Professor Richard Gearry

Consultant Gastroenterologist

Christchurch Hospital, Professor of Medicine,
University of Otago, Christchurch

Sunday, August 14, 2016

(Room 6)

8:30 - 9:25 WS #140: A Revolution in Reflux: Tackling the Therapeutic Gap

9:35 - 10:30 WS #150: A Revolution in Reflux: Tackling the Therapeutic Gap (Repeated)

A revolution in reflux

Tackling the therapeutic gap

Richard Gearry

Professor of Medicine, University of Otago, Christchurch

Gastroenterologist, CDHB

Gastroenterologist, Gastroenterology and Endoscopy Specialists

Workshop tools

- Quiz
- Case
- Lecture
- Questions
- Discussion

Key Message Slides

- If it was a late night last night and an early start this morning, feel free to let what I have to say drift over you …..

- I will let you know when we get to the key messages on these slides

Why have I been asked to run this workshop?

- Gastroenterologist (CDHB)
- Gastroenterologist (GAES)
- Professor of Medicine (UOC)

Gastroenterology and Endoscopy Specialists

Gastroenterology and Endoscopy Specialists

- Gastroenterology consultation
- Endoscopy and colonoscopy
- Capsule endoscopy
- Dietitians
- Breath testing for carbohydrate malabsorption
- 24 hour ambulatory oesophageal pH and impedence monitoring

Quiz 1

- How common is reflux?
- Why might GORD be becoming more common?
- What are the two classic reflux symptoms?
- What are UGI alarm symptoms?
- Name 5 extra-oesophageal symptoms of reflux

What is GORD?

- “a condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complications”

Montreal definition

Epidemiology of reflux symptoms / GORD

- Reflux symptom prevalence
  - Europe / North America 11-28%
  - Asia 2-5%
  - Australia 11.6%

- Erosive oesophagitis prevalence (endoscopy)
  - 15.5% (Sweden) 37% of these had no GORS
  - 11.8% (Italy)
  - 6% (China) 12% of those with GORS

Rising rates of reflux

- 50% increase in GORD prevalence in studies pre / post 1995
- Barrett’s oesophagus incidence is increasing
- Oesophageal adenocarcinoma – one of the most rapidly increasing cancers

Rising rates of reflux

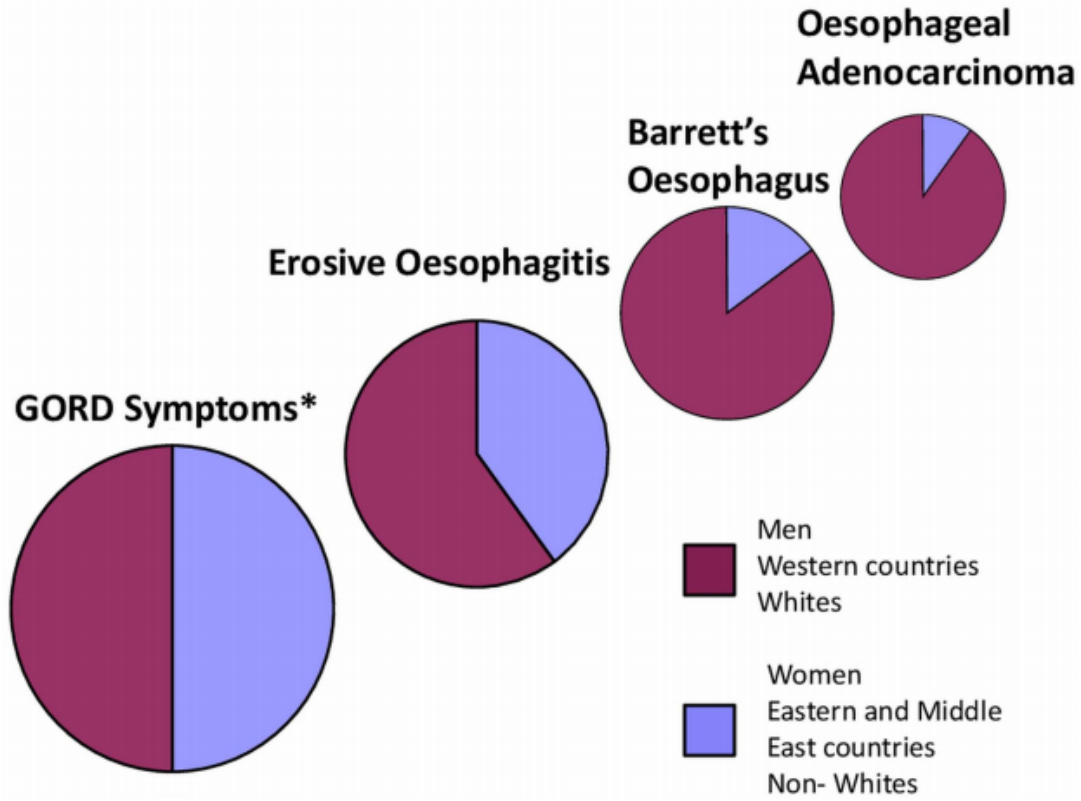
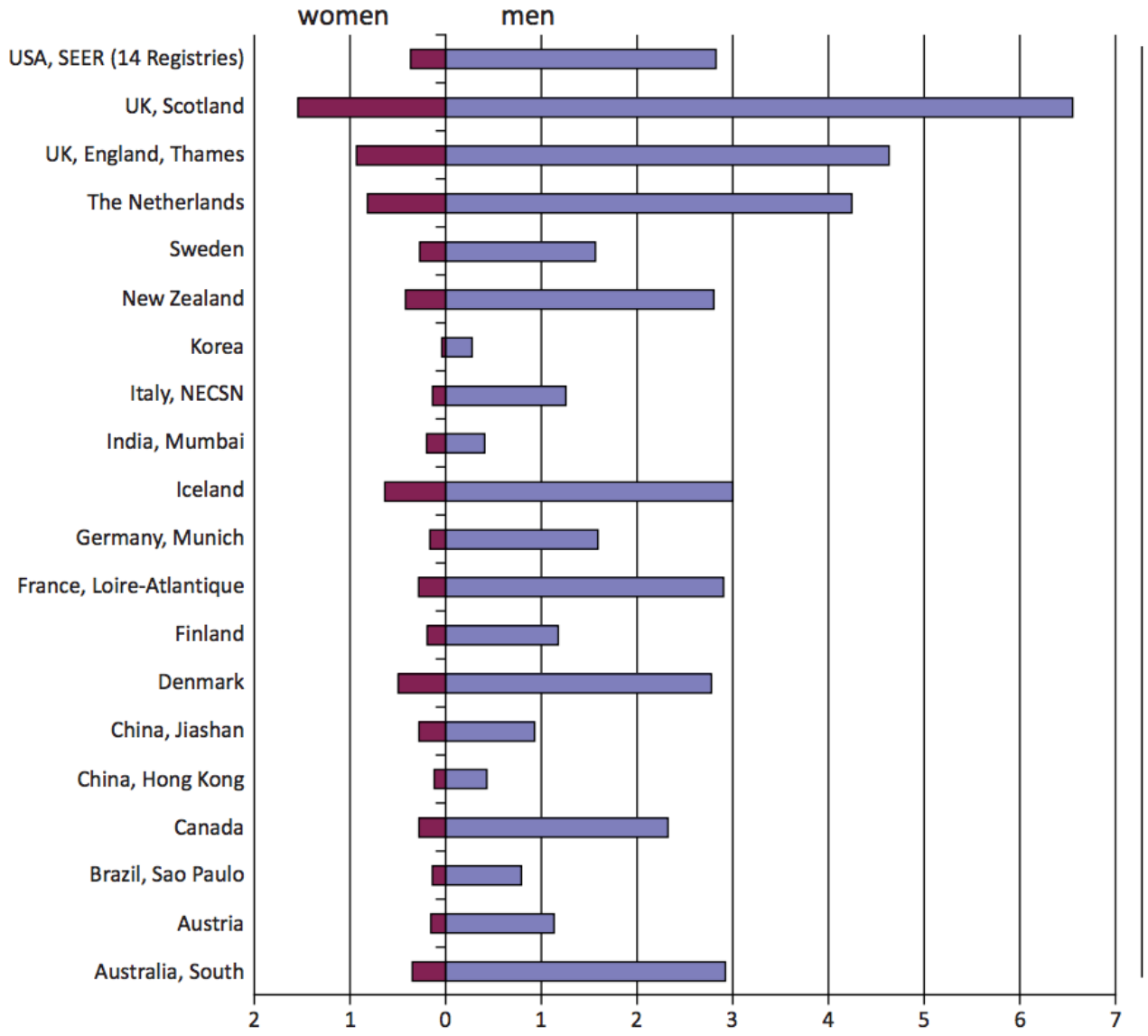


Figure 1 Schematic presentation of epidemiological trends in GORD-related disorders. While typical GERD symptoms are balanced between comparator groups, the distribution of complications becomes progressively skewed in gender, geographic and racial distribution. *GORD symptoms are similar between Western and Middle Eastern countries, but are lower in Eastern countries.

Rising rates of oesophageal cancer



Why more reflux?

- More obesity (especially central)
- Less *Helicobacter pylori* infection
- More GORD in infants / children
- ???

Typical reflux syndrome

- Heartburn
  - translates poorly
  - ~50% will have a positive pH study
  - overlap with functional dyspepsia
- Regurgitation

Upper GI alarm symptoms

- Dysphagia / odynophagia
- Unexplained weight loss
- Unexplained iron deficiency anaemia
- Haematemesis or melaena
- Abdominal mass
- Persistent / protracted vomiting
- New / worsening symptoms >50 years age

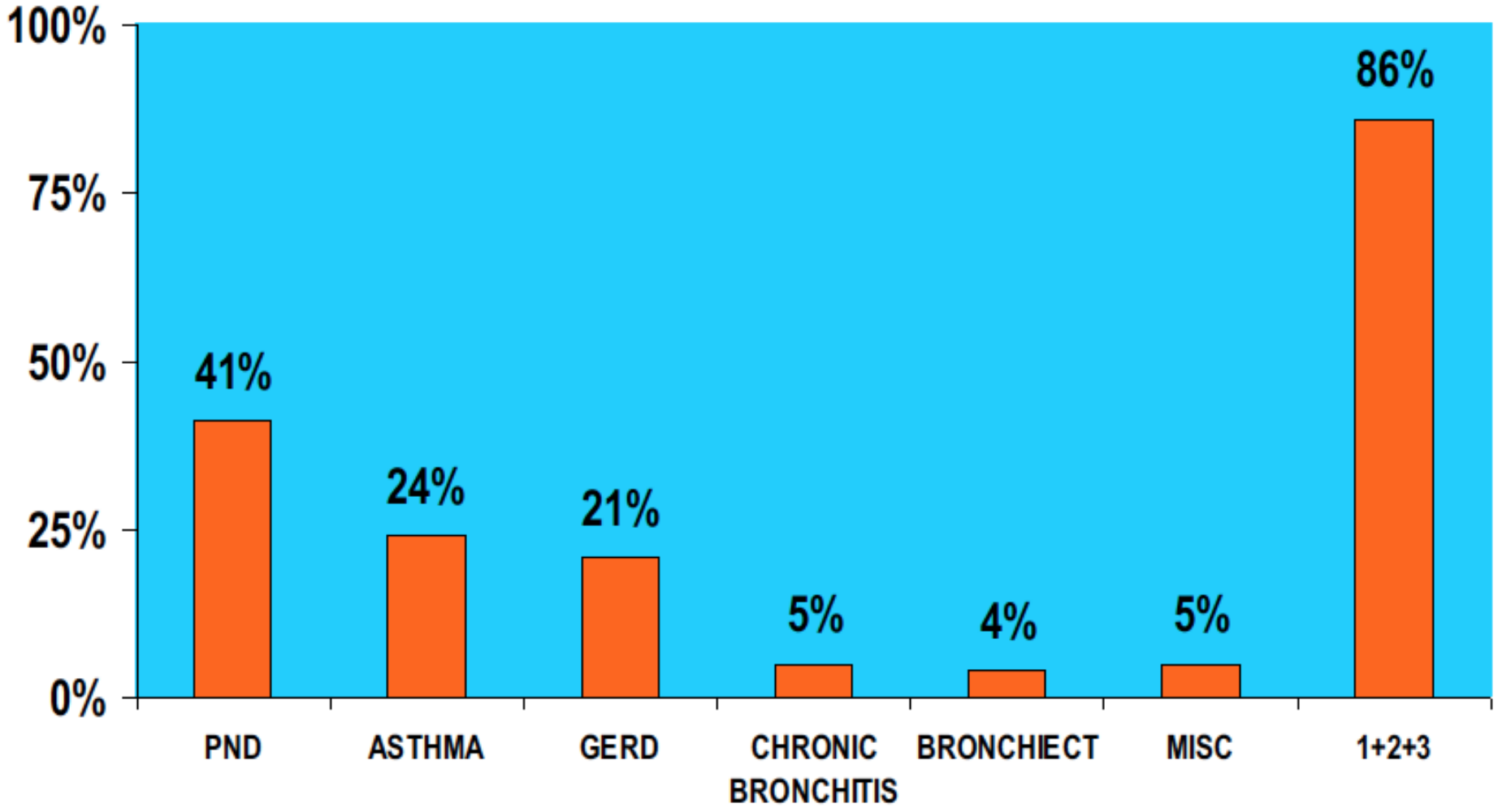
Extra-oesophageal symptoms

- 1/3 patients with GORD may have extra-oesophageal symptoms (EOS)

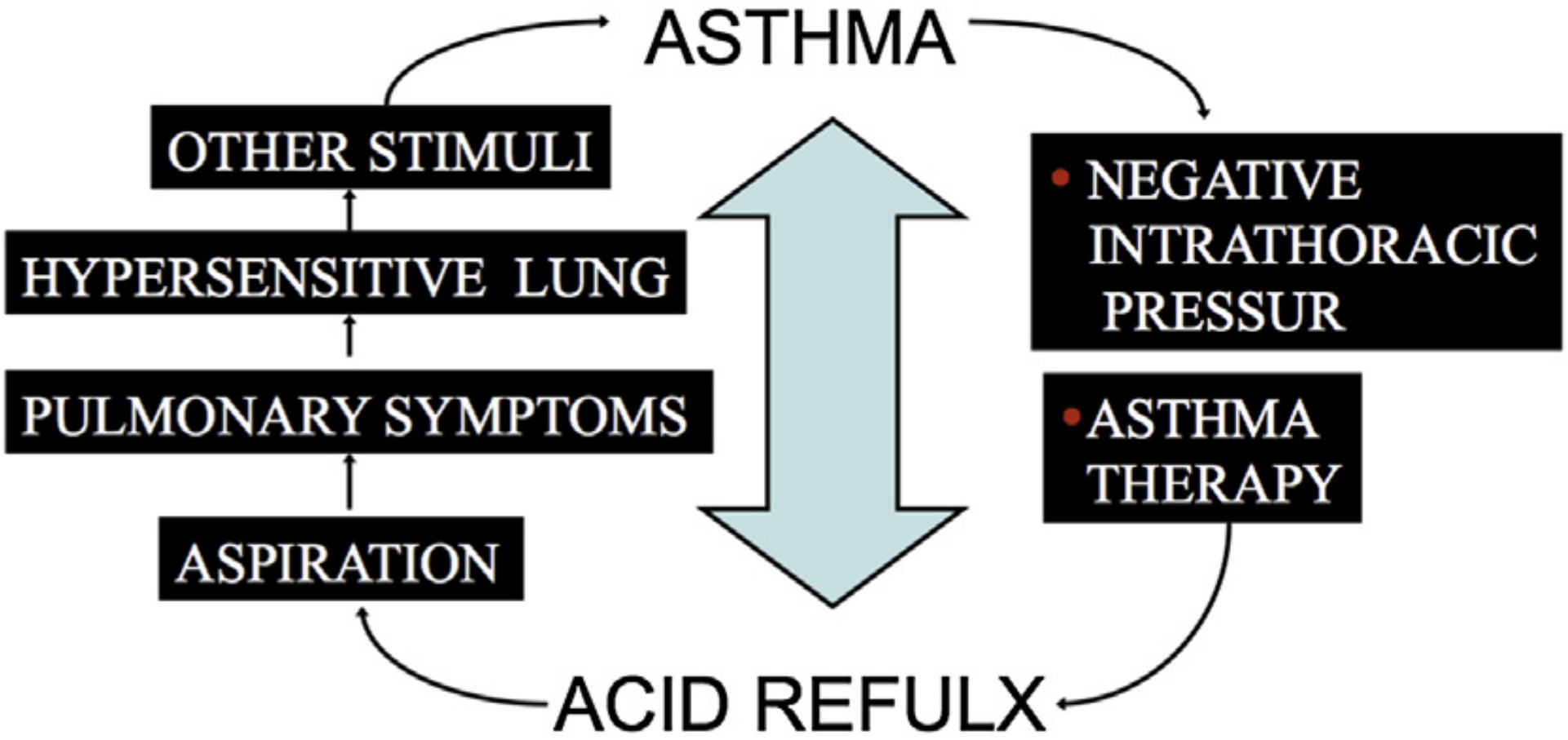
Extra-oesophageal symptom	Prevalence (%)
Chest pain	14.5%
Chronic cough	13%
Laryngeal disorders	10.4%
Asthma	4.8%
Dental erosions	20%

