

Different management for *Helicobacter pylori* positive and negative patients with gastro-oesophageal reflux disease?

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Summary

Available evidence would suggest that *Helicobacter pylori* infection does not contribute to the pathogenesis of gastro-oesophageal reflux disease. The prevalence of *H pylori* infection in patients with reflux disease is no greater than that in control populations. There are some data suggesting that the organism has a protective role: patients with duodenal ulcers develop reflux disease after *H pylori* eradication, whereas in patients with oesophageal reflux those with *H pylori* infection have less severe reflux changes. There is also evidence indicating that the presence of *H pylori* augments the anti-secretory properties of both the H₂ receptor antagonists and proton pump inhibitors (PPIs), suggesting that eradication therapy may not be beneficial. However, the considerable recent interest in the association between *H pylori* and reflux disease has largely been generated by studies outlining the interactions between *H pylori* infection and acid suppression in the long term. In *H pylori* positive patients, therapy with PPIs is associated with a proximal extension of the infection and its associated gastritis. In addition long term PPI therapy is reported to be associated with an accelerated development of atrophic gastritis, suggesting that *H pylori* should be diagnosed and treated. Although these latter findings in particular need confirmation, *H pylori* eradication therapy should be considered in this patient group, at least until there is evidence to the contrary.

Introduction

Gastro-oesophageal reflux disease (GORD) refers to the abnormal exposure of the oesophageal mucosa to refluxed gastric contents, resulting in symptoms and/or tissue damage. It is a common condition with epidemiological studies indicating that up to 10% of the adult population experience heartburn on a daily basis, and up to 44% report this symptom at least once a month.¹⁻⁴ Long term follow up studies indicate that GORD is not a self limiting condition and many patients still have significant morbidity many years after their initial diagnosis.⁵⁻⁶ Since the discovery of *Helicobacter pylori* in the early 1980s, a role for this organism in the pathogenesis of peptic ulcer disease has been well established. In addition, the benefit of eradicating the organism in this setting is not in doubt.⁷⁻¹⁰ Studies also indicate an epidemiological link with gastric adenocarcinoma.¹¹ The association between *H pylori* and GORD has not been as thoroughly

investigated, but despite this there has recently been great interest in the role of *H pylori* in reflux disease. The decision to eradicate this bacteria in patients with GORD is not clear-cut—there are differing opinions expressed by many national and international groups.¹⁰ If we are to suggest different management strategies for patients with GORD with and without *H pylori* infection, we need to evaluate the evidence that this organism has a role in the pathogenesis of reflux disease. The impact of *H pylori* infection on both the efficacy and long term safety of agents currently used in the management of GORD also needs to be considered.

H pylori and the pathophysiology of GORD

GORD is regarded as a multifactorial disease, and the proposed factors contributing to pathological gastro-oesophageal reflux include the presence of a hiatus hernia, oesophageal sphincter incompetence, the aggressive nature and impaired clearance of refluxed material, impaired oesophageal epithelium defence mechanisms, and finally impaired gastric emptying.¹²⁻¹⁹ A role for *H pylori* in the pathogenesis of GORD according to present data is speculative, but theoretically *H pylori* could contribute to the development of GORD by several different mechanisms: (a) inflammation of the cardia causing impairment of sphincter function; (b) increased gastric acid secretion associated with antral predominant gastritis; (c) impairment of gastric emptying; and (d) the production of cytotoxins harmful to the oesophageal mucosa. Conversely, there are also potential mechanisms by which the presence of *H pylori* may prevent the development of reflux disease: (a) decreased gastric acid secretion with corpus predominant gastritis; (b) proximal gastric inflammation may paradoxically contribute to the barrier function of the gastro-oesophageal junction; and (c) ammonia production by *H pylori* could offer a potential buffering system.

