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Treatment Failure of Norfloxacin against *Campylobacter pylori* and Chronic Gastritis in Patients with Nonulcerative Dyspepsia

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Several reports have been published to show the in vitro susceptibility of *Campylobacter pylori* to different classes of antibiotics, including fluoroquinolones. The purpose of this study was to describe the clinical effect of norfloxacin on eradication of *C. pylori* in patients with gastritis. Endoscopy was performed in 38 patients with symptoms of nonulcerative dyspepsia. Of these, 20 patients had a *C. pylori*-positive culture. From this group, 17 patients were treated with norfloxacin for 1 month. After therapy, 15 patients still had positive cultures, and in 9 cases the strain was resistant to norfloxacin. These data, which confirm previous studies, support the concept that the in vitro activity of norfloxacin against *C. pylori* cannot be transposed to an in vivo effect.

Campylobacter pylori is closely associated with chronic active gastritis and may be an etiological factor in nonulcerative dyspepsia and peptic ulcer disease (3, 5, 6). *C. pylori* is susceptible to several antibiotics (1, 2, 4). The effects of these antibiotics on *C. pylori* in vivo, however, are disappointing, probably because they do not easily penetrate the mucous layer in which the bacteria are located. *C. pylori* has recently been found to be susceptible to norfloxacin in vitro (7). The aim of our study was to examine the in vivo effect of norfloxacin on the eradication of the bacterium. Norfloxacin is a fluorinated quinolone carboxylic acid derivative, mainly used as an effective agent for the treatment of urinary tract infections.

Endoscopy was performed in 38 patients with symptoms of nonulcerative dyspepsia. For this examination, the only premedication was lidocaine spray of the pharynx. Peptic ulcers, upper gastrointestinal malignancies, or reflux esophagitis was not found in any of these patients. Multiple biopsies were taken from the prepyloric antrum and lower gastric body by a predetermined protocol. Separate biopsies were used for histological examination and bacteriological culture. The degree of gastritis was classified by the method of Whitehead et al. (8) into chronic superficial or chronic atrophic gastritis of a mild, moderate, or severe degree. The pattern of inflammation was categorized as "active" or "quiescent." The biopsies for bacteriological culture were transported to the bacteriological laboratory in phosphate-buffered saline. After crushing of the biopsies, smears were colored with Gram stain and the specimens were inoculated to both chocolate and blood agars with *Campylobacter* selective supplement and incubated at 37°C for 7 days in microaerobic conditions. A microorganism was determined to be *C. pylori* if the Gram stain of the isolated colonies showed curved gram-negative rods and the strains produced catalase, oxidase, and urease in urea broth base supplemented with 40% urea solution. Susceptibility to penicillin, amoxicillin, erythromycin, tetracycline, cephradine, nalidixic acid, and norfloxacin was determined by the agar diffusion method.

On histological examination, 26 of the 38 patients showed chronic superficial active gastritis (Fig. 1), 11 to a mild and 15 to a moderate degree. Of these 26 patients, 77% had *C. pylori*-positive cultures and 23% had negative cultures. Of the group of 11 patients with mild gastritis, 8 (72%) had *C. pylori*-positive cultures; of the group of 15 patients with moderate gastritis, 12 (80%) had positive cultures. Of the 20 patients with positive cultures, 17 were treated with 400 mg of norfloxacin twice daily for 1 month. From the start of this treatment, all previous therapy for nonulcerative dyspepsia was stopped; of the 17 antibiotic-treated patients, 14 were older than 40 years of age. Gastroscopy was repeated within 2 days after the end of norfloxacin therapy. Biopsies were taken according to the protocol for histological examination and culture; also, the symptoms of nonulcerative dyspepsia were recorded. Fifteen patients continued to have positive cultures after antibiotic therapy. In these 15 patients, as well as in the sole patient whose cultures became negative, the histological degree of gastritis in 13 patients did not change after therapy. They represented 10 patients with a moderate degree and 3 patients with a mild degree of chronic superficial active gastritis. In two patients the degree of superficial gastritis reverted from a mild form to a moderate one, and one patient showed a change from a moderate to a mild degree of chronic superficial active gastritis. In all patients the symptoms of nonulcerative dyspepsia remained unchanged. One patient did not return for the second gastroscopy. Of the 17 strains obtained from patients who were treated subsequently with norfloxacin, 14 were shown to be susceptible to this antibiotic; the other 3 strains died during susceptibility testing.