- Many patients with EOS do not have typical GORD symptoms

GORD - a common cause of chronic cough

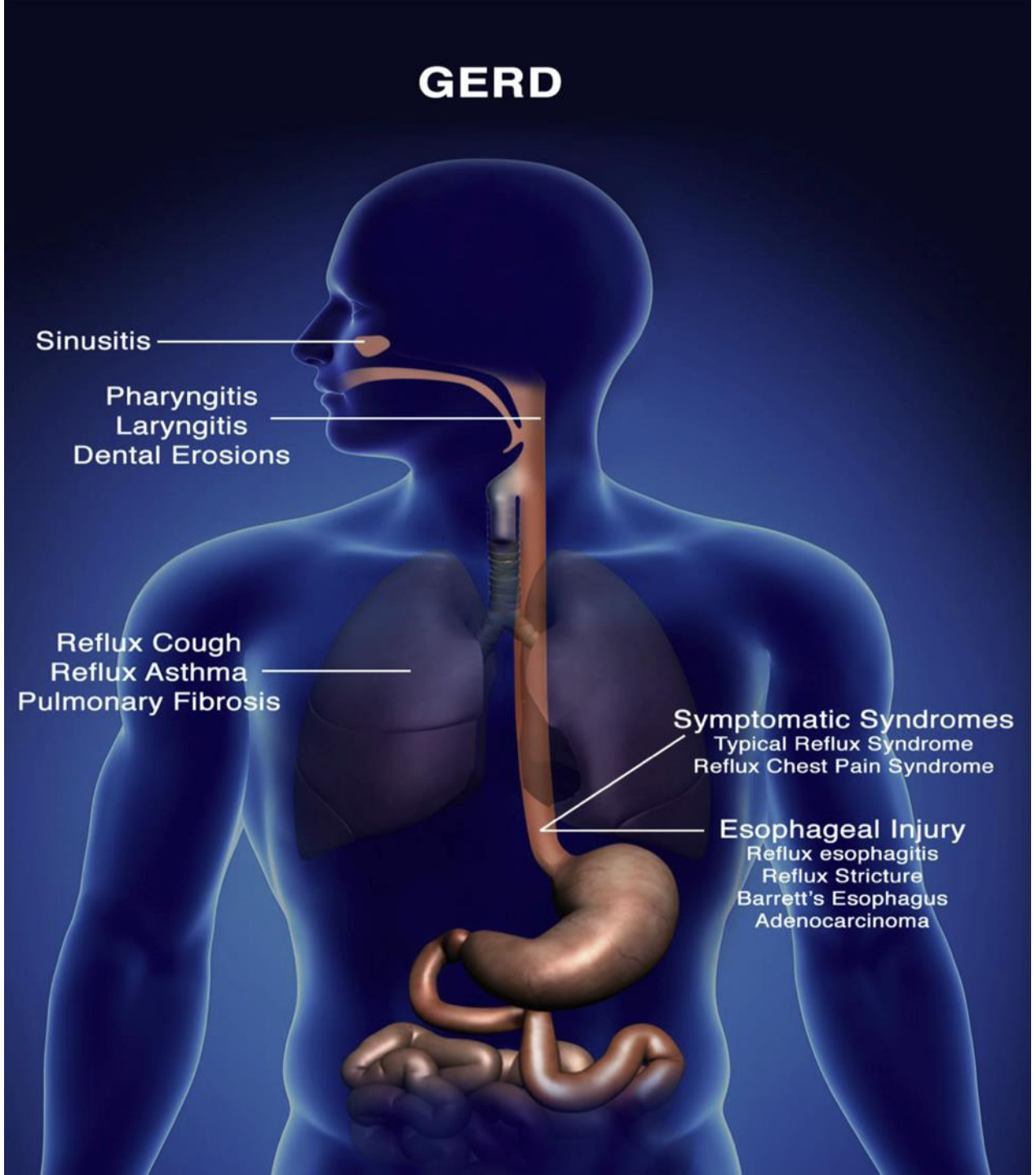


Asthma and GORD



Symptoms associated with GORD-laryngitis

- Hoarseness
- Dysphonia
- Sore / burning throat
- Excessive throat clearing
- Chronic cough
- Globus
- Apnoea
- Laryngospasm
- Dysphagia
- Post-nasal drip
- Neoplasm


GERD
Sinusitis
Pharyngitis
Laryngitis
Dental Erosions
Reflux Cough
Reflux Asthma
Pulmonary Fibrosis
Symptomatic Syndromes
Typical Reflux Syndrome
Reflux Chest Pain Syndrome
Esophageal Injury
Reflux esophagitis
Reflux Stricture
Barrett's Esophagus
Adenocarcinoma

Remember dyspepsia is not GORD

- Dyspepsia
  - post prandial fullness
  - bloating
  - Belching
  - early satiety
  - anorexia
  - nausea

Episodic

Recurrent

Chronic

Most people with dyspepsia do not have underlying pathology, may not seek medical attention and will not require investigation

Key messages

- There is a lot of GORD out there – think carefully about how patients present …
- Typical GORD symptoms
- Atypical GORD symptoms
- Extra-oesophageal symptoms
- Alarm symptoms

Heartburn and regurgitation

Cough, laryngitis, asthma, dental erosions

Dysphagia, wt loss, GI bleeding, abdo mass, ongoing vomiting, age > 50 years

Case 1

- 54 year old Caucasian male
- BMI 30, smoker, moderate alcohol

- Complains of 6 years of increasing
  - Acid regurgitation / heartburn
  - Nocturnal cough
  - antacid use most days

What are the issues to deal with?

Quiz 2

- What is the underlying pathogenesis of GORD?
- What is (a) NERD?
- Are hiatus hernias important in reflux?
- How common are functional disorders of the upper GI tract?

How does reflux cause symptoms?

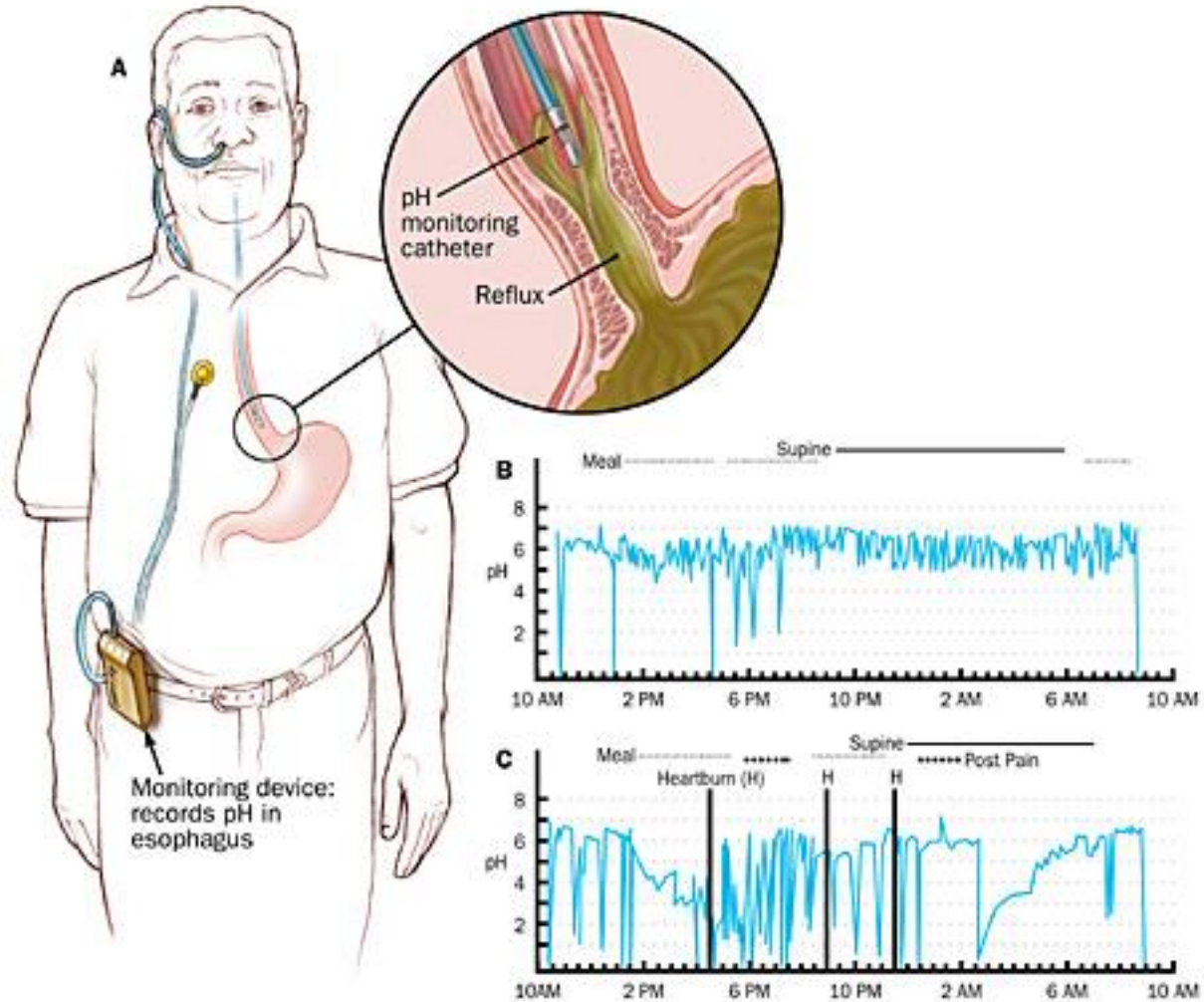
- Everyone refluxes, some people have symptoms
- Discrepancy between acid exposure / symptoms

- Mechanical factors
- Altered oesophageal sensitivity

Sub-types of reflux

- How to classify reflux?
- Endoscopy
  - oesophagitis (LA classification)
  - Normal
    - NERD (non-erosive reflux disease)
    - Hypersensitive oesophagus
    - Functional heartburn
- 24H pH study / 24 hour pH-impedance study
  - number of episodes or duration of exposure

24 hour oesophageal pH study



Characteristics of GORS subtypes

	Endoscopy	pH study	pH/impedance	PPI response
Reflux oesophagitis	Oesophagitis	Positive off PPI	Positive on or off PPI	Good
Non-erpsove reflux disease (NERD)	Normal (possible subtle signs on biopsy)	Sometimes positive	Always positive	Variable
Hypersensitive oesophagus	Normal	Normal acid exposure but clear association of symptoms with reflux events	Normal acid exposure but clear association of symptoms with reflux events	Variable
Functional Heartburn	Normal	Negative	Negative	Negative

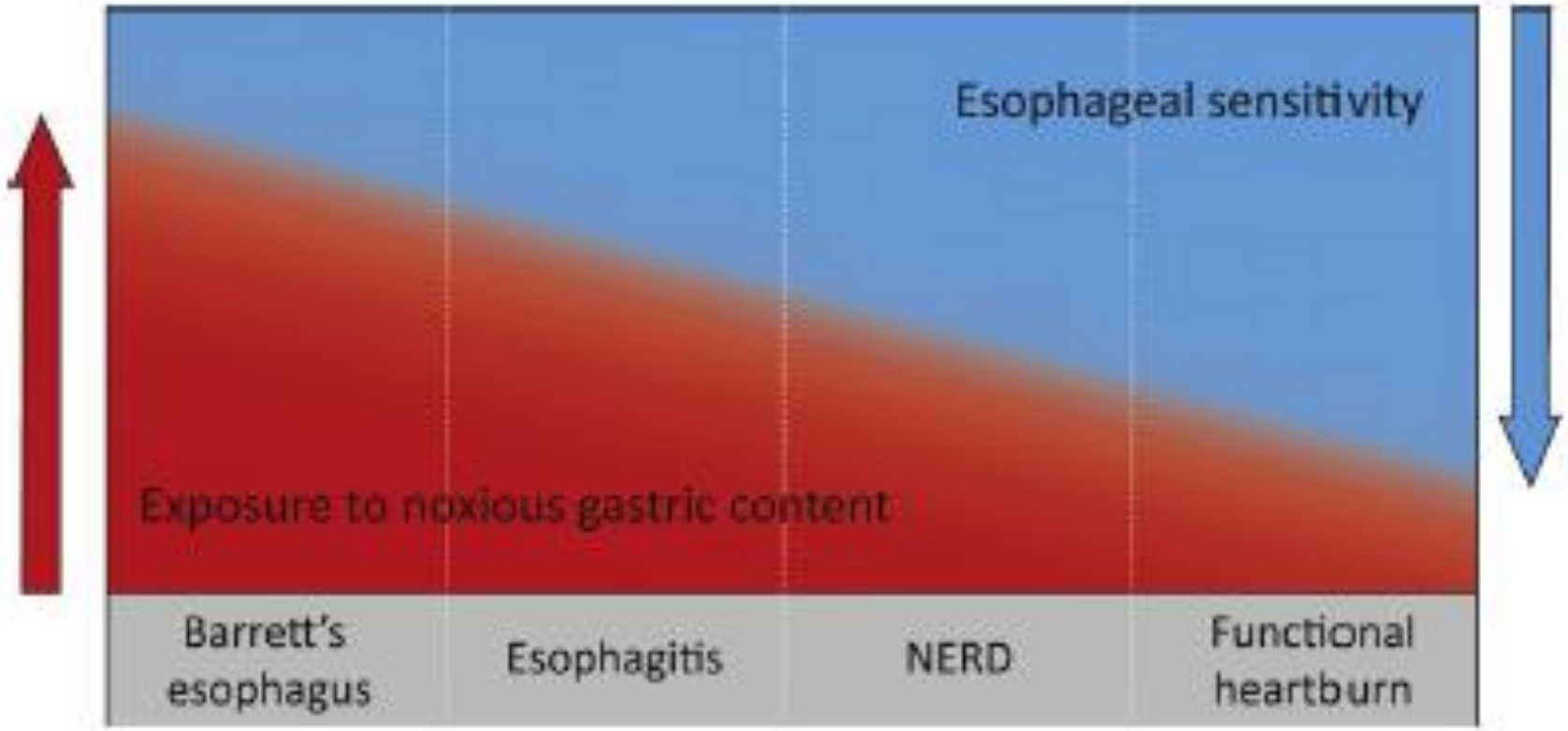
Functional oesophageal disease

- Functional chest pain
- Functional heart burn
- Reflux hypersensitivity
- Globus
- Functional dysphagia

Functional heartburn

- 6 months of symptoms with criteria fulfilled for the last 3 months
- Frequency of ≥2X/week with all of:
  - burning retrosternal discomfort or pain
  - no symptom relief with optimal PPI
  - normal pH / impedance study, no EosOes
  - absence of oesophageal motor disorders

Interaction between refluxate and oesophageal sensitivity



How does reflux cause symptoms?

