Helicobacter pylori and Less Common Gastric Diseases

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Abstract

Helicobacter pylori (*H. pylori*) is associated with a wide spectrum of gastroduodenal diseases. Strong evidence has shown that *H. pylori* is implicated in the development of gastritis, gastric and duodenal ulcers, MALT lymphoma and gastric cancer. The result of multiple clinical trials had also found out that eradication of *H. pylori* results in cure of gastric and duodenal ulcers. The improvement of gastric inflammation after therapy is well documented and a substantial proportion of MALT lymphoma can be well treated by *H. pylori* eradication regimen. Progress has been made to widen the spectrum of gastric diseases associated with *H. pylori* infection. In recent years there were reports relating this microorganism with the less common gastric diseases. The long term complication of peptic ulcer disease, gastric outlet obstruction was found to be related to *H. pylori* infection in a substantial number of cases and eradication treatment can dilate the stenosis. As high as 90% of Menetrier's disease had been found to be related to *H. pylori* infection. Possible elimination of gastric hyperplastic polyps by *H. pylori* eradication therapy had been reported. The possible role of *H. pylori* in lymphocytic gastritis and granulomatous gastritis had been well investigated. Revolutionalized concept to treat these diseases by antimicrobial therapy had been substantiated by the successful experience of various authors. However, large series of prospective randomized clinical trials are still lacking in these fields. (J Intern Med Taiwan 2002;13:1-9)

Key Words：Helicobacter pylori, Gastric outlet obstruction, Menetrier's disease, Gastric hyperplastic polyps, Lymphocytic gastritis, Granulomatous gastritis.

Introduction

Since Warren and Marshall disclosed *Helicobacter pylori (H. pylori)* in gastric mucosa of gastritis patients in 1983, multiple studies have shown that *H. pylori* is associated with the development of gastritis, gastric and duodenal ulcers, MALT lymphoma and even gastric adenocarcinoma. There had been strong evidence relating *H. pylori* infection with chronic gastritis [1, 2], gastric ulcer [2, 3] and duodenal ulcer [2, 3]. Effective eradication therapy of *H. pylori* infection had resulted in over 90% of cure rate of gastric and duodenal ulcers [4, 5]. In addition, a substantial number of cases of MALT lymphoma, especially low grade lymphoma, had been well treated with this antibacterial therapeutic regimen[1,6]. Evidence from pathological and epidemiological studies has also identified the relationship between chronic *H. pylori* infection and the subsequent development of gastric cancer [7, 8]. This had led the working group of the WHO International Agency for Research on Cancer to place *H. pylori* in the list of group 1 carcinogen in humans in 1994. Greater awareness of spectrum of diseases associated with *H. pylori* had prompted more investigational studies. In recent years there were also reports relating this microorganism with the less common gastric diseases. This category included gastric outlet obstruction, hypertrophic gastropathy, gastric polyps, lymphocytic gastritis, granulomatous gastritis and miscellaneous rarer gastric diseases.

Helicobacter pylori and Gastric Outlet Obstruction

Benign gastric outlet obstruction (GOO) may be a long term complication of chronic peptic ulcer disease [9], or in the minority of cases, a result of nonsteroidal anti-inflammatory drug-related disease [10]. The incidence of GOO is estimated to be 2-8% of peptic ulcer disease [11]. In the past, patients of GOO with clinical symptoms were first treated medically by acid suppression therapy. Aggressive intervention such as surgical operation [12] or balloon dilatation [13] would be undertaken if the initial treatment option failed, or in severe intractable condition such as long standing fibrotic stenosis.

In recent years, clinical reports regarding *H. pylori* eradication therapy in these patients had been interesting and fascinating. Accumulating evidence suggests that *H. pylori* infection was related to a substantial proportion of peptic ulcer induced GOO, and antibacterial therapy was efficient to relieve the symptoms and ultimately dilate the stenosis[14-18]. The authors suggested that oral eradication therapy should be attempted before operational procedure.

There was evidence showing that even long standing fibrotic stricture appears to dilate after *H. pylori* eradication. W. de Boer in 1995 reported two cases of pin-point pyloric stenotic patients with successful treatment by oral eradication regimen14. Both cases had been treated previously with acid suppression therapy without effective outcome, but the pyloric stenosis disappeared rather "unexpectedly" after *H. pylori* eradication therapy. In this report, the author emphasized the preference for quadruple therapy regimen for optimal treatment, and stated that the regimen works even in non-empty stomach, presumably by their topical effect, which was in agreement with Kimura's work [19]. The therapeutic success of W. de Boer was supported by clinical report (1996) of Italian authors, who successfully treated stenotic cases with one week triple therapy [15]. The Australian group had followed up patients of stenosis for 4 to 8 years, and had concluded that these patients, some with near pin-point stricture, responded well to quadruple therapy. They stated that tight stricturing and presumably associated fibrosis could be reversible [16].

