

Gastro-oesophageal reflux disease: The Montreal definition and classification

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Abstract

Guidelines come and go, and each successive guideline hopefully brings with it an improvement in the understanding, diagnosis and management of the condition in question. The Montreal definition and classification of gastro-oesophageal reflux disease (GORD) is an excellent, well-constructed guideline, compiled by world authorities on the subject, after exhaustive consultation.¹ The aim of any guideline is to achieve wide recognition and ensure uniformity in approach.

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The global definition of gastro-oesophageal reflux disease (GORD)

1. GORD is a condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complications.

This definition allows the diagnosis of GORD to be made independent of the diagnostic method employed, i.e.:

- typical symptoms alone,² or
- investigations that demonstrate the reflux of stomach content, e.g. pH or impedance monitoring to prove the reflux of acid, bile or air, or
- the injurious effect of the reflux (endoscopy or histology).

This definition allows patients with complications of GORD, such as Barrett's oesophagus, to be included. It also recognises that the refluxate causing symptoms may be weakly acidic or gaseous.

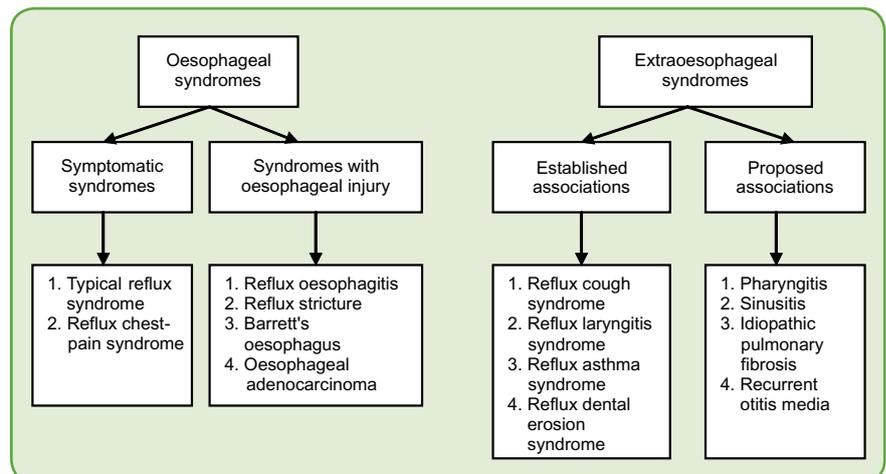
A proposal that GORD-related symptoms be presented as a set of syndromes was debated and accepted by the panel members. This is a reflection of the diverse presentations of GORD. The algorithm (Figure 1) elegantly classifies the proven and suspected associations and complications of GORD.

2. Symptoms related to gastro-oesophageal reflux become troublesome when they adversely affect an individual's well-being.

It has been demonstrated that an individual's quality of life deteriorates as the severity of GORD increases.³

Figure 1. The overall definition of GORD and its constituent syndromes

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



3. Reflux symptoms that are not troublesome should not be diagnosed as GORD.

Most panel members accepted this statement. Occasional heartburn is common and does not by itself constitute a disease. An important exception to this statement is the patient with Barrett's oesophagus or erosive oesophagitis who may be asymptomatic. Such a patient would, according to Definition 1, be classified as having GORD.

4. In clinical practice, the patients should determine if their reflux symptoms are troublesome.

The panel agreed that the determination of "troublesome symptoms" should be

patient centred without arbitrary cut-offs for frequency and duration.

A. OESOPHAGEAL SYNDROMES: SYMPTOMATIC

Typical reflux syndrome: The typical reflux syndrome is defined by the presence of troublesome heartburn and/or regurgitation. Patients may have other symptoms, such as epigastric pain or sleep disturbance.

5. Heartburn is defined as a burning sensation in the retrosternal area (behind the breastbone).

It is important that both the patient and the doctor understand what is meant by heartburn. With this definition, misunderstanding can be avoided.