Oesophageal characteristics / hypersensitivity

Peripheral sensitization

Central sensitization

Mucosal barrier function

Sustained oesophageal contractions

Psychological factors

Genetic factors

Reflux characteristics

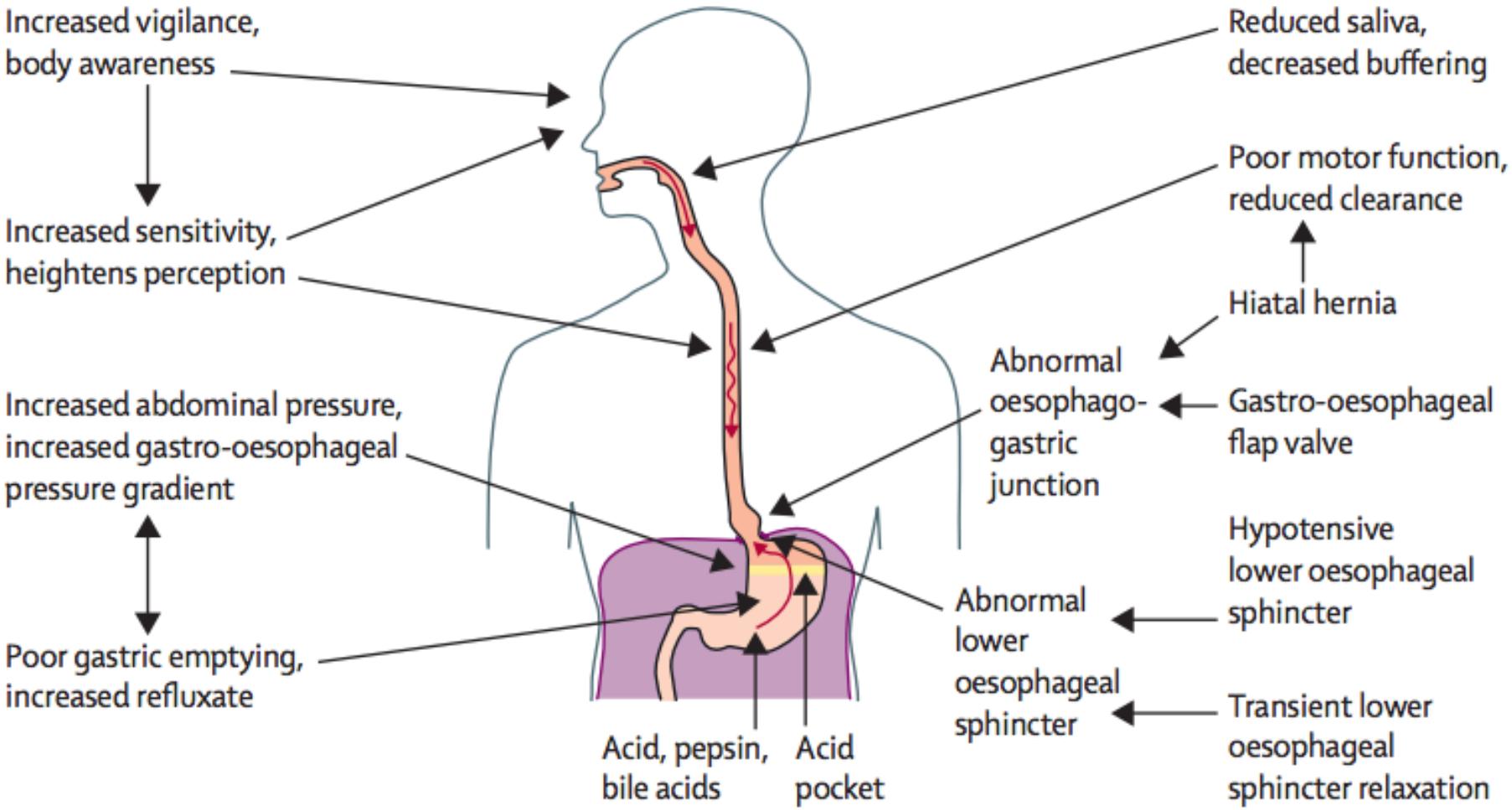
Acidity

Duodenogastric-oesophageal reflux / pepsin

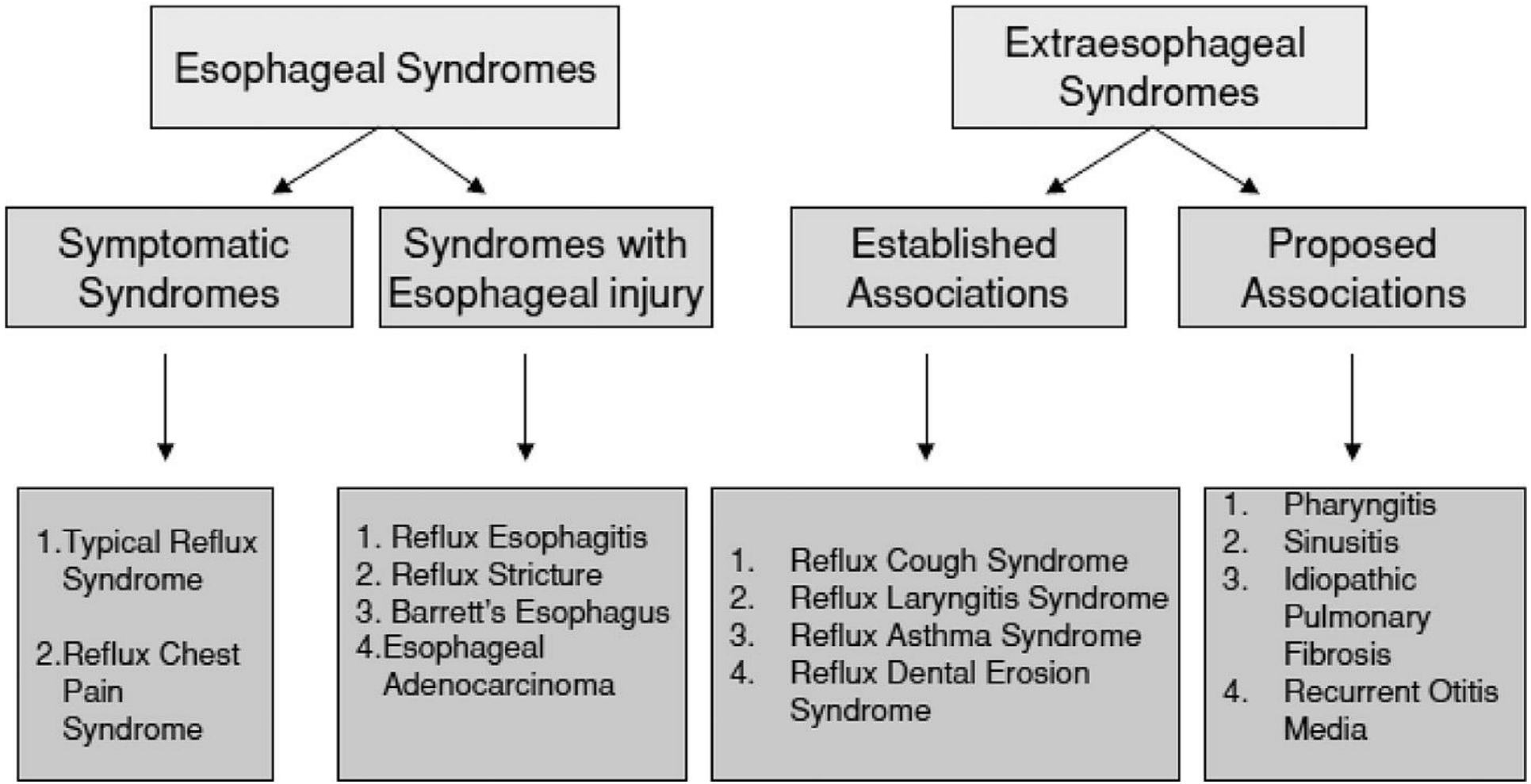
Gas reflux

Proximal extent

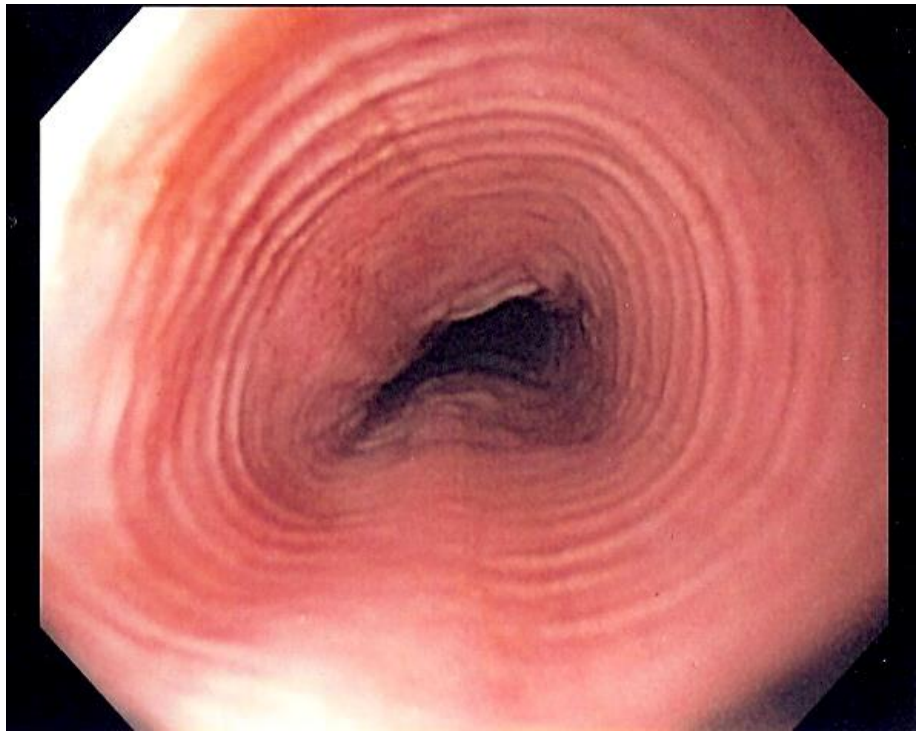
Pathogenesis of GORD



GERD is a condition which develops when the reflux of gastric content causes troublesome symptoms or complications



Eosinophilic oesophagitis

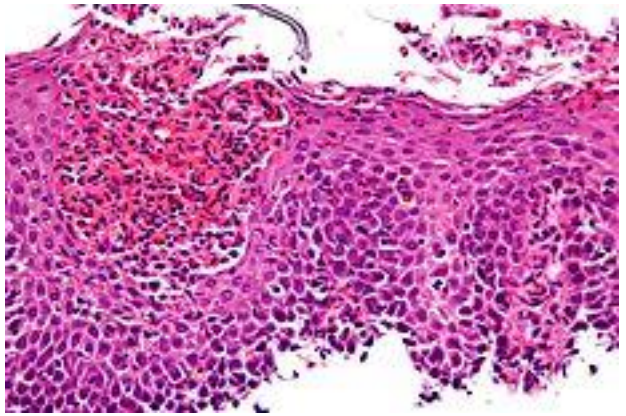


Typically …..

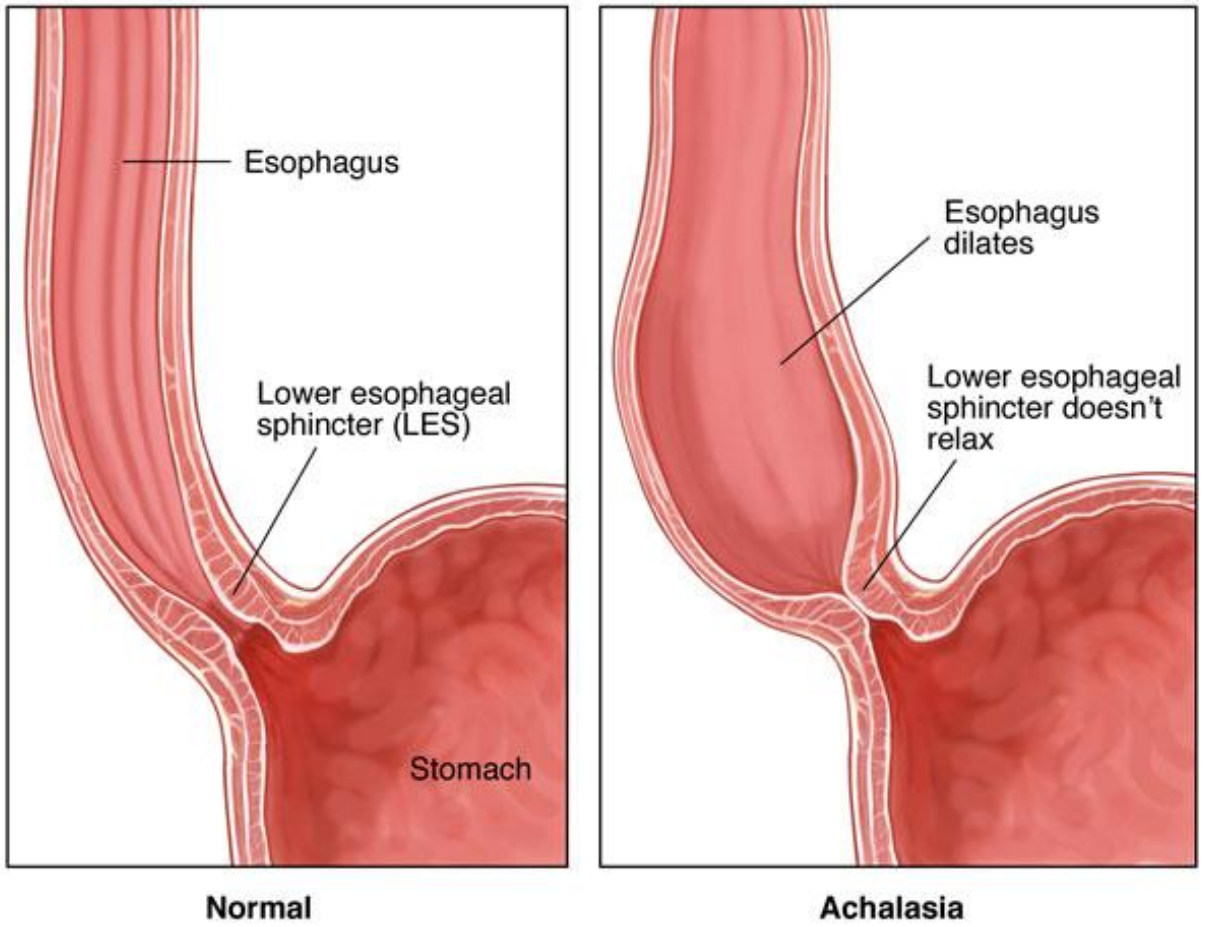
Young males

History of atopy / asthma

Recurrent dysphagia / food bolus obtruction



Achalasia



Esophageal Achalasia

Case

- 26 year old woman
- 12 months of intermittent regurgitation and heartburn, atypical chest pains
- Normal gastroscopy – “no evidence of reflux oesophagitis”
- Partial response to PPI

Where to from here?

Key Messages

- Most people who reflux will not have erosive oesophagitis
- NERD / functional heartburn comprise most patients
- The pathogenesis of GORD is complex
  - multiple targets for therapy
- Eosinophilic oesophagitis is also becoming more common

Quiz 3

- How do we diagnose GORD
- What investigations are required for GORD?
- Which is the most useful test for GORD

Investigation-based testing of GORD

- Endoscopy
- 24 hour pH / impedance study
- The PPI test

Endoscopy

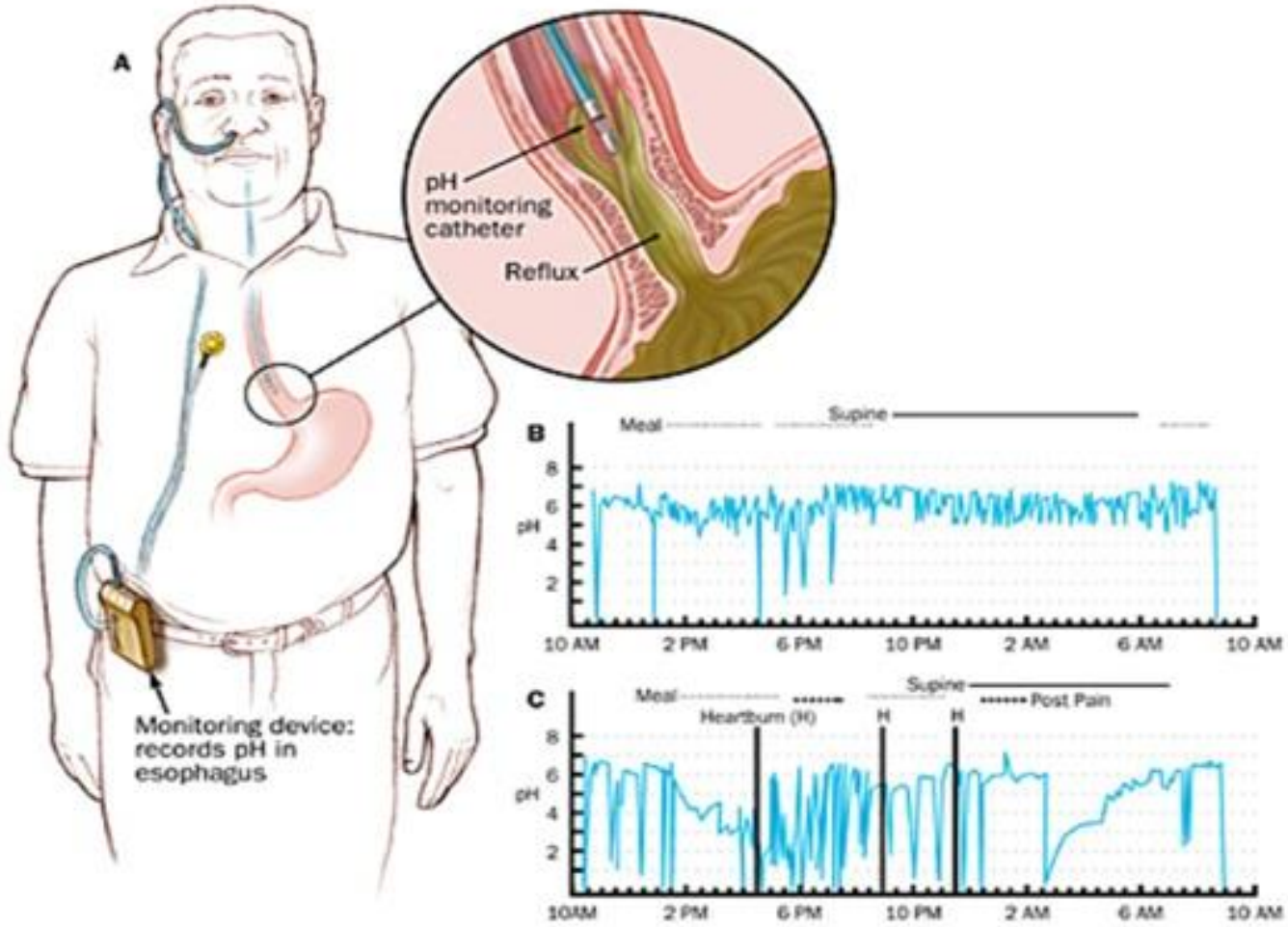
- In primary care 50% of patients with GORD symptoms have a normal endoscopy

- Expensive and invasive

What is the role of endoscopy in GORD management?

