Comparison of five latex agglutination kits for detecting group A streptococcal antigen

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The sensitivity and specificity of five latex agglutination kits for rapid detection of group A *Streptococcus* (GAS) antigen in direct throat swabs were compared. A total of 1,007 clinical specimens for diagnosis of GAS pharyngitis were randomly tested against one of the kits as well as by standard cultural methods. β -hemolytic streptococci were isolated from 291 specimens (29%). Of these isolates 128 (44%) were presumptively identified as GAS by bacitracin susceptibility and 129 (44%) were identified as GAS by serotyping. The sensitivity value of the rapid detection kits in comparison with standard cultural methods ranged from 60% to 68%; the specificity ranged from 91% to 98%; the positive predictive value ranged from 43% to 80%, and the negative predictive value ranged from 94% to 96%. When tested in vitro with varying dilutions of antigen, the test kits did not differ substantially in detecting the low concentrations of antigen.

Classically, the definitive diagnosis of streptococcal pharyngitis has been made by isolation and identification of group A β -hemolytic streptococci from pharyngeal specimens. Presumptive identification of this organism is made by demonstrating in vitro susceptibility to 0.04 units of bacitracin.¹ Unfortunately, this method of presumptive identification often yields incorrect results: false-positive because occasional group C streptococci are sensitive to bacitracin, and false-negative because of fail-

ure to detect β -hemolysis in oxygen-sensitive strains of group A streptococci.² Some authors³ have reported discrepant results in which one inoculated agar plate yielded moderate to heavy growth of β -hemolytic streptococci and a second plate, inoculated from the same throat swab, showed no such growth.³ The standard Lancefield precipitation test for serologic identification of the β -hemolytic streptococci⁴ remains the reference standard for identification; however, the procedure is time consuming and expensive. Newer serologic procedures employing a latex agglutination immunoassay are less time consuming and are as sensitive and specific as the Lancefield precipitation technique; however, they are more expensive than the bacitracin method commonly employed by most laboratories.⁵

Interest in immunologic procedures that directly detect infectious agents in specimens without cultivation has been increasing.⁶⁻⁹ Several kits for direct detection of group A streptococcal antigen in oropharyngeal swabs are now marketed. Most of the kits are based on a latex particle agglutination immunoassay and differ in their antigen extraction method, that is, acid¹⁰⁻¹¹ or enzymatic.¹²⁻¹³ They also differ in minimum time for test results, ranging from 5 to 60 minutes. Most of these kits have been evaluated singly by comparison to standard cultural techniques,¹⁰⁻¹⁸ and a few two-kit comparative trials have been reported.^{15,19} The usefulness and importance of comparative evaluations of both antigen and antibody detection kits is amply evidenced in the literature.²⁰⁻²⁴ Therefore the purpose of this study was to conduct a direct comparison of the sensitivity, specificity, and the predictive values (positive and negative) of five commercially available group A streptococci direct de-

tection kits, and compare the efficiency of each kit to the standard culture techniques of a single testing laboratory.

Methods

Throat specimens were obtained from outpatients with suspected GAS pharyngitis by swabbing the tonsillar region and posterior pharynx with a rayon-tipped swab (Culturette, Marion Scientific, Kansas City, Mo). All specimens were submitted to the microbiology laboratory to be routinely screened for streptococcal pharyngitis.

The swab for each patient was inoculated on trypticase soy agar supplemented with 5% sheep blood (BBL Microbiology Systems, Cockeysville, Md). The specimen was streaked for isolation, and the agar was stabbed across the primary streak. Cultures were incubated aerobically at 35°C in 5% CO₂ for 18 to 24 hours. β -hemolytic streptococcal colonies were presumptively identified as small (0.5 to 1.0 mm), white-gray colonies surrounded by a clear zone of hemolysis. β -hemolytic colony-forming units (CFU) of streptococci were quantified as follows: rare, less than 10 colonies per plate; few, 10 to 50 colonies per plate; moderate, 50 to 100 colonies per plate; and many, more than 100 colonies per plate. β -hemolytic colonies were subcultured from the primary plate, tested for bacitracin susceptibility according to standard methods,¹ and identified definitively by serologic techniques (Streptex; Wellcome Diagnostics, Research Triangle Park, NC).