It seems that the associated luminal edema resolves early after *H. pylori* eradication, with improvement of gastric emptying and symptoms, whereas the scarred lesion requires more time to soften. The explanation held by these authors is "that the long standing fibrotic stricture appears to dilate presumably due to the incessant pump action akin to a built-in dilator, which progressively stretches the softening fibrosis— provided the underlying *H. pylori*-driven inflammation is removed" [16].

There were also different opinions presented by other aurthors [20-23]. A Tursi and his coworkers pointed out that *H. pylori* eradication is not necessarily effective in older stenosis [21]. Rinaldi and Zullo emphasized the importance of the width of pyloric opening in predicting successful therapy [22]. Gibson DM recently reviewed a cohort of 24 patients underwent surgery, and found that only 8 (33%) were *H. pylori* positive.

In conclusion, based on the successful experience of many authors, *H. pylori* eradication therapy might be considered as a first-line treatment for GOO, if *H. pylori* infection is documented, and quadruple therapy appears to be the optimal treatment regimen. Dilatation or surgery should be reserved for patients who do not improve after antibacterial treatment. Finally it remained to be reminded that long term prospective comparative trial is still lacking in this field.

Helicobacter pylori and Hypertrophic Gastropathy

Hypertrophic gastropathy comprises entities of diseases associated with thickened gastric folds. The most common form of these diseases is hypertrophic gastritis which is histologically characterized by hypertrophy of glandular and foveolar layers associated with severe *H. pylori* infection [24]. It is believed that the majority of cases is simply a rugal hyperplasia condition secondary to *H. pylori* infection [24]. Normally no severe clinical condition is found associated to this form of gastritis, but in the long run, as in other chronic *H. pylori* related gastritis, it may proceed to atrophic gastritis and intestinal metaplasia, which subsequently may be predisposed to increased frequency of cancer transformation [25].

Another well known disease in this category is Menetrier's disease. The histological features of this disease is characterized by foveolar hyperplasia, atrophy of glands and increased mucosal

thickness [26]. It is a rare disease often regarded as of unknown etiology, and clinically manifested as protein-losing gastropathy and hypoproteinemia [27]. Increased incidence of gastric cancer association as high as 13% had been reported [28]. There was some evidence that the altered expression of transforming growth factor-alpha might play a role in its etiology [29, 30]. Recently *H. pylori* has been implicated as a pathogenic factor in the cause of this disease [31]. In 1992, the Dutch Menetrier's study group has reported a low prevalent rate of *H. pylori* infection in adult Menetrier's disease [32]. More recently, Stolte and Bayerdorffer et al in 1995 had retrospectively investigated 138 patients with hypertrophic gastropathy, and found that this disease was associated with *H. pylori* infection in more than 90% of cases [33]. In view of this finding, the study group treated a case of Menetrier's disease associated with protein losing gastropathy, with documented *H. pylori* infection. This case was treated previously with cimetidine for more than 3 years, with little benefit. A 14-day course of dual therapy with amoxicillin and omeperazole led to *H. pylori* eradication and normalization of the giant folds in a 4-week period, and increased serum protein concentration to normal range in 6-week period [34]. Several other reports had also shown that effective *H. pylori* eradication therapy resulted in remission of protein-losing hypertrophic gastropathy [35-37]. Some authors have proposed that *H. pylori* might act as a local antigen to sensitize the gastric mucosa, which leads to an abnormal response ultimately resulting in hypertrophic gastropathy [38]. It has been shown that gastric mucosa infected with *H. pylori* is in a state of hyperproliferation, evidenced from expression of PCNA [39]. Animal study of infected transgenic mice has shown sustained anti-Helicobacter felis serum antibody response, with subsequent development of adenomatous and cystic hyperplasia of the surface foveolar epithelium [40]. H.
pylori had been implicated in cases of hypertrophic gastropathy in both adults and children [35, 41]. Yamada M. in 1997 had reported a 3-year-old boy with severe protein-losing gastropathy [35]. Abdominal scintigraphy using IV 99m Tc-labelled albumin showed massive protein excretion from the stomach. A 2 week antibacterial treatment was prescribed and this resulted in rapid improvement of protein loss with subsequent improvement of hypoproteinemia and edema in 4 weeks time.