- Eosophageal symptoms unresponsive to PPI
  - make a positive diagnosis of / rule out GORD
  - diagnose / rule out another oesophageal condition
- Extra-oesophageal symptoms
  - diagnosing or ruling out GORD
- Prolonged GORD / alarm features
  - diagnose / rule out GORD injury syndromes
    - stricture, erosions, Barrett's, adenocarcinoma

pH testing


A
pH monitoring catheter
Reflux
Monitoring device: records pH in esophagus
B
Meal
Supine
pH
8
6
4
2
10 AM
2 PM
6 PM
10 PM
2 AM
6 AM
10 AM
C
Meal
Supine
Heartburn (H)
Post Pain
H
H
pH
8
6
4
2
10AM
2 PM
6 PM
10 PM
2 AM
6 AM
10 AM

pH / impedance testing

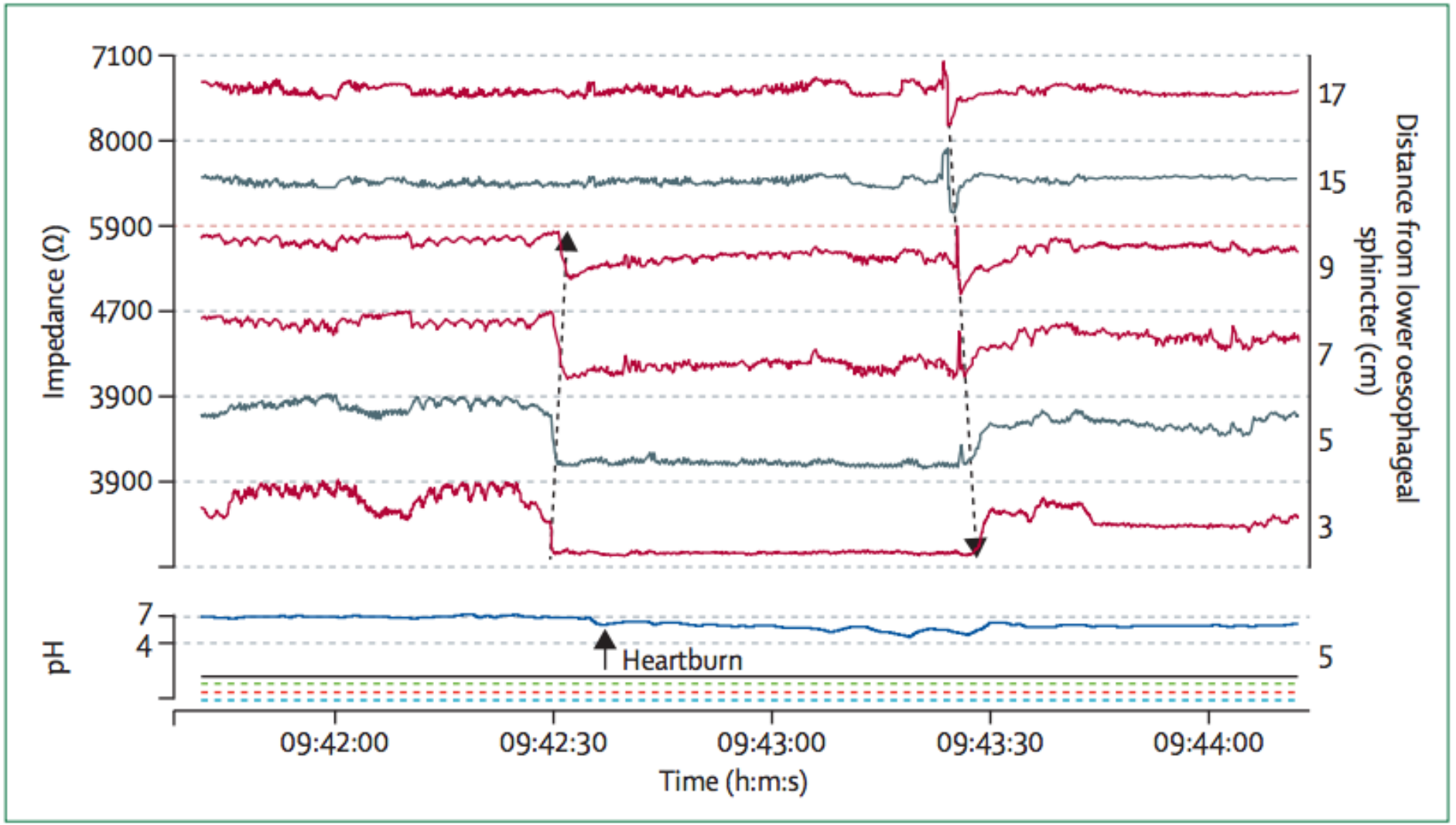


Figure 5: **Combined pH and impedance monitoring to identify non-acid reflux**

Case

- 45 year old male
- Typical reflux symptoms
- Controlled with prn PPI
- Now a change in symptoms
  - atypical pain
  - cough despite PPI

Where to from here?

Quiz

- What lifestyle modifications are effective for GORD?
- What drugs make GORD worse?
- Why do H2RAs not work as well as PPIs?
- Which PPI is most likely to interact with other drugs?

Management of reflux-related symptoms

- Goals of therapy:
  - symptom relief
  - heal the oesophagus
  - prevent long-term complications
    - Barrett's, stricture, adenocarcimona

- Induction and then maintenance of symptom control

What are the targets of therapy?

- GORD has multiple aetiologies
  - lower oesophageal sphincter dysfunction
- Noxious refluxate causes most symptoms
- Primary target is making refluxate less noxious
  - PPI therapy

- Other targets
  - enhancing oesophageal clearance
  - promoting gastric emptying
  - providing mucosal protection
  - decreasing tissue hypersensitivity

Lifestyle modifications

	↓ LOS pressure	↓ oesophageal pH	Modification leads to ↓ GORD symptoms
Smoking	✓	✓	
Coffee	✓		
Chocolate	✓	✓	
Alcohol		✓	
Carbonated beverages	✓		
Fatty food		✓	
Right lateral decubitus	✓		
Elevating head of the bed		✓	✓
Targeted weight loss			✓
Abdominal breathing			✓

Review of drugs associated with GORD

- NSAIDs
- steroids
- calcium channel antagonists
- nitrates
- theophyllines
- bisphosphonates

Medical management of GORD

- Acid suppression
- TLOSR inhibitors
- Increasing oesophageal clearance
- Improving visceral hypersensitivity
- Mucosal protection
- Mucosal healing

Acid suppression

- Antacids
- H2 receptor antagonists
- Proton pump inhibitors

Antacids

- Aluminium hydroxide
- Magnesium hydroxide

- Sodium bicarbonate

- Calcium containing compounds
- Simeticone
- Alginate / raft-forming compounds

Rapid

No role in healing

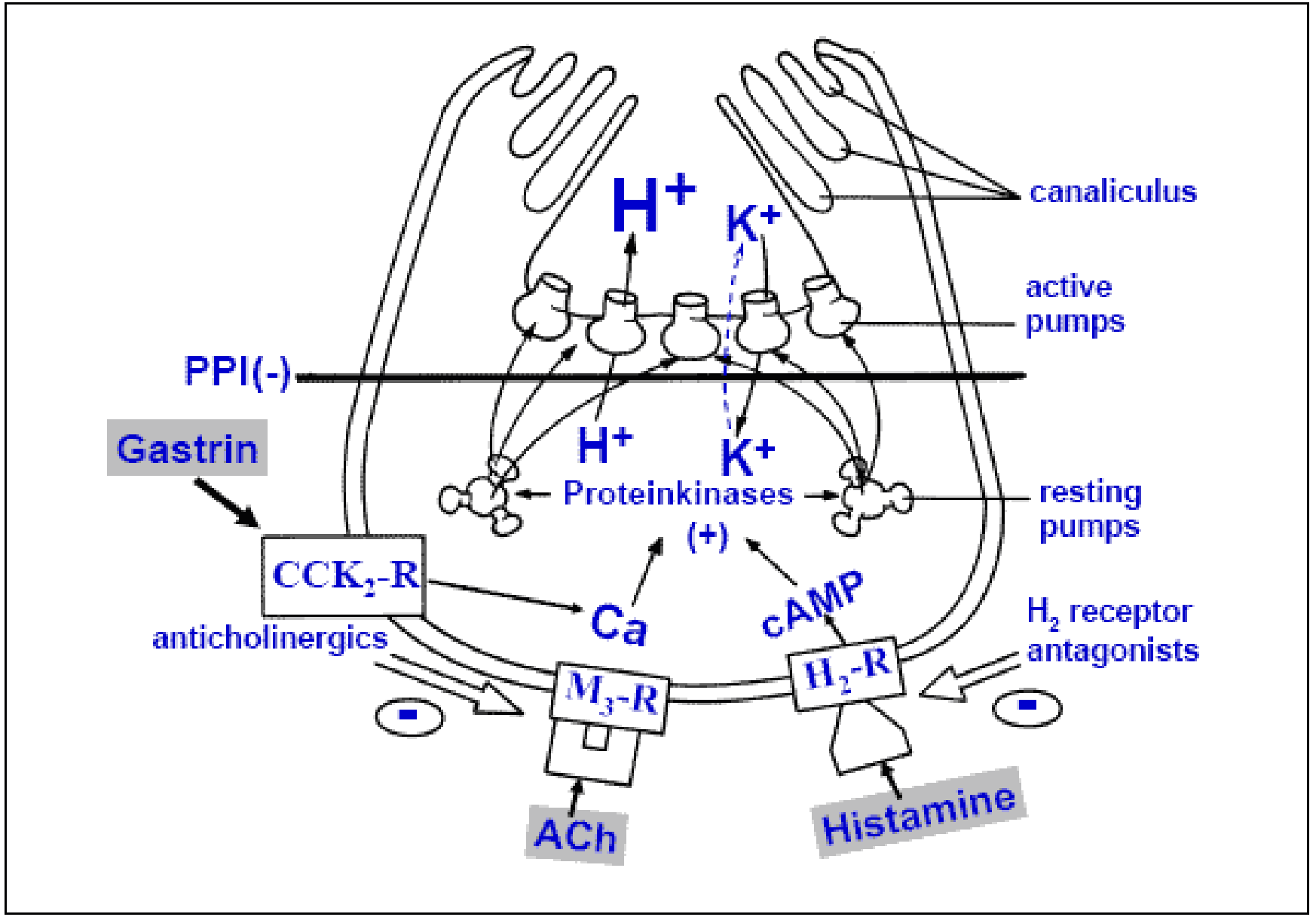
Mild or break-though symptoms

Other GI side effects

Recent study of NERD patients PPI+alginate better than PPI alone (57% v 27%, $p<0.005$)

H2 Receptor Antagonists

- Cimetidine
- Famotidine
- Ranitidine
- Better for GI-II (80%) than III-IV (30-50%) oesophagitis
- Safe and cheap but ADRs, tachyphylaxis, interactions
- Effective in addition to PPI for nocturnal reflux


H+
K+
canaliculus
active
pumps
PPI(-)
H+
K+
Gastrin
Proteinkinases
(+)
resting
pumps
CCK2-R
Ca
cAMP
H2 receptor
antagonists
anticholinergics
M3-R
H2-R
ACh
Histamine

Proton Pump Inhibitors

- Most effective class for acid suppression
- Cornerstone of GORD therapy
  - Symptom relief
  - Mucosal healing
  - Prevent long-term complications

PPIs available in NZ

	Omeprazole	Pantoprazole	Lansoprazole
Formulation	20 / 40mg caps	20 / 40mg caps	15 / 30 mg caps
Bioavailability	Variable	Constant	Constant
Food effect on absorption	Minimal	Minimal	Delayed absorption
Cytochrome P450 metabolism	Mostly 2C19	Low P450 affinity	Lower P450 affinity
Drug interactions	Phenytoin, warfarin, carbemazepine, diazepam …	No p450 interactions	Minimal P450 interactions

PPI fast facts

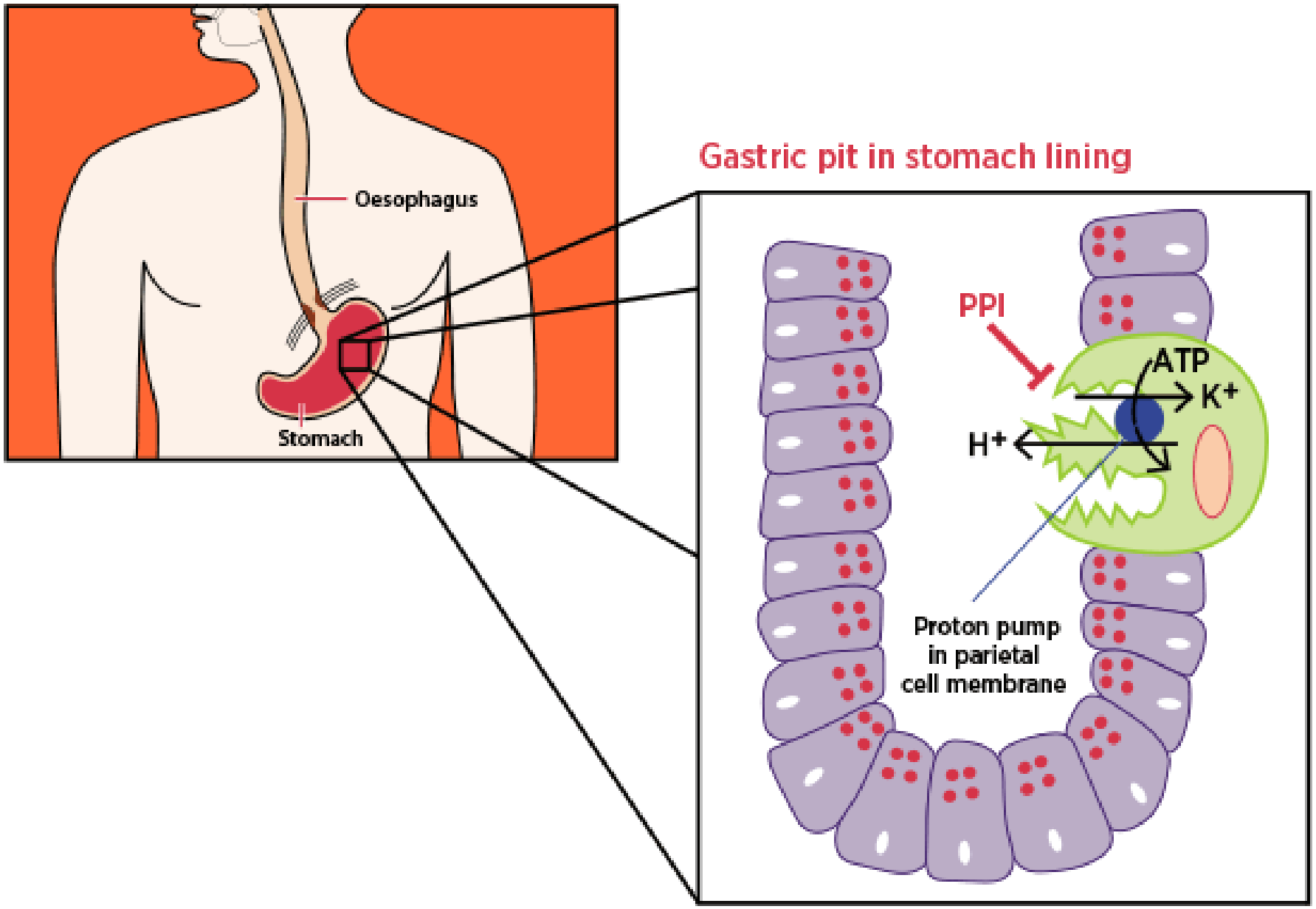
- Irreversibly binds H/K ATPase on parietal cell
- Pro-drugs – activated in secretory canaliculus
- All are enteric coated (acid labile)
- Short half life 1-1.5 hours
- Maximal acid suppression >5 days
- Acid suppression optimised when PPI taken with meal-stimulated acid secretion