The same swab submitted for culture was also used for detection of GAS antigen after inoculation of agar plate. At the beginning of each collection day, a direct latex agglutination kit was chosen by random number for that day's testing. The kits tested are shown in Table 1. Strict adherence to the protocol specified by each manufacturer was followed. All the kits used in this study were generously supplied by the manufacturers.

The relative sensitivity of each kit was determined according to a modification of the procedure described by Petts.⁸ Briefly, an overnight broth culture of a clinical isolate of GAS was diluted tenfold in sterile saline solution, and colony counts were performed in triplicate for each dilution. Sterile swabs were placed in each dilution and allowed to absorb fluid, removed, drained, and subsequently treated as a clinical throat swab for GAS antigen detection. The volume of fluid absorbed by each swab was determined by weighing before and after loading.

Analysis of the data to determine sensitivity, specificity, predictive value for a positive result and predictive value for a negative result was done by the method of Griner et al.²⁵ The χ^2 test was used to compare discrete variables.

Results

Oropharyngeal specimens were collected from 1,007 patients with pharyngitis and were processed according to the procedure described. β -hemolytic streptococci were recovered from 291 (29%) specimens by cultural methods. The predominant serogroups identified were group A, accounting for 44% (129/291), and group C, accounting for 32% (93/291) of the β -hemolytic streptococcal isolates. The percentage of isolates in each of groups B, F, and G were 8%, 9%, and 6%, respectively. Two 1% isolates were group D and were identified serologically only after the antigen-enzyme extraction mixture was incubated an additional 30 min. Of the 129 serologically identified group A isolates, 115 were presumptively identified to be GAS by bacitracin susceptibility (sensitivity, 89%), and 149 of the 162 non-group A isolates were resistant to bacitracin (specificity, 92%). Overall, bacitracin tests were in 91% (264/291) agreement with serologic identification of GAS.

A comparison of each kit with standard culture methods for detecting GAS on the basis of serologic identification is shown in Table 2. The total number of tests for each kit represents, to the extent possible, random selection of a kit for a given day's testing and ranged from 169 to 240 tests. A total of 49 test kit results were false positive with 71% (35/49) occurring in specimens that produced no β -hemolytic CFU on culture. The serotype distribution of the non-group A isolates representing the remaining 14 false positives did not appear to be substantially different from the general distribution observed for all cultures yielding β -hemolytic CFU. The comparative sensitivities, specificities, positive predictive values, and negative predictive values are given in Fig 1. The greatest variation in the performance of the test kits occurred

TABLE 1. DIRECT LATEX AGGLUTINATION KITS.

Kit	Abbreviation or Acronym	Antigen Extraction Method	Manufacturer
Detect-A-Strep Direct Antigen Identification Kit	DAS	Acid	Antibodies, Inc.
Directigen	DAD HWD	Enzymatic Enzymatic	Difco Hynson, Westcott and Dunning
Group A Strep ID	SID	Acid	Marion Diagnostic Products
Pathodex A	PDX	Acid	

TABLE 2. COMPARISON OF DIRECT LATEX AGGLUTINATION KITS WITH STANDARD CULTURAL METHODS FOR DETECTION OF GAS IN THROAT SWABS.

Test Kit	Kit Results	No. Positive	Culture Result No. Negative	Total
DAS	Positive	13	14	27
	Negative	7	150	157
	Total	20	164	184
DAD	Positive	21	6	27
	Negative	10	183	193
	Total	31	189	220
HWD	Positive	12	3	15
	Negative	8	146	154
	Total	20	149	169
SID	Positive	20	10	30
	Negative	12	198	210
	Total	32	208	240
PDX	Positive	12	16	28
	Negative	8	158	166
	Total	20	174	194

Fig. 1. Comparison of the sensitivity (SENS), specificity (SPEC), and predictive values for positive results (PVP) and for negative results (PVN) of the five test kits for detection of GAS in throat swabs.

in the positive predictive values, which ranged from 43% (PDX) to 80% (HWD). No significant differences among the kits with regard to sensitivity (60% to 68%), specificity, (91% to 98%) or negative predictive value (94% to 96%) were shown.

