symptoms even after giving PPI.
- Catheter is placed nasally at the level of LES for 24 hrs → Continuous measurement of pH.
- Normal people : Acid exposure time is <5 % of total time.
- If acid exposure time is >6% it indicates reflux.
- more than 80 episodes of reflux in 24 hrs → GERD.

Esophageal manometry :

It is usually done before doing a surgery to know the normal pressures in the esophagus preoperatively.

Natural history of disease

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Non erosive disease :

- Around 70% patients have non erosive disease.
- Young females thin with functional complaints.
- < 1% develops barret's esophagus at the end of 2 years.

Reflux testing :

It is categorized into 3 types :

- Abnormal reflux : Responds well to PPI's.
- Reflux hypersensitive patients : Patients have symptoms for normal reflux → They are difficult to treat.
- Completely normal patients with normal reflux testing results : Functional heartburn patients → Require psychiatric evaluation.

Erosive disease :

- Around 30% patients have erosive disease.
- Seen in older men.
- Severe symptoms are present.
- Will have findings suggestive of erosion in endoscopy.
- only 25% of erosive disease progresses to severe esophagitis /Barrets esophagus.

Risk of developing Barret's esophagus :

- Non erosive esophagitis : <1% at the end of 2 years.
- Los Angels Grade A/B : 1.5%
- Los Angels Grade C/D : 5 %.

Complications and treatment

01:00:08

Complications :

- Peptic strictures :
  - Long standing inflammation of esophagus leads to stricture formation.
  - Symptoms will be longstanding leading to decrease in reflux symptoms.
  - Dysphagia increases.
  - Management : Endoscopy.
- Barrett's esophagus.

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Treatment :

Lifestyle modifications :

- Head end elevation.
- Left lateral decubitus position.
- Weight loss.
- Small meals.
- Decrease spicy foods, chocolate and nicotine.
- Complete abstinence from alcohol.

Drugs :

1. Proton pump inhibitors :

- H_a receptor antagonist were used initially.
- PPI reduces meal stimulated & nocturnal acid secretion effectively than H_a receptor antagonist.
- H_a receptor antagonist reduce pH for 4-8hrs while PPI reduce pH for 10-14hrs.
- Patient on PPI's will have nocturnal breakthrough.
- To avoid nocturnal breakthrough H_a receptor antagonist can be given as add on therapy.
- PPI's are given 20-30 min before food.
- Long term therapy can lead to :
  - Enteric infections/SIBO.
  - High risk of aspiration pneumonia.
  - Deficiency of calcium, magnesium, iron and vitamin B12.

2. Other drugs :

- Baclofen : GABA B Agonist used for transient LES relaxation.
- H2 Receptor antagonist.
- Antacids : Gaviscon.

Surgical therapy :

- Nissens 360 degree fundoplication.
- Toupet partial fundoplication :
- Indications :
  - Patient is non compliant for long term PPI therapy.
  - Even after double dose PPI treatment if the patient is in the risk of developing strictures or erosions.

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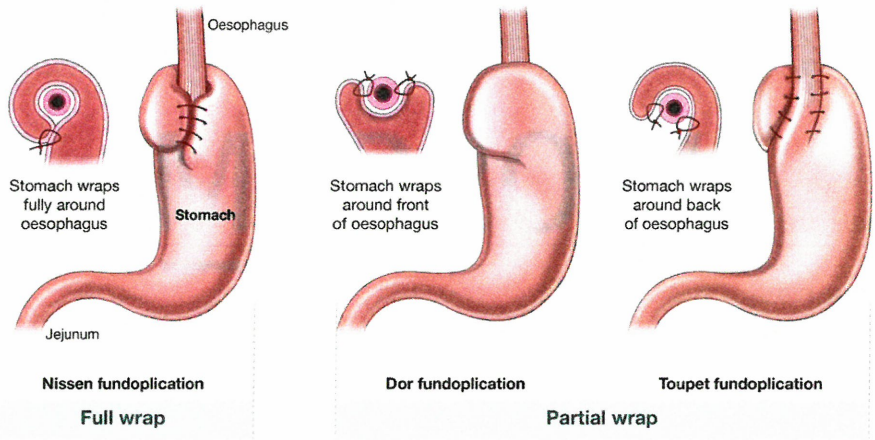

Fundoplication

Novel therapies :

- Stretta : RF ablation is done at LES using electrodes endoscopically.
- TIF : Transoral incisionless fundoplication.
- ARMS/ARMA : Antirefulx mucosectomy/ Anti reflux mucosal ablation.
- Magnetic sphincter.
- LES electrical stimulation.

Treatment of peptic esophageal stricture :

- Endoscopic dilatation.
- Dye is passed and the LES is located → Guide wire is introduced → Bougie dilatation → Savary dilators are used.
- Esophageal lumen <13 mm : Dysphagia is present.

