Gastro-Esophageal Reflux Disease (GERD)

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Financial Interest Disclosure

Commercial Interest	Relationship*
AVIR Pharma	Consultant/ ad board (2019-)
Medtronic	Consultant/ ad board (2011-) Speaker Bureau

* e.g. advisory board, consultant, investigator, speaker, research support, stockholder, employee

Objectives

- *Review the updated guidelines on the diagnosis and treatment of gastro-esophageal reflux disease (GERD).*
- *Define the role of endoscopy in the management of this condition.*
- *Establish the relative contribution of the various life-style modifications and pharmacological therapies available*

Consultation

- Nancy B.: 51 year-old ER nurse; Single mother of two teenagers
- Severe heartburn and regurgitation for the last 6 years. Has occasional nausea but no other GI issues.
- Symptoms occur several times per week, especially when she does TSO/16-hours shift. Eats when she can and what she can while at work
- Self-treated with antacids and OTC H2-RA with some short-term relief
- Symptoms are much worse lately, especially at night, with significant impact on her quality of life and sleep
- Drinks 3-4 cups of coffee/shift. Smokes 5-10 cig per day; no cannabis
- 5’2’’; 175 lbs. (BMI= 32)

Tell me, Dr…..

- What do I have ? Is this reflux ?
- Do I need a gastroscopy ?
- What can I do to help myself ?
- Should I start a proton pump inhibitor right away ? For how long ?
- I am concerned about cancer. Should I be worried ?

Clinical Features

- *Heartburn is the classic symptom of GERD:* burning feeling, rising from the stomach or lower chest and radiating toward the neck, throat, and occasionally the back.
  - Specificity (43 % - 89%) and sensitivity (38 % -73 %) for GERD (24-hour esophageal pH)
  - Predictive of symptoms resolution during treatment with omeprazole 20 mg
- *Effortless regurgitation of acidic fluid/air/food* (specificity 95%; sensitivity 6%)

Diagnosis

American College of Gastroenterology Guidelines
January 2022

- The diagnosis of GERD can be made without investigation, based on the predominant presence of the typical symptoms of heartburn, with or without regurgitation.
- GERD is essentially a clinical diagnosis
- If chest pain is present: cardiac work-up first

Katz, PO et al AM J GI 2022; Katz, PO et al Am J GI 2013
Alberta Health Services: GERD Primary Care Pathway: Primary Care Networks 2021

Upper endoscopy Referral

- Not required in the presence of typical GERD symptoms (heartburn/regurgitation)
- Indicated if:
  - "Alarm" symptoms
  - Consideration for Barrett's esophagus screening *(intestinal metaplasia)*
    - Main risk factor for development of esophageal adenocarcinoma
    - Up to 30-fold risk increase (relative risk)
    - Risk of annual progression to high-grade dysplasia/ Cancer: 0,5 %/year/pt
  - **Lack of response after trial of life style modifications/ PPI tx*

Katz, PO et al. Am J GI 2013 ; Qumseya, B et al GIE 2019; Peters, Y et al. Clin GI Hepatol 2019
Kamboj, AK et la GIE Clin NA 2020; Shaheen, NJ et al Am J GI 2022; Katz, PO et al AM J GI 2022

Upper Endoscopy Referral
"Alarm Signs"

- Dysphagia/odynophagia
- Unintended Weight loss (> 5 % over 6-12 months)
- Bleeding/ iron deficiency anemia
- Persistent vomiting
- Abdominal mass

Katz, PO et al AM J GI 2022
Alberta Health Services: GERD Primary Care Pathway: Primary Care Networks 2021

Endoscopic Screening for Possible Barrett's

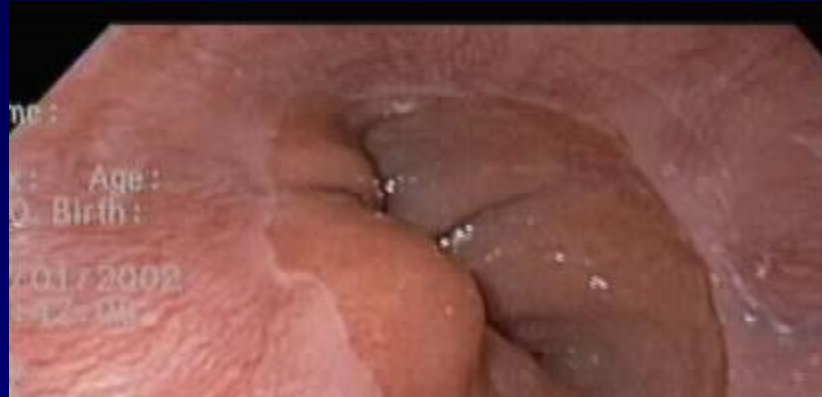
American College of Gastroenterology (ACG) 2022 Guidelines