Table 3 summarizes the individual performances of each kit for the in vitro testing of the lower limits of antigen detection. Tenfold dilutions were made from a broth culture of GAS containing 3.0×10^6 CFU/mL. Swabs were placed in the dilutions and the volume retained by the swab was calculated from the increased weight and ranged from 0.159 to 0.178 mL with a mean of 0.168 ± 0.01 mL. The results showed that each test kit gave a positive reaction at a dilution of 10^{-3} (460 CFU/swab). The PDX kit showed a borderline positive result at the 10^{-4} dilution.

Discussion

The predominant β -hemolytic *Streptococcus* isolated in this study was group A, which accounted for 44% of the isolates. The most common non-A β -hemolytic *Streptococcus* was group C, which accounted for 32% of all β -hemolytic streptococci and 57% of all non-A β -hemolytic streptococci. The distribution of non-group A isolates from patients with pharyngitis varies in the literature, although group C²⁶ and group G²⁷ frequently predominate as the most common non-group A isolates. Both group C²⁸ and group G²⁹ streptococci can cause a pharyngitis that is clinically indistinguishable from illness associated with the group A streptococci. Some authors argue that patients with group C streptococcal infection should undergo treatment so that local and metastatic suppurative complications can be avoided³⁰; however, other evidence has shown that therapy neither significantly modifies the severity nor affects the duration of symptoms associated with non-group A streptococcal pharyngitis.³¹ Perhaps the evidence should be re-examined in light of recent findings that early administration of antimicrobics for group A streptococcal pharyngitis alters the course of disease.³²

The standard cultural methods used in this study included serologic identification of β -hemolytic streptococcal isolates as the reference method. The sensitivity of presumptive identification by bacitracin susceptibility as compared to serologic identification was 89%. Among the 13 false-positive bacitracin-sensitive strains, group C accounted for 10 (77%) of the isolates, and group G accounted for the remaining 3 isolates (23%). The serotype distribution of the false-positive bacitracin-suscepti-

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ble isolates was significantly different from that observed for all isolates ($P < .001$). Therefore, the use of bacitracin sensitivity to evaluate direct latex agglutination kits for GAS would have limitations in studies yielding a high proportion of group C and group G isolates. Such isolates could increase the number of false negative results (bacitracin sensitive, latex negative), thereby decreasing the sensitivity value.

The sensitivity of the test kits varied from 60 to 68%. Generally, our findings were in the lower range of reported sensitivities for comparative studies on direct latex agglutination kits.¹⁰⁻¹⁸ However, previous studies have shown that sensitivity of a single kit may range from 62%¹⁰ to 95%.¹⁸ This variation reflects, in part, variation among laboratories in specimen collection and standard culturing techniques. Throat culture technology is not sufficiently standardized; therefore, comparisons among studies are difficult.³³ In our study all kits were evaluated by use of the uniform standard techniques of a single laboratory, so that the cultural methods used to evaluate kit performance had some standardization or uniformity. Under these conditions, no significant differences in either sensitivity or specificity were found among the five DLAKs tested.

A possible explanation for decreased sensitivity would include the use, in our study, of a single-swab specimen for both culture and the antigen detection tests. The literature includes conflicting reports that culture plate inoculation may sufficiently deplete the swab of GAS as to preclude a positive antigen detection test.^{3,10,33} Poorly collected specimens further increase the likelihood of false negative DLAK results.¹⁰ One study has shown that a minimum of 2×10^5 CFU of GAS per swab is necessary for a positive latex test.³⁴ These data differ significantly from our findings of a positive latex agglutination reaction for swabs containing 4.6×10^2 CFU of GAS. Nevertheless, 67% (30/45) of false-negative latex agglutination test results occurred from specimens that yielded less than 50 β -hemolytic CFU on primary culture.

The positive predictive values of the kits differed significantly. Kits (DAD and HWD) that utilize an enzymatic extraction method for release of GAS antigen had substantially higher predictive values of positivity than those using an acid extraction method. The positive predictive values showed that between 20% to 57% of the patients diagnosed as having GAS pharyngitis by direct antigen detection tests would receive unnecessary antimicrobial therapy. The decision whether to use a direct antigen detection test as a primary diagnostic tool as the basis for therapy should depend on whether a

TABLE 3. IN VITRO COMPARISON OF LOWER LIMIT OF GAS ANTIGEN DETECTION BY TEST KITS. DILUTIONS ARE FROM CULTURE CONTAINING 3.0×10^6 CFU/ML *STREPTOCOCCUS PYOGENES*.