6. Regurgitation is defined as the perception of the flow of refluxed gastric content into the mouth or hypopharynx.

7. Heartburn and regurgitation are the characteristic symptoms of the typical reflux syndrome.

The panel expressed the hope that the more rigorous definitions of heartburn and regurgitation would result in more robust data in future clinical trials of GORD.⁴

8. Gastro-oesophageal reflux is the most common cause of heartburn.

Indirect evidence for acid causing most heartburn comes from the multitude of clinical trials of acid suppression in GORD. A Cochrane meta-analysis of the short-term treatment of GORD showed that relative risk (RR) of relief from heartburn increased with greater degrees of acid suppression: prokinetic agents RR 0.86, H₂-receptor antagonists RR 0.77 and PPIs RR 0.37.⁵

9. Heartburn can have a number of non-reflux-related causes. Their prevalence is unknown.

Duodenogastric reflux, as evidenced through the use of pH and Billitec monitoring, has been shown to play a role in some cases. Impedance studies have demonstrated that gas reflux, both with and without drops in pH, coincide with symptoms. It is clear that acid reflux is more common than non-acid reflux. This pattern changes when treatment with a PPI is instituted.^{6,7}

10. The typical reflux syndrome can be diagnosed on the basis of the characteristic symptoms without diagnostic testing.

This statement is important, particularly at primary-care level. General practitioners should be able to make a confident diagnosis based on typical symptoms. It is equally important, however, that "alarm symptoms" are recognised and investigated without delay. Alarm symptoms include:

- dysphagia
- upper gastrointestinal bleeding or anaemia
- loss of weight
- worsening symptoms in the older patient (older than 50).

11. Non-erosive reflux disease (NERD) is defined by the presence of troublesome reflux-associated symptoms and the absence of mucosal breaks at endoscopy.

The absence of visible erosions at endoscopy is reported in over 50% of patients presenting with reflux symptoms in primary care. If their symptoms are troublesome, they have the typical reflux syndrome. Once again, the general practitioner should diagnose GORD and commence treatment, thus minimising expensive investigation. Patients are frequently referred for endoscopy after having been on PPIs for some time. The endoscopist is then unable to differentiate between NERD and healed erosive oesophagitis.

12. Epigastric pain can be a major symptom of GORD.

This symptom may be due to the perfusion of dilute acid into the lower oesophagus. Trials have shown a strong correlation between the resolu-



tion of heartburn and the resolution of epigastric pain with acid-suppressive therapy.⁸

13. GORD is frequently associated with sleep disturbance.

Sleep disturbance is reported in 23 to 81% in several surveys.⁹

14. Night-time heartburn and sleep disturbance reported by patients with GORD are substantially improved by PPI therapy or antireflux surgery.

Therapeutic studies support a causal link between reflux and sleep disturbance.

B. REFLUX CHEST-PAIN SYNDROME

15. Chest pain indistinguishable from ischaemic cardiac pain can be

caused by GORD.

In this situation, it would be safer to assume that the symptoms are of cardiac origin, and only once heart disease has been ruled out would one consider oesophageal causes for the pain.

16. Gastro-oesophageal reflux can cause chest pain without accompanying heartburn or regurgitation.

Levels of non-cardiac chest pain have been reported in up to 25% of chest-pain sufferers.¹⁰

C. OESOPHAGEAL SYNDROMES: SYNDROMES WITH OESOPHAGEAL INJURY

17. Oesophageal complications of GORD are reflux oesophagitis, haemorrhage, stricture, Barrett's oesophagus and adenocarcinoma.

Reflux oesophagitis is seen in less than 50% of patients with typical GORD symptoms. It is, however, the most common consequence of oesophageal injury. Reflux oesophagitis can be easily documented at endoscopy and provides an objective criterion for diagnosis. Oesophagitis can be diagnosed histologically but reliability has been questioned.¹¹ Findings may include increased polymorphonuclear and mononuclear cells, basal cell hyperplasia and elongation of the papillae. The other complications are less common.