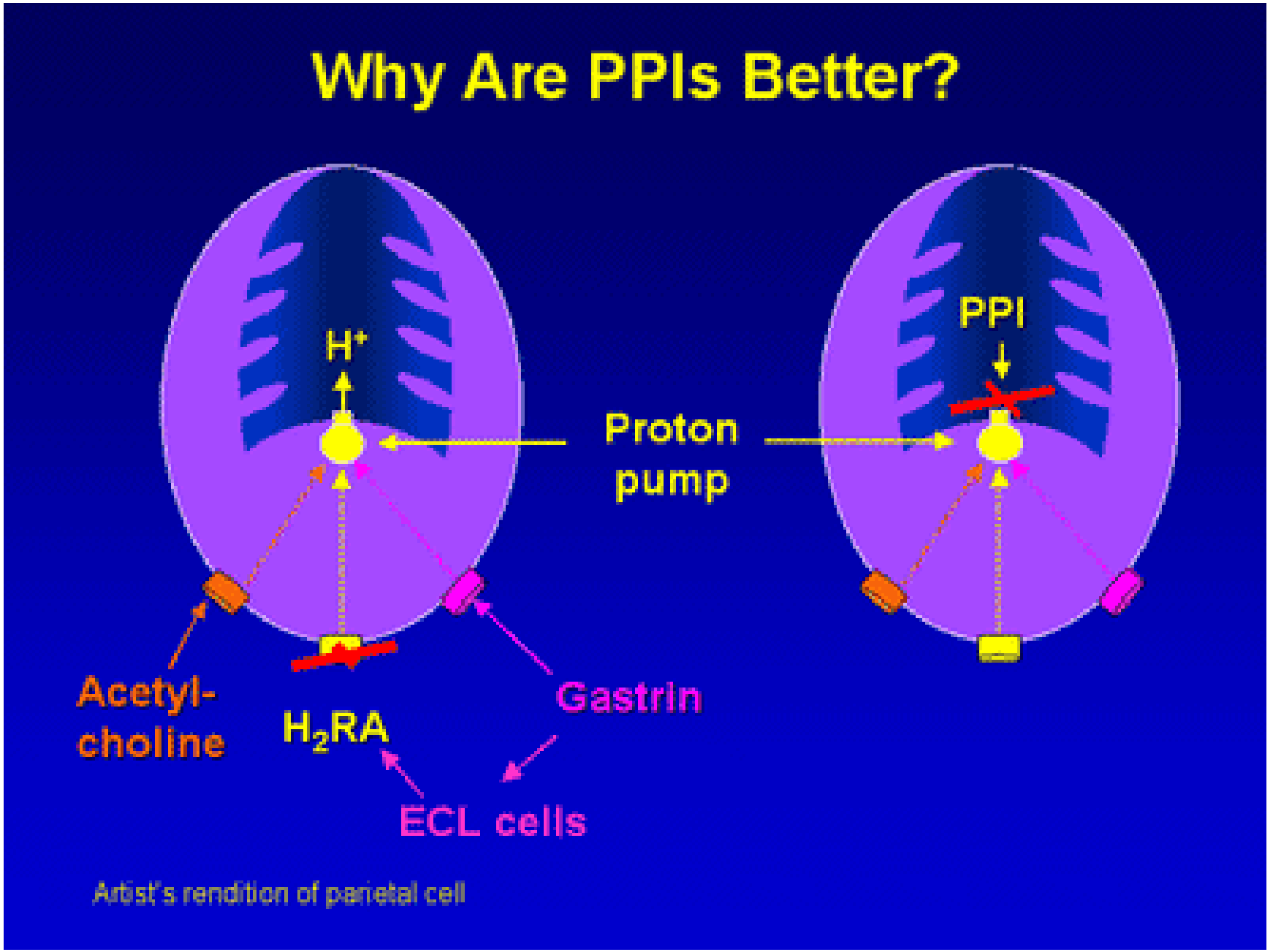
PPI /Reflux fast facts

- Oesophagitis
  - efficacy is associated with longer ↑ gastric pH
  - double dose PPI has an additive effect
  - all Grade B/C patients relapse on PPI cessation
- NERD
  - PPI is superior to H2RA and prokinetic
  - 2/3 of NERD patients relapse on PPI cessation
  - intermittent PPI may be as good as continuous PPI
- Barrett's oesophagus
  - PPIs reduce the risk of dysplasia

Timing of PPIs

- Acid suppression optimised when PPI taken with meal-stimulated acid secretion
- Best consumed 30-60 minutes before the first meal of the day
  - Recommended by only 30% of physicians
  - Adhered to by <10% of patients


Oesophagus
Stomach
Gastric pit in stomach lining
PPI
ATP
K+
H+
Proton pump
in parietal
cell membrane


Why Are PPIs Better?
H+
PPI
Proton pump
Acetyl-choline
H2RA
Gastrin
ECL cells
Artist's rendition of parietal cell

Transient Lower Oesophageal Sphincter Relaxation Inhibitors

- Persistent reflux despite PPI is a big problem
  - 16% GORD patients on BD PPI
  - >50% GORD patients have reflux symptoms on PPI
- Baclofen
  - 60% reduction in TLOSRs
  - increases basal LOS pressure
  - reduces acid, weak acid and bile reflux
  - Poorly tolerated, multiple dosing (5-20mg tds)

Improving oesophageal clearance

- Prokinetics
  - inferior to PPI as monotherapy
  - given with PPI in those with gastric dysmotility
- Macrolides
  - erythromycin and azithromycin have shown efficacy physiologically and clinically for those with GORD

Reducing visceral hypersensitivity

- Some efficacy for antidepressants in reducing visceral pain and hypersensitivity

Pain modulation in functional oesophageal disorders

Table 2. Pain Modulators for the Treatment of Functional Esophageal Disorders

Class of drug	Dose	Disorder	RCT	Side effects	Response
TCAs					
Imipramine	50 mg/day	NCCP	+	+/-	57%
Amitriptyline	10–20 mg/day	NCCP, globus	+	+/-	52%
SSRIs					
Sertraline	50–200 mg/day	NCCP	+	+	57%
Paroxetine	50–75 mg/day	NCCP	+	+/-	Modest
Citalopram	20 mg/day	ES	+	+/-	Significant
Trazodone					
Vs clomipramine	50/25 mg/day	NCCP	-	+	Modest
Trazodone alone	100–150 mg/day	dysmotility	+	+/-	29%–41%
SNRIs					
Venlafaxine	75 mg/day	NCCP	+	++	52%
Other					
Theophylline	200 mg twice/day	NCCP	+	+/-	58%
Gabapentin	300 mg 3 times/day	globus	+	+/-	66%

ES, esophageal hypersensitivity; RCT, randomized control trial; SNRI, serotonin norepinephrine reuptake inhibitor.

Mucosal protection

- Sucralfate
  - binds to inflamed mucosa and reduces acid exposure and promotes healing in oesophagitis
  - Heals mild erosive oesophagitis and NERD
  - Multiple dosing
  - Safe in pregnancy

Case

- 34 year old woman
- heartburn for 5 years intermittently
- Normal gastroscopy
- Normal 24 hour pH study
- responds partially to PPI

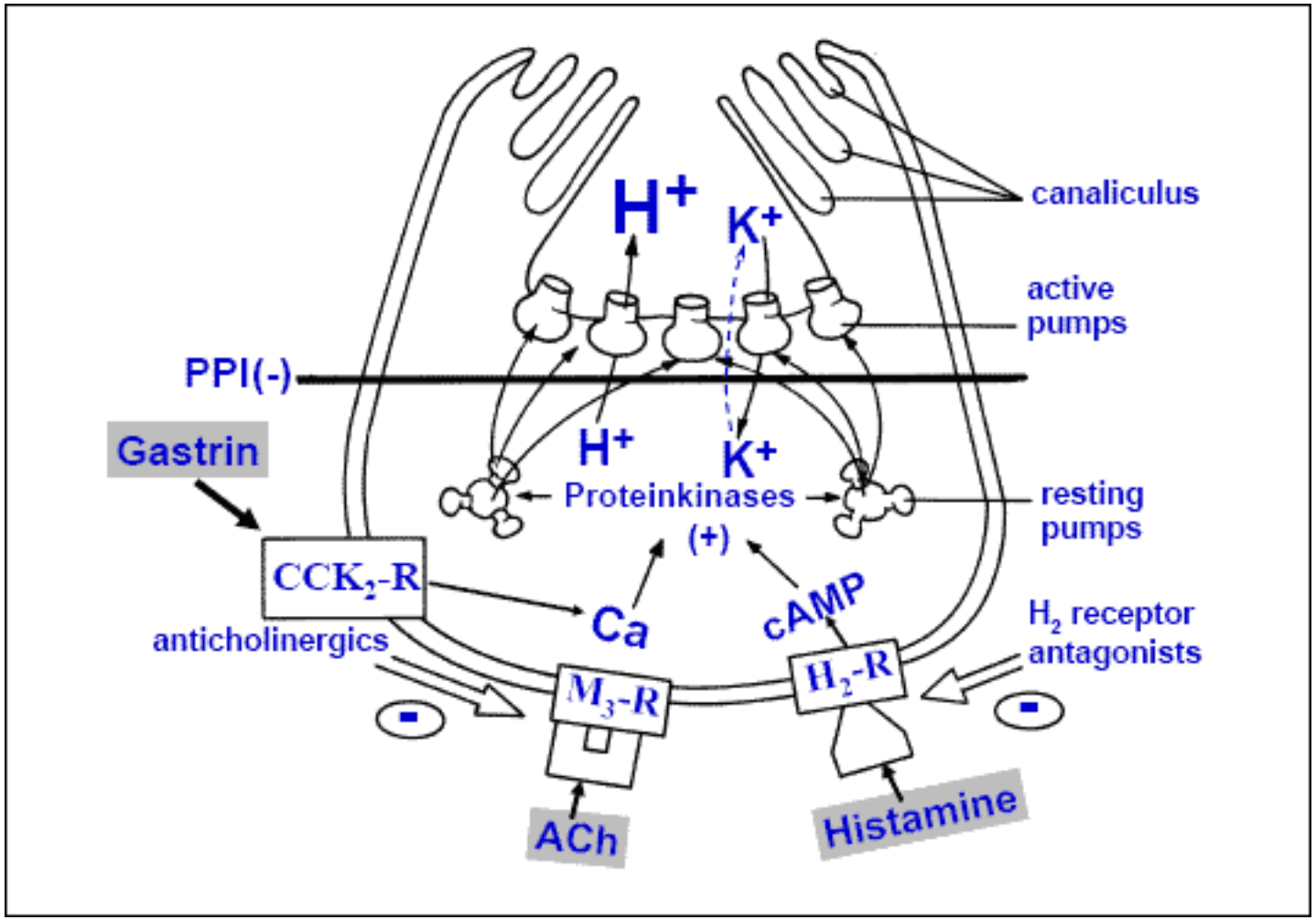
Where to from here?

Key Messages

- Weight loss and raising the head of the bed are the most useful lifestyle factors to improve reflux symptoms
- PPIs are the most effective therapy for ERD / NERD
- Other drugs work well in combination with PPI
  - nocturnal H2RA, baclofen, alginate antacids
- Consider baclofen / anti-depressants

Quiz

- Which of the following does not come up on google searches of PPI adverse reactions:
  - Pneumonia
  - Hypomagnesaemia
  - myocardial ischaemia
  - Enteric infections
  - iron deficiency
  - Psychosis


H+
K+
canaliculus
active
pumps
PPI(-)
H+
K+
Gastrin
Proteinkinases
(+)
resting
pumps
CCK2-R
Ca
cAMP
H2 receptor
antagonists
anticholinergics
M3-R
H2-R
ACh
Histamine

PPI Adverse Effects

- Overall, PPIs are exceptionally well tolerated
- Common
  - headache, diarrhoea, rash, nausea, constipation
- Less common but more worrying …

Risk of fracture

- Possible mechanisms
  - reduction of Ca absorption???
  - impairment of osteoclast activity???
- Four retrospective association studies
  - OR 1.18 [1.12-1.45] – 1.6 [1.4-1.8]
- Two case-control studies
  - No independent risk of hip fracture

Risk of fracture

- Meta-analysis of 10 observational studies (>200,000 #)
  - overall poor quality and high heterogeneity
  - Hip # OR 1.2 [1.1-1.4]
  - Vertebral # OR 1.5 [1.3-1.7]
  - Wrist / forearm # OR 1.1 [0.9-1.2]
- Prospective BMD studies – mixed results

- “Concern for fracture and osteoporosis should not prevent otherwise indicated long-term PPI therapy”

Hypomagnesaemia

- Mg – cofactor in >300 enzymatic reactions
- Early signs
  - Anorexia, nausea, fatigue, weakness
- Late signs
  - tremor, agitation, fasciculation, arrhythmia, depression, seizures (often with ↓ Ca / K)
- First reported with PPIs 2006
  - likely secondary to reduced absorption
  - Often other causes for low Mg

Hypomagnesaemia

- Rotterdam study of ~10,000 with serum [Mg]
  - 36 cases of ↓ Mg + PPI exposed
- 2X increased risk of ↓ Mg with PPI
- 7X increased risk with PPI + loop diuretic

- Italian study of patients with admission for ↓ Mg
  - 2X more likely to be on a PPI
  - 3X more likely to have diabetes, 20X more likely to have chronic diarrhoea

B12 Deficiency

- In diet, B12 is protein bound and requires acid-activated proteolytic digestion
- However studies have not been conclusive
  - positive studies are small and non-controlled

- The quality of available evidence does not justify routine B12 measurement in all patients receiving long-term PPI

Fe deficiency

- Gastric acid facilitates absorption of non-haem fe to more soluble ferrous form
- Odd case report etc
- Routine screening cannot be recommended

Enteric infections

- Gastric pH<4 is a major defense mechanism
  - Gastric pH>4 allow 50% of bacteria to escape acid
  - altered gastric and small intestinal flora
- Multiple retrospective cohort / C-C studies
  - Salmonalla, *Campylobacter jejuni, C difficile*
- Salmonella 2X CC studies – adjusted RR 4-8
- C jejuni 4X CC studies – adjusted RR 4-11
- Clostrium difficile…

Clostrium difficile

- Two large meta-analyses (similar results)
- 17-30 CC, 6-12 cohort studies (~300K subjects)

- RR of CDI in PPI-treated patients 1.69 [1.4-1.9]
  - No duration of treatment data
  - 15 studies suggested a reduced rate of CDI in H2RA-treated patients (RR 0.71 [0.53-0.97])

Enteric infections

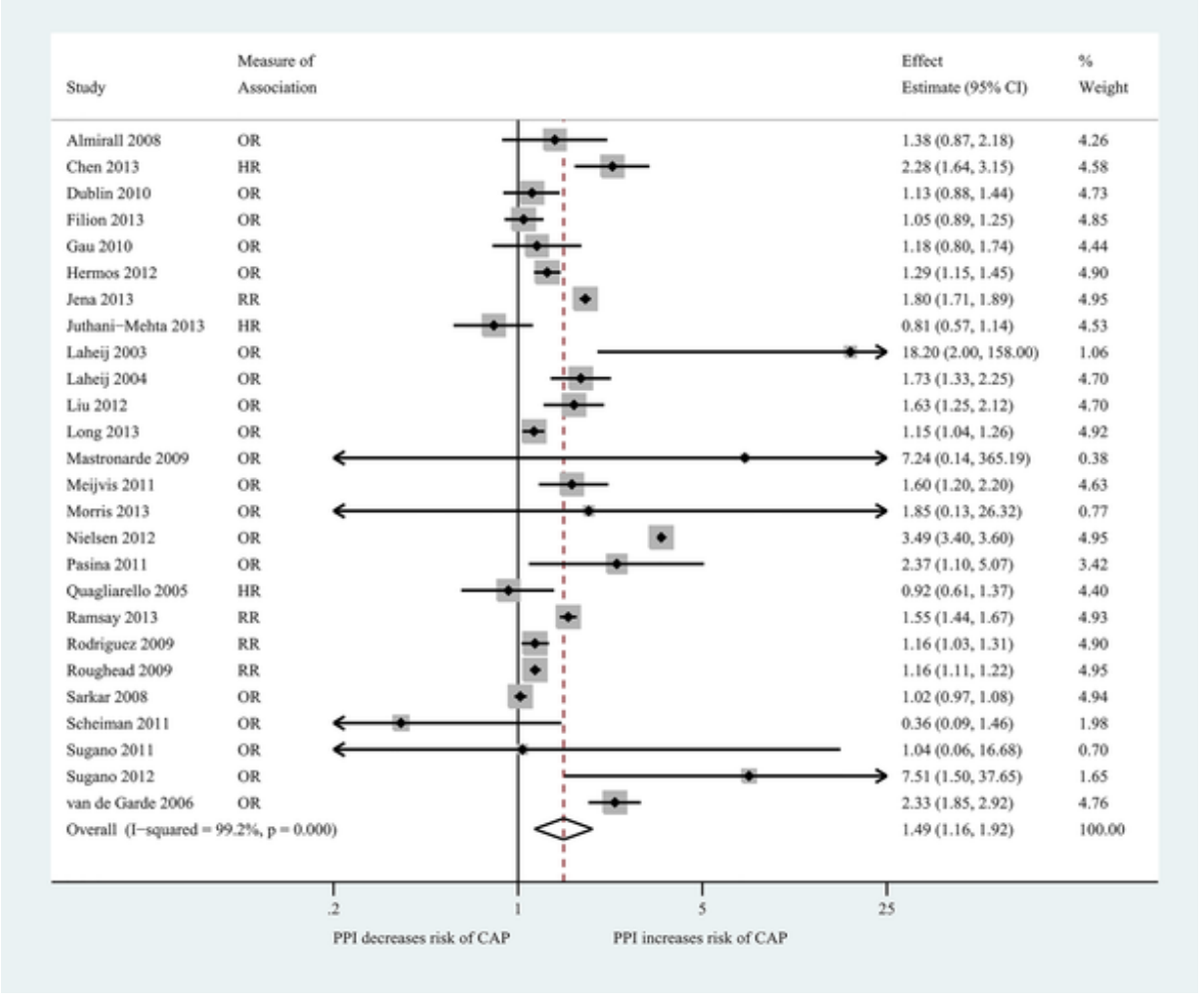
- PPIs may be risk factor for CDI
  - weak association
  - observational studies (low quality, unmeasured confounders and co-morbidity)

- Awareness of this association, particularly in hospitalised elderly patients

Pneumonia

- Gastric pH<4 increases pathogens in UGI tract?
  - possible micro-aspiration
- Initial CC studies suggested RR 1.5-1.7
- Nested CC study – significant confounders
- If there is an effect, it appears to be early
  - effect lessens with time
- Biologically plausible association but not strong and significant confounding

Fig 2. Summary Forest Plot of Overall Risk of Community-Acquired Pneumonia with Outpatient Proton Pump Inhibitor Use, subdivided by study design and effect estimate.