Dilutions	CFU/swab	Test Kit Result*				
		DAS	DAD	HWD	PDX	SID
10^{-2}	4.90×10^3	2+	4+	4+	4+	3+
10^{-3}	4.60×10^2	1+	1+	2+	2+	1+
10^{-4}	4.90×10^1	—	—	—	±	—

*Intensity of agglutinations graded as follows: 1+, very slight, fine granular; 2+, moderate agglutination with uniform small clumps; 3+, heavy agglutination with uniform large clumps; 4+, heavy agglutination with widely scattered large clumps and clearing of suspending fluid.

culture will be performed. If no culture will be done, the direct antigen detection test may be used to supplement the physician's physical findings. The test could provide a rapid means of improving the diagnosis of GAS pharyngitis and increase the chance of appropriate therapy.

The results of this study showed that the five DLAKs tested performed equally well with regard to sensitivity and specificity. The choice of which kit to use could be based on cost and ease of operation.

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WARNINGS

CIPROFLOXACIN SHOULD NOT BE USED IN CHILDREN OR PREGNANT WOMEN. The oral administration of ciprofloxacin caused lameness in immature dogs. Histopathological examination of the weight-bearing joints of these dogs revealed permanent lesions of the cartilage. Related drugs such as nalidixic acid, cinoxacin, and norfloxacin also produced erosions of cartilage of weight-bearing joints and other signs of arthropathy in immature animals of various species (SEE ANIMAL PHARMACOLOGY SECTION IN FULL PRESCRIBING INFORMATION).

PRECAUTIONS

General:

As with other quinolones, ciprofloxacin may cause central nervous system (CNS) stimulation, which may lead to tremor, restlessness, lightheadedness, confusion, and very rarely to hallucinations or convulsive seizures. Therefore, ciprofloxacin should be used with caution in patients with known or suspected CNS disorders, such as severe cerebral arteriosclerosis or epilepsy, or other factors which predispose to seizures (SEE ADVERSE REACTIONS).

Crystals of ciprofloxacin have been observed rarely in the urine of human subjects but more frequently in the urine of laboratory animals. Crystalluria related to ciprofloxacin has been reported only rarely in man, because human urine is usually acidic. Patients receiving ciprofloxacin should be well hydrated, and alkalinity of the urine should be avoided. The recommended daily dose should not be exceeded. Alteration of the dosage regimen is necessary for patients with impairment of renal function (SEE DOSAGE AND ADMINISTRATION).

Drug Interactions:

Concurrent administration of ciprofloxacin with theophylline may lead to elevated plasma concentrations of theophylline and prolongation of its elimination half-life. This may result in increased risk of theophylline-related adverse reactions. If concomitant use cannot be avoided, plasma levels of theophylline should be monitored and dosage adjustments made as appropriate.

Antacids containing magnesium hydroxide or aluminum hydroxide may interfere with the absorption of ciprofloxacin, resulting in serum and urine levels lower than desired; concurrent administration of these agents with ciprofloxacin should be avoided.

Probenecid interferes with the renal tubular secretion of ciprofloxacin and produces an increase in the level of ciprofloxacin in the serum. This should be considered if patients are receiving both drugs concomitantly.

As with other broad-spectrum antibiotics, prolonged use of ciprofloxacin may result in overgrowth of non-susceptible organisms. Repeated evaluation of the patient's condition and microbial susceptibility testing is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Information for Patients:

Patients should be advised that ciprofloxacin may be taken with or without meals. The preferred time of dosing is two hours after a meal. Patients should also be advised to drink fluids liberally and not take antacids containing magnesium or aluminum concomitantly or within two hours after dosing. Ciprofloxacin may cause dizziness or lightheadedness; therefore patients should know how they react to this drug before they operate an automobile or machinery or engage in activities requiring mental alertness or coordination.