GASTRIC ACID SECRETION

There are conflicting results in studies evaluating the association between gastric acid secretion and reflux oesophagitis,²⁰⁻²³ but increased gastric acid production is important in at least a subset of patients.^{22 24 25} There is considerable evidence that *H pylori* is involved in the modulation of gastric acid production through alterations in the function of both gastric exocrine and endocrine cells either directly, or

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via the inflammatory mediators associated with *H pylori* gastritis. Most of these data, however, come from patients with *H pylori* and associated peptic ulcer disease, or from studies at an animal or cellular level, and not from patients with documented reflux disease. *H pylori* positive subjects have been shown to have increased basal, meal stimulated and gastrin releasing peptide (GRP) stimulated gastrin concentrations.²⁶⁻³⁰ Factors proposed to account for the increase in gastrin associated with *H pylori* infection include a local alkalinisation as a result of ammonium ion production secondary to urease activity, and the increased expression of mucosal cytokines.³¹ This increase in gastrin has been demonstrated in both patients with duodenal ulceration and non-ulcer dyspepsia.^{29 30 32} Eradication of *H pylori* results in a decrease in gastrin concentrations.^{33 34} The increased basal acid and GRP stimulated acid secretion associated with increased gastrin concentrations has been more noticeable in patients with duodenal ulcer compared with other patient groups.^{29 30 35 36} Again, eradication of *H pylori* results in the normalisation of this acid response,^{29 30 36} indicating that the infection is probably causative. Although the mechanisms are unclear, several studies have also reported reduced somatostatin levels associated with *H pylori* infection both at a protein and mRNA level.³⁷⁻⁴² Somatostatin, which is usually released from D cells, has widespread inhibitory effects on both endocrine and exocrine cells including G cells, enterochromaffin-like (ECL) cells and parietal cells.³¹ Its reduction could thus account for the observed alterations in both gastrin and acid secretion. It is thus clear that *H pylori* infection is associated with abnormalities leading to increased acid secretion. These data, however, do not come directly from patients with GORD, but mainly from patients with duodenal ulceration and associated antral gastritis, so a degree of caution is necessary if extrapolation to patients with GORD is considered.

A subgroup of subjects with chronic *H pylori* infection exhibit a lowering of gastric acid secretion or complete achlorhydria associated with a body predominant bacterial colonisation and gastritis.⁴³ Theoretically, *H pylori* infection would protect against GORD in this setting, but more importantly this pattern of colonisation and inflammation is associated with an increased risk of gastric cancer. Eradication of *H pylori* in this group produces partial reversal of the gastric acid hyposecretory state.⁴⁵ *H pylori* thus has divergent effects on gastric secretory function and patterns of gastritis. In some patients it results in notably increased acid secretion associated with a predominant antral gastritis, which could increase the likelihood of GORD, and in others it results in profound inhibition of acid secretion associated with severe corpus gastritis, which may well be protective.

GASTRO-OESOPHAGEAL SPHINCTER FUNCTION

Many authors would consider altered motility the dominant pathophysiological abnormality in GORD. It is now established that transient

lower oesophageal sphincter relaxation (TLOS) is the dominant mechanism underlying reflux events.⁴⁴ The mechanisms controlling TLOS are not fully understood, but it is thought that stimulation of receptors through distension of the proximal stomach may trigger some TLOSs by a vagal reflex.⁴⁵ Hypothetically, proximal extension of bacterial colonisation and inflammation could increase the frequency of TLOS via increased triggering of these vagally mediated receptors. In addition, the presence or absence of *H pylori* in the peri-sphincter area may influence sphincter pressure and competence through structural alterations independent of TLOS. All of these proposed mechanisms are at present highly speculative however and the overall significance, if any, of *H pylori* infection in this context remains unclear.

OTHER FACTORS

Evidence of delayed gastric emptying of a solid or semi-solid meal is very variable in patients with GORD, and studies indicate prevalences from 6 to 80%.⁴⁶⁻⁴⁸ The degree of abnormality detected is also very variable, and the overall significance of abnormal gastric emptying in the pathophysiology of GORD is uncertain. The relation between *H pylori* and delayed gastric emptying has been evaluated in other patient groups and at least three studies failed to indicate a difference between *H pylori* positive or negative patients.⁴⁹⁻⁵¹ There is some indirect evidence that *H pylori* has a role in altering gastric motility in patients with GORD. In a small series of patients with reflux disease and histological evidence of antral gastritis, the degree of delayed gastric emptying did correlate with the severity of antral inflammation.⁵² Although the presence or absence of *H pylori* was not formally determined by recommended diagnostic tests, it is accepted that *H pylori* is the most common cause of this pattern of gastritis. Despite this latter small study, however, overall present evidence would suggest that *H pylori* does not predispose to GORD through alterations in gastric emptying.

