

Upper GIT Conditions

- GORD
- PPI
- Eosinophilic oesophagitis
- Helicobacter pylori
- Barrett's oesophagus

Gastroenterology/Hepatology workshop

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RBWH

CHRONIC GORD

GORD

- GOR common
 - GORD if impact on QoL or $>2x$ per week
 - Prevalence GORD 10-20%

GORD

- General and lifestyle changes
 - Weight loss
 - Smaller meals, avoid late meals
 - Physical activity
 - Avoid alcohol
 - Stop smoking
 - Elevate head of bed
- Empiric trial of PPI
 - 40mg daily for 4-6 weeks
- Consider GE referral if not responding or any red flags

GORD Red Flags

- GI bleeding
 - Weight loss >5% in 6 months
 - Dysphagia
 - Vomiting
 - Unexplained iron deficiency
-
- Beware: New onset in older people

Erosive GORD

- 10-20% have GORD, 1/3 of these have endoscopic erosions
- 8 weeks of PPI (40mg/d) highly effective in healing (>80%)
 - Double dose more effective
- Maintenance Rx often needed



NERD



- *Non Erosive Reflux Disease* – normal endoscopy
- If pH confirms acid reflux – PPI as effective as in GORD
- If not acid related → variable response to PPI
 - Reflux hypersensitivity
 - Volume / bile reflux
 - Functional heartburn / functional dyspepsia
 - these may also benefit from visceral analgesics

GORD / NERD

- Both are chronic diseases
- Relapse rate 6 months after stopping PPI:
 - 90% in GORD
 - 75% in NERD

PPI dosing

- 30-60 minutes before meals
- Chronic PPI or escalation of dose not recommended if no initial response
 - ?functional or bile reflux
- Try to stop or step down
- Lowest effective dose
- PRN dosing okay
- Beware of rebound

Chronic GORD - Treatment

- Maintenance therapy
 - Life style modifications
 - Weight loss – of patients compliant with hypocaloric diet
 - 54% could stop PPI
 - 32% halved PPI dose
 - Avoid trigger foods/alcohol, elevate head of bed, stop smoking etc
 - PPI: Individualised dosing / step down
 - H2RA: 300mg nocte
 - Prokinetics: domperidone 10mg BD – selected cases only
 - Regular review
 - Fundoplication / RYGB
- Health Pathways Website

PPI: INDICATIONS AND LONG TERM USE

Healing of peptic ulcers



- Find the cause
 - Cut out offending agents
 - Treat H pylori
- All patients with significant PU should have PPI
- PPIs more effective than H2RA
- Duration
 - 4-8 weeks if cause treated
 - No cause found → long term PPI with reviews
- Repeat endoscopy after 2 months to document healing

PPI in NSAID-related PUD

- Reduces ulcer risk in regular NSAIDs / low dose aspirin users (OR 0.2-0.3)
- NSAIDs user ***with risk factors*** should be on PPI
 - Age>65
 - High dose NSAIDs
 - History of ulcer disease
 - Concurrent aspirin, steroids, or anticoagulants
- Joint statement American College of Gastroenterology, AC of Cardiology, and American Heart Association (AHA) 2008

PPI in Barrett's



- For symptom control
- Chemoprophylaxis
 - Meta-analysis: OR 0.29 for HGD/cancer in Barrett's
 - Retrospective cohort and case-control studies
 - Controversial
 - American Gastroenterological Society and the American College of Gastroenterology agree,
 - The British Society of Gastroenterology disagrees
 - Australian Barrett's Guidelines not endorsing mandatory PPI use

Harmful effects of PPI

- Multiple publications describing associations of PPI with adverse effects
 - Media hype
- Often epidemiologic studies
 - Multiple confounders, some will be unknown and unadjustable
 - Causality difficult to ascertain

Harmful effects of PPI

- Described for
 - Malabsorption
 - Iron, Vit B12, calcium, magnesium
 - Fractures
 - Hip RR 1.26
 - Any site RR 1.33
 - Microbiome changes / infections
 - Drug interactions
 - Clopidogrel – not clinically significant
 - Atrophic gastritis / gastric cancer
 - Renal failure
 - Dementia

Long term PPI use

- Generally safe
 - Reassure pts
 - Ensure appropriate indication

- Overutilisation
 - Small risk of adverse effects
 - Health care cost

PBS data 15-16: cost

Table 10(a): PBS Drugs (Generic Name) Sorted by Highest Government Cost, 2015-16.
Section 85 only; incl. Drs Bag.