Carcinogenesis, Mutagenesis, Impairment of Fertility:

Eight *in vitro* mutagenicity tests have been conducted with ciprofloxacin and the test results are listed below:

- Salmonella/Microsome Test (Negative)
- E. coli* DNA Repair Assay (Negative)
- Mouse Lymphoma Cell Forward Mutation Assay (Positive)
- Chinese Hamster V₇₉ Cell HGPRT Test (Negative)
- Syrian Hamster Embryo Cell Transformation Assay (Negative)
- Saccharomyces cerevisiae* Point Mutation Assay (Negative)
- Saccharomyces cerevisiae* Mitotic Crossover and Gene Conversion Assay (Negative)
- Rat Hepatocyte DNA Repair Assay (Positive)

Thus, two of the eight tests were positive, but the following three *in vivo* test systems gave negative results:

- Rat Hepatocyte DNA Repair Assay
- Micronucleus Test (Mice)
- Dominant Lethal Test (Mice)

Long-term carcinogenicity studies in animals have not yet been completed.

Pregnancy—Pregnancy Category C:

Reproduction studies have been performed in rats and mice at doses up to six times the usual daily human dose and have revealed no evidence of impaired fertility or harm to the fetus due to ciprofloxacin. In rabbits, as with most antimicrobial agents, ciprofloxacin (30 and 100 mg/kg orally) produced gastrointestinal disturbances resulting in maternal weight loss and an increased incidence of abortion. No teratogenicity was observed at either dose. After intravenous administration, at doses up to 20 mg/kg, no maternal toxicity was produced, and no embryotoxicity or teratogenicity was observed. There are, however, no adequate and well-controlled studies in pregnant women. SINCE CIPROFLOXACIN, LIKE OTHER DRUGS IN ITS CLASS, CAUSES ARTHROPATHY IN IMMATURE ANIMALS, IT SHOULD NOT BE USED IN PREGNANT WOMEN (SEE WARNINGS).

Nursing Mothers:

It is not known whether ciprofloxacin is excreted in human milk; however, it is known that ciprofloxacin is excreted in the milk of lactating rats and that other drugs of this class are excreted in human milk. Because of this and because of the potential for serious adverse reactions from ciprofloxacin in nursing infants, a decision should be made to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use:

Ciprofloxacin should not be used in children because it causes arthropathy in immature animals (SEE WARNINGS).

ADVERSE REACTIONS

Ciprofloxacin is generally well-tolerated. During clinical investigation, 2,799 patients received 2,868 courses of the drug. Adverse events that were considered likely to be drug related occurred in 7.3% of courses, possibly related in 9.2%, and remotely related in 3.0%. Ciprofloxacin was discontinued because of an adverse event in 3.5% of courses, primarily involving the gastrointestinal system (1.5%), skin (0.6%), and central nervous system (0.4%).

The most frequently reported events, drug related or not, were nausea (5.2%), diarrhea (2.3%), vomiting (2.0%), abdominal pain/discomfort (1.7%), headache (1.2%), restlessness (1.1%), and rash (1.1%).

Additional events that occurred in less than 1% of ciprofloxacin courses are listed below. Those typical of quinolones are italicized.

CONVENIENT B.I.D. DOSAGE

Recommended dosage schedule

Infection Site	Severity of Infection	Dosage
Respiratory Tract	Mild/Moderate	500 mg B.I.D.
Bone and Joint	Severe/Complicated	750 mg B.I.D.
Skin/Skin Structure	Severe/Complicated	750 mg B.I.D.
Urinary Tract	Mild/Moderate	250 mg B.I.D.
	Severe/Complicated	500 mg B.I.D.
Infectious Diarrhea	Mild/Moderate/Severe	500 mg B.I.D.

GASTROINTESTINAL: (See above), painful oral mucosa, oral candidiasis, dysphagia, intestinal perforation, gastrointestinal bleeding.

CENTRAL NERVOUS SYSTEM: (See above), dizziness, lightheadedness, insomnia, nightmares, hallucinations, manic reaction, irritability, tremor, ataxia, convulsive seizures, lethargy, drowsiness, weakness, malaise, anorexia, phobia, depersonalization, depression, paresthesia.

SKIN/HYPERSENSITIVITY: (See above), pruritus, urticaria, photosensitivity, flushing, fever, chills, angioedema, edema of the face, neck, lips, conjunctivae or hands; cutaneous candidiasis, hyperpigmentation, erythema nodosum.

SPECIAL SENSES: blurred vision, disturbed vision (change in color perception, overbrightness of lights), decreased visual acuity, diplopia, eye pain, tinnitus, bad taste.

MUSCULOSKELETAL: joint or back pain, joint stiffness, achiness, neck or chest pain, flare up of gout, decreased visual acuity, diplopia, eye pain, tinnitus, bad taste.

