Letters

Helicobacter pylori, Peptic Ulcer, and Cimetidine

We read with interest the article by Fich and associates in the February 1990 issue of the *Proceedings* (pages 187 to 191). An interesting association between *Helicobacter pylori* (formerly called *Campylobacter pylori*) and gastritis or peptic ulcer diseases has been claimed by many authors.[1-6] Although we agree with Dooley and colleagues[7] that *H. pylori* infection may be of potential importance in the asymptomatic population, suggesting that the bacterium is a commensal of the stomach, we would like to ask Fich and colleagues whether *H. pylori* is an opportunistic pathogen in the gastroduodenal region, similar to *Pneumocystis carinii* in the lung areas.

Because cimetidine, which is being widely used for the treatment of peptic ulcer disease, has been shown to enhance T-cell function,[8] we investigated whether this drug has any antibacterial effect through enhancement of humoral immunity. Cimetidine was diluted with brain-heart infusion broth (100 mg, 50 mg, 20 mg, 10 mg, and 5 mg/ml), and one drop of solution that contained a 10^{-4} dilution of *H. pylori* isolated from the gastric juice of a 14-year-old child with gastritis was added and cultured for 24 hours. Examination at 4, 8, and 24 hours showed that bacteria had grown in each tube; this result should naturally lead to the conclusion that cimetidine has no antibacterial effect on *H. pylori*.

Subsequently, we investigated the effect of cimetidine on the phagocytic functions of the macrophages. Peritoneal macrophages were collected from mice by washing the peritoneal cavity with phosphate-buffered Ringer's solution. Macrophages were purified by Ficoll-Hypaque gradient centrifugation.[9] Bacteria and macrophages were mixed in a 50:1 ratio in phosphate-buffered Ringer's solution that contained 10 mg/ml of cimetidine and 10% heat-activated guinea pig serum and incubated at 37°C for 30 minutes. Phagocytosis was then quantitatively evaluated on Giemsa-stained specimens prepared by cytocentrifugation. At least 250 macrophages were scored for each sample. Statistical analysis revealed no difference between the cimetidine and control groups ($P>0.05$) (Table 1).

Table 1.—**Effect of Cimetidine on Bacteria and Phagocytic Function of Macrophages**

Group	Macrophages with associated bacteria (%)	No. of bacteria/ 100 macrophages
Cimetidine	6.0	12.0
Control	8.0	10.0

In summary, both groups of experiments revealed no evidence in support of antibacterial or phagocytosis-promoting effects of cimetidine.

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The authors reply

We appreciate the comments of Kaya and colleagues; however, more information about the inoculum size used, the adequacy of the broth, the response in controls, and the use of any quantitative determination of inhibitor activity is necessary to interpret the data they cite.

The issue remains whether *Helicobacter pylori* is a pathogen or a commensal. At least in the stomach, overwhelming evidence is available in support of a causative role for *H. pylori* in chronic gastritis, and Koch's postulates have been fulfilled.[1-3] The clinical significance of *H. pylori* gastritis, however, remains controversial; clearly, *H. pylori* gastritis is common in totally asymptomatic persons.[4]

A very strong association has been noted between *H. pylori* gastritis and chronic duodenal ulcer disease.[1,2] In their letter, Kaya and co-workers report that cimetidine, which effectively promotes healing of ulcers, did not have antibacterial or phagocytosis-promoting effects. Other investigators have shown that the 90% minimal inhibitory concentration of the H_2 antagonists is more than 1,000 mg/liter.[5] The lack of effect of cimetidine on phagocytic function of macrophages is of interest; although little information has been published on the role of macrophages in *H. pylori* gastritis, they are usually considerably increased in this condition. One study suggested that, in vitro, the speed of ingestion of *H. pylori* by mouse peritoneal macrophages varied with different bacterial strains, but the importance of this finding in vivo is unknown.[6]

Clearly, ulcers heal with H_2-receptor blockers despite the continued presence of *H. pylori*.[7] This result implies that a decrease in gastric acid is sufficient to allow healing of ulcers, and *H. pylori* is not independently capable of inhibiting this process. This finding does not, however, negate a possibly important role of *H. pylori* in duodenal ulcer disease. Indeed, relapse rates for chronic duodenal ulcer disease seem to be substantially less at 1 year in those patients who have had *H. pylori* infection eradicated in comparison with those who have not,[8,9] although further data are needed.

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