Taking account of the fact that protein-losing gastropathy with intractable hypoproteinemia is sometimes a life-threatening condition, this report

Table 1 Clinical Features of Patients with Hyperplastic Gastric Polyps Treated by *Hp* Eradication Therapy Reported in English Literature

Reference	Case number	Description of lesions	Associated clinical features	Treatment	Follow up
Veerman et al.	2	multiple polyps size not stated	mild chronic gastritis	amoxicillin+ bismuth x 2w	disappearance and recurrence of polyps(1y, 2y)
		2 polyps 2mm, 7 mm	diffuse gastritis healed GU		disappearance of symptoms (no follow-up endoscopy)
Mocek et al.	1	multiple polyps size not stated	post gastrectomy status 5 y with	bismuth+ tetracycline+ metronidazole	disappearance of polyps (less than 1 y)

			recurrence of polyps	x 2w	
Suzuki et al.	1	15 polyps 8-26 mm		lanzoprazole+ amoxicillin x 2w	disappearance of polyps(1 y) ↓ gastrin level ↑ pepsinogen I/ II ratio
Ohkusa et al.	12	mean no. 4½ polyps mean size 9.3 mm	mostly presence of chronic gastritis some with DU, GU	PPI+ amoxicillin+ clarithromycin/ ecabet sodium	disappearance of polyps, average 7.1 m. ↓ gastrin level ↓ *Hp* Ab
Koay et al. (Taiwan)	1	8 polyps largest size 18 mm	post-gastrectomy status moderate degree gastritis	amoxicillin+ omeprazole+ clarithromycin x 2w	disappearance of smaller polyps 3 m. and large polyps 9 m.

GU= gastric ulcer; y= year; *Hp* Ab= *Helicobacter pylori* antibody; DU= duodenal ulcer; w= week; m= month; ↓ = decreased; ↑ = increased

should encourage a prompt treatment option aiming at eradication of *H. pylori in* cases of protein-losing gastropathy with severe hypoproteinemia.

In conclusion, the data presented suggest that *H. pylori is* a pathogenic factor in substantial cases with hypertrophic gastropathy. It seems rational to treat *H. pylori*-associated hypertrophic gastropathy with antibacterial eradication regimen.

Gastric Hyperplastic Polyps and Helicobacter pylori Treatment

The etiology of gastric hyperplastic polyps had been obscured. The polyps often appear as a late consequence of chronic gastritis. Usually small polyps less than 1 cm in size have little predisposition to malignant change, but large polyps greater than 2 cm may present clinical risk of bleeding, obstruction and malignant transformation (1.5-3% incidence) [42]. Therefore, larger polyps are often removed endoscopically or surgically to avoid later complications.

In recent years, reports regarding *H. pylori* infection with hyperplastic polyps, and disappearance of polyps after eradication treatment has been inte-resting and encouraging (Table 1) [43]. In 1990 Veereman et al has reported that in cases with persistent pre-sence of *H. pylori*, along with chronic gastritis and hyperplastic polyps for more than three years, success-ful *H. pylori* eradication treatment had resulted in di-sappearance of hyperplastic polyps [44]. In 1994 Mocek et al reported multiple recurrences of hyperplastic gastric polyps in 6-year period, despite sessions of treatment by acid suppression therapy and surgery. These polyps ultimately subsided after *H. pylori* era-dication [45]. In 1997 Ohkusa et al had reported elimination of multiple hyperplastic gastric polyps 1 year after *H. pylori* eradication therapy [46]. In 1998 the same Japanese group conducted a randomized controlled study of 35 patients with *H. pylori* infection and hyperplastic polyps. Successful clearance of *H. pylori* with omeperazole-based triple therapy regimen resulted in 80% disappearance of polyps, which was associated with regression of gastritis and lowering of both

serum gastrin level and IgG titer [47]. The authors proposed that *H. pylori* promotes inflammation and contributes to the reactive hyperplasia of the gastric mucosa which leads to the formation of hyperplastic polyps, and they recommended that eradication therapy should be attempted before endoscopic removal of the polyps.

