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Susceptibility of Clinical Isolates of *Campylobacter pyloridis* to 11 Antimicrobial Agents

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The activities of 11 antimicrobial agents, including two bismuth salts, against 70 strains of *Campylobacter pyloridis* isolated from gastric biopsy specimens were tested. The isolates were very susceptible to penicillin (the MIC for 90% of the strains tested [MIC_{90}] was 0.03 μg/ml), erythromycin, cefoxitin (MIC_{90}, 0.12 μg/ml), gentamicin, and ciprofloxacin (MIC_{90}, 0.25 μg/ml). The bismuth salts and nalidixic acid had moderate activity (MIC_{90}, 16 to 64 μg/ml). Twenty percent of the isolates were resistant to metronidazole (MIC, >1 μg/ml), and all were resistant to sulfamethoxazole and trimethoprim (MIC_{90}, >256 μg/ml).

Campylobacter-like organisms isolated from the gastric antrum have been reported recently from many centers (5, 6, 9). These organisms (now called *Campylobacter pyloridis*) are found in the gastric antrum of patients with histologically confirmed gastritis (6). They lie on the gastric mucosa and in the gastric pits and are probably protected from gastric acid by the mucus layer (13). *C. pyloridis* is a fastidious organism requiring 3 to 5 days of microaerobic incubation for growth on blood agar (3). It will also grow in liquid media if supplemented with blood or serum (unpublished observations).

These organisms may be involved in the etiology of gastritis and peptic ulceration (9). It is not yet known if antimicrobial chemotherapy is an appropriate alternative to antacid or gastric acid reduction in the therapy of this condition. In this study, we examined susceptibility of clinical isolates to a number of potential chemotherapeutic agents, including two bismuth salts.

Seventy isolates were obtained from antral biopsy specimens taken at routine endoscopy for investigation of upper gastrointestinal symptoms and stored in liquid nitrogen. Sixty-two of the isolates were from patients with histologically confirmed gastritis; the remaining eight were from patients with other gastric pathology. The organisms were identified as *C. pyloridis* by Gram stain and positive oxidase, catalase, urease, and alkaline phosphatase tests by previously described methods (5, 11).

MICs were determined by a routine agar dilution technique with IsoSensitest agar (pH 7.2) (Oxoid Ltd., London, United Kingdom) supplemented with 10% horse blood. The medium was prepared immediately prior to use.

The antimicrobial agents tested were penicillin (Beecham Laboratories, Bristol, Tenn.), erythromycin (Abbott Laboratories, North Chicago, Ill.), ciprofloxacin (Bayer AG, Wuppertal, Federal Republic of Germany), nalidixic acid (Winthrop Laboratories, Div. Sterling Drug Inc., New York, N.Y.), trimethoprim (Roche Diagnostics, Div. Hoffman-La Roche Inc., Nutley, N.J.), sulfamethoxazole (Wellcome Research Laboratories, Beckenham, United Kingdom [Div. Burroughs Wellcome Co.]), gentamicin (Roussel Laboratories, Wembley, United Kingdom), cefoxitin (Merck Sharp & Dhome, West Point, Pa.), and metronidazole (May & Baker Ltd., Dagenham, United Kingdom). The two bismuth salts used were tripotassium dicitratobismuthate (De-nol; Brocades, Weybridge, United Kingdom) and bismuth sodium tartrate (Procter & Gamble, Cincinnati, Ohio).

The isolates were grown for 3 days in tryptone soya broth supplemented with 10% horse blood, yielding a viable count of about 10^9 CFU/ml. The inocula were obtained by transferring 1 μl of undiluted 3-day-old culture to the surface of the antibiotic-containing medium by a multipoint inoculating device (Denley-Tech Ltd., Billingshurst, United Kingdom). The final inoculum on the plates was therefore about 10^6 CFU. The control organisms *Staphylococcus aureus* (NCTC 6571) and *Escherichia coli* (NCTC 10418) were included on each plate.

