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Treatment of Genitourinary Tract Infections with Fluoroquinolones: Clinical Efficacy in Genital Infections and Adverse Effects

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INTRODUCTION

In the first minireview (66) we considered the activity in vitro, pharmacokinetic properties, and efficacy of fluoroquinolones for the treatment of urinary tract infections and prostatitis. In this minireview we review the role of fluoroquinolones in the treatment of genital infections and summarize the adverse effects of these agents when used for the treatment of genitourinary tract infections.

CLINICAL EFFICACY IN GENITAL TRACT INFECTIONS

Gonorrhea. *Neisseria gonorrhoeae* strains are exquisitely susceptible to the newer fluoroquinolones (66), and potency in vitro has been translated into efficacy in vivo at least with uncomplicated gonococcal infections. In seven randomized studies comparing single doses of fluoroquinolones with single doses of ampicillin, amoxicillin, or penicillin in combination with probenecid or of ceftriaxone or spectinomycin alone for the therapy of uncomplicated gonorrhea (Table 1), eradication rates with the fluoroquinolones were comparable to those with the comparison regimen and ranged from 94 to 100% for both urethritis and cervicitis. In an additional nonrandomized study (15), norfloxacin (two 600-mg doses given 4 h apart) cured all 59 patients with gonococcal urethritis and was comparable to spectinomycin.

Other open or comparative studies with single doses of norfloxacin (800 mg) (9, 44), ciprofloxacin (100 to 500 mg) (30, 48, 56), ofloxacin (200 to 600 mg) (3, 14, 33, 42), enoxacin (200 to 600 mg) (4, 38, 50, 55, 60), or fleroxacin (400 mg) (8) confirmed the efficacy of fluoroquinolones in the treatment of uncomplicated gonorrhea. Treatment failures for gonococcal urethritis or cervicitis have been rare with these agents, except for patients treated with lower doses of enoxacin. In only one instance was failure associated with the isolation of a resistant (64-fold increase in the MIC to 2 μg/ml) strain of *N. gonorrhoeae* identical to the susceptible pretherapy isolate in serovar and lectin groups and auxotype (60).

Single doses of fluoroquinolones were effective in eradicating rectal (173 of 174 cases [99%]) and pharyngeal (37 of 41 cases [90%]) infections in both comparative (Table 1) and open (4, 8, 30, 44, 55, 60) studies. In the comparative studies, rectal and pharyngeal infections were eradicated in 80 to 100% of patients given fluoroquinolones, in contrast to 16 to 33% of patients given ampicillin plus probenecid.

Infections caused by penicillinase-producing *N. gonorrhoeae* strains (3, 4, 9, 11, 15, 27, 30, 38, 39, 46, 48, 50, 55, 56, 60) and strains with chromosomally mediated resistance to penicillin (11) responded similarly to those caused by penicillin-susceptible strains.

Treatment of complicated or disseminated gonococcal infections with fluoroquinolones has been reported uncommonly. A single case of gonococcal salpingitis (31) and two cases of gonococcal septic arthritis (41) all responded to ciprofloxacin given for 7 or 10 days, respectively.

***Chlamydia trachomatis* infections.** None of the currently available antimicrobial agents, including fluoroquinolones, is effective as a single dose in eradicating *C. trachomatis* genital infections, which most often occur as the syndrome of nongonococcal urethritis (NGU) or mucopurulent cervicitis. Studies which used single doses of norfloxacin (44), ciprofloxacin (30, 43, 48), ofloxacin (6, 42), enoxacin (55, 60), or fleroxacin (29) for the treatment of gonorrhea uniformly reported the substantial persistence of *C. trachomatis* or the development of postgonococcal urethritis (3, 9, 38, 46, 56), which is often caused by *C. trachomatis*.