H pylori infection is more often asymptomatic than symptomatic and the reasons for this are not clearly understood. Several bacterial genotypic markers including *cagA*, *vacA*, *slsA*, and *iceA1* are associated with an increased risk of gastroduodenal disease.⁵³ *CagA* positive strains—for example, colonise the host with increased density and are associated with higher degrees of epithelial injury, interleukin 8 secretion and mucosal inflammation.⁵³ Most patients with duodenal ulcer are infected with such strains, and it has been reported that *cagA* strains are associated with a higher gastrin output in response to GRP when these patients are compared with those harbouring *cagA* negative strains.⁵⁴ There are very few data specifically tackling these issues in patients with GORD but a study from Tee and colleagues,⁵⁵ which included 11 patients with GORD, indicated that 80% of patients with erosive oesophagitis had cytotoxin producing strains, whereas only

one (17%) of six patients without erosive changes had a cytotoxin producing strain.

***H. pylori* and GORD: the epidemiological link**

A number of studies have attempted to evaluate the relation between *H. pylori* and GORD by determining the prevalence of *H. pylori* infection in this condition.⁵⁶⁻⁶⁷ Although all of the studies did not have adequate numbers of patients or control populations, the overall prevalence of *H. pylori* is not significantly greater in patients with GORD than what would be expected in the general population (table 1). *H. pylori* had been diagnosed by various methods in just 35% of almost 700 patients with varying degrees of reflux disease (table 1). Exclusion of those studies that evaluated paediatric⁵⁹ or elderly⁶³ populations only does not alter this figure significantly. Where control populations were reported, the majority of investigators chose patients with normal endoscopic studies to form this group. Other than one study where the prevalence of *H. pylori* was significantly higher in the control group,⁶⁶ there was no significant difference between the prevalence of *H. pylori* in patients with reflux disease and control populations. In over half of the studies to date, the oesophagus has also been evaluated for evidence of *H. pylori* (table 1). In one of the earlier studies which enrolled patients with either grade 3 or 4 oesophagitis only, evidence of *H. pylori* was reported in 45%.⁵⁷ Since then, there have been a number of studies which have failed to detect *H. pylori* in the squamous oesophageal mucosa of patients with reflux disease.^{58-61 65 67} In one of the larger series of patients where the prevalence of *H. pylori* was 54% in the stomach, evidence of the organism was found in a hiatus hernia in 44% of 64 patients.⁶² Although the evaluation of *H. pylori* in GORD was not the primary aim in a number of these studies,^{36 60 64} when all of these studies are evaluated collectively, the overall

low prevalence of *H. pylori* would indicate that this organism is very unlikely to have an important role in the pathogenesis of GORD.

***H. pylori* influencing the current treatment of GORD**

Given that the outlined evidence would indicate that *H. pylori* does not cause GORD, recent studies would suggest that we do need to consider both the diagnosis and treatment of *H. pylori* in our approach to the management of this condition. Acid suppression, with either H₂ receptor antagonists or proton pump inhibitors (PPIs), is now firmly established as an effective method of treating GORD in terms of initial symptom relief and mucosal healing.⁶⁸ Symptom relapse in the majority of patients on withdrawal of therapy, no matter what agent is used, has generated a need for long term treatment. It is the relatively recent evidence questioning the safety of long term acid suppression, particularly with PPIs, in patients with concomitant *H. pylori* infection, that has generated most interest in the association between *H. pylori* and GORD.

PPIs AND THE DEVELOPMENT ATROPHIC GASTRITIS
Kuipers *et al* reported that patients with *H. pylori* infection requiring long term proton pump inhibition for the treatment of GORD have an increased risk of developing atrophic gastritis.⁶⁹ Of 59 *H. pylori* positive Dutch patients treated with omeprazole, 31% developed atrophic gastritis during a mean follow up of five years, whereas only 3% of 31 *H. pylori* positive Swedish patients who were treated surgically with a fundoplication had evidence of atrophic gastritis during a similar period of follow up. Atrophic gastritis, via the subsequent steps of intestinal metaplasia and dysplasia, increases the risk of developing gastric cancer, and this obviously is where the real worry lies. There are however some other factors that need attention in the analysis of the data from