The issue of large polyps management is important due to their tendency to induce complications and malignant transformation. In the previously mentioned articles, no information had been provided specifically regarding the larger polyps. In our own experience, we had reported a case of multiple hyperplastic gastric polyps of variably sized, associated with *H. pylori* infection [43]. The largest polyp was measured to be 18 mm in size. We prescribed a 2-week therapeutic regimen with omeperazole, amoxicillin and clarithromycin, and follow up endoscopy after 3 months and 9 months. We found successful eradication of *H. pylori* was accompanied by dramatic disappearance of most of the polyps and partial resolution of the large polyp in a 3-month period. Complete elimination of polyps with normal appearance of gastric mucosa was noted in 9-month period. Now the patient had been followed up in our outpatient clinic for 3 years, without clinical evidence of polyps recurrence and *H. pylori* reactivation. We therefore concluded that multiple hyperplastic polyps may be treated by *H. pylori* eradication therapy, if there is a well documented *H. pylori* infection, before attempting endoscopic or surgical resection. Eradication therapy for large gastric polyps may be tried, but it is too early to draw conclusion for large polyp, as the experience is limited till now.

The pathogenesis of the *H. pylori*-induced mucosal hyperplasia and hyperplastic polyp is being elucidated. In 1993 Correa had proposed that *H. pylori* induced a chronic inflammatory response that leads to an increased rate of mucosal proliferation [48]. Subsequent studies by other authors have shown increased proliferative indices, proliferating cell nuclear antigen (PCNA) staining, 5-bromo-2'-deoxy-uridine (BrdU) incorporation in patients with *H. pylori* infection [49, 39, 50]. In 1992, Saito et al proposed that *H. pylori* infection induces increased inflammatory cell infiltration of gastric mucosa, and results in reactive epithelial cell proliferation and hyperplastic polyp formation [51]. In 1998 Ohkusa et al had investigated patients of gastric hyperplastic polyps with *H. pylori* infections. Successful clearance of *H. pylori* caused subsidence of polyps which correlated well with decreased number of inflammatory cell infiltration of gastric mucosa [47]. These evidences clearly indicated a close relation between *H. pylori* infection, inflammatory cell infiltration and hyperlastic polyp.

Further investigation of its pathophysiology was done by several authors. Experiment performed on mice had shown that host immune response notably the adaptive immune response, specifically T-cells, is an important mediator contributing to the gastric epithelial hyperproliferation seen after *H. pylori* infection [52]. Clinical studies on interleukin-1 β and hepatocyte growth factor had shown that increased production of these factors after *H. pylori* infection may stimulate epithelial cell proliferation and foveolar hyperplasia [53].

The Role of Helicobacter pylori in Lymphocytic Gastritis

Lymphocytic gastritis (LG) was first described by Haot et al in 1988 [54]. It is a rare disease which involves an increase in intraepithelial lymphocytes in the surface and foveolar epithelium of gastric mucosa [54]. Endoscopically LG may present a picture of multiple chronic raised erosions or giant folds gastritis, mostly located over corpus. Its etiopathogenesis has been linked to celiac disease and *H. pylori* infection. The exact relationship between *H. pylori* and LG is still unclear. There were several case reports of LG association with *H. pylori* infection [55-58]. Some authors had suggested that LG represents an abnormal response of gastric mucosa to a local antigen, which may be the pathogen, *H. pylori* in many cases. Dixon et al had reported a 41% positive rate of *H. pylori* infection in biopsied specimen of LG, and 82% positive rate when tested serologically [56]. Wu et al had investigated 103 patients with LG and identified a distinct etiology in 84 patients (82%). This included 39 with celiac disease, 30 with *H. pylori* infection, 4 with varioliform gastritis and 11 with other entities of diseases [57]. Niemela et al had followed up cases of LG associated with *H. pylori* infection for 10 years. The authors observed that LG was associated with increase in the grades of corpus gastritis, neutrophilic granulocytes and intestinal metaplasia during the 10 year interval [58].

LG was also found to be more prevalent in patients with gastric adenocarcinoma (12.3%) and primary gastric lymphoma (13.7%) than in unselected patients undergoing endoscopy (0.83%, 2.5%) [59].

Healing of LG by pharmacologically eradicating *H. pylori* has been reported [60, 61, 62]. Hayat et al had treated 11 patients of LG associated with *H. pylori* infection, with a one week course of omeperazole, clarithromycin and metronidazole. Two months after treatment, they found a significant reduction of gastric intra-epithelial lymphocyte counts, improvement of corpus inflammation, and all patients turned *H. pylori* negative histologically [61]. More recently, Mullel et al had treated 61 patients of LG with documented *H. pylori* infection (29 by histology, 32 by serology), with a control group of 37 patients of LG without *H. pylori* association. They found much improvement of gastritis parameters including normalization of intra-epithelial lymphocyte counts in both the treatment groups in 93.1% and 84.3% of cases [62]. This study supports the notion that most cases of LG might be a consequence of *H. pylori* infection.