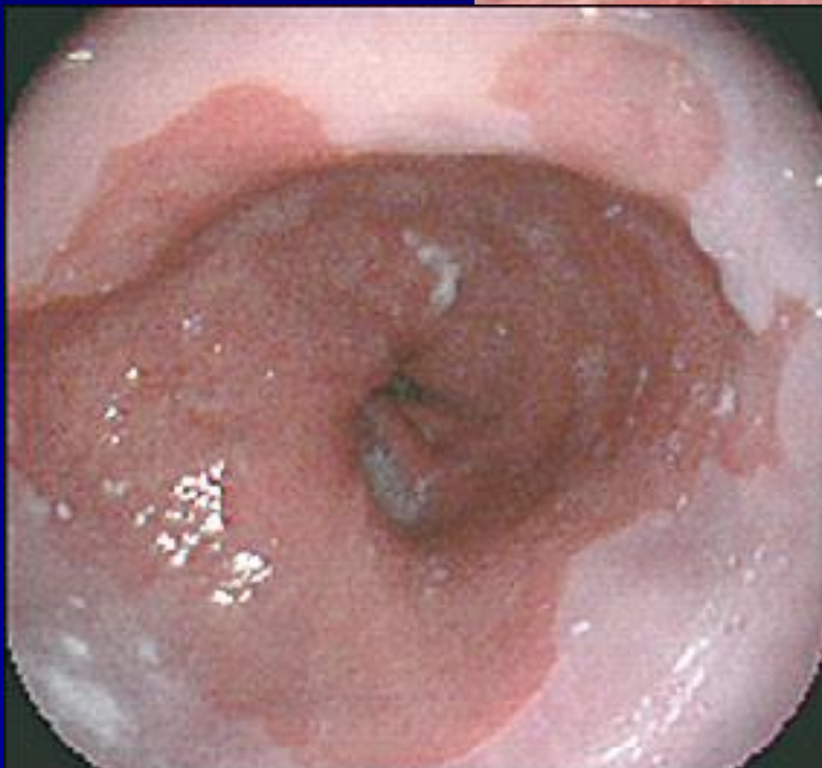
- Patients with chronic GERD (> 5 years) and/or frequent symptoms (weekly or more) (heartburn and/or regurgitation) and *at least 3 or more risk factors for BE/EAC:*
  - Male gender
  - Caucasian race
  - Age > 50 years old
  - Central obesity (W > 102 cm or WHR > 0.9)
  - Smoking (present or past)
  - Confirmed family Hx of BE/EAC (1st degree relative)

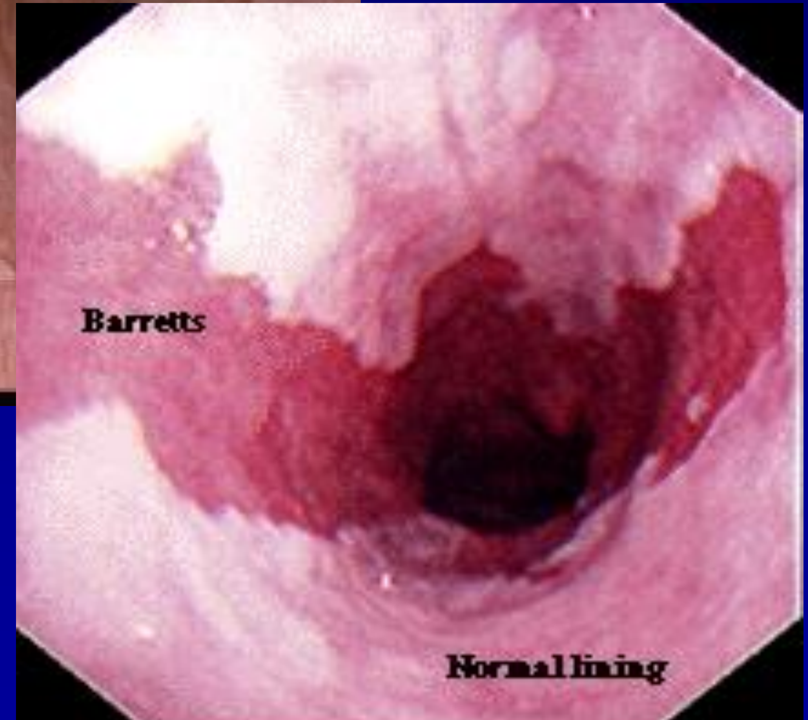
Controversial !
Based on consensus expert opinions
Consider overall-life expectancy/Discussion with patient

