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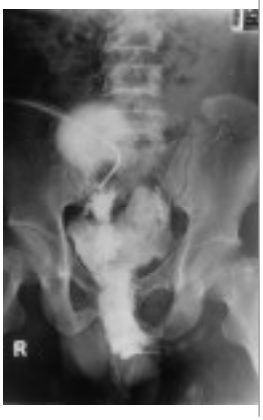

Cover Picture:
Initial cystography performed through the indwelling suprapubic catheter.
(Refer to page 511)

Editorial

Helicobacter pylori Infection and its Treatment in Singapore

K G Yeoh

Helicobacter pylori infection is now recognised to be the most important aetiology for peptic ulcer disease and a significant risk factor for gastric cancer. Half the world's population is infected and it is a global health problem. The infection is common in Singapore and its epidemiology has been well described. The prevalence of infection increases with age in all races, from 3% in children below 5 years to 71% in adults above 65 years[1]. The pattern is similar to that in developed countries. However there are marked differences among the three major ethnic groups[2]. The prevalence of *H pylori* infection is highest in Indians, followed by Chinese and lowest in Malays. For instance in the age group 51-60 years, the prevalence of *(H pylori)* antibodies is 70% in Indians, 43% in Chinese and 35.7% in Malays ($p<0.01$). The corresponding odds ratio for infection in Indians and Chinese are 3.0 (1.5 to 5.9) and 1.5 (0.7-2.9) respectively, compared to Malays.

The majority of people with *H pylori* infection do not develop clinical disease or symptoms, and the lifetime risk of developing ulcer disease is estimated at 10-15% while that of gastric cancer is 1-2%. *Who should be treated?* Consensus guidelines[3,4] have been developed to provide guidance on indications for therapy (Table I) and treatment regimes. The strongest evidence for the treatment of *H pylori* is in association with peptic ulcer disease. Eradication has been shown to heal ulcers, dramatically reduce recurrence and produce long term remission[5]. It is also cost-effective because it prevents recurrence of ulcer disease and its complications. Whether the infection should be treated in patients with non-ulcer dyspepsia is still a matter of controversy. *What is the best treatment?* Evidence from randomised controlled trials show that the best results are obtained with a

Table I. Recommendations for treatment of *H pylori* infection:

Treatment of H pylori infection is recommended when associated with the following (modified from reference 4):

Indication	Level of evidence
Duodenal ulcer	Randomised controlled trials
Gastric ulcer	Randomised controlled trials
Complicated ulcer (bleeding or perforation)	Randomised controlled trials
NSAID* therapy, past history of ulcer	Expert Committee report
NSAID therapy, in patients with dyspepsia	Expert Committee recommendation
Following resection of early gastric cancer	Expert Committee report
Low-grade MALT** lymphoma	Expert Committee report
Non-ulcer dyspepsia, case-by-case basis	Expert Committee report

** Non-steroidal anti-inflammatory drug; ** Mucosa-associated lymphoid tissue*

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triple therapy regimen comprising a proton-pump inhibitor and two antibiotics (clarithromycin and either amoxycillin or metronidazole), which give eradication rates exceeding 90% on per-protocol analysis[6]. There is a relatively high rate of primary metronidazole resistance in *H pylori* strains in this region and therefore the combination of clarithromycin and amoxycillin may be preferred. In this issue, Fock and co-authors report the results of an earlier randomised trial on dual therapy comparing amoxycillin versus clarithromycin in combination with omeprazole[7]. This study showed the combination of omeprazole and clarithromycin produced an eradication rate of 75% and was well tolerated. It is now recognised that dual therapy is less effective than triple therapy, and as a result the latter is the treatment of choice.

There are peculiar features of *H pylori* infection in Singapore and some differences compared to western populations. There appears to be a lower prevalence of *H pylori* among local peptic ulcer patients compared to western figures. The study by Vu in this issue diagnosed *H pylori* in 85% of duodenal ulcer patients and 68% of gastric ulcer patients presenting to a local hospital endoscopy unit[8], which is lower than the corresponding prevalence of 95% among Caucasian patients with duodenal ulcer[9]. The author was careful in documenting the use of non-steroidal anti-inflammatory drugs (NSAIDS), although since patient particulars were retrieved from case files it is possible that this was under-recorded. An earlier study by Kang *et al* in 1990 showed similar results[10]. Besides *H pylori*, the next most important cause of ulcer disease are NSAIDS, however even after exclusion of the latter, Vu found no obvious cause in 13% and 28% of duodenal and gastric ulcer disease respectively. The author was also careful in screening out possible confounding factors such as the use of recent antibiotics and proton pump inhibitors which could potentially result in false negative *H pylori* status. If this suspicion of a lower than expected prevalence of *H pylori* in local peptic ulcer patients is substantiated, it suggests other factors contributing to the development of ulcer disease that have not been elucidated. Yet another significant difference is the high prevalence of *cag*A-positive *H pylori* strains (73 to 89% in Singapore)[11,12] compared to western figures (60%). *cag*A is a marker for a complex of many genes, which some workers have linked with more severe disease outcomes in western studies. It is associated with increased mucosal IL-8 and inflammation, however it does not seem to be predictive of disease outcomes in our population[11,12].

Interesting questions remain to be answered. Why do only a minority of *H pylori*-infected people develop disease? Possibilities include differences in bacterial strains and virulence genes, host factors or host-bacterial interaction. Our group found no difference in the prevalence of putative bacterial virulence genes such as *cag*A, *vac*A and *ice*A in patients with peptic ulcer compared to those with non-ulcer dyspepsia[11,13]. Furthermore, the ethnic prevalence of *H pylori* infection does not adequately explain the differences in ulcer frequency in the three races in Singapore. Recent evidence suggests that host factors such as Lewis blood group antigens, which are also expressed by *H pylori*, may be important in determining the development of peptic ulcer in people with *H pylori* infection[13]. Our group's hypothesis is that disease outcomes of *H pylori* infection are due to host-bacterial interaction rather than specific bacterial virulence factors *per se*.

The remarkable progress over the last decade in clarifying the role of *H pylori* in duodenal and gastric ulcer disease has led to simple and effective treatment which has almost eliminated complicated ulcer disease. This triumph of modern medicine is a model of how an understanding of

Eradication has been shown to heal ulcers, dramatically reduce recurrence and produce long term remission.

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pathophysiology is translated into cure of disease. The "classical ulcer sufferer" described in the textbooks need suffer no longer after a one week course of triple therapy. However as in many other fields, the challenge now is to work out an understanding of the molecular mechanisms. Why does *H pylori* cause disease in only a minority of people? What is its role in gastric carcinogenesis? Can the progression to gastric cancer be reversed by its eradication? The final goal would be a therapeutic and prophylactic vaccine to eliminate the infection, without problems associated with antibiotic use and drug resistance. SMJ

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ERRATUM

In the article "Paediatric One Lung Anaesthesia by Selective Bronchial Intubation" published in Vol 41 issue 8 August 2000, Table I should read "ph at PCO2 of 40mmhg= measured pH + (measured PCO2 – 40)mmHg x 0.008".