Rank	Drug	Script Volume	Government Cost	Total Cost*	Ave. Price**
1	Ledipasvir + Sofosbuvir	15,776	\$357,875,840	\$358,203,581	\$22,705.60
2	Adalimumab	193,120	\$334,694,252	\$339,560,312	\$1,758.29
3	Ranibizumab	146,736	\$217,812,843	\$219,604,664	\$1,496.60
4	Sofosbuvir	10,702	\$213,273,366	\$213,465,013	\$19,946.27
5	Aflibercept	142,372	\$213,134,445	\$214,882,554	\$1,509.30
6	Esomeprazole	6,747,706	\$166,509,203	\$210,238,799	\$31.16
7	Etanercept	95,884	\$164,684,806	\$166,777,684	\$1,739.37
8	Fluticasone + Salmeterol	3,006,437	\$148,510,188	\$194,793,783	\$64.79
9	Fingolimod	64,468	\$147,542,266	\$149,158,012	\$2,313.68
10	Insulin Glargine	366,896	\$146,557,692	\$151,574,150	\$413.13
11	Pregabalin	3,150,492	\$139,093,159	\$171,497,777	\$54.44
12	Rosuvastatin	6,465,792	\$136,915,124	\$172,331,151	\$26.65
13	Denosumab	403,366	\$121,961,712	\$126,361,836	\$313.27
14	Imatinib	26,570	\$98,153,433	\$98,668,809	\$3,713.54
15	Rivaroxaban	1,246,539	\$96,288,227	\$112,155,727	\$89.97
16	Tiotropium	1,786,709	\$94,597,554	\$108,689,695	\$60.83
17	Budesonide + Eformoterol	1,829,094	\$90,950,660	\$122,663,679	\$67.06
18	Atorvastatin	7,490,700	\$85,103,958	\$121,514,059	\$16.22
19	Daclatasvir	9,918	\$79,114,622	\$79,291,724	\$7,994.73
20	Golimumab	45,576	\$76,256,407	\$77,350,463	\$1,697.18



Helicobacter pylori

Helicobacter pylori

- Motile spiral Gram negative bacillus
- Found in deep mucus layer
- urease → ammonia
- Nobel Prize 2005 Warren and Marshall

Worldwide Prevalence of H. pylori



Hp prevalence in Australia

- Overall *Hp* prevalence in controls 23%
 - Birth cohort effect

• <40y	5%
• 40 - 49yrs	12%
• 50 - 59yrs	19%
• 60 - 69yrs	25%
• 70 - 79yrs	31%
- *Hp* a/w low education, smoking

The bad Helicobacter

- Complications, definite
 - Gastric and duodenal ulcers
 - Distal gastric cancer
 - MALT lymphoma
- Complications, probable
 - Idiopathic Thrombocytopenic Purpura (ITP)
 - Iron deficiency anaemia
 - Non-ulcer dyspepsia

Hp may protect against...

- GORD, Barrett's, EoE
 - Good data: negative correlation
- Atopic disease / allergy
 - No convincing evidence

Hp – an old companion

- In humans >60,000 yrs
- Part of “normal” gastric flora?
- 90% have no clinical problems
- Possible beneficial effects on the immune system

Cascade to distal gastric cancer



Normal mucosa



Chronic active gastritis



Atrophy



Intestinal metaplasia



Dysplasia



Gastric adeno-ca



Correa. Lancet 1975

Cascade to distal gastric cancer



Normal mucosa



← *H. pylori*

Chronic active gastritis



Atrophy



Intestinal metaplasia



Dysplasia



Gastric adeno-ca



Correa. Lancet 1975

Eradicate Hp to reduce risk of Gastric Cancer?