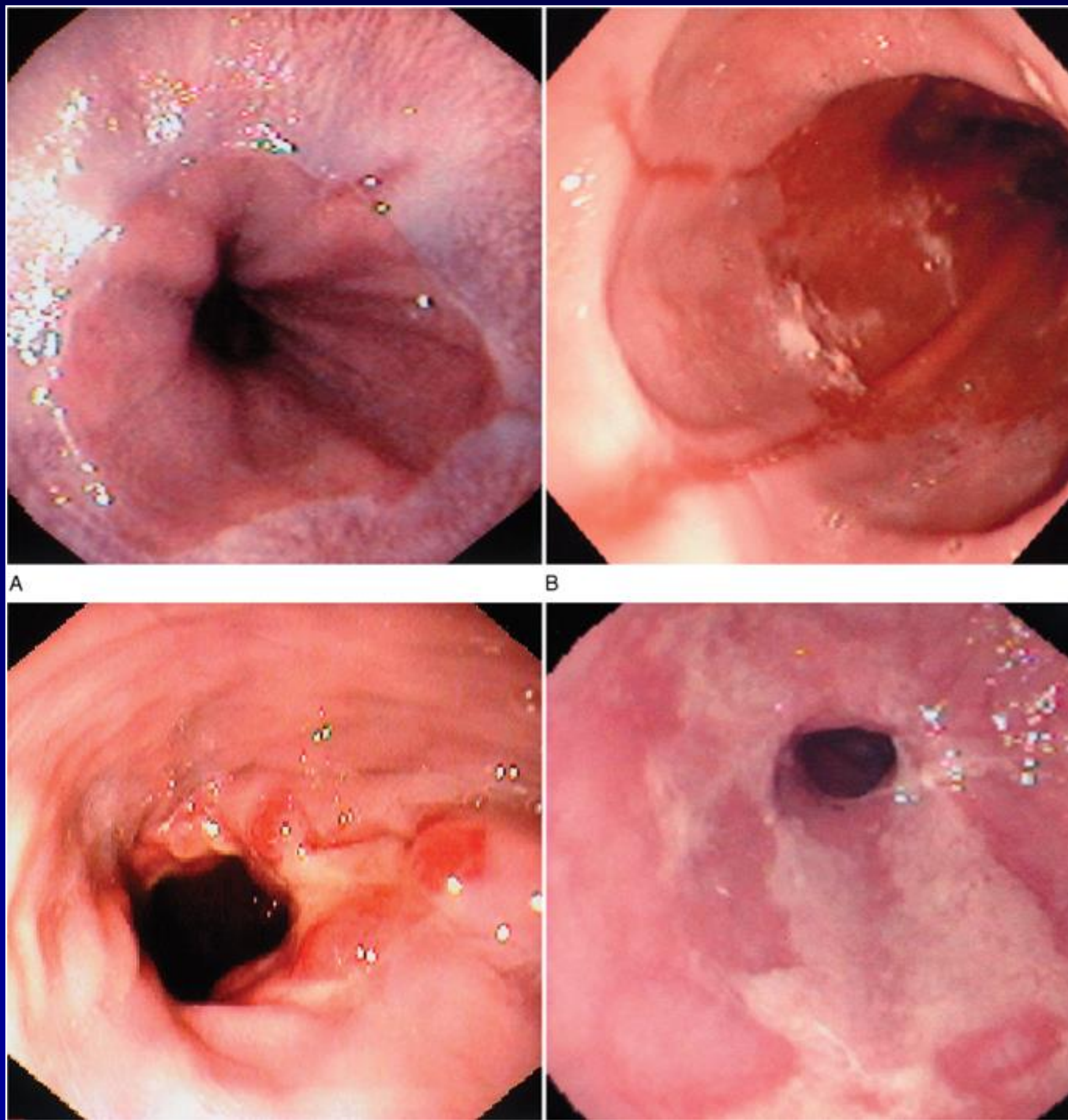
Shaheen, NJ et al Am J GI 2022; Qumseya, B et al GIE 2019 ; Shaheen, NJ et al Am J GI 2016

