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# Comparison of Antimicrobial Susceptibility Patterns of *Campylobacter jejuni* and *Campylobacter coli*

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**To determine whether employing antibiograms is useful to separate *Campylobacter jejuni* and *Campylobacter coli*, we determined the MICs of 12 antibiotics for 104 human clinical strains and 74 swine strains. Of 74 swine strains, 5 (7%) were hippurate positive, as were 93 (89%) of 104 human strains. The 12 antimicrobial agents tested were ampicillin, amoxicillin, clindamycin, chloramphenicol, erythromycin, furazolidone, norfloxacin, nalidixic acid, rosoxacin, rosaramicin, tetracycline, and Sch 32063. Isolates from humans were significantly ($P < 0.001$) more susceptible than swine strains to clindamycin, erythromycin, rosaramicin, and Sch 32063. Of 11 human hippurate-negative strains, 3 (27%) were resistant to clindamycin, erythromycin, rosaramicin, and Sch 32063, compared with 1 of 93 (1%) hippurate-positive strains. Nearly all human and swine strains were susceptible to furazolidone and nalidixic acid. *Campylobacter* isolates from humans and swine have different antibiograms, and the susceptibility to certain antibiotics, such as clindamycin, may be helpful for differentiation of *C. jejuni* from *C. coli*.**

*Campylobacter jejuni* is a common cause of human enteritis and has been isolated from 3 to 14% of patients with diarrhea in Europe, North America, Australia, Africa, and Asia (2, 4). The *C. jejuni* isolates cited in these references, however, may be *C. jejuni*, *Campylobacter coli*, or *Campylobacter laridis* according to the newer terminology (5, 12). In the clinical laboratories, these thermophilic *Campylobacter* strains have been separated by biochemical tests and susceptibility to nalidixic acid (12, 13). Most *Campylobacter* isolates from humans hydrolyze hippurate, which is a marker for *C. jejuni* (14), whereas most hog isolates do not hydrolyze hippurate, thus identifying them as *C. coli* (9). To supplement the existing tests for the separation of these strains, we determined the MICs of 12 antimicrobial agents for 104 human clinical strains and 74 hog strains from farms. The results of our tests showed that the hog isolates, predominantly *C. coli*, required for inhibition significantly higher MICs for four antibiotics, clindamycin, erythromycin, rosaramicin, and Sch 32063, than did the predominantly *C. jejuni* human isolates.

## MATERIALS AND METHODS

**Sources of specimens.** Eighty-one strains from humans were isolates obtained from the Clinical Microbiology Laboratories of the Denver Veterans Administration Medical Center and the University of Colorado Hospital, Denver; 20 isolates were from the culture collection of R. Weaver at the Centers for Disease Control, Atlanta, Ga., and 3 isolates were from V. Bokkenheuser, St. Luke's Hospital, New York, N.Y. Twenty-seven strains were isolates from different fresh stools in the pens of feeder pigs on hog farms near Denver. Forty-seven strains were isolates from rectal swabs collected from individual piglets on farms in the Denver area.

**Sources of antimicrobial agents.** The agents used in this study and their sources were as follows: ampicillin (Bristol Laboratories), amoxicillin (Hoffmann La Roche Inc.), chloramphenicol (Parke Davis & Co.), clindamycin (The Upjohn Co.), erythromycin (Abbott Laboratories), furazolidone (Norwich), norfloxacin (Merck Sharp & Dohme), nalidixic acid (Sterling-Winthrop), rosoxacin (Sterling-Winthrop), rosaramicin (Schering Corp.), tetracycline (Pfizer Inc.), and Sch 32063 (Schering).

**Identification of strains.** All the strains were confirmed by the following characteristics: gram-negative curved, S-shaped, or spiral forms typical for *Campylobacter* spp.; oxidase, catalase, and $H_2S$ positivity on lead acetate paper; growth at 42 to 43°C but not at 24 to 26°C; and susceptibility to a 30-mg disk of nalidixic acid (12). All strains were tested for the ability to hydrolyze hippurate by the method of Harvey (6). Thermophilic nalidixic acid-susceptible campylobacters were considered to be *C. jejuni* if hippurate positive and *C. coli* if hippurate negative, as previously defined (12, 14).