- Most studies from Asia, suggest some benefit from eradication (relative risk reduction 45%)
 - » Lee. Gastroenterology 2016
- Australia: Different strains, different host genetics
 - Benefit likely smaller than in literature
 - Gastric cancer 1% by age 85 in Australia
 - Some are proximal cancers
 - Absolute benefit very small
- Concerns re cost effectiveness and growing resistance
- To be effective one would have to treat young people, before development of atrophy

Hp and Ulcers

- Hp causes ulcers in $\leq 10\%$ patients
- Risk higher with ASA / NSAIDs
- Eradication reduces risk
- Consider testing before long-term NSAIDs
 - Benefit not as great as of PPI therapy

Hp and GORD

- Eradication has variable effect on GORD symptoms
 - Usually none
 - Can lead to increase or decrease in acid production
- Don't test for Hp in classic GORD symptoms

When to treat Hp

- Once H pylori has been found, eradication should be offered
- The decision is when to look for H pylori
 - Testing is not expensive, but the implications may be

Who to test for H pylori

- History of peptic ulcer
- Long term NSAIDs use and risk factors
- MALT lymphoma, ITP
- Controversial
 - Aspirin users
 - Non-ulcer dyspepsia
 - Eradication of Hp to treat symptoms: NNT=14
 - Long term PPI use
 - Iron deficiency anaemia after negative investigations

Initial Therapy

- Standard therapy:
 - PPI, amoxicillin, clarithromycin
 - Eradication rates 85%
 - Clarithromycin resistance growing
 - Increased by previous macrolide monotherapy
- Metronidazole resistance 50%
 - Despite this, metronidazole can be substituted for amoxicillin in penicillin allergy, with response rate of 80%
 - Can be overcome by high doses (>1500mg / day)

1st line

Amoxicillin
1g BD

Clarithromycin
500mg BD

Omeprazole
20mg BD

7 days

If penicillin sensitive:

Metronidazole
500mg BD

Clarithromycin
500mg BD

Omeprazole
20mg BD

7 days

After treatment

- Check eradication success
- IgG serology may stay positive for years
- Use urea breath test, faecal antigen, or gastric biopsy (if endoscopy for other reasons)
 - >6 weeks after treatment finishes
 - Off PPI / antibiotics for 1-2 weeks
- If still positive – don't try the same again

2nd line

Amoxicillin
1g BD

Clarithromycin
500mg BD

Omeprazole
20mg BD

Bismuth
subcitrate
120mg QID

Amoxicillin
1g BD

Moxifloxacin
400mg daily

Esomeprazole
20mg BD

Bismuth
subcitrate
120mg QID

Furazolidone
200mg QID

Amoxicillin
1g BD

Omeprazole
20mg BD

Bismuth
subcitrate
120mg QID

Tetracycline
200mg QID

Metronidazole
200mg QID

Omeprazole
20mg BD

Culture and sensitivities available

2nd/3rd line

Amoxicillin
1g TDS

Rabeprazole
20mg TDS

10 days

+

Rifabutin
150mg BD

Ciprofloxacin
500mg BD

5 days starting from day 6

If penicillin sensitive:

Rabeprazole
20mg TDS

Ciprofloxacin
500mg BD

Rifabutin
150mg BD

Bismuth
subcitrate
240mg QID

10 days

EOSINOPHILIC OESOPHAGITIS

Eosinophilic Oesophagitis

- Common cause of dysphagia and food bolus
- Non-IgE related allergy
 - Food antigen
 - Elemental diet, elimination diet
- Incidence increasing
 - Hygiene hypothesis
 - Inverse relationship with H pylori
- Male predominance, often young age
- 70% will have other atopic or allergic disease
 - Asthma, atopic dermatitis, hayfever etc

EOE - Presentation

- Childhood: pain, nausea, vomiting
- Adults: dysphagia
- Food bolus obstructions
- Diagnosis delayed several years
 - Slow progression
 - Coping mechanism
- Remodeling
 - Progressive fibrosis
 - Strictures (predictor: duration of disease)
 - Narrow calibre oesophagus



Endoscopic features

- Rings
- Furrows
- Oedema
- White plaques
- Strictures
- Narrow calibre



- Diagnosis only by endoscopy

Histological features

- >15 eosinophils per HPF
- Inflammation involves deep layers too
- Subepithelial fibrosis
- Microabscess formation

EOE - Management

- 50% of patients respond to PPI
- PPI first line for all, continue if it works

EOE - Management

- Swallowed fluticasone (500mcg BD)
 - Not TGA approved
- With small sip of water
- Rinse out mouth
- Candidiasis (asymptomatic)
- Almost universal relapse after stopping
- Safe – first pass effect
- Compliance issues