Table 1 Prevalence of *Helicobacter pylori* in GORD: summary of studies to date

Author	Number of patients	Prevalence of <i>H. pylori</i> (%)		Comments
		Stomach	Oesophagus	
Marshall <i>et al</i> ⁵⁶ (1984)	34	41	NA	"Abnormal oesophagus" not defined
Borkent <i>et al</i> ⁵⁷ (1988)	20	40	45	Only patients with grade III-IV reflux oesophagitis
Cheng <i>et al</i> ⁵⁸ (1989)	27	41	0	No <i>H. pylori</i> in oesophagus (assessed by histology, microbiology and RUT)
Stewart <i>et al</i> ⁵⁹ (1990)	26	4	0	Paediatric population, mean age 3 years
Shalcross <i>et al</i> ⁶⁰ (1990)	31	51.6	0	51.6% of patients taking NSAIDs
Francoual <i>et al</i> ⁶¹ (1990)	21	33	0	21 patients with "clinical" GORD, 13 with GORD on endoscopy/histology
O'Connor <i>et al</i> ⁶² (1994)	93	54	NA	44% of 64 patients with a hiatus hernia had <i>H. pylori</i> in the hernia
Liston <i>et al</i> ⁶³ (1996)	37	75.5	NA	Mean age 78.9 years. <i>H. pylori</i> prevalence in controls (OGD normal) = 81.8%
Hatlebakk <i>et al</i> ⁶⁴ (1996)	18	44	NA	Only patients with grade I reflux disease. <i>H. pylori</i> diagnosed by UBT
Newton <i>et al</i> ⁶⁵ (1997)	36	42	0	<i>H. pylori</i> prevalence in controls (asymptomatic, investigation of anaemia) = 36%
Werdmuller <i>et al</i> ⁶⁶ (1997)	118	30	NA	<i>H. pylori</i> prevalence higher in controls (normal endoscopy) at 51%
Csendes <i>et al</i> ⁶⁷ (1997)	236	20-25	0	No difference in prevalence of <i>H. pylori</i> in different grades of oesophagitis
Total				
All inclusive	697	247/697 (35.48%)		
Excluding references 59 and 63	659	218/659 (33.1%)		

RUT, rapid urease test; NSAID, non-steroidal anti-inflammatory drug; UBT, urea breath test; OGD, oesophagogastrroduodenum.

this study. In particular the groups were not age matched—the mean ages after follow up were 58 and 67 years in the surgical and medically treated groups, respectively. Increasing age has been associated with a higher prevalence of atrophic gastritis, and the greater age of the patients receiving drug therapy initially looks like a reasonable factor to at least partly explain the results of this study. However, when we consider the absence of atrophic gastritis in the relatively elderly population (mean age of 62 years) at enrollment in the medically treated group, the argument for age difference explaining the new emergence of atrophic gastritis is less convincing. Other factors which could have influenced results include the lack of randomisation, the different male:female ratios and the fact that the two cohorts were treated in different hospitals and different countries. In addition, no significant increase in the prevalence of intestinal metaplasia was seen after a mean of five years of follow up in the *H pylori* positive medically treated group. The findings of this study, though important, need to be confirmed in other studies. There has been some preliminary data from a long term follow up study by Lundell *et al* which would not support these data.⁷⁰

PPIs AND THE REDISTRIBUTION OF *H PYLORI*

There is also evidence that treatment with PPIs alters the distribution of *H pylori*.^{71 72} In a study of 29 *H pylori* positive patients by Logan *et al* the histological density of *H pylori* in the antrum and corpus had decreased whereas that in the fundus had increased after four weeks of treatment with omeprazole 40 mg daily.⁷¹ These results were confirmed by Kuipers *et al* who also demonstrated a shift in organism distribution after eight weeks of omeprazole therapy.⁷² *H pylori* cultures from the antrum became negative in 61% of 33 patients, whereas corpus inflammation increased. Similar findings have also been found with the use of lansoprazole.^{73 74} These results have implications for the diagnosis of *H pylori* as the sensitivity of diagnostic tests based on analysis of biopsy samples from the antrum alone would be reduced. Although the reduced acid output with a pangastritis would theoretically make GORD less likely, the more relevant message suggested by these data is that PPI therapy is associated with a change in the distribution of *H pylori* to a pattern more likely to be associated with gastric cancer. Although this certainly does not indicate a causal link, it again raises the question of the need to treat *H pylori* infection when long term acid suppression is being considered.