Lambert AA, Lam JO, Paik JJ, Ugarte-Gil C, Drummond MB, et al. (2015) Risk of Community-Acquired Pneumonia with Outpatient Proton-Pump Inhibitor Therapy: A Systematic Review and Meta-Analysis. PLoS ONE 10(6): e0128004. doi:10.1371/journal.pone.0128004
http://journals.plos.org/plosone/article?id=info:doi/10.1371/journal.pone.0128004

Acid rebound

- PPI >8 weeks ↑ acid secretion (temporarily)
- Affects ~50% of those stopping PPI
  - healthy volunteers
  - more likely in H pylori negative patients
  - smaller studies of GORD patients on PPI - no effect
- Possible explanation for long term PPI use…

Cancer

- Long term PPIs increase gastrin
  - gastrin has a trophic effect on gut epithelium
- Gastric fundic gland polyps
  - increased risk but no clinical significance
- Gastric cancer
  - ?H pylori increased risk –eradicate first
- Gastric carcinoids
  - ?H pylori increased risk –eradicate first
- Colorectal cancer
  - no effect in large CC studies

Safety in Pregnancy

- Acid-related symptoms - common in pregnancy
- Meta-analysis (7 CC studies, 1500 women, T1)
  - Major malformations OR1.29 [0.86-1.4]
- Danish nation-wide registry study
  - 5082 cases from 840,000 births
  - no effect

Mortality

- Large UK study (18,000 patients on PPI)
  - First year mortality, OR=1.4 [1.3-1.6], then no ↑ risk
  - marked confounding

- Mixed results from smaller studies
  - mostly of elderly / long term facility residents

Case

- A 89 year old woman on a wide range of drugs including PPI, frusemide and B-Blocker presents with lethargy

Where to from here?

Key Messages

- The risks of long-term PPI ADRs are small in comparison to a good indication for PPI
- The elderly are most likely to be affected by long-term PPI ADRs but are also most likely to have the poorest indications for PPI
- PPIs are the drug class most likely to be questioned by patients regarding ADRs

Quiz

- How long should patients with erosive oesophagitis remain on PPI?
- Why might we not perform surveillance for patients with Barrett’s oesophagus?
- What are the risk factors for Barrett’s oesophagus?

Complications of GORD

- Erosive oesophagitis
- Peptic strictures
- Barrett’s oesophagus
- Adenocarcinoma

Erosive oesophagitis

- Population-based study
  - 2/3 of those with reflux symptoms have no erosive oesophagitis

NERD

  - 1/3 of those with oesophagitis had reflux

Asymptomatic EO group

- Treatment with PPI
  - higher grades heal at lower rates

The Los Angeles Classification System for Esophagitis

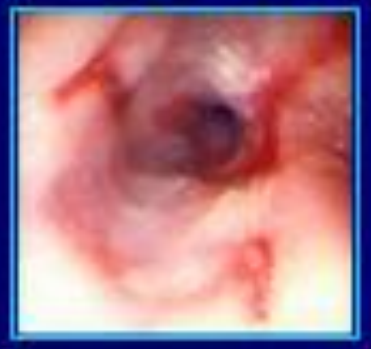
Los Angeles Grade A

One or more mucosal breaks no longer than 5 mm, not bridging the tops of mucosal folds

Los Angeles Grade B

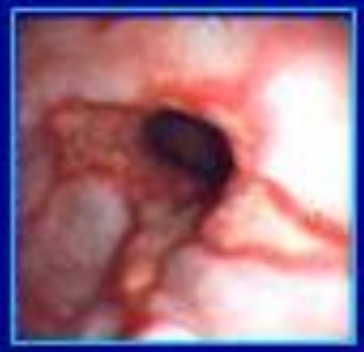
One or more mucosal breaks longer than 5 mm, not bridging the tops of mucosal folds

Los Angeles Grade C



One or more mucosal breaks bridging the tops of mucosal folds involving <75% of the circumference

Los Angeles Grade D



One or more mucosal breaks bridging the tops of mucosal folds involving >75% of the circumference

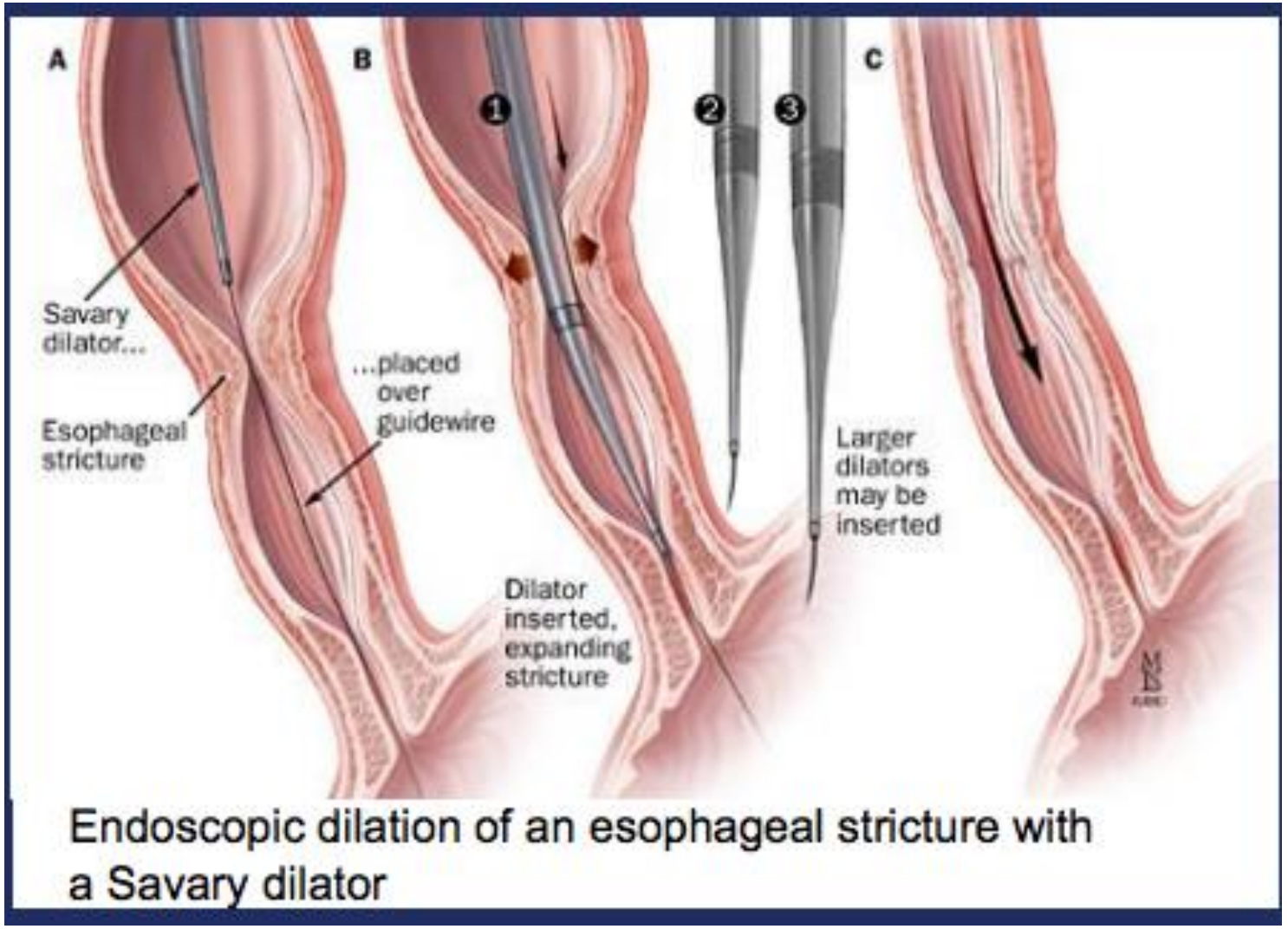
Lundell LR, et al. *Gut*. 1999;45:172–180.
Armstrong D, et al. *Gastroenterology*. 1996;111:85–92.

Peptic strictures

- Secondary to healing and fibrosis

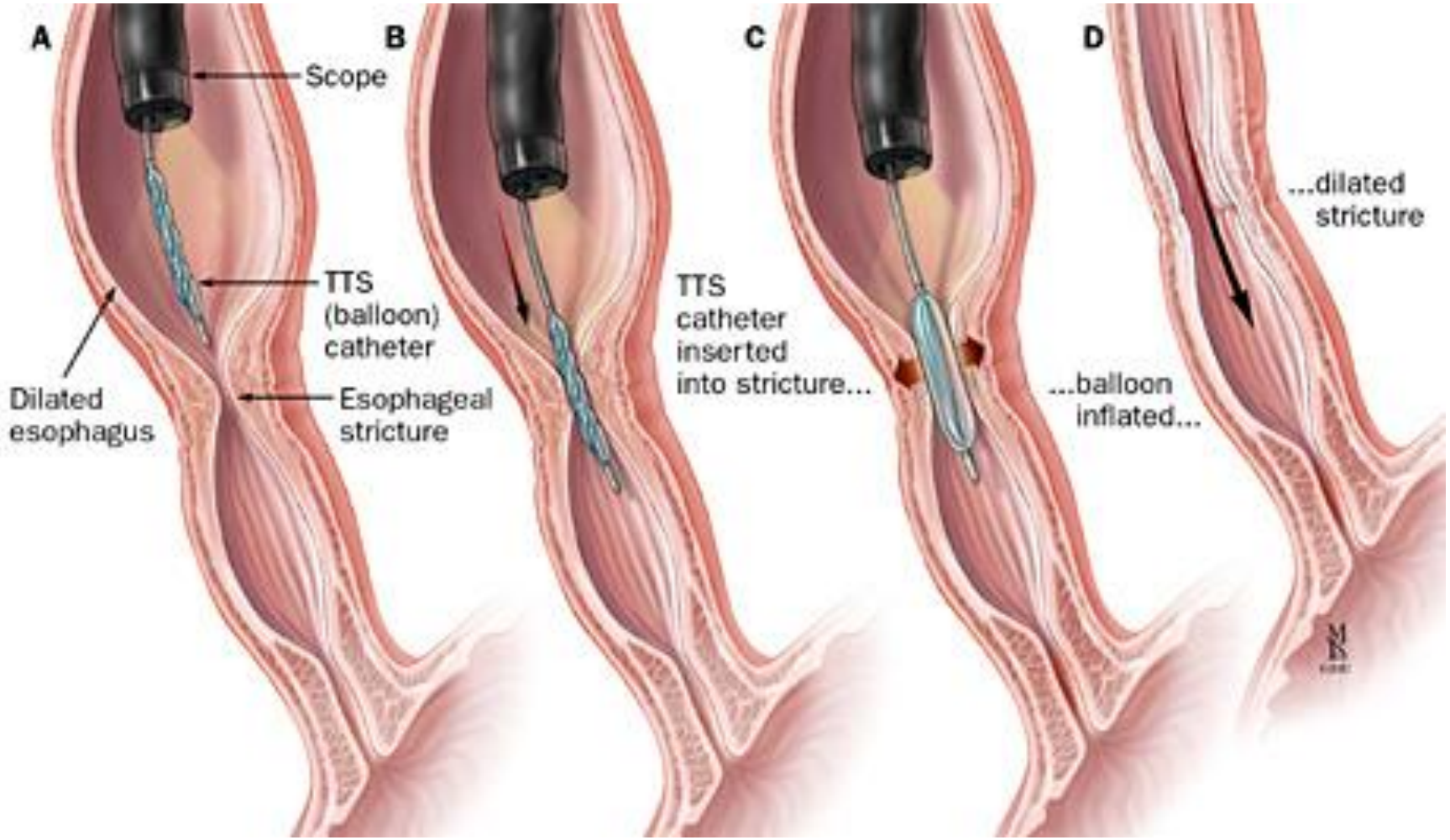
- Dilatation is standard therapy
  - Savary bougie
  - TTS balloon