EOE - Management

- Budesonide 1mg BD
 - Not TGA approved
- Respules (nebulising solution) mixed with artificial sweetener
 - Slurry to coat oesophagus
 - Don't eat or drink for 30 minutes
- Only on authority script for severe chronic asthma
 - Patients have to pay (\$2.50/day)

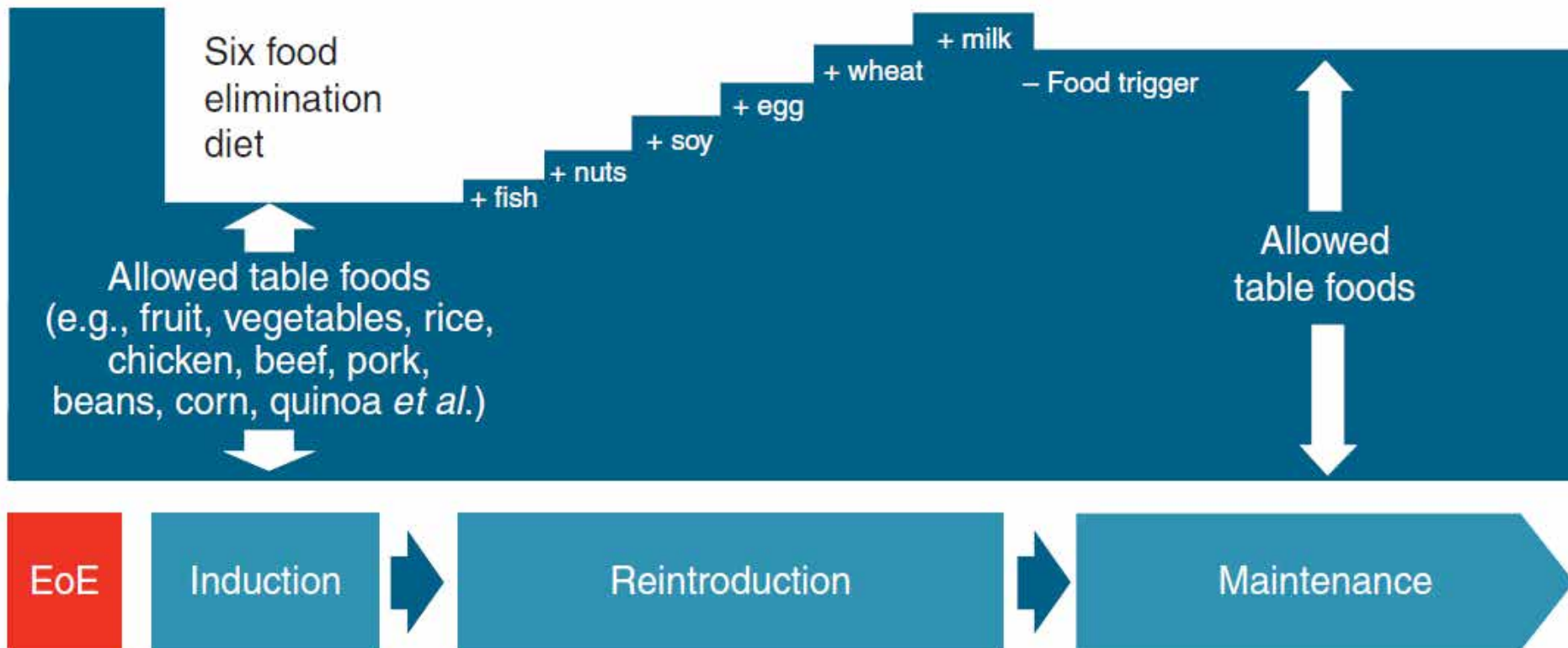
Dilatation in EOE

- Initially unpopular – perforation risk
- Useful for fibrotic strictures
- Does not arrest the inflammation

Dietary manipulation

- Elemental diet (amino acids rather than protein) very high response rate in children
- 6 food elimination diet
 - **Wheat**
 - **Dairy**
 - Nuts
 - Soy
 - Seafood
 - Eggs