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MEDICINE INDUCED ESOPHAGITIS

Introduction

00:00:21

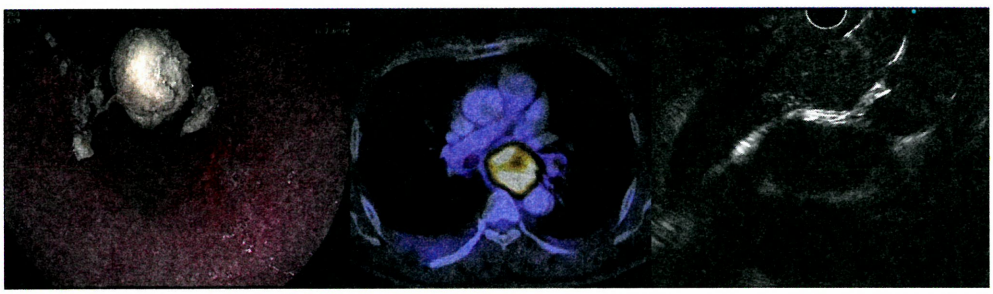
Case scenario :

50 year old man came with c/o sudden onset worsening chest pain for few weeks. Dysphagia aggravated on intake of NSAIDS. History of intake of medications for chronic lower back pain present and weight loss.

Investigations :

- Endosocopy : Ulcerations in the esophagus.
- CT : Multiple bone metastases.
- PET CT : Increased uptake, EUS showed large hypoechoic area seen around the esophagus.
- Diagnosis in biopsy : Polydifferentiated adenocarcinoma.

Hence medication induced esophagitis/pill esophagitis can be an indicator for an underlying malignancy.



Endoscopy PET CT EUS

Epidemology :

- It is a common presentation.
- It is unrecognized due to the differential diagnosis like cardiac pathology, GERD etc.
- Anyone is susceptible to pill induced esophagitis based on their pill taking habits.
- While prescribing drugs in the night, patient should be advised to take the drug 30 mins before going to bed, after food intake.

Predisposition :

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- Middle third of the esophagus is commonly affected.
- Trough zone : Diffusion area between the skeletal muscle of the upper part of the esophagus that joins with the smooth muscle area.

Normal anatomy	Abnormal anatomy	Mucosal/ Functional anatomy	Behavioural	Drug related
• Aortic arch • Left atrium • Left main brochus • Trough zone	• Cardiomegaly • Mitral stenosis • Aortic aneurysm • Zenker's • Achalasia cardia	• Scleroderma • Eosinophilic esophgitis • Reflux esophagitis	• Dry swallow • Recumbent Sleep	• Size • Capsule • Ex-tended release

Pathophysiology 00:15:18

Mechanism of esophageal injury :

- Acidic injury : Ascorbic acid, ferrous sulphate, tetracycline.
- Alkaline injury : Alendronate.
- Hyperosmolar trauma : Potassium chloride.
- Direct drug toxicity : Tetracycline.

Pills get deposited in the subepithelial layer of esophagus.

Medications commonly associated with esophagitis or esophageal injury :

Antibiotics	Antiviral agents	Bisphosphonates	Chemotherapeutics	Others
• Clindamycin. • Doxycycline. • Penicillin. • Rifampicin. • Tetracycline. • Cloxacillin.	• Nelfinavir. • Zalcitabine. • Zidovudine.	• Alendronate. • Etidronate. • Pamidronate. • Risedronate (Lower risk).	• Bleomycin. • Cytarabine. • Dactinomycin. • Danorubicin. • 5-Fluorouracil. • Methotrexate. • Vincristine. • Crizotinib.	• Ascorbic acid. • Ferrous sulphate. • Lansoprazole. • Multivitamins. • Potassium chloride. • Quinidine. • Theophylline.

Features of bisphosphonates induced esophagitis :

- Women are more affected.
- Will have sloughing appearance in endoscopy similar to candidiasis (whitish plaques).
- Image like esophageal dissecans superficialis can also be seen.

NSAIDS : Aspirin, ibuprofen, Naproxen may also be involved in some cases.

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Note :

- Pill induced esophagitics due to antibiotics is seen more in young people.
- Incidence of pill induced esophagitis is seen more in old people generally due to recumbency.
- Female : male is 60 : 40.

Clinical features and diagnosis 00:19:30

Clinical features :

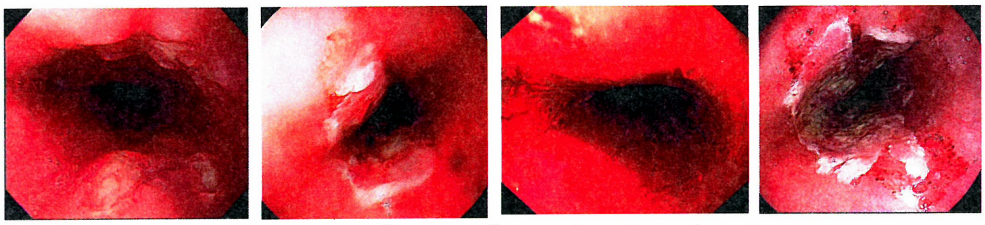
- Chest pain.
- Odynophagia.
- Dysphagia.
- Others.
- Onset of symptoms : It will be within hours/1 to 2 days/overnight after taking a larger size pill.