18. Over a 20-year period, the severity of reflux oesophagitis does not increase in most patients.

Limited data are available. The available evidence suggests that the severity of GORD symptoms, both on and off treatment, does not, in most patients, change over time. In most patients, GORD is a chronic condition and symptoms persist. Older patients tend to have more severe oesophagitis, supported by the increased rates of Barrett's oesophagus and cancer with age. A confounding factor in many studies and certainly in clinical practice is that by the time that patients are referred for endoscopy they are often on therapy, with possible healing of mucosal breaks.

19. Although heartburn frequency and intensity correlate with the severity of mucosal injury, neither will accurately predict the severity of mucosal injury in the individual patient.

Factors that predict the presence of oesophagitis are the frequency and duration of reflux episodes, the occurrence of day and night-time reflux episodes and the presence of a hiatal hernia.¹²

Symptoms do not accurately predict the endoscopic findings in an individual patient. Elderly patients may have less severe heartburn despite more severe grades of oesophagitis. By relying on heartburn severity, one could therefore underestimate the severity of oesophagitis in elderly patients. There is some evidence that patients with Barrett's oesophagus may report less frequent or less severe symptoms.

20. The characteristic symptom of a stricture is persistent troublesome dysphagia.

Dysphagia is a perceived impairment of the passage of food from the mouth to the stomach. A reflux stricture can develop as a result of severe reflux disease. This is seen in fewer than 5% of GORD patients. Patients usually complain of persistent and troublesome dysphagia. Treatment usually requires endoscopic dilatation in addition to acid-suppressive therapy. The term "dysphagia" should not be confused with oropharyngeal dysphagia, which is unrelated to GORD. Odynophagia is defined as painful swallowing and is a common symptom in infectious oesophagitis, e.g. candida and herpes oesophagitis.

An important aspect of the new GORD definition is that symptoms are troublesome. Troublesome dysphagia is more related to solids than liquids. Non-troublesome dysphagia is common in GORD. Thirty-seven per cent of 11 495 patients reported dysphagia when a symptom checklist was used. Dysphagia resolved in 83% of patients following treatment with a PPI.¹³

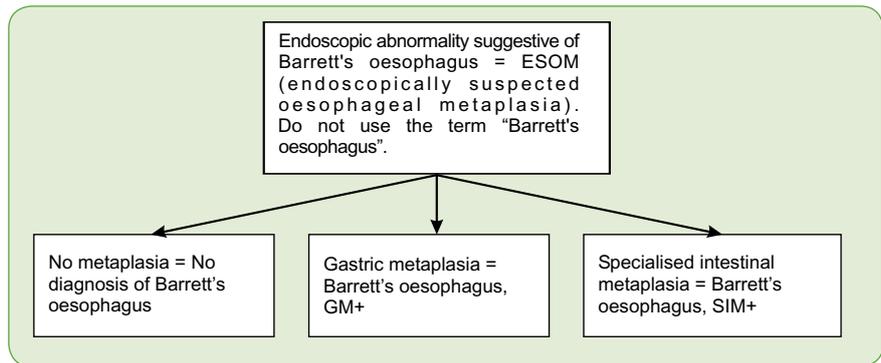
21. Persistent progressive or troublesome dysphagia is a warning symptom of stricture or cancer of the oesophagus and warrants investigation.

There is agreement that troublesome and worsening dysphagia, especially for solids, is an alarm symptom. It warrants investigation, as it could be indicative of more serious pathology, such as peptic stricture or cancer of the oesophagus. Having dysphagia increases the risk (the odds ratio is 3:4) of the presence of an upper GI malignancy.¹⁴

22. The term "Barrett's oesophagus" is currently interpreted in various ways and lacks the clarity needed and scientific communication about columnar metaplasia of the oesophageal mucosa.