6 Food Elimination Diet



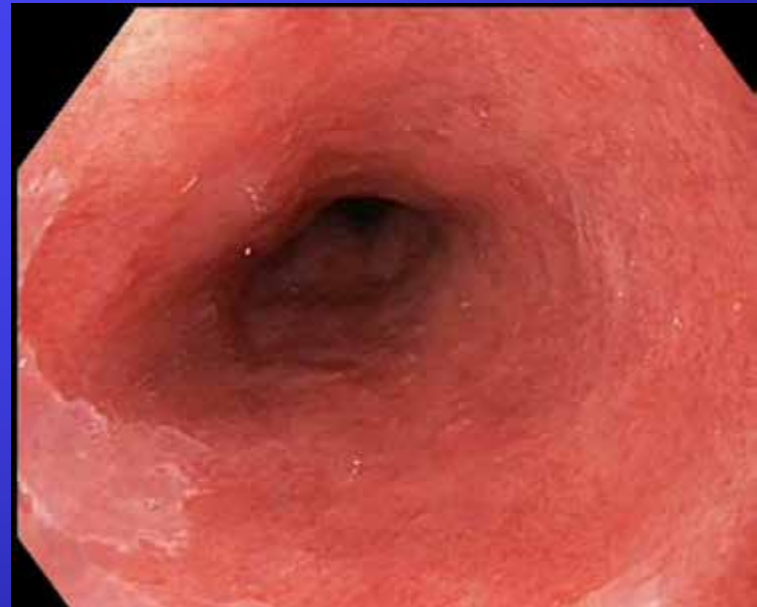
6 Food Elimination Diet

- Long process
 - 1 year, 6 endoscopies + biopsies, multiple dietitian reviews, dietary discipline
- Success rate 60-70% PP
 - ITT much lower
 - Patient's motivation / severity of symptoms
 - Travel distance / interference with pt's work etc
 - Compliance with diet
- Fibrotic strictures need dilatation

BARRETT'S

Barrett's Oesophagus (BO)

- Change of the oesophageal epithelium, from squamous to columnar with intestinal metaplasia



Barrett's Oesophagus (BO)

- Caused by reflux
- Columnar epithelium more resistant to acid
 - Less ulceration
 - Fewer symptoms of reflux
- Predisposes to adeno-carcinoma
 - Absolute risk 0.1% per year
 - Lifetime risk <2%

Barrett's Oesophagus (BO)

- Prevalence unknown, about 1-5%
- Probably rising
 - Adeno-ca incidence increasing
- Risk factors
 - Central obesity
 - Male
 - Older age (>50)
 - Reflux symptoms
 - Hiatus hernia
- Screening in those with multiple risk factors

Management of BO

- PPI for
 - Symptoms
 - Inflammatory changes
 - Chemoprophylaxis (?)
- Fundoplication in selected patients
 - if free reflux / hiatus hernia, poorly responding to PPI
 - Unclear if prevents cancer
- Endoscopic surveillance