The Controversial Role of Helicobacter pylori in Granulomatous Gastritis

Granulomatous gastritis has long been considered as part of a local or systemic disease. The frequency of its association with other local or systemic diseases varies widely, and the more commonly related entities are Crohn's disease, sarcoidosis and infection [63]. In 1963 Fahimi et al reported 3 cases of granulomatous gastritis without evidence of associated local or systemic disease, and proposed that idiopathic granulomatous gastritis (IGG) could be regarded as a distinct clinicopathologic condition [63]. The concept of IGG had later gained acceptance by clinicians and pathologists [64]. The possible role of *H. pylori* infection in garnulomatous gastritis was proposed early by Dhillon in 1989, who reported 3 cases of granulomatous gastritis associated with "Campylobacter-like organisms" [65]. Ectors et al in 1993 had found that in a series of 71 patients with granulomatous gastritis, a pattern of chronic gastritis with atrophy was noted in 95 % of patients and *H. pylori* was detected in 92% of the biopsies [66]. On the contrary, Shapiro et al (1996) had retrospectively reviewed 42 cases with granulomatous gastritis, and concluded that granulomatous gastritis per se was not associated with *H. pylori*. In this series, performed in a Crohn's disease referral center, the majority of cases belongs to Crohn's diseases (55%) and sarcoidosis. However, as stated by the author, in cases of IGG, a statistically significant association with *H. pylori* infection was found [67].

Conclusion

The spectrum of *H. pylori*-related gastroduodenal diseases is still expanding. New and accumulating experience of *H. pylori*-relating disease entities is still being studied and reported. There were recent reports of a rare case of *H. pylori*-induced gastric lymphonodular hyperplasia with gastric outlet obstruction, which improved after *H. pylori* treatment [68], and a case of metaplastic duodenal polyp with complete resolution after *H. pylori* eradication therapy [69]. The possible causal role of *H. pylori* in the development of gastric polyposis and double pylorus [70] had been reported and is still under investigation. There is also evidence that lymphoid hyperplasia and nodular gastritis appear to be more frequent in children, and usually regress well after *H. pylori* eradication [41]. At present, it may be concluded that there were evidences of *H. pylori* association with gastric outlet obstruction, Menetrier's disease, gastric hyperplastic polyps, granulomatous gastritis and lymphocytic gastritis. However, long term prospective clinical studies are still lacking in these fields. In addition, further research concerning the host factors, subtypes of *H. pylori*, molecular basis for pathogenic interaction and animal models for pathogenic elucidation are required to explain the different clinical outcomes of *H. pylori* infection.

References

1、Marshall BJ. Helicobacter pylori. Am J Gastroenterol 1994;89:5116-28.

2、Helicobacter pylori in peptic ulcer disease. NIH Consensus Statement 1994 Feb 7-9;12:1-22.

3、Graham DY, Lew GM, Klein PD, et al. Effect of treatment of Helicobacter pylori infection on the long term recurrence of gastric or duodenal ulcer. A randomized, controlled study. Ann Intern Med 1992;116:705-8.

4、Lind T, Veldhuyzen van Zanten S, Unge P, et al. Eradication of Helicobacter pylori using one-week triple therapies combining omeprazole with two antimicrobials: The MACH 1 study, Helicobacter 1996;1:138-44.

5、Satoh K, Kimura K, Takimoto T, et al. Efficacy of Clarithromycin in eradicating Helicobacter pylori J Gastroenterol 1996;31(suppl XI):53-5.

6、Wotherspoon AC, Ortiz Hidalogo C, Falozon MR, et al. Helicobacter pylori-associated gastritis and primary B-cell gastric lymphoma. Lancet 1991;338:1175-6.

7、Eurogast Study Group. An international association between Helicobacter pylori and gastric cancer. Lancet 1993;341:1359-62.

8、Parsonette J, Friedman GD, Vandersteen DP, et al. Helicobacter pylori infection and the risk of gastric carcinoma. N Engl J Med 1991;325:1127-131.

9、Kreel L, Ellis H. Pylorus stenosis in adults: a clinical and radiological study of 100 consecutive patients. Gut 1965;6:253-61.

10、Weaver GA, Merrell NB, Harper RL, et al. Nonsteroidal antiinflammatory drugs are associated with gastric outlet obstruction. J Clin Gastroenterol 1995;20:196-8.

11、Graham DY. Ulcer complications and their non-operative treatment. In: Sleisenger MH, Fordtram JS, eds, Gastrointestinal disease. Pathophisiology, diagnosis, management. Philadelphia: WB Saunders Co; 1993; 698-712.