Endoscopic Appearance









Endoscopic photographs of the four grades of esophagitis (A to D) using the Los Angeles classification system

Gastrointestinal and Liver Disease 8ed Elsevier 2007

Management

Lifestyle interventions

Pharmacological therapy

Life-Style modifications
Recommended for symptoms control

- Weight loss in overweight/obese (also useful for symptomatic pt with normal BMI but recent weight gain)
  - 40 % reduction in GERD symptoms, if reduction of BMI > 3.5 or more (women)
- Avoid meals within 2-3 hours of bedtime/reclining
- Avoid/stop smoking/tobacco products
- Avoid trigger foods (i.e chocolate, caffeine, carbonated drinks, alcohol, acidic/citrus/spicy/fatty food etc.)
- Elevate the head of bed (4-6 inches ; "bedge") for night time GERD symptoms
  (extra pillow not sufficient)
- Preferable to sleep on left side (compared to right side or flat)

Katz, PO et al Am J GI 2022; Ness-Jensen, E. et al. Am J GI 2013; Jacobson, T. et al NEJM 2006; Hampel, H. et al. AIM 2005

Medical options

- *First line Tx*: Life-style modifications…*but life "happens"*

- Antiacids/ H2RA (OTC): for on-demand Tx of short term symptoms relief. Short acting (fast relief): Problem of tolerance (tachyphylaxis) with H2RA on the long term

  - Proton pump inhibitors form the basis of effective GERD Tx.
    - Superior healing rate for all grades of esophagitis
    - Faster healing rate
    - Faster/more complete heartburn relief

Katz, PO et al Am J GI 2022; Labenz, J et al. World J GI 2005; Chiba, N et al. GI 1997

Proton Pump Inhibitors

GERD (heartburn/regurgitation/no alarm signs)

- 8-weeks trial/Tx once daily (standard dose) PPI (30 - 60 min ac meal)
- *If adequate response*:
  - For most patients (not all*): try to titrate down to the lowest effective dose or discontinue PPI *(may or may not be possible in all patients)*
  - * To be avoided:
    - ✓ Proven Barrett's esophagus
    - ✓ Endoscopic evidence of severe esophagitis (Los Angeles Grade C or D)
    - ✓ Frequent symptoms of GERD (2 times per week or more) and/ or prolonged symptoms that have a significant effect on daily activities.
  - Concept of "acid rebound" (mild; < 1 week; interim strategy with H2RA/ anti-acids)
  - Concept of once-a-year attempt at tapering/"de-prescribing"if patient on maintenance Tx

Katz, PO et al AM J GI 2022;Alberta Health Services:GERD Primary Care Pathway: Primary Care Networks 2021

Proton Pump Inhibitors

GERD (heartburn/regurgitation/no alarm signs)

- 33 % of patients will not have an adequate response (obesity, poor adherence, psychological factors)
- *If inadequate response*: optimize PPI tx (8 weeks)
  - Double the dose (ac breakfast and ac supper)
  - Switch to another PPI (once)
- *If no response still*: consider referral/ endoscopy (off PPI 2-4 weeks to increase yield of esophagitis detection)

Katz, PO et al AM J GI 2022;Alberta Health Services:GERD Primary Care Pathway: Primary Care Networks 2021

Proton Pump Inhibitors
"GERD Maintenance strategies"

- *Structured stopping of the PPI, dose tapering and on-demand therapy* are all safe and effective (see exceptions). Patients should be able to choose which method *works best for them.*

- ***Stop*** once-a-day use of PPI:

  – If patients have a rebound hypersecretion of acid beyond two weeks they likely will require long term PPI. In that case titrate to the lowest dose of PPI which controls symptoms (see on demand strategy).

- ***Tapering*** can be achieved by reducing twice-daily to once-daily or halving the once-daily dose. The aim is to reduce the frequency of PPI dosing to a threshold whereby symptoms are still well controlled.