The plates were incubated for 72 h at 37°C in an atmosphere of 5% O_2 and 10% CO_2 (GasPak; BBL Microbiology Systems, Cockeysville, Md.). The MIC of an antimicrobial agent was defined as that concentration (in micrograms per ml of agar) at which there was a reduction (by counting) to 10 or fewer colonies in the original inoculum. The susceptibilities of the isolates to the antimicrobial agents, expressed in terms of inhibitory range (MICs for 50 and 90% of the strains tested [MIC_{50} and MIC_{90}, respectively]), are shown in Table 1. The MICs of *E. coli* and *S. aureus* were within 1 dilutional step of those previously reported (12).

All of the strains were highly susceptible to penicillin and erythromycin. Of the two quinolones tested, ciprofloxacin was markedly more active (MIC_{90}, 0.25 μg/ml) than nalidixic acid (MIC_{90}, 64 μg/ml), although there was a wide range of susceptibility to the latter. Susceptibility to gentamicin was very similar to susceptibility to ciprofloxacin. All strains were susceptible to cefoxitin. The majority of strains were susceptible to metronidazole, that is, 80% had an MIC of 1 μg/ml or less, 88.7% had an MIC of 2 μg/ml or less, but a few strains had a higher MIC of 8 μg/ml with this agent. This bimodal distribution has been described for other members of the *Campylobacter* genus (17). Like other campylobacters, all strains were resistant to trimethoprim and sulfamethoxazole (16), the MIC_{90} being >256 μg/ml. The bismuth salts both had MICs in the range of 4 to 32 μg/ml.

There is little data on the susceptibility of *C. pyloridis* to antimicrobial agents. In a brief report, Kasper and Dickgiesser (4) used a different range of antimicrobial agents, but their results for metronidazole suggested a lower activity.

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TABLE 1. Comparative in vitro activities of 11 agents against 70 isolates of *C. pyloridis*

Agent	MIC_{50}[a]	MIC_{90}[a]	MIC range[a]
Penicillin	0.015	0.03	0.002–0.06
Erythromycin	0.06	0.12	0.015–0.5
Gentamicin	0.12	0.25	0.06–0.5
Cefoxitin	0.12	0.12	0.015–0.5
Nalidixic acid	32	64	1.0–64
Ciprofloxacin	0.12	0.25	0.06–0.5
Metronidazole	1.0	8.0	0.5–8.0
Sulfamethoxazole	128	>256	32–>256
Trimethoprim	512	1024	256–1024
Tripotassium dicitratobismuthate	8	16	4–32
Bismuth sodium tartrate	8	16	2–32

[a] Micrograms per ml.

This may be related to the prolonged period of incubation (4 days) or the different inoculum and medium employed. Marshall et al. (7) have also reported several isolates resistant to penicillin—our results disagree with these findings, but again these differences may be related to methodology.

Compared with other *Campylobacter* spp., *C. pyloridis* is highly susceptible to penicillin. The other susceptibilities are similar to those found by Michel et al. (10).

If antimicrobial agents are found to be effective in the therapy of gastritis, this could be due to topical action, following systemic absorption, or both. It is possible that the activity of compounds such as β-lactams and erythromycin might be altered considerably by the low gastric pH (14). Tripotassium dicitratobismuthate and bismuth subsalicylate have both been used for the treatment of gastrointestinal associated symptoms (1, 2, 8, 18,) and could be useful agents for the treatment of gastritis. Preliminary studies in this department suggest this may be the case (C. A. M. McNulty, B. Crump, J. C. Gearty, D. M. Lister, M. Davis, I. A. Donovan, V. Melikian, and R. Wise. 3rd Int. Workshop *Campylobacter* Infect., in press, 1985). These bismuth salts are not absorbed and hence are presumed to act locally in the stomach, where concentrations greater than their MICs would be expected.

C. pyloridis strains are resistant to trimethoprim and sulfamethoxazole. These compounds could therefore be useful antimicrobial agents in selective agars for isolation of *C. pyloridis* from gastric biopsies when oral contaminants may be a problem. Trimethoprim is already being used in a selective medium for isolation of other *Campylobacter* spp. (15).

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