12、Pollard SG, Friend PJ, Dunn DC, et al. Highly selective vagotomy with duodenal dilatation in patients with duodenal ulceration and gastric outlet obstruction. Br J Surg 1990;77:1365-6.

13、Lau JYW, Chung SCS, Sung JJY, et al. Through-the-scope balloon dilation for pylori stenosis: long term results. Gastrointest Endosc 1996;43:98-101.

14、de Boer WA, Driessen WMM. Resolution of gastric outlet obstruction after eradication of Helicobacter pylori. J Clin Gastroenterol 1995;21:329-30.

15、Tursi A, Cammarota G, Papa A, et al. Helicobacter pylori eradication helps resolve pyloric and duodenal stenosis. J Clin Gastroenterol 1996;23:157-63.

16、Borody TJ, Bampton P, Moont M, et al. Re: W de Boer: Gastric outlet obstruction and Helicobacter pylori. Am, J Gastroenterol 1997;92:1576-7.

17、George LL, Borody TJ, Andrews P et al. Cure of duodenal ulcer after eradication of Helicobacter pylori. Med J Aust 1990;153:145-9.

18、de Boer WA. Gastric outlet obstruction and Helicobacter pylori. Am J Gastroenterol 1997;92:362-3.

19、Kimura K, Ido K, Saifuku K, et al. A one-hour topical therapy for the treatment of Helicobacter pylori infection. Am J Gastroenterol 1995;1:118-9.

20、Perng C, Lin H, Lo W, et al. Characteristics of patients with benign gastric outlet obstruction requiring surgery after endoscopic balloon dilatation Am J Gastroenterol 1996;91:987-90.

21、Brandimarte G, Tursi A, Di Cesare L, et al. Antimicrobial treatment for peptic disease: a prospective study. Eur J Gastroenterol Hepatol 1999;11:731-4.

22、Rinaldi V, Zullo A, Diana F, et al. Duodenal stenosis may not regress after eradication of Helicobacter pylori. J Clin Gastroenterol 1997;24:288-9.

23、Gibson JB, Behrman SW, Fabian TC, et al. Gastric outlet obstruction resulting from peptic ulcer disease requiring surgical intervention is infrequently associated with Helicobacter pylori infection. J Am College of Surgeons 2000;191:32-7.

24、Lanza FL. Gastropathy and Gastritis. In: Anthony J, DiMarino Jr, Stanley BM, eds. Gastrointestinal disease, an endoscopic approach. Blackwell Science Inc 1997:308-12.

25、Forman D, Newell D, Fullerton F, et al. Association between Helicobacter pylori and risk of gastric cancer. Evidence from a prospective investigation. Br Med J 1991;302:1302-5.

26、 Lewin KJ, Riddell RH, Weinstein WM. Gastritis. In: Lewin KJ, ed. Gastrointestinal pathology and its clinical implications. Igaku-Shoin New York. Tokyo 1992:544.

27、 Searcy RM, Malagelada J-R. Menetrier's disease and idiopathic hypertrophic gastropathy. Ann Intern Med 1984;100:565-70.

28、 Whitehead R: Menetrier's disease. In: Gastrointestinal and Oesophageal Pathology. Edited by Whitehead R. Edinburgh: Churchil Livingstone;1989:424.

29、 Dimpsey PJ, Goldenring JR, Soroka CJ, et al. Possible role of transforming growth factor alfa in the pathogenesis of Menetrier's disease: supportive evidence from humans and transgenic mice. Gastroenterol 1992;103:1950-63.

30、 Coffey RJ, Romano M, Goldenring J. Roles for transforming growth factor-alpha in the stomach. J Clin Gastroenterol 1995;21(suppl):S36-9.

31、 Bayerdorffer E, Ritter M, Hatz R, et al. Menetrier's disease and Helicobacter pylori. N Engl J Med 1993;329:60.

32、 Meuwissen SGM, Ridwan BU, Hasper HJ, et al. The Dutch Menetrier's Study Group: Hypertrophic protein-losing gastropathy. A retrospective analysis of 40 cases in the Netherlands. Scand J Gastroenterol 1992;27(194):1-7.

33、 Stolte M, Batz CH, Bayerdorffer E, et al. Helicobacter pylori eradication in the treatment and differential diagnosis of giant folds in the corpus and fundus of the stomach. Z Gastroenterol 1995;33:198-201.