In our study, norfloxacin did not eradicate *C. pylori*. It also did not improve the degree of gastritis, except possibly in one patient in whom the biopsy changed from a moderate to a mild degree. That norfloxacin did not eradicate *C. pylori* contrasts with a recent study in which norfloxacin was shown to be effective in vitro (7), although we must admit that in our study one patient's cultured microorganism was not susceptible to norfloxacin before therapy with this antibiotic. However, acquired bacterial resistance to norfloxacin seems to be a major factor in the persistence of *C. pylori*. This resistance to new fluoroquinolones has been described previously (Y. Glupczynski, M. Labbe, A. Burette et al.,

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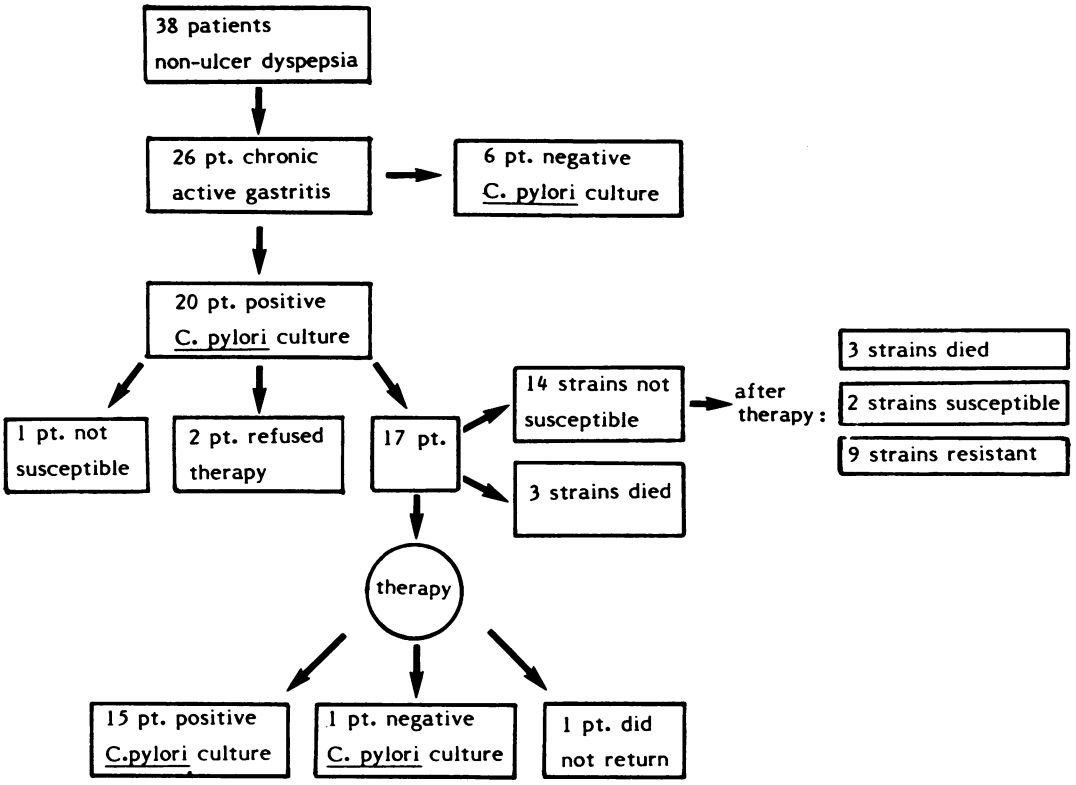

FIG. 1. Composition of the study group. pt., Patient.

Letter, Lancet i:1096, 1987). In two patients from whom strains remained susceptible after therapy, however, *C. pylori* was not eradicated.

We assume that norfloxacin does not penetrate in sufficient concentration to eradicate the bacteria, even the susceptible strains in the deeper layers of the gastric mucus. The addition of a mucolytic agent might be helpful in antibiotic treatment of *C. pylori*.

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