**Methods of susceptibility testing.** The standard agar dilution method was used for the MIC tests (10). After preliminary testing for optimal conditions, we used Mueller-Hinton agar in an atmosphere of 5% $O_2$ and 10% $CO_2$ and 48 h of incubation at 35°C for all the MIC plates. Strains of *Escherichia coli* (ATCC 25922) and *Staphylococcus aureus* (ATCC 25923) were used as controls for the MICs.

## RESULTS

The MICs required to inhibit 104 thermophilic *Campylobacter* isolates from humans and 74 isolates from hogs are shown in Table 1. Tetracycline resistance (MIC, 8) was widespread (86%) among the hog isolates and considerable (30%) among the human isolates. Susceptibility to furazolidone, nalidixic acid, and rosoxacin was common among both groups of strains. The swine strains were significantly more resistant to clindamycin, erythromycin, rosaramicin, and Sch 32063 than those of humans (Table 2). Hippurate-positive strains, regardless of source but preponderantly (93%) from humans, were significantly more susceptible to these four antibiotics than the hippurate-negative strains, chiefly from hogs (Table 3). Data also show that significantly ($P < 0.001$) more hog strains (53 of 74) and hippurate-negative strains (51 of 80) regardless of source were multiply

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TABLE 1. Susceptibility of thermophilic *Campylobacter* isolates to 12 antimicrobial agents

| Antimicrobial agent | MIC (μg/ml) for following type of isolate: | | | | | |
|---|---|---|---|---|---|---|
| | Human ($n$ = 104) | | | Hog ($n$ = 74) | | |
| | Range | 50% | 90% | Range | 50% | 90% |
| Ampicillin | 1–>32 | 8 | 16 | 1–>32 | 8 | 16 |
| Amoxicillin | 1–>32 | 8 | 32 | 1–>32 | 32 | >32 |
| Clindamycin | 0.25–>32 | 0.5 | 1 | 0.5–>32 | 32 | >32 |
| Chloramphenicol | 4–16 | 4 | 8 | 2–16 | 4 | 16 |
| Erythromycin | 0.5–>32 | 2 | 4 | 0.5–>32 | >32 | >32 |
| Furazolidone | 0.6–1 | 0.25 | 0.5 | 0.06–0.25 | 0.12 | 0.25 |
| Norfloxacin | 0.25–8 | 1 | 2 | 0.12–8 | 1 | 2 |
| Nalidixic acid | 2–>32 | 8 | 8 | 4–>32 | 8 | 16 |
| Rosoxacin | 0.25–2 | 0.25 | 1 | 0.25–>32 | 0.5 | 1 |
| Rosaramicin | 0.25–>32 | 0.5 | 1 | 0.5–>32 | >32 | >32 |
| Tetracycline | 0.25–>32 | 2 | >32 | 1–>32 | >32 | >32 |
| Sch 32063 | 0.25–>32 | 1 | 2 | 0.25–>32 | >32 | >32 |

resistant to these four antimicrobial agents than were human strains (4 of 104) or hippurate-positive strains (3 of 98) (Table 4).

## DISCUSSION

The thermophilic *Campylobacter* group presently consists of *C. jejuni*, *C. coli*, and *C. laridis* strains (5). Our previous work (9) showed that all 28 hog strains tested were hippurate negative (*C. coli*), and 99% of the 155 human clinical strains isolated in Denver were hippurate positive (*C. jejuni*). Our present study confirmed these findings, with few *C. coli* strains found among our human isolates and fewer *C. jejuni* strains found among the hog isolates.

Hog strains required for inhibition significantly higher MICs than did human strains for four antibiotics, clindamycin, erythromycin, rosaramicin, and Sch 32063. Reviewing the susceptibility of these four antibiotics, we found that use of the arbitrarily selected breakpoints shown in Table 2 effectively separated the human and hog strains. The resistance pattern of the hippurate-negative hog and human strains to these four antibiotics suggests that antimicrobial susceptibility testing may also aid in the differentiation of *C. coli* from *C. jejuni*.

*C. jejuni* caused acute enteritis and other diseases, such as colitis (1) and arthritis (8). It is desirable to learn the source of the strains involved in these diseases for epidemiological purposes. Using MICs for differentiation of hog and human isolates could thus be helpful in identifying sources of outbreaks.