34、 Bayerdorffer E, Ritter MM, Hatz R, et al. Healing of protein losing hypertrophic gastropathy by eradication of Helicobacter pylori —Is Helicobacter pylori a pathogenic factor in Menetrier's disease? Gut 1994;35:701-4.

35、 Yamada M, Sumazaki R, Adachi H, et al. Resolution of protein-losing hypertrophic gastropathy by eradication of Helicobacter pylori. Eur J Pediatr 1997;156:182-5.

36、 Kaneko T, Akamatsu T, Gotoh A, et al. Remission of Menetrier's disease after a prolonged period with therapeutic eradication of Helicobacter pylori. Am J Gastroenterol 1999;94:272-3.

37、 Kapsoritakis AN, Potamianos S, Matrella E, et al. Helicobacter pylori-associated protein-losing hypertrophic gastropathy with hypercholesterolemia. Dig Dis Sci 1999;44(9):1843-7.

38、 Johnson MI, Spark JI, Ambrose NS, et al. Early gastric cancer in a patient with Menetrier's disease, lymphocytic gastritis and Helicobacter pylori. Eur J Gastroenterol Hepatol 1995;7:187-90.

39、 Brenes F, Ruiz B, Correa P, et al. Helicobacter pylori causes hyperproliferation of the gastric epithelium: pre and post-eradication indices of proliferating cell nuclear antigen. Am J Gastroenterol 1993,88:1870-5.

40、 Fox JG, Li XT, Cahill R, et al. Hypertrophic gastropathy in Helicobacter felis-infected wild-type C57 BL/6 mice and P53 hemizygous transgenic mice. Gastroenterology 1996;110:155-66.

41、 Riddell RH. Pathobiology of Helicobacter pylori infection in Children. Canadian J Gastroenterol 1999;13:599-603.

42、 Daibo M, Itabashi M, Hirota T. Malignant transformation of gastric hyperplastic polyps. Am J Gastroenterol 1987;82:1016-25.

43、 Koay LB, Sun CS, Lin CN, et al. Elimination of multiple hyperplastic polyps by eradication of Helicobacter pylori: report of a case. Gastroenterol J Taiwan 2001;18:167-74.

44、 Veereman WG, Ferrell L, Ostroff JW, Heyman MB. Hyperplastic gastric polyps associated with persistent Helicobacter pylori infection and active gastritis. Am J Gastroenterol 1990;85:1395-7.

45、 Mocek FW, Ward WW Jr, Wolfson SE, et al. Elimination of recurrent hyperplastic polyps by eradication of Helicobacter pylori. Ann Intern Med 1994;120:1007-8.

46、 Suzuki S, Ohkusa T, Shimoi K et al. Disappearance of multiple hyperplastic polyps after the eradication of Helicobacter pylori. Gastrointest Endosc 1997;6:566-8.

47、 Ohkusa T, Takashimizu I, Fujiki K et al. Disappearance of hyperplastic polyps in stomach after eradication of Helicobacter pylori. Ann Intern Med. 1998;129:712-5.

48、 Correa P, Fox JG. Gastric cancer and Helicobacter pylori. In: Pajares JM, Pena AS, Malfertheiner P, eds. Helicobacter pylori and gastroduodenal pathology. New York: Springer-Verlag, 1993:239-43.

49、 Cahill RJ, Sant S, Beattle S, et al. Helicobacter pylori and increased epithelial cell proliferation: a risk factor for cancer. Eur J Gastroenterol Hepatol 1994;6:1123-7.

50、 Lynch DAF, Mapstone NP, Clarke AMT, et al. Cell proliferation in Helicobacter pylori associated gastritis and the effect of eradication therapy. Gut 1995;36:346-50.

51、 Saito Y, Ohukusa T, Endo S, et al. Detection of Helicobacter pylori in gastric hyperplastic polyps: Comparison between foveolar and fundic polyps. Eur J Gastroenterol Hepatol 1992;4 (suppl 1):89-92.

52、 Roth KA, Kapadia SB, Martin SM. Cellular immune responses are essential for the development of Helicobacter felis-associated gastric pathology. Journal of Immunology 1999;163: 1490-7.

53、 Yasunaga Y, Shinomura Y, Kanayama S, et al. Increased production of interleukin-1 β and hepatocyte growth factor may contribute to foveolar hyperplasia in enlarged fold gastritis. Gut 1996;39:787-94.

54、 Haot J, Hamichi L, Wallez L, et al. Lymphocytic gastritis: a newly described entity: a retrospective endoscopic and histological study. Gut 1988;29:1258-64.