There is universal agreement that the

Figure 2. Consensus terminology for Barrett's oesophagus



core component of the definitions of Barrett's oesophagus is the partial replacement, from the gastro-oesophageal junction proximally, of oesophageal squamous epithelium with metaplastic columnar epithelium. The term "Barrett's



oesophagus" is currently confusing and ambiguous because of varying definitions used in the diagnosis of Barrett's. Some clinicians make this diagnosis solely on the basis of the endoscopic appearances of the proximal extension of the squamo-columnar junction of any extent, to the requirement that intestinal type oesophageal columnar metaplasia be proven histologically before this diagnosis is made. It has been demonstrated that the consistency of endoscopic and histological findings at index endoscopy compared to one performed two years later was poor. In patients with suspected Barrett's oesophagus, biopsies were shown in 42% of patients to be negative for Barrett's oesophagus.

A diagnosis of Barrett's oesophagus carries with it significant implications for the patient. These include the fear of

having a premalignant condition, undergoing regular surveillance endoscopies and the impact of the diagnosis on the cost of life assurance.

23. Neither the frequency nor the severity of heartburn is useful for the prediction of the presence, type or extent of oesophageal columnar metaplasia.

It was readily agreed that these criteria are not discriminatory. Between 5,6 and 25% of older people free of troublesome heartburn have evidence of oesophageal columnar metaplasia. Risk factors for having oesophageal columnar metaplasia include age, gender and the duration and pattern of reflux symptoms.¹⁵

24. Endoscopically suspected oesophageal metaplasia (ESOM) describes the endoscopic findings consistent with Barrett's oesophagus that await histological evaluation.

It was agreed that there should be terminology that differentiates a purely endoscopic diagnosis of oesophageal columnar metaplasia from one that is confirmed histologically. Available data suggest that the endoscopic diagnosis needs confirmation with histology and that a term that acknowledges the possibility that endoscopic appearance may not be diagnostic was chosen. The chosen terminology is more neutral and will be of less concern to patients and their insurers.

25. Multiple, closely spaced biopsies are necessary to characterise ESOM.

Effective management for the risk of oesophageal adenocarcinoma requires the sensitive detection of intestinal-type metaplasia and high-grade dysplasia. High-grade dysplasia frequently occupies a very small proportion of the surface area of columnar metaplasia. Newer modalities for detecting areas of dysplasia, such as narrow-band

imaging and magnification chromoendoscopy, are not yet in routine clinical practice. The best researched biopsy protocol is four-quadrant biopsies every 1 cm for circumferential metaplastic segments, which is substantially more sensitive than the currently recommended 2 cm intervals. This protocol is onerous and expensive and is generally not accepted as best practice.¹⁶ Even with the use of such protocols, there is significant sampling inaccuracy. It has been found that the intestinal-type metaplasia is most prevalent at the proximal extent of metaplasia.

26. The description of ESOM should include a standardised measure of endoscopic extent.

The risk of adenocarcinoma is significantly influenced by the extent of metaplasia. About 75% of cases have metaplasia less than 3 cm in extent and the cancer risk is less in these patients than in those with more extensive metaplasia. There appears to be an increasing risk of cancer with an increasing extent of metaplasia beyond 3 cm. An attempt at standardisation has recently been released as the Prague criteria.¹⁷

27. When biopsies of ESOM show columnar epithelium, it should be called Barrett's oesophagus and the presence or absence of intestinal metaplasia specified.

It was decided that all types of histologically proven oesophageal columnar metaplasia should be included under the umbrella word "Barrett's", with the important added descriptors of either "intestinal-type metaplasia positive" or "negative".

28. Adenocarcinoma of the oesophagus is a complication of GORD.

29. The risk of adenocarcinoma of the oesophagus rises with an increasing frequency and duration of heartburn.

There is strong epidemiological evidence, especially from case-controlled studies in Sweden, that oesophageal adenocarcinoma is a complication of GORD and that chronic GORD symptoms increase the risk of oesophageal adenocarcinoma. Lagergren et al.¹⁸ found that the risk of oesophageal adenocarcinoma was increased (OR 7.7) in patients suffering from long-standing reflux symptoms. Reflux greater than three times a week and a long duration – 10 to 20 years of symptoms – further increased the OR to 16.4 and 20 respectively. In the USA, oesophageal adenocarcinoma has now overtaken

oesophageal squamous carcinoma in incidence. There appears to be an increasing incidence of Barrett's oesophageal adenocarcinoma in Japan, where the disease used to be rare. However, the lifetime risk of developing adenocarcinoma is still less than 1%.