- ***On-demand therapy*** is using a PPI for a period sufficiently long to achieve symptoms resolution followed by discontinuation until symptoms recur. This is effective in patients with mild GERD/NERD

Alberta Health Services :GERD Primary Care Pathway: Primary Care Networks 2021;
Alberta Health Service. PPI Deprescribing. Scheelar, R. 2021

GERD

Natural History

- GERD is one of the most common *chronic* disorder
- Up to 66 % of patient with non–erosive GERD will experience symptomatic relapse off PPI
- Almost 100 % of patients with severe erosive esophagitis (LA grade C-D) will relapse within 6 months
- Most patients will require *long-term combination* of life-style modifications and pharmacological Tx

Schindlbeck NE. et al. Gut 1992
Katz, PO et al AM J GI 2022

Long-Term PPI issues

PPIs are the ***most effective medical treatment*** for GERD.

Some studies have identified an ***association*** between the long-term use of PPIs and the development of numerous adverse conditions *(intestinal infections, pneumonia, stomach cancer, osteoporosis-related bone fractures, chronic kidney disease, deficiencies of certain vitamins and minerals, ischemic heart disease, strokes, dementia, and early death)*

Those studies have flaws, are not considered definitive and do not establish a ***cause-and-effect relationship*** between PPIs and the adverse conditions.

Katz, PO et al AM J GI 2022

Long-Term PPI issues

GERD

- Placebo- RCT
- 17 598 pts (> 65 y old) with CAD on Rivaroxaban +/- ASA
- Randomized to receive Pantoprazole 40 mg po q day vs Placebo
-

However, cannot (…may never be able to….? No matter how large a study)exclude the possibility that PPIs might confer a (very) small increase in the risk of developing these adverse conditions. Risk 0 does not exist !*

- Pneumonia, c.diff, enteric infections, fractures, gastric atrophy, CRD, DM, COPD, Cancer, Hospit, deaths(all –causes)

No significant difference between the PPI group and the placebo group except for enteric infections (OR: 1,33; 1,45 % vs 1,0 %)

Moayyedi P, Eikelboom JW, Bosch J, et al. Safety of proton pump inhibitors based on a large, multi-year, randomized trial of patients receiving rivaroxaban or aspirin. Gastroenterology 2019

Long-Term PPI issues
GERD

- ✓ If no other risk factors for bone disease, no recommendations for increasing the intake of calcium or vitamin D or undergoing routine monitoring of bone mineral density.

- ✓ If no other risk factors for vitamin B12 deficiency, no recommendation that to raise the intake of vitamin B12 or to routinely monitor serum B12 levels.

- ✓ If no other risk factors for kidney disease (or in the absence of established renal insufficiency) , no recommendation to routinely monitor serum creatinine levels

Katz, PO et al AM J GI 2022

Tell me, Dr…..

- What do I have ? Is this reflux ? Yes indeed !
- Do I need a gastroscopy ? Depends on your response to Tx/ ? Barrett's screening consideration
- What can I do to help myself ? YES: Frist Stop Smoking/loose weight
- Should I start a proton pump inhibitor ? For how long ? Yes: PPI once a day for 8 weeks
- I am concerned about cancer. Should I be worried ? Risk factors for Barrett (smoker, obesity, severe GERD, age >50) but less frequent in women….Stop smoking !

Key Messages I

- *GERD is essentially a clinical diagnosis (based on the presence of predominat heartburn and/or regurgitation) which does not require further investigations, in the initial stage.*

- *Indications for upper endoscopy/GI referral include the presence of: alarms signs, an unsatisfactory response to pharmacologic therapies, and consideration for Barrett's esophagus screening (based on individual risk profile, and after discussion with the patient)*

Key Messages II

- *Life-style modifications (weight loss, avoiding late meals, stopping smoking, elevating head of bed) represent the first steps in managing uncomplicated GERD.*
- *An eight-week trial of PPI once-a-day (standard dose) can be considered in those patients failing non-pharmacologic Tx*
- *In responders, with uncomplicated disease (non-erosive GERD or milder symptoms, and no Barrett's) PPI should be discontinued (stopped) or tapered to lowest effective dosing.*
- *Various maintenance strategies can be considered ("on-demand"/ daily continuous use) for symptoms recurrence, tailored to the individual patient's profile and preference.*
- *In spite of several observational studies associating PPI with multiple long-term side-effects, patients should be informed/reassured about these drugs favorable innocuity profile, while putting in perspective their considerable benefits.*

Thank you….

? Questions