Savary dilator

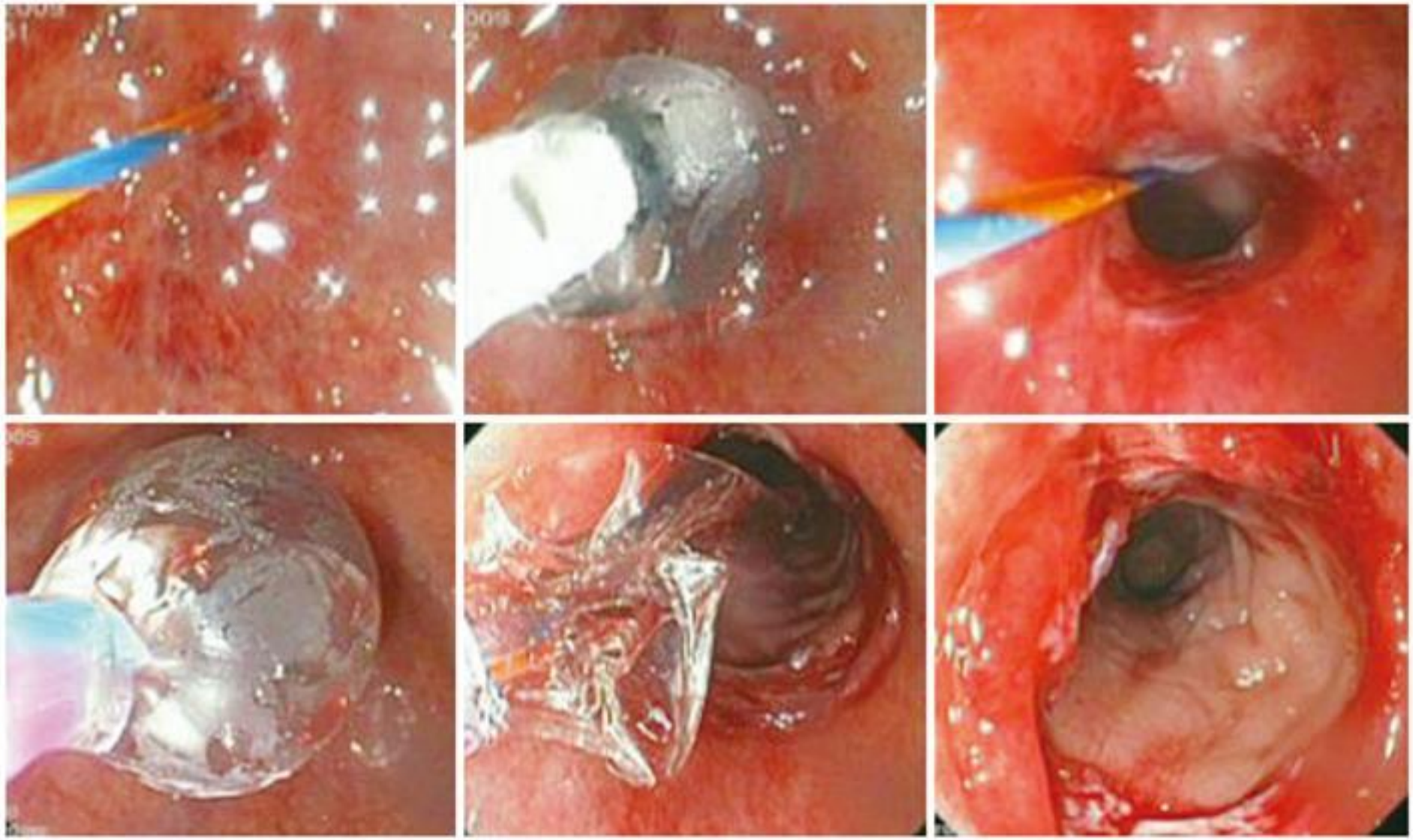


Endoscopic dilation of an esophageal stricture with a Savary dilator

TTS Ballon dilatation



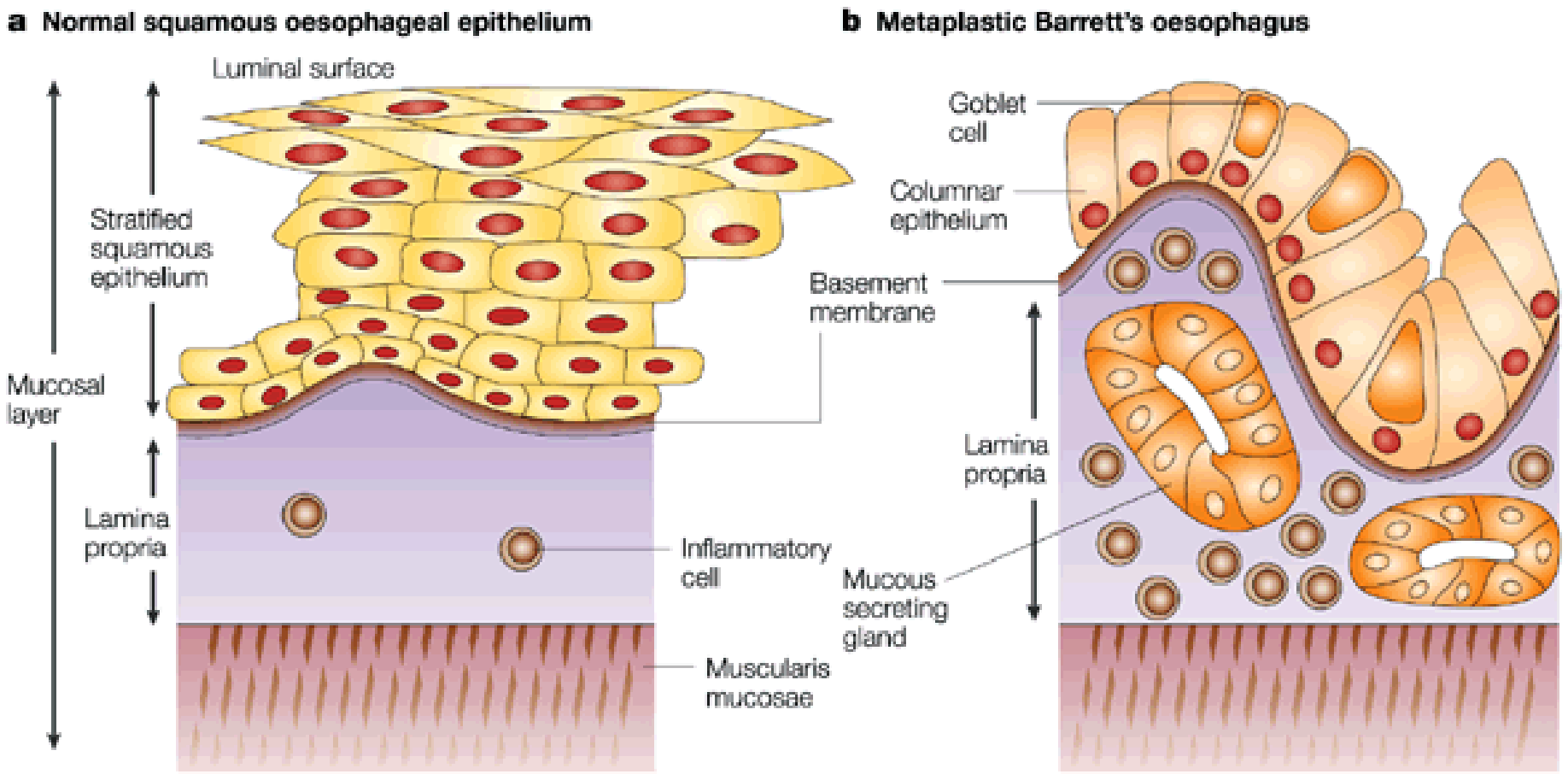
TTS balloon dilatation



Barrett’s oesophagus

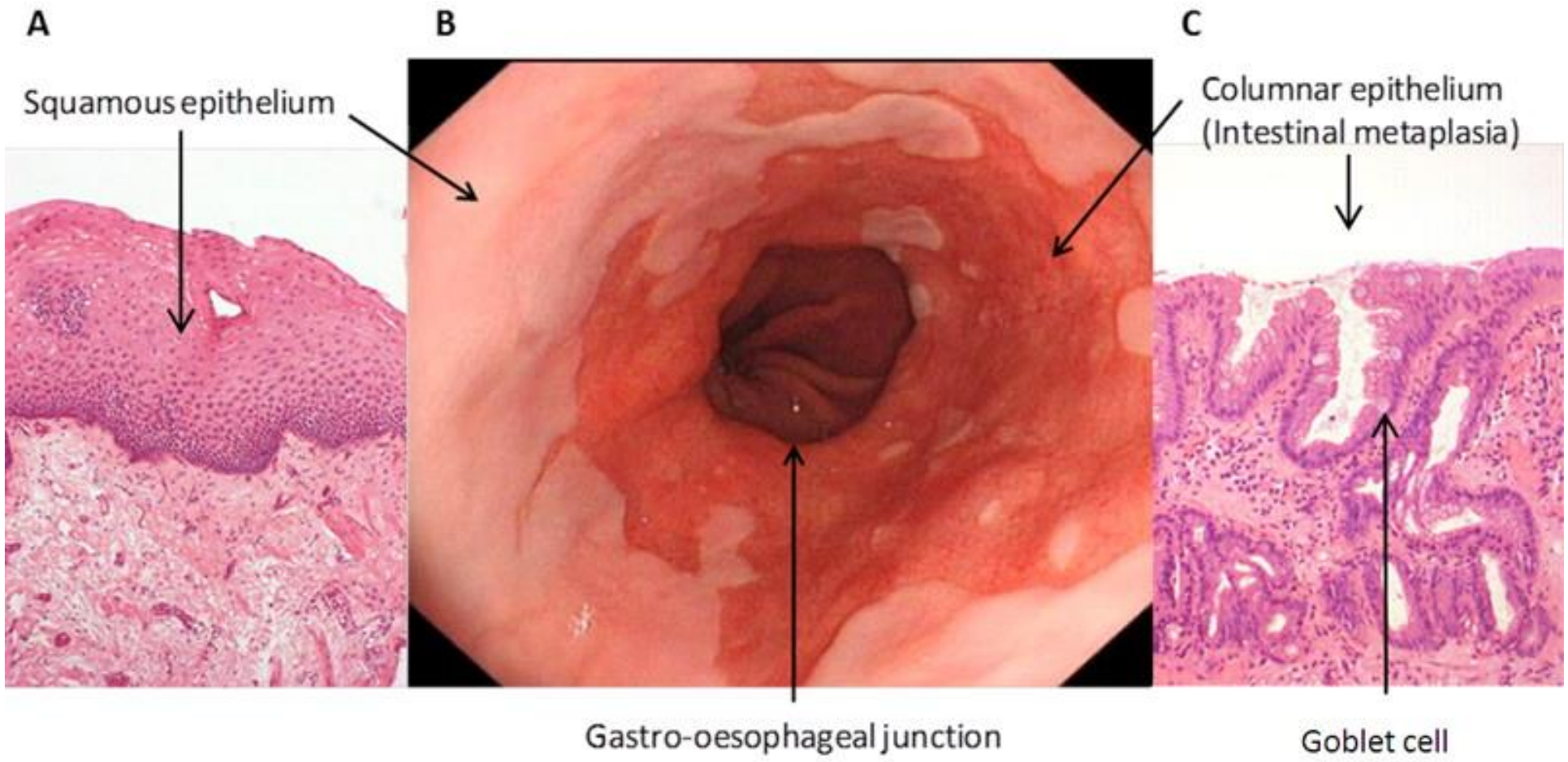
- Pre-malignant condition
- Oesophageal squamous epithelium undergoes columnar change with metaplasia
- Prevalence ?1.6%
- Rapidly increasing incidence

Barrett’s oesophagus

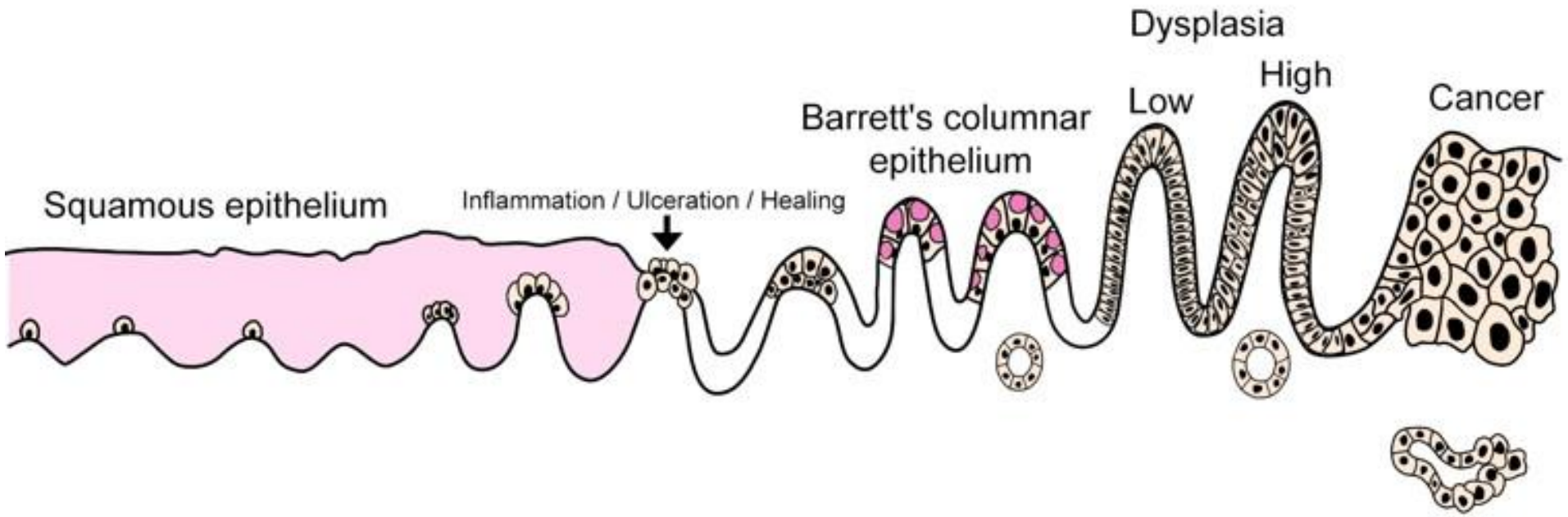


Nature Reviews | Cancer

Barrett’s oesophagus



Barrett’s oesophagus



Risk factors for Barrett's oesophagus

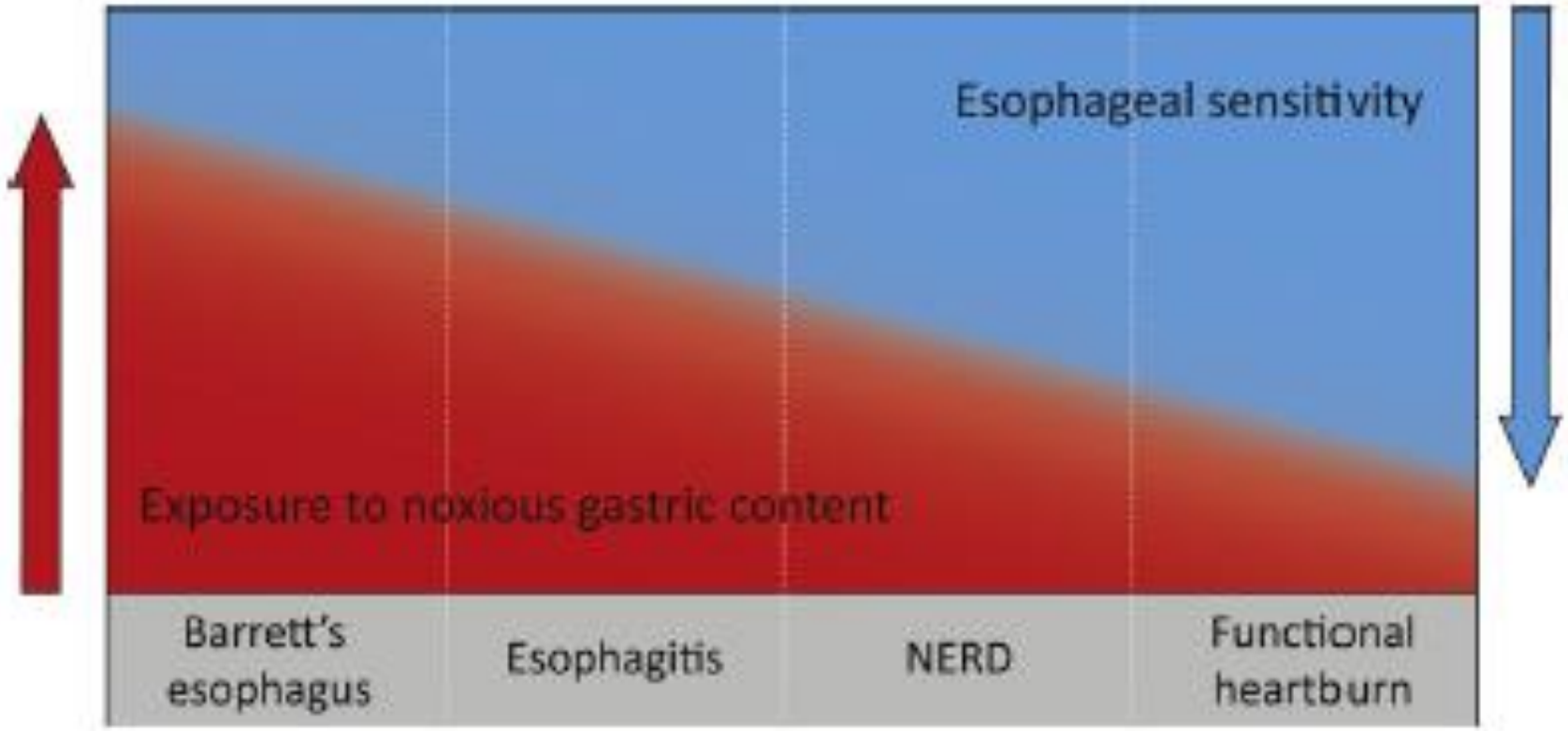
- GORD (EO associated with BE, OR 5.2 [1.2-23])
- Hiatus hernia
- Smoking
- Central obesity / overweight
- White race
- Males
- Age >50 years
- Genetic factors

Barrett's oesophagus

- Usually found at endoscopy for those under-going evaluation for UGI symptoms

- ? screening
  - GORD symptoms and $\geq$ 2 risk factors
  - lower threshold for those with FHx

Interaction between refluxate and oesophageal sensitivity



How do we manage Barrett's oesophagus?

- Symptom control of GORD / healing
- Endoscopic surveillance for dysplasia / adenoCa
  - in the right groups
- Consideration of endoscopic / surgical treatment for those with dysplasia

Symptom control of GORD

- PPI – probably at higher doses
- NSAIDs, aspirin and statins all ↓ risk of BE and progression of BE to dysplasia
  - observational studies
- Surgery and medical therapy are equally effective in patients with BE

Endoscopic surveillance for dysplasia

- Rate of progression differs for individuals
  - no prospective studies showing efficacy but all guidelines support surveillance
- Non-dysplastic BE → adenoCa 0.2-0.4% / year
  - surveillance Q3-5 years
- Dysplastic BE → adenoCa 0.6-5% / year
  - surveillance Q6-12 months

Endoscopic management of BE

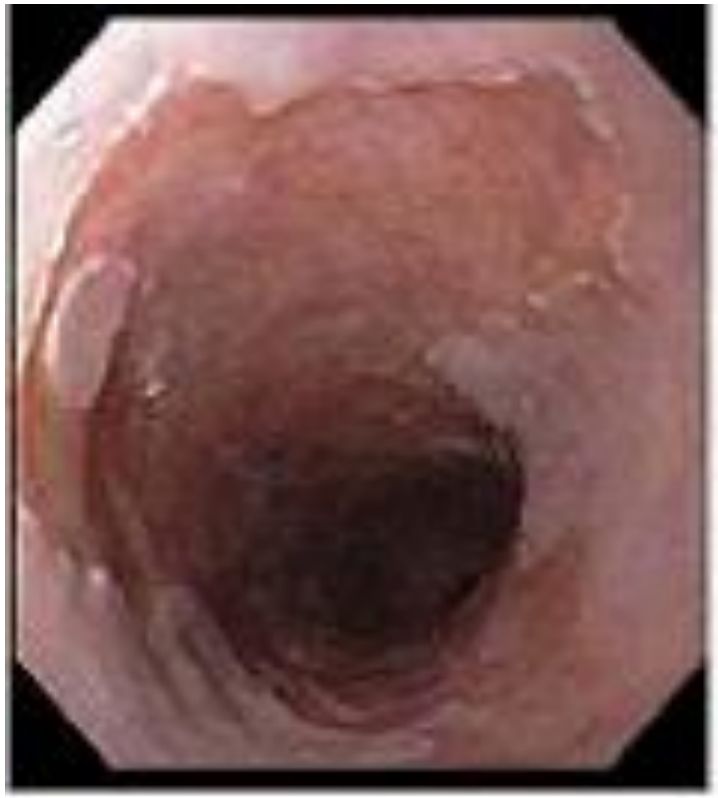
HALO 360+ catheter is introduced over a guidewire