Surveillance

- <3cm: repeat endoscopy in 3-5 years
- ≥3cm: repeat endoscopy in 2-3 years

- Low grade dysplasia: repeat in 6 months
- High grade dysplasia: intervention

- Australian Barrett's Guidelines
 - Cancer Council Website

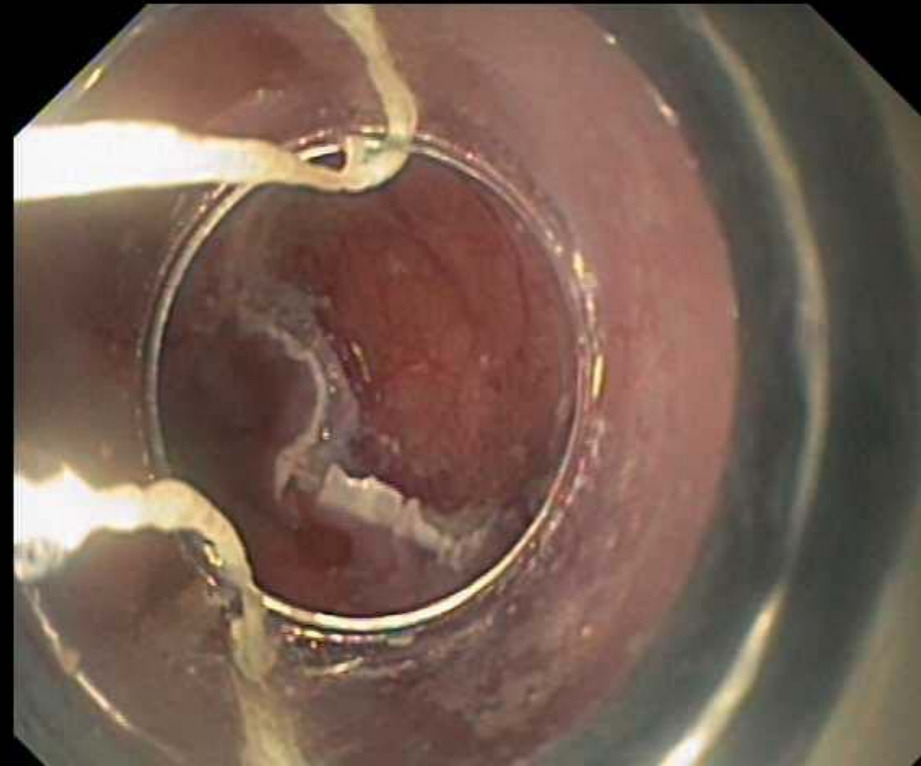
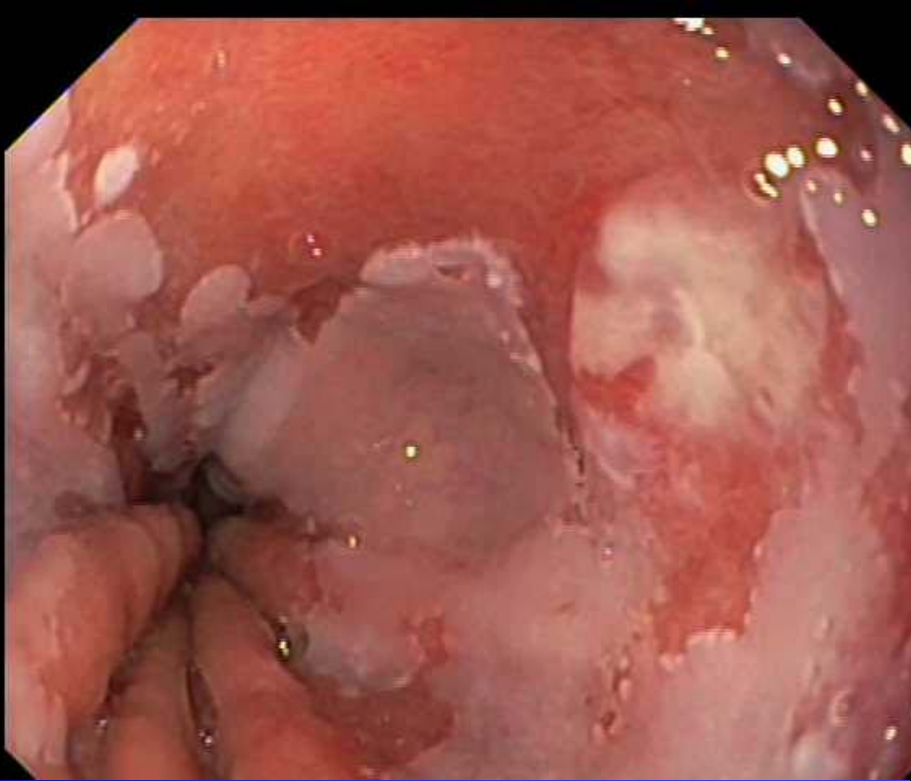
Endoscopic treatment

- To cure
 - dysplasia
 - intramucosal cancer
- Two treatment options:
 - Radiofrequency ablation (RFA): only for flat dysplasia
 - Endoscopic mucosal resection (EMR) – for flat and nodular lesions, cancer
- Tertiary centres only

EMR

- Removing the mucosa is 1-2cm pieces
- Day procedure
- Curative for early cancers
- Small risk of bleeding, perforation, stricture
- Often in combination with RFA

EMR



RFA



- Day procedure
- Expensive
- Approved for HGD, selected LGD
- Burning of the mucosa to a depth of 0.5 to 1mm
- Heals with non-dysplastic squamous mucosa
- Adverse events:
 - Common: Pain, strictures, multiple procedures
 - Uncommon: bleeding, perforation
- Close endoscopic follow up is paramount
 - Every 3-6 months for first 2-3 years, then 6-12 months
- Double dose PPI

Aspirin in Barrett's

- Reduces risk of oesophageal adeno-ca by 40%
- But absolute benefit small
- Give aspirin if other reasons, such as CV risk factors

Thank you!