In Vitro Susceptibility of Campylobacter fetus subsp. jejuni to N-Formimidoyl Thienamycin, Rosaramicin, Cefoperazone, and Other Antimicrobial Agents

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The activities of 11 antimicrobial agents against 36 strains of Campylobacter fetus subsp. jejuni were studied by a broth microdilution method. All strains were susceptible to 7 of the 11 antimicrobial agents. Of the newer agents tested N-formimidoyl thienamycin (MK0787) and rosaramicin had very good activity, whereas ceftaxime, moxalactam, and cefoperazone had poorer activity.

Enteric and disseminated diseases caused by Campylobacter fetus subsp. jejuni are being reported in increasing numbers, and the spectrum of pathology due to this bacterium is expanding (3, 6, 8, 9, 13). The current drug of choice, based only on in vitro data, is erythromycin, although tetracycline, gentamicin, and chloramphenicol have also been used successfully (6). This study was done to determine whether there has been any change in the pattern of susceptibility of C. fetus subsp. jejuni to certain established antibiotics and to evaluate the activity of some newer antimicrobial agents, namely, N-formimidoyl thienamycin (MK0787), rosaramicin, and cefoperazone, against this bacterium.

A total of 36 strains of C. fetus subsp. jejuni were studied, and they consisted of 20 obtained from patients with diarrhea and 16 from the rectal contents of chickens. All strains were isolated by filtration technique (4) or by direct plating of stool specimens onto selective media (BBL Microbiology Systems, Cockeysville, Md; Oxoid Ltd., Columbia, Md; Scott Laboratories, Inc., Fiskeville, R.I.). Typical colonies were picked off and identified to subspecies level as described by Grant et al. (4).

The antimicrobial agents tested were N-formimidoyl thienamycin (Merck & Co., Inc., Rahway, N.J.), rosaramicin and gentamicin (Schering Corp., Bloomfield, N.J.), erythromycin (Abbott Laboratories, North Chicago, Ill.), ampicillin (Beecham Laboratories, Bristol, Tenn.), ceftaxime (Hoechst-Roussel Pharmaceuticals, Inc., Somerville, N.J.), moxalactam (Eli Lilly & Co., Indianapolis, Ind.), cefoperazone (Pfizer Inc., New York, N.Y.), rifampin (Ciba-Geigy Corp., Summit, N.J.), chloramphenicol (Parke, Davis & Co., Detroit, Mich.), and vancomycin (USP). Twofold serial dilutions of solutions of the susceptibility test powders were prepared in Mueller-Hinton broth (Difco Laboratories, Detroit, Mich.), supplemented with laked blood.

Minimal inhibitory concentrations (MICs) were determined by the broth microdilution technique. Isolates were reconstituted in Trypticase (BBL) soy broth and plated on chocolate agar. The plates were incubated for 48 h at 37°C in about 10% carbon dioxide and about 10% O2. Suspensions of colonies were incubated in Mueller-Hinton broth for 48 h, as described above, and then diluted to approximately 106 colony-forming units per ml. An MIC 2000 apparatus (Dynatech Laboratories Inc., Alexandria, Va.) was used to prepare the antibiotic solutions and dispense inocula into microtiter plates. The plates were examined after incubation for 48 h. The MIC was defined as the lowest concentration that showed no growth. The minimal bactericidal concentrations were determined by plating MIC cultures on Mueller-Hinton agar and incubating for 48 h under the conditions stated above. Bactericidal activity was defined original inoculum, determined by quantitative subcultures. However, because the 90% minimal bactericidal concentrations were equal to or one tube dilution higher than the 90% MICs (MIC90's) for all the drugs tested, only MICs are shown.

Table 1 summarizes the MICs, in order of activity, of 11 antimicrobial agents for 36 strains of C. fetus subsp. jejuni. N-Formimidoyl thienamycin, rosaramicin, gentamicin, and erythro-
TABLE 1. Susceptibility of C. fetus subsp. jejuni to antimicrobial agents