RENAL/UROGENITAL: interstitial nephritis, nephritis, renal failure, polyuria, urinary retention, urethral bleeding, vaginitis, acidosis.

CARDIOVASCULAR: palpitations, atrial flutter, ventricular ectopy, syncope, hypertension, angina pectoris, myocardial infarction, cardiopulmonary arrest, cerebral thrombosis.

RESPIRATORY: epistaxis, laryngeal or pulmonary edema, hiccough, hemoptysis, dyspnea, bronchospasm, pulmonary embolism.

Most of these events were described as only mild or moderate in severity, abated soon after the drug was discontinued, and required no treatment.

In several instances, nausea, vomiting, tremor, restlessness, agitation, or palpitations were judged by investigators to be related to elevated plasma levels of theophylline possibly as a result of a drug interaction with ciprofloxacin.

Adverse Laboratory Changes: Changes in laboratory parameters listed as adverse events without regard to drug relationship:

Hepatic—Elevations of: ALT (SGPT) (1.9%), AST (SGOT) (1.7%), Alkaline Phosphatase (0.8%), LDH (0.4%), serum bilirubin (0.3%).

Hematologic—eosinophilia (0.6%), leukopenia (0.4%), decreased blood platelets (0.1%), elevated blood platelets (0.1%), pancytopenia (0.1%).

Renal—Elevations of: Serum creatinine (1.1%), BUN (0.9%).

CRYSTALLURIA, CYLINDRURIA, AND HEMATURIA HAVE BEEN REPORTED.

Other changes occurring in less than 0.1% of courses were: Elevation of serum gamma-glutamyl transferase, elevation of serum amylase, reduction in blood glucose, elevated uric acid, decrease in hemoglobin, anemia, bleeding diathesis, increase in blood monocytes, and leukocytosis.

OVERDOSAGE

Information on overdosage in humans is not available. In the event of acute overdosage, the stomach should be emptied by inducing vomiting or by gastric lavage. The patient should be carefully observed and given supportive treatment. Adequate hydration must be maintained. In the event of serious toxic reactions from overdosage, hemodialysis or peritoneal dialysis may aid in the removal of ciprofloxacin from the body, particularly if renal function is compromised.

DOSAGE AND ADMINISTRATION

The usual adult dosage for patients with urinary tract infections is 250 mg every 12 hours. For patients with complicated infections caused by organisms not highly susceptible, 500 mg may be administered every 12 hours.

Respiratory tract infections, skin and skin structure infections, and bone and joint infections may be treated with 500 mg every 12 hours. For more severe or complicated infections, a dosage of 750 mg may be given every 12 hours.

The recommended dosage for infectious diarrhea is 500 mg every 12 hours.

In patients with renal impairment, some modification of dosage is recommended (SEE DOSAGE AND ADMINISTRATION SECTION IN FULL PRESCRIBING INFORMATION).

HOW SUPPLIED

Cipro[®] (ciprofloxacin HCl/Miles) is available as tablets of 250 mg, 500 mg, and 750 mg in bottles of 50, and in Unit-Dose packages of 100 (SEE FULL PRESCRIBING INFORMATION FOR COMPLETE DESCRIPTION).

References: 1. Barry, A.L., Jones, R.N., Thornberry, C., et al.: Antibacterial activities of ciprofloxacin, norfloxacin, oxolinic acid, cinoxacin, and nalidixic acid. *Antimicrob. Agents Chemother.* 25:633-637, 1984. 2. Guimaraes, M.A., and Noone, P.: The comparative *in-vitro* activity of norfloxacin, ciprofloxacin, enoxacin and nalidixic acid against 423 strains of gram-negative rods and staphylococci isolated from infected hospitalised patients. *J. Antimicrob. Chemother.* 17:63-67, 1986. 3. Van Caekenbergh, D.L., and Pattyn, S.R.: *In vitro* activity of ciprofloxacin compared with those of other new fluorinated piperazinyl-substituted quinolone derivatives. *Antimicrob. Agents Chemother.* 25:518-521, 1984.

For further information, contact the Miles Information Service:
1-800-642-4776. In VA. call collect: 703-620-2799.

COMMITTED TO THERAPEUTIC EFFICIENCY

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