55、 Johnson MI, Spark JI, Ambrose NS, et al. Early gastric cancer in a patient with Menetrier's disease, lymphocytic gastritis and Helicobacter pylori. Eur J Gastroenterol Hepatol 1995;7:187-90.

56、 Dixon MX, Wyatt JI, Burke DA, et al. Lymphocytic gastritis-relationship to Campylobacter pylori infection. J Pathol 1988;154:125-32.

57、 Wu TT, Hamilton SR. Lymphocytic gastritis: association with etiology and topology. Am J Surg Pathol 1999;23:153-8.

58、 Niemela S, Karttunen T, Kerola T, et al. Ten year follow up study of lymphocytic gastritis: further evidence on Helicobacter pylori as a cause of lymphocytic gastritis and corpus gastritis. J Clin Pathol 1998;51:83-4.

59、 Griffiths AP, Wyatt J, Jack AS, et al. Lymphocytic gastritis, gastric adenocarcinoma, and primary gastric lymphoma. J Clin Pathol 1994;47:1123-4.

60、 Groisman GM, George J, Berman D, et al. Resolution of protein-losing hypertrophic lymphocytic gastritis with therapeutic eradication of Helicobacter pylori. Am J Gastroenterol 1994;89:1548-51.

61、 Hayat M, Arora DS, Dixon MF, et al. Effects of Helicobacter pylori eradication on the natural history of lymphocytic gastritis. Gut 2000;47:314-5.

62、 Mullel H, Volkholz H, Stolte M, et al. Healing of lymphocytic gastritis by eradication of Helicobacter pylori. Digestion 2001; 63:14-9.

63、 Fahimi HD, Deren JJ, Gottlieb LS, et al. Isolated granulomatous gastritis: its relationship to disseminated sarcoidosis and regional enteritis. Gastroenterology 1963;45:161-75.

64、 Heatley RV, Wyatt JI. Gastritis and duodenitis. In: Haubrich WS, Schaffner F, Berk, JE, eds. Bockus gastroenterology, 5th ed. Philadelphia: WB Saunders Co; 1995;649-50.

65、 Dhillon AP, Sawyerr A. Granulomatous gastritis associated with Campylobacter pylori. APMIS 1989;97:723-7.

66、 Ectors NL, Dixon MF, Geboes KJ, et al. Granulomatous gastritis: a morphological and diagnostic approach. Histopathology 1993;23:55-61

67、 Shapiro JL, Goldblum JR, Petras RE. A clinico-pathologic study of 42 patients with granulomatous gastritis. Am J Surg Pathol 1996;20:462-70.

68、 Misra SP, Misra V, Dwivedi M, et al. Case report: Helicobacter pylori-induced lymphonodular hyperplasia: a new cause of gastric outlet obstruction. J Gastroenterol Hepatol 1998;13:1191-4.

69、 Yousfi MM, E l-Zimaity HMT, Cole RA, et al. Resolution of a metaplastic polyp after cure of Helicobacter pylori infection. J Clin Gastroenterol 1996;23:53-4.
70、 Hu TH, Tai DI, Changchien CS, et al. Double pylorus: report of a longitudinal follow-up in two refractory cases with underlying diseases. Am J Gastroenterol 1995;90:815-8

幽門螺旋桿菌與罕見胃疾病

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摘　　要

幽門螺旋桿菌（Helicobacter pylori, H. pylori）已被証實與許多胃腸疾病有關，包括慢性胃炎、胃及十二指腸潰瘍，胃黏膜相關淋巴瘤（MALT lymphoma）以及胃癌。許多臨床研究顯示根除治療幽門螺旋桿菌（H. pylori eradication therapy），可使消化性潰瘍癒合，促使慢性胃炎改善。部份胃黏膜相關淋巴瘤（MALT lymphoma）亦可經由 H. pylori eradication therapy 治愈。 近年已有文獻報告 H. pylori 與一些較罕見的胃腸疾病有關係。學者發現部份因長期消化性潰瘍導致的 gastric outlet obstruction 與 H. pylori infection 有關，根除治療 H. pylori 可改善 pyloric stenosis 以及其引發的阻塞症狀。其他醫學研究亦發現 90% 的 Menetrier's disease 與 H. pylori infection 有關， 單一或多發性的 gastric hyperplastic polyps 可經由 H. pylori eradication therapy 後消失，另外 lymphocytic gastritis 及 granulomatous gastritis 與 H. pylori infection 之關係亦有不少研究文獻。上述研究的發表已引發一些比較革命性的疾病思考觀念及治療方法，但是值得提醒的是較大規模的前瞻性臨床研究仍然相當匱乏。