| Drug                  | MIC (µg/ml) | MIC50 | MIC90 |
|-----------------------|-------------|-------|-------|
|                       | Range       |       |       |
| N-Formimidoyl thienamycin | 0.01–0.03  | 0.03  | 0.03  |
| Rosaramicin           | 0.03–1.0    | 0.06  | 0.5   |
| Gentamicin            | 0.03–0.5    | 0.25  | 0.5   |
| Erythromycin          | 0.06–2.0    | 0.25  | 0.5   |
| Cefotaxime            | 2.0–4.0     | 2.0   | 4.0   |
| Ampicillin            | 2.0–8.0     | 2.0   | 4.0   |
| Chloramphenicol       | 2.0–8.0     | 2.0   | 4.0   |
| Moxalactam            | 4.0–32      | 16    | 16    |
| Rifampin              | ≥0.5        | ≥128  | ≥128  |
| Cefoperazone          | ≥128        | ≥128  | ≥128  |
| Vancomycin            | ≥128        | ≥128  | ≥128  |

N-Formimidoyl thienamycin exhibited very good activity, with MIC50's ranging from 0.03 to 0.25 µg/ml and MIC90's ranging from 0.03 to 0.5 µg/ml. Overall, N-formimidoyl thienamycin showed the best activity, inasmuch as all strains were susceptible to 0.03 µg/ml. Rosaramicin was the next most active drug, with an MIC50 of 0.5 µg/ml. Only one strain had an MIC higher than 0.5 µg/ml. Gentamicin and erythromycin showed overall equal activity; the MIC50 was 0.5 µg/ml for both drugs. All but two strains were inhibited by 0.5 µg of erythromycin per ml, and all strains were susceptible to 0.5 µg of gentamicin per ml.

Cefotaxime, ampicillin, and chloramphenicol had lower activity, with MIC50's of 2 µg/ml and MIC90's of 4.0 µg/ml. With 4 µg/ml inhibiting all strains, cefotaxime was the most active in this group. Moxalactam had an MIC50 of 16 µg/ml, showing only slight activity against most strains. Rifampin, cefoperazone, and vancomycin did not inhibit any strains at a concentration of 128 µg/ml.

N-Formimidoyl thienamycin demonstrated the highest activity against C. fetus subsp. jejuni in this study, confirming earlier reports of overall superior activity of the thienamycin antibiotics in comparison with established antimicrobial agents and the newer cephalexin or cephalexin antibiotics with an expanded gram-negative antibacterial spectrum (7, H. C. Neu and P. Labthavikul, Program Abstr. Intersci. Conf. Antimicrob. Agents Chemother. 20th, New Orleans, La., abstr. no. 260, 1980). The clinical significance of this in vitro finding awaits further investigation. Rosaramicin also showed very good activity and appeared better than erythromycin, an observation that has been made of the activity of the two drugs against several species (12). Thus rosaramicin is potentially an alternative drug (with superior activity) to erythromycin, which is currently the recommended drug for C. fetus subsp. jejuni enteritis (6).

The activities of gentamicin and cefotaxime were judged good from our results and compared favorably with the results of other investigators (10). In this study ampicillin and chloramphenicol inhibited over 90% of the strains tested at concentrations that are easily achievable in the blood. Previous studies have shown the activity of ampicillin to range from good (1) to poor (5) in vitro and similarly variable in vivo (2, 11). The high MIC90's of moxalactam would appear to preclude its use for C. fetus subsp. jejuni infections in spite of the good serum concentrations achievable by parenteral administration of this drug. All of the newer antibiotics had good activity against C. fetus subsp. jejuni in this study, with the exception of cefoperazone. Their clinical usefulness remains to be confirmed.

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ERRATA

Treatment of Uncomplicated Gonorrhea with Rosoxacin

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Volume 20, no. 5, p. 625: The affiliations of Franklyn N. Judson and King K. Holmes should be transposed.
Page 625: The receipt and acceptance dates should be transposed.
Page 625, abstract, line 5: “Susceptibility to rosoxacin was determined for 6” should read “Susceptibility to rosoxacin was determined for 106.”
Page 628, column 2, line 29: Reference 12 should be reference 9.

Dose-Ranging Study of Ceftriaxone for Uncomplicated Gonorrhea in Men

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Volume 20, no. 6, p. 840, column 1, line 24: “0.50 µg/ml” should read “0.35 µg/ml.”

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Volume 20, no. 6, p. 850, column 2, line 26: “Bactericidal activity was defined original inoculum, determined by quantitative subcultures” should read “Bactericidal activity was defined as a reduction of 99% of the colonies in the original inoculum, determined by quantitative subcultures.”