H PYLORI AND THE EFFICACY OF ANTI-SECRETORY MEDICATIONS

There is evidence suggesting that *H pylori* augments the pH increasing effect of PPIs. Verdu *et al* have shown that omeprazole produces greater acid suppression in subjects with *H pylori* than in those without the infection.⁷⁵ This group has also reported that omeprazole produces less acid suppression after *H pylori* eradication.⁷⁶ Labenz *et al* have reported that in

patients with duodenal ulcers treated with omeprazole, intragastric pH depended significantly on *H pylori* status: eradication of *H pylori* also resulted in a notable decrease in the pH increasing effect of omeprazole.⁷⁷ Cure of *H pylori* infection has also been shown to decrease the anti-secretory effect of the H₂ receptor antagonist ranitidine, particularly at night.⁷⁸ It may thus be argued that *H pylori* eradication therapy may not be in the best interest of patients requiring long term acid suppression for the control of symptoms, in that the available anti-secretory agents may not achieve sufficient inhibition of gastric acid output for the optimal treatment of GORD in the absence of *H pylori*. These findings do require further consideration as it is not established to what degree they are clinically relevant. They would suggest that the dose of anti-secretory agent required for appropriate control of gastric acidity may have to be increased in some patients after *H pylori* eradication.

ERADICATION THERAPY IN PATIENTS WITH GORD

Numerous studies have evaluated the efficacy of *H pylori* eradication therapy in the treatment of both peptic ulcer disease and non-ulcer dyspepsia, despite the continued uncertainty among some groups concerning the role of *H pylori* in the pathogenesis of the latter condition. There is very limited data tackling this issue in patients with GORD. In a small double blind study of patients with grades III–IV oesophagitis 10 patients received cimetidine 800 mg at night, and 10 patients received cimetidine plus colloidal bismuth. In the latter group, healing of oesophagitis was significantly better.⁵⁷ At entry evidence of *H pylori* was present in nine patients—in the five patients treated with combination therapy cultures were negative within one week, while they were negative in two of four patients treated with cimetidine alone. Although these findings do suggest a benefit for eradication therapy at least in patients with severe oesophagitis, patient numbers were small, and the efficacy of diagnostic tests for *H pylori* is limited during continued acid suppression. Again, this area warrants further evaluation if any conclusions are to be drawn.

DEVELOPMENT OF GORD AFTER *H PYLORI* ERADICATION

The treatment of patients with peptic ulceration with *H pylori* eradication therapy has recently been associated with the subsequent development of reflux oesophagitis. Hirschel *et al* reported the development of reflux oesophagitis in 10 of 16 patients who were successfully treated for *H pylori*.⁷⁹ Labenz *et al* recently reported on the follow up of 460 patients who also had treatment for duodenal ulcers associated with *H pylori* infection.⁸⁰ After four weeks, eradication was successful in 244 patients, whereas the infection persisted in 216. During a mean follow up of 17.3 months endoscopically confirmed GORD developed in seven *H pylori* positive patients. Over 17.7 months GORD was found in 32 *H pylori* negative patients. From lifetime analysis the incidence of reflux

oesophagitis within three years was estimated to be 12.9% and 25.8% in the *H pylori* positive and negative groups respectively. Patients who later developed GORD had higher scores for body gastritis before eradication. Although the increase in gastric acid output associated with the healing of proximal gastritis is one explanation for the development of reflux after *H pylori* eradication, other potential explanations include the masking of symptoms by the use of acid suppressants before eradication therapy and weight gain due to dietary changes. In addition, there is a recent study reporting that 20% of 244 patients with *H pylori* positive peptic ulcer disease had associated GORD on initial presentation.⁸¹ The GORD tended to improve or remain stable in the short term after eradication therapy. Of patients who presented with a normal oesophagus only 7% developed GORD during follow up. These findings suggest that the reporting of GORD after eradication therapy may simply reflect pre-existing disease. This area also needs further investigation and clarification.

Could *H pylori* have a protective role in GORD?

The new development of GORD after the eradication of *H pylori* would suggest that this may well be the case. However, these initial studies need to be confirmed. Another argument for a protective role is the higher prevalence of *H pylori* in some control groups with normal endoscopies than patients with endoscopic evidence of oesophagitis.⁶⁰ There is also some preliminary evidence that *H pylori* negative patients present with more severe oesophagitis than *H pylori* positive ones.⁸² It has also been documented that although the prevalence of *H pylori* is decreasing in some populations, the incidence of oesophagitis and cancer of the distal oesophagus and proximal stomach is increasing in the same populations. If *H pylori* was causative in these disease processes such opposing trends would not be expected—they suggest that *H pylori* may have a protective role.