30. Long-segment Barrett's oesophagus with intestinal-type metaplasia is the most important identified risk factor of oesophageal adenocarcinoma.

D. EXTRAESOPHAGEAL SYNDROMES: ESTABLISHED ASSOCIATIONS

The panel came to the following conclusions:

- I. An association does exist between extraoesophageal syndromes and GORD.



- II. Extraoesophageal syndrome rarely occurs in isolation without a concomitant manifestation of the typical oesophageal syndrome.
- III. These symptoms are usually multifactorial, with GORD as one of several potential aggravating factors.
- IV. Data substantiating a beneficial effect of reflux treatments on the extraoesophageal symptoms are weak.

31. Chronic cough, laryngitis and asthma are significantly associated with GORD.

32. Chronic cough, chronic laryngitis and asthma are usually multifactorial disease processes and gastro-oesophageal reflux can be an aggravating cofactor.

33. Gastro-oesophageal reflux is rarely the sole cause of chronic cough, chronic laryngitis or asthma.

Studies have shown an increased risk of ENT and pulmonary symptoms in patients with oesophagitis or reflux symptoms, with nocturnal cough having the strongest association.¹⁹ Chronic cough, chronic laryngitis and asthma symptoms may be improved but not completely resolved by PPI therapy or antireflux surgery. Commonly implicated cofactors with laryngitis include heavy voice usage, habitual throat clearing, allergic rhinitis with postnasal drip, infectious laryngitis and environmental irritants, including smoking.

A significant improvement in asthma symptoms and a reduction in asthma medication have been shown with GORD treatment but no improvement has been shown in pulmonary function.²⁰ Commonly implicated cofactors include allergens, exercise, temperature or climate changes and emotional conflict.

In two series of highly selected chronic-cough patients, 51% of 133 showed a complete response following Nissen fundoplication²¹ and two out of eight patients' refractory to medical therapy showed a complete response to antireflux surgery.

These data in no way support the routine use of antireflux surgery in patients with chronic cough, chronic laryngitis and asthma.

34. Potential causal mechanisms of reflux cough, reflux laryngitis and reflux asthma syndromes include direct (aspiration) or indirect (neurally mediated) effects of gastro-oesophageal reflux.

35. In the absence of heartburn or regurgitation, unexplained asthma and laryngitis are unlikely to be related to GORD.

This statement achieved a high grade of agreement for asthma and low-level agreement for laryngitis. Most asthmatics have objective evidence of reflux disease and reflux symptoms. In a study of 770 asthmatics on twice-daily PPI therapy, only those with nocturnal respiratory and GORD symptoms showed a response over placebo.²²

In a group of patients with chronic laryngitis but excluding those with frequent heartburn, PPI therapy showed no benefit over the placebo treated group.

36. Medical and surgical treatment trials aimed at improving presumed

reflux cough, reflux laryngitis and reflux asthma syndromes by treating GORD are associated with uncertain and inconsistent treatment effect.

Asthmatics placed on antireflux medication may benefit by having fewer symptoms and a reduction in asthma medication but there is no improvement in lung function.

In reflux-cough syndrome, the data are conflicting, with some small studies showing benefit from PPIs and antireflux surgery.

For reflux laryngitis, the trial results have also yielded inconsistent results.

In patients presenting with ENT symptoms, a careful history needs to be obtained with regard to reflux symptoms. Patients presenting with both ENT and GORD symptoms will most likely derive the greatest benefit from antireflux treatment.

37. The prevalence of dental erosions, especially on the lingual and palatal tooth surfaces, is increased in patients with GORD.

38. It is unclear whether GORD is a significant causal or exacerbating factor in the pathogenesis of sinusitis, pulmonary fibrosis, pharyngitis or recurrent otitis media.

The panel found insufficient evidence to support an association between GORD and these conditions. 🐾

See CPD Questionnaire, page 48

P This article has been peer reviewed

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