Investigations :

Endoscopy :

Not all patients with pill esophagitis will require endoscopy.

Kissing ulcers : Characteristic of pill induced esophagitis.



Endoscopic findings of pill induced esophagitis

Treatment 00:26:57

Prevention :

Patient should be in upright position 30 min after taking pill before going to bed.

About 80 ounces (250 ml) of water should used while taking medicine.

Treatment :

- No need of endoscopy in all pill induced esophagitis.
- Medications used are :
    i. PPI.
    ii. Sucralfate suspension.
- Liquid diet for few days.
- I/V pain killers.
- Ryle's tube in advanced cases.

BARRETT'S ESOPHAGUS

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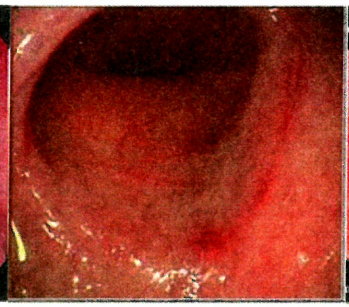
Introduction 00:00:21

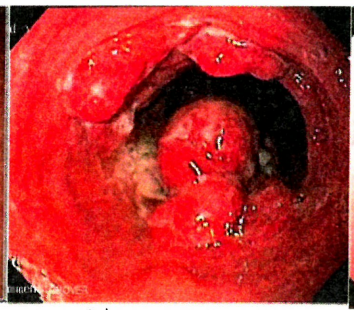
Features :

- Complication arising from chronic GERD (Gastro-Esophageal Reflux Disease).
- Previously thought to be a common complication of GERD and associated with high chances of conversion to adenocarcinoma.
- Recent studies show that conversion rates of Barrett's esophagus into esophagitis and adenocarcinoma is much lesser.

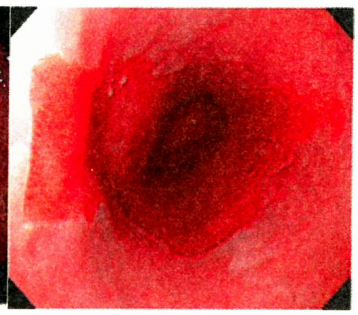
Normal lower end view of oesophagus



Erosive oesophagitis



Adenocarcinoma



Velvety pouching from LES & stomach

- Mucosal changes occur from stratified squamous to columnar epithelium (metaplasia).
- D/t constant exposure of acid coming from stomach.
- Barrett's esophagus occurs by transdifferentiation and not entirely by dysplasia.
- Higher chance of conversion to esophageal adenocarcinoma if dysplasia is seen with Barrett's esophagus.

Diagnosis 00:06:04

Diagnosed by :

- Endoscopy :
  - Velvety gastric mucosa in lower part of oesophagus.
  - Erosive esophagitis with suspicion of Barrett's esophagus : Do not take biopsy (Overdiagnosis), give PPI for 4 weeks, repeat endoscopy.
- Histopathology : After taking biopsy and look at intestinal/gastric columnar lined mucosa (Barrett's metaplasia).

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Note :

Endoscopy is the only way to diagnose barrett's oesophagus.

Epidemiology and progression 00:07:34

Progression :

- 2-5 % of GERD cases progress to barret's oesophagus.
- Types of barret's oesophagus :
  - Short barrett's : <3 cm of barrett's mucosa.
    (Low chance of conversion into adenocarcinoma).
  - Long barrett's : >3 cm of barrett's mucosa.
    (High chance of conversion into adenocarcinoma).
- Atleast 1 cm of abnormal gastric mucosa is needed for it to be diagnosed as barrett's oesophagus.

Non erosive esophagitis to Barrett's :

- <0.5% chance of conversion at the end of 2 years.

Erosive esophagitis to Barrett's :

- LA Grade A, B : 1.5% at the end of 2 years.
- LA Grade C, D : 5% at the end of 2 years.

Barrett's to esophageal adenocarcinoma (EAC) :

- 0.5 to 1 % of all barrett's oesophagus turn into EAC per year.
- Barrett with non dysplastic changes, risk of turning into EAC is 0.25 %.
- Barrett's with low grade dysplasia has 0.9 to 1 % risk.
- Barrett's with high grade dysplasia has 3 to 4 % risk.

Biopsy :

Seattle protocol :

Once detected, 1-2 cm sized 4 quadrant circumferential multiple biopsies are taken.

Defining Barrett's :

PRAGUE classification :

- Based on circumferential extent and maximum extent.
- Used to diagnose endoscopically.