H pylori and Barrett's mucosa

It is established that chronic GORD is an important predisposing factor for the development of Barrett's oesophagus. However, only a small percentage of patients with GORD develop Barrett's mucosa, indicating a potential role for host or environmental factors. The

incidence of adenocarcinoma of the oesophagus is increasing⁸³⁻⁸⁵ and the only recognised risk factor for adenocarcinoma of the oesophagus is Barrett's mucosa.⁸³ The risk of malignancy in patients with Barrett's oesophagus is more than 30 times higher than that of the general population.⁸⁶⁻⁸⁸ It is a premalignant condition in which the normal stratified squamous epithelium of the distal oesophagus is replaced by a columnar epithelium. With this columnar epithelium, particularly of the gastric type, one would expect some colonisation by *H pylori*. It is conceivable that the bacteria may either have a role in determining which patients with GORD develop Barrett's mucosa, or in determining which patients with Barrett's mucosa develop adenocarcinoma of the oesophagus. Available data would not support either. A number of studies have determined the prevalence of *H pylori* in both gastric and oesophageal specimens from patients with Barrett's mucosa (table 2). Evidence of oesophageal colonisation was found in 23.2% of over 360 patients. A number of these studies were retrospective, and data outlining *H pylori* infection of gastric mucosa were available in only 71% of cases. Of 261 patients, 22% had documented gastric infection. This figure is not above that expected in the general population, and would not support a role for *H pylori* in the pathogenesis of Barrett's mucosa. A possible role for *H pylori* in the evolution of Barrett's mucosa to adenocarcinoma has not been extensively investigated to date, but in a study by Quddus *et al* there was no evidence of *H pylori* in 19 patients with adenocarcinoma arising in Barrett's oesophagus.⁸⁹ Although these results are preliminary, and require confirmation, they do suggest that *H pylori* probably does not have a role in the pathogenesis of oesophageal adenocarcinoma on background Barrett's mucosa.

Different management for *H pylori* positive and negative patients with GORD?

Available data would suggest that *H pylori* probably does not have a role in the pathogenesis of GORD or Barrett's mucosa. Although *H pylori* has been shown to contribute to the development of pathophysiological abnormalities, particularly through altered gastric acid production, which would theoretically make GORD more likely, most of the data in this context are circumstantial, and have come from patients with duodenal ulceration and not directly from patients with GORD. The low prevalence of *H pylori* infection in patients with GORD would suggest that the organism does not have a causal role in disease development. Indeed there is some evidence to suggest that the infection may be protective. In addition, there is not sufficient evidence to suggest eradication therapy on the basis of a greater risk of Barrett's mucosa, a premalignant condition for which chronic GORD is a predisposing factor. The reports of reduced efficacy of both H₂ receptor antagonists and PPIs in the absence of *H pylori* would suggest that the organism should not be eradicated. The data

Table 2 Prevalence of *Helicobacter pylori* in patients with Barrett's mucosa: summary of studies to date

Author	Number of patients	Prevalence of <i>H pylori</i> (%)	
		Stomach	Oesophagus
O'Connor <i>et al</i> ⁹² (1994)	8	62	12.5
Paull <i>et al</i> ⁸¹ (1988)	26	37	15
Loffield <i>et al</i> ⁸² (1992)	71	NA	62
GOSPE ⁸³ (1991)	100	21*	19
Talley <i>et al</i> ⁸⁴ (1988)	23	NA	52
Walker <i>et al</i> ⁸⁵ (1989)	7	NA	29
Francoval <i>et al</i> ⁸¹ (1990)	11	36	0
Newton <i>et al</i> ⁸⁵ (1997)	16	25	12.5
Csendes <i>et al</i> ⁸⁷ (1997)	100	20-25	0

*Gastric mucosa available in 63 of 100 patients.

outlining the efficacy of eradication therapy for the actual treatment of oesophagitis and its associated symptoms are too limited to guide a recommendation. However, there are data available indicating that we should consider *H pylori* eradication in our patients with GORD for other reasons. The reports of organism redistribution, the development of proximal gastritis and particularly the development of atrophic gastritis with long term acid suppression, though controversial, are the most compelling. These latter areas in particular require further evaluation, but until evidence to the contrary is available the recommendation of the European *Helicobacter pylori* Study Group, who considered it "advisable" on the basis of "supportive" evidence that *H pylori* should be eradicated when GORD requires treatment with long term PPIs, is a reasonable one.⁹ In other words patients with GORD with *H pylori* infection, particularly when long term acid suppression is required, should be considered for eradication therapy.

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