Ablation Effect

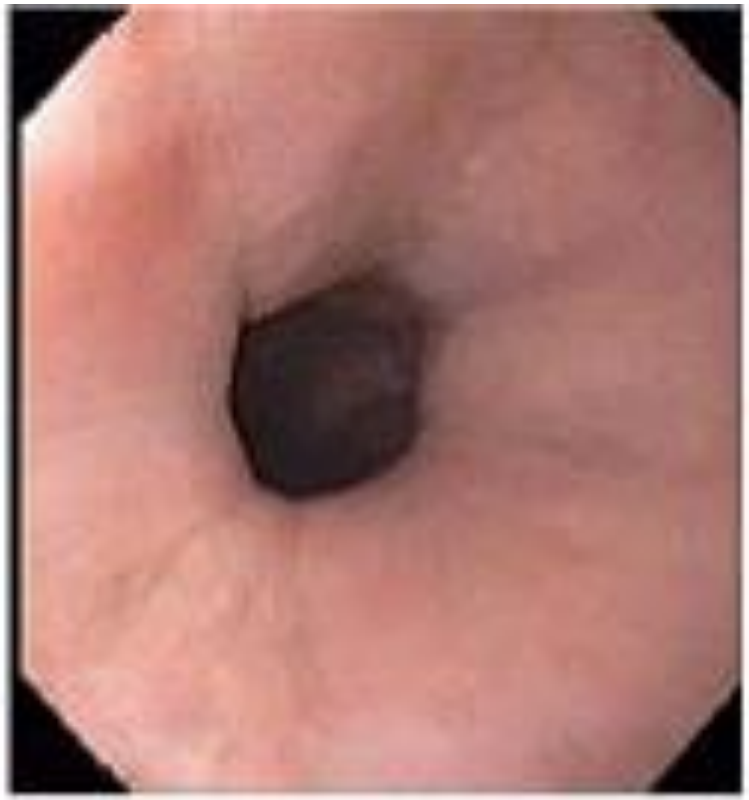
HALO 90 catheter is mounted on the endoscope

Ablation Effect

Endoscopic management of BE

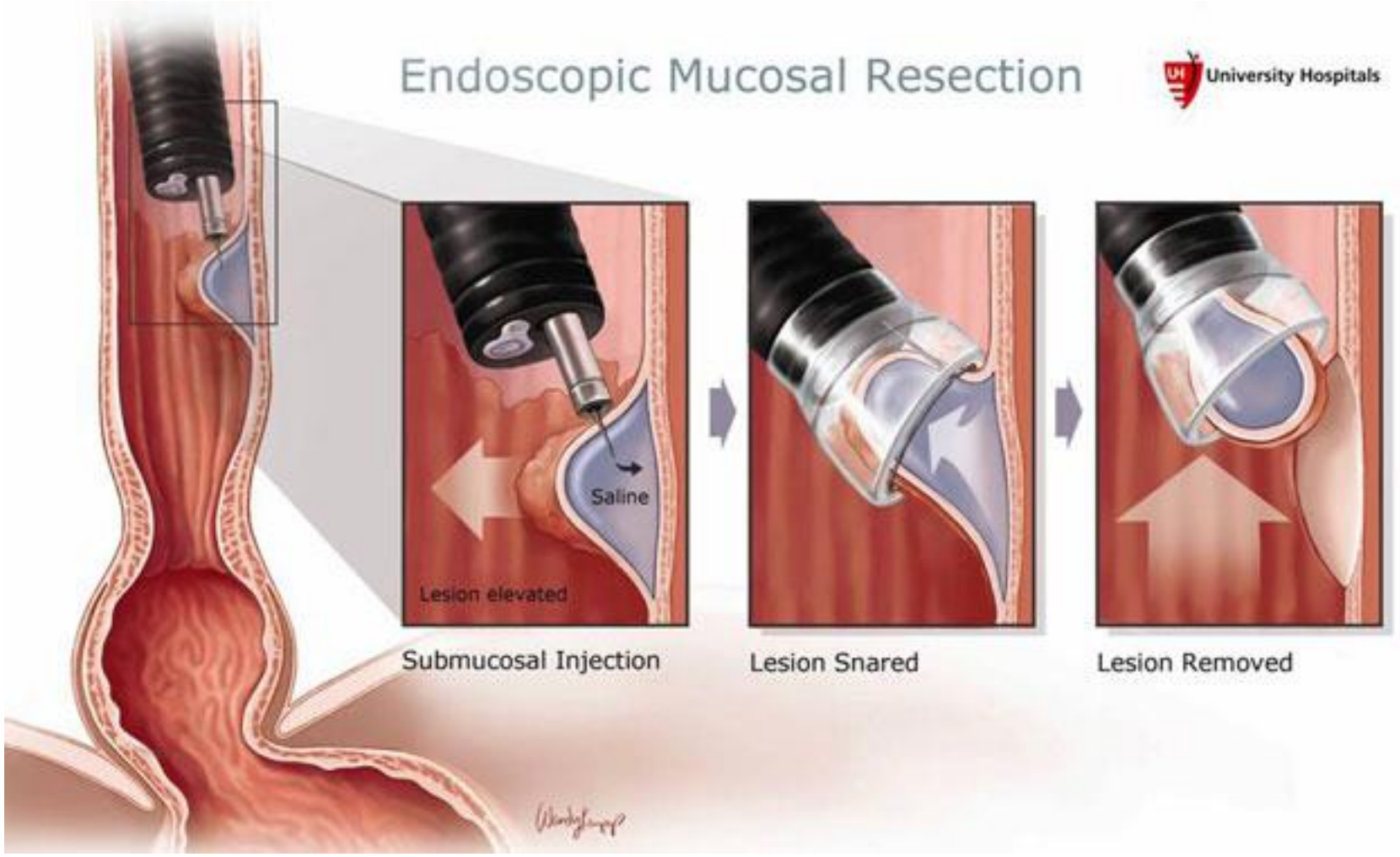


Barrett's column before treatment

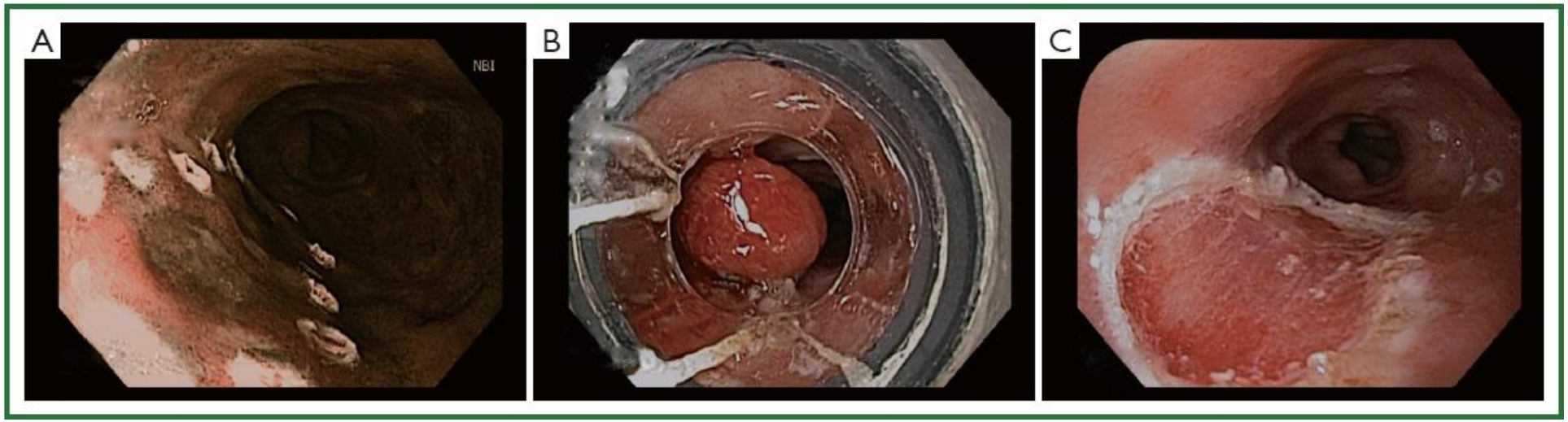


Barrett's eradicated by HALO RFA

Endoscopic management of BE



Endoscopic management of BE



Dr Gary Lim,
Interventional Endoscopist

CDHB

Gastroenterology & Endoscopy Specialists

Case

- 54 year old male with occasional reflux symptoms managed with intermittent PPI
- Gastroscopy for dysphagia shows 6cm length of Barrett's oesophagus

Where to from here?

Key Messages

- Erosive oesophagitis is a great indication for long-term PPI
- Peptic stricture responds well to dilatation(s)
- Erosive oesophagitis, Barrett's and AdenoCa oesophagus are all becoming more frequent
- Endoscopic therapy for Barrett's is revolutionalising management

Final Quiz
Bridging the therapeutic gap

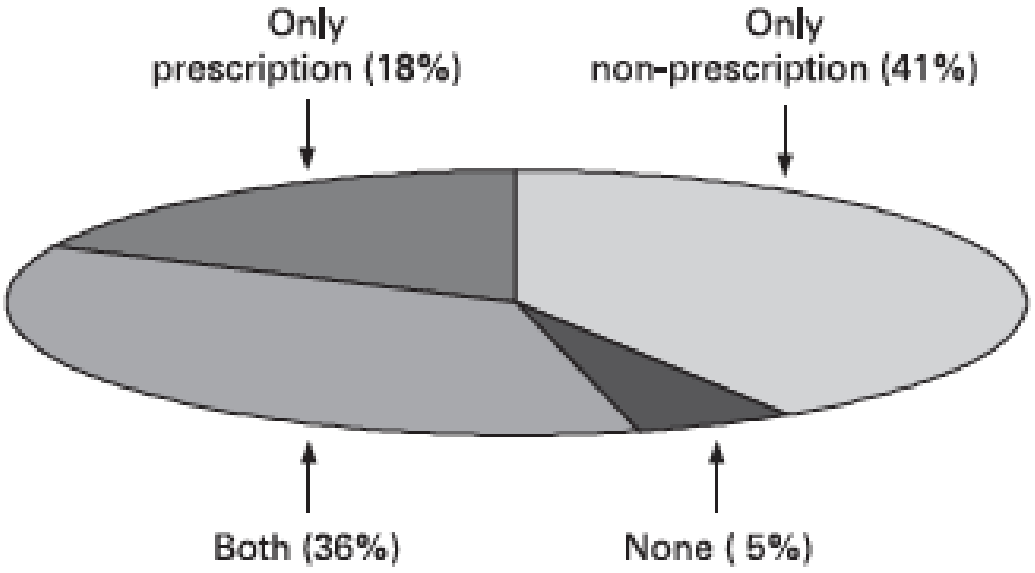
- What are the mechanisms of PPI non-responsive GORD?

- How do you manage heartburn not responding to PPI?

PPI non-responsive GORD

- 10-50% of people with GORD do not completely respond to a PPI
- 1997 - 2004 – 50% ↑ in double dose PPI
- <50% of people with GORD are satisfied with Rx
- PPI escalation beyond potential efficacy is common
- PPI non-responsive GORD patients
  - NERD / functional heartburn

PPI non-responsive GORD



- 56% "breakthrough symptoms"
- 28% "only combination works"
- 21% "non-prescription is faster acting"

Figure 1 Reported type of medications used in the past 30 days by 1009 surveyed subjects with gastro-oesophageal reflux disease (GORD). The box shows the common explanations given by patients with GORD for adding a non-prescription drug to a prescription drug.[4]

Psychological comorbidity

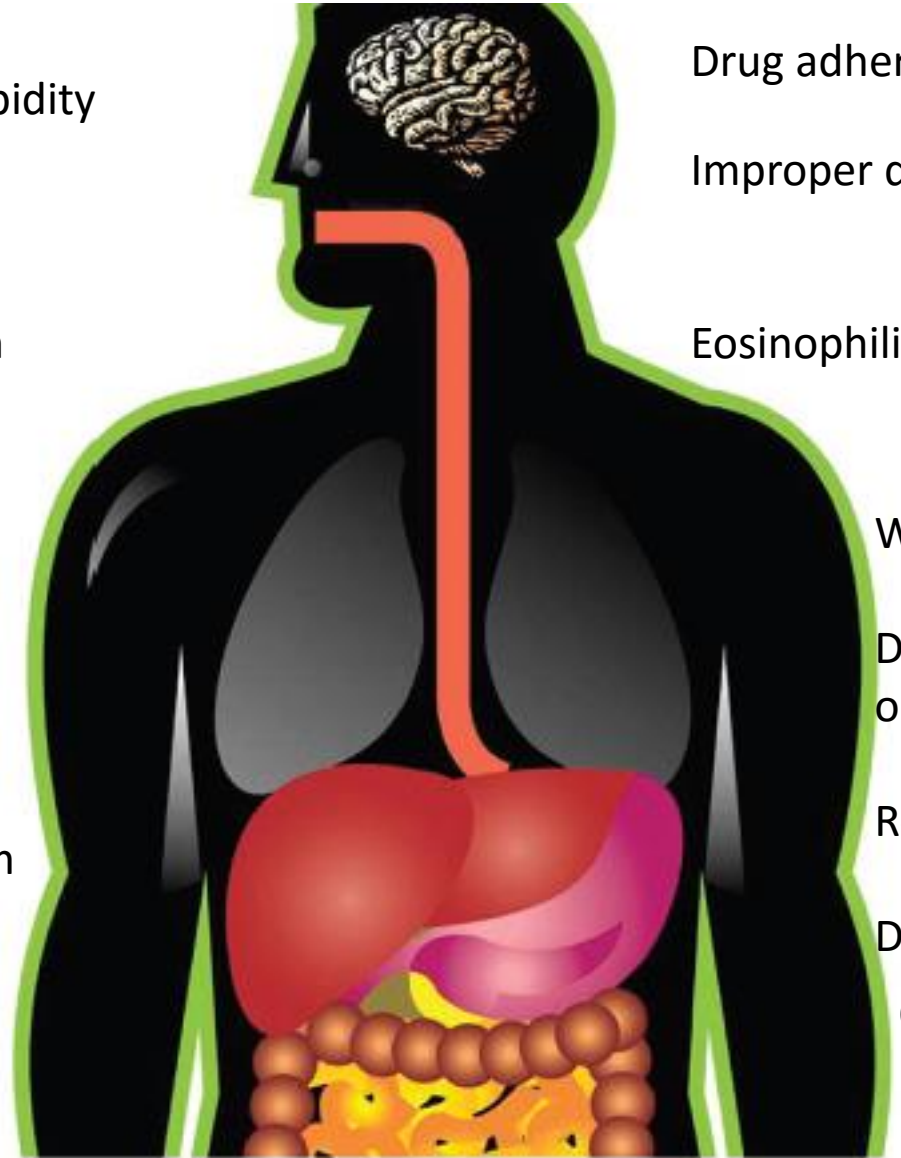
Functional heartburn

↓PPI availability

Rapid PPI metabolism

PPI resistance

Others



Drug adherence

Improper dosing time

Eosinophilic oesophagitis

Weakly acid reflux

Duodenogastric-oesophageal reflux

Residual acid reflux

Delayed gastric emptying

Concomitant functional bowel disorder

PPI adherence for GORD

- 1 month 55%
- 6 months 30%

- Presence of symptoms
- Severity of symptoms
- Personal preference

PPI dose timing

- 30 minutes prior to eating

- 100 patients with persistent GORD on PPI
  - 46% dosed optimally
  - 39% dosed at bed time or prn

Weakly acidic / alkaline reflux

- PPIs stop acid but not volume
- 168 refractory GORD (pH / impedance testing)
  - 11% acid reflux
  - 37% non-acid reflux
- Need to consider the lower oesophageal junction

Duodenogastro-oesophageal reflux / Bile reflux

- less common cause of symptoms

- Need to consider the lower oesophageal junction

Oesophageal hypersensitivity

- 50% of GORS patients with normal endoscopy have normal pH studies
- People with erosive oesophagitis have lower oesophageal pain thresholds than those without
- 58% of BD PPI-failure patients have functional heartburn

Residual acid reflux

- Up to 40% of patients taking once daily PPI have a positive pH study

- PPI daily 31%
- PPI BD 4%

- BD PPI trials are worthwhile

Nocturnal acid breakthrough

- Oesophageal pH <4 for greater than one hour overnight in symptomatic GORD patients on BD PPI

- Nocturnal symptoms do not correlate strongly with daytime symptoms or pH testing abnormalities

Psychological co-morbidity

- Patients with a poor correlation between symptoms and acid reflux events have higher rates of anxiety and depression

Eosinophilic oesophagitis

- All have dysphagia
- 1/3 have classic heartburn

- Eosinophilic oesophagitis and GORD may co-exist

Investigation for PPI non-responsive GORD

- Upper GI endoscopy
  - may reveal an alternative diagnosis
  - often normal – NERD / functional heartburn
- 24H oesophageal pH / impedance monitoring
  - defines the physiology
  - allows definitive diagnosis to be made
- Barium swallow / manometry
  - only if considering anti-reflux surgery

Treatment approaches

- Addressing poor PPI adherence and timing
- Confirming lifestyle measures
- Nocturnal H2RA in addition to BD PPI
- Switching to another PPI brand / dose escalation
- TLOSR reducers (baclofen)
- Prokinetics (only if impaired gastric emptying)

Treatment approaches

- Visceral pain modifiers
- Botox injections of the pylorus
  - especially with gastroparesis
- Anti-reflux surgery
  - works best if a positive response to PPI
  - patients need careful evaluation
- Endoscopic treatment (coming)

Thank you


UNIVERSITY of OTAGO
Te Whare Wānanga o Otāgo
NEW ZEALAND
SAPERE AUDE


Canterbury
District Health Board
Te Poari Hauora ō Waitaha


Gastroenterology and
Endoscopy Specialists