Erythromycin is recognized as the drug of choice to treat *Campylobacter* infections in humans (2), but strains resistant to erythromycin have been previously observed (16). Vanhoof et al. (16) found in Belgium that 8.4% of isolates from humans in 1978 were resistant to erythromycin, but in 1980 (15) only two strains (2.3%) tested were resistant. Walder's study in Sweden (17) found 8% of strains to be resistant, whereas Karmali et al. (7) in Canada and Brunton et al. (3) in England showed that only 0.5 to 1% of strains studied were resistant to erythromycin. Our data suggest that these discrepancies in susceptibility could be based on the source of the strains, since strains from hogs were more resistant to erythromycin. More hog strains from different geographic areas should be tested to reach a definite conclusion.

Our study showed that hippurate-negative isolates, from humans as well as from hogs, were often erythromycin resistant. Therefore, we believe that if a *Campylobacter* strain isolated from a patient is hippurate negative, erythromycin should not be used to treat these patients until laboratory susceptibility results are available.

The other three antibiotics, clindamycin, rosaramicin, and Sch 32063, also showed MIC differences between *C. jejuni* and *C. coli*; these characteristics may be utilized to help differentiate the species. Furthermore, since *C. jejuni* was found more commonly among the clinical strains, these antibiotics might be considered as alternative agents for the treatment of diarrhea caused by *C. jejuni*.

Tetracycline has also been used as an alternative drug to treat *Campylobacter* enteritis (2). Our results show that the hog strains are more resistant to tetracycline than the human strains. Studies of other human isolates showed a $MIC_{90}$ range of 0.5 to 64 μg of tetracycline per ml (7, 11). These differences might also be related to the ultimate source of strains tested.

In conclusion, the differences in susceptibility to antimicrobial agents among isolates of *C. jejuni* and *C. coli* may be

TABLE 2. Comparison of susceptibility of thermophilic *Campylobacter* isolates from humans and hogs to four antimicrobial agents

| Antimicrobial agent | MIC (μg/ml) | % of strains susceptibile[a] | |
|---|---|---|---|
| | | Human ($n$ = 104) | Hog ($n$ = 74) |
| Clindamycin | 2 | 96 | 8 |
| Erythromycin | 8 | 96 | 26 |
| Rosaramicin | 2 | 96 | 21 |
| Sch 32063 | 2 | 95 | 8 |

[a] Each difference was significant at $P < 0.001$.

TABLE 3. Susceptibility of hippurate-positive and -negative thermophilic *Campylobacter* isolates from humans and hogs to four antimicrobial agents

| Antimicrobial agent | MIC (μg/ml) | % of strains susceptibile[a] | |
|---|---|---|---|
| | | Hippurate positive (*C. jejuni*) ($n$ = 98[b]) | Hippurate negative (*C. coli*) ($n$ = 80[c]) |
| Clindamycin | 2 | 94 | 18 |
| Erythromycin | 8 | 97 | 30 |
| Rosaramicin | 2 | 97 | 25 |
| Sch 32063 | 2 | 95 | 16 |

[a] Each difference was significant at $P < 0.001$.
[b] 93 isolates from humans, 5 isolates from hogs.
[c] 11 isolates from humans, 69 isolates from hogs.

TABLE 4. Susceptibility of 178 *Campylobacter* isolates to four antimicrobial agents by resistance

| Resistance | No. of isolates from: | | No. of isolates from strains | |
|---|---|---|---|---|
| | Humans ($n$ = 104) | Hogs ($n$ = 74) | Hippurate positive (*C. jejuni*) ($n$ = 98) | Hippurate negative (*C. coli*) ($n$ = 80) |
| Susceptible to all 4 antibiotics | 99 | 2 | 92 | 10 |
| Resistant to | | | | |
| One antibiotic | 1 | 5 | 1 | 3 |
| Two antibiotics | 0 | 10 | 2 | 8 |
| Three antibiotics | 0 | 4 | 0 | 5 |
| Four antibiotics | 4 | 53 | 3 | 54 |

useful for epidemiological recognition of probable sources of these strains as well as their identification in the laboratory. Moreover, the greater resistance of *C. coli* to commonly used antimicrobial agents has implications for therapy of these thermophilic *Campylobacter* infections.

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