When given for 7 to 10 days, however, some fluoroquinolones had efficacy in eradicating *C. trachomatis* from genital sites (Table 2). Norfloxacin (10) and ciprofloxacin (17) had little or limited efficacy in patients with NGU, and ciprofloxacin was significantly less effective than doxycycline, the current preferred agent, in one comparative study (17). In contrast, ofloxacin or fleroxacin produced high rates of eradication of *C. trachomatis* (Table 2), and ofloxacin was comparable to doxycycline in one study (19).

In seven of eight patients (88%) with acute epididymitis associated with the isolation of *C. trachomatis* from the urethra, ofloxacin (200 mg twice daily for 14 days) (63) eradicated the organism, but the local painful swelling responded slowly, persisting in two men for 12 weeks.

C. trachomatis and *N. gonorrhoeae* may coexist at genital sites in substantial numbers of infected heterosexual patients, and resistance in up to 15% of *N. gonorrhoeae* strains may limit the use of tetracycline in the treatment of such concurrent infections (52). Thus, ofloxacin and fleroxacin offer the prospect of effective single-agent therapy of these commonly coexisting pathogens.

NGU caused by agents other than *C. trachomatis*. Fluoroquinolones have limited activity in vitro against *Ureaplasma urealyticum* and *Mycoplasma hominis* (67), other pathogens that have been implicated in the NGU syndrome. In a substantial number of cases of NGU no pathogen is identified.

U. urealyticum was eradicated from the urethra of 17 of 27 men (63%) with NGU given norfloxacin for 10 days, and in 15 of these men (56%) all symptoms resolved (10). In the only comparative study (17), ciprofloxacin given in high doses (750 mg twice daily) for 7 days eradicated *U. urealyticum* from 9 of 13 patients (69%) and was somewhat more effective than doxycycline, which eradicated the organism from 9 of 20 patients (45%) ($P = 0.12$) (17). Data on the response of *M. hominis* genital infections to fluoroquinolones are not available, but a patient with an *M. hominis*

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TABLE 1. Randomized comparative studies of single doses of quinolones in the treatment of gonorrhea

Reference	Agent	Dose (mg)	No. cured/total no. treated (%) for the following site of infection:			
			Urethra	Cervix	Rectum	Pharynx
27	Norfloxacin	800	26/27 (96)	18/19 (95)	8/8 (100)	2/2 (100)
	Ampicillin + probenecid	3,500 + 1,000	34/36 (94)	20/20 (100)	7/8 (88)	1/3 (33)
39	Norfloxacin	800	142/142 (100)	97/97 (100)	49/49 (100)	
	Spectinomycin	2,000[a]	144/145 (99)	97/98 (98)	43/43 (100)	
43	Ciprofloxacin	250	49/49 (100)		4/5 (80)	1/1 (100)
	Ampicillin + probenecid	3,500 + 1,000	47/51 (92)		1/1 (100)	1/6 (17)
46	Ciprofloxacin	250	31/34 (91)		3/3 (100)	4/5 (80)
	Ampicillin + probenecid	2,000 + 1,000	37/40 (93)		3/3 (100)	1/3 (33)
6	Ofloxacin	400	48/48 (100)	50/50 (100)	13/13 (100)	7/8 (88)
	Amoxicillin + probenecid	3,000 + 1,000	52/54 (96)	43/44 (98)	17/17 (100)	7/8 (88)
11	Enoxacin	400	40/40 (100)			
	Ceftriaxone	250[a]	40/40 (100)			
29	Fleroxacin	400	39/39 (100)			
	Penicillin G + probenecid	2.4[b] + 1,000	39/39 (100)			

[a] Given intramuscularly.
[b] Million units given intramuscularly.

infection of a prosthetic joint responded to ciprofloxacin (51). Patients with NGU and negative cultures for *C. trachomatis* and *U. urealyticum* had similar clinical responses to norfloxacin (10), ciprofloxacin (17), and doxycycline (17) (61 to 69%). Men with chlamydia-culture-negative urethritis (*U. urealyticum* cultures were not done) responded similarly to ofloxacin (58%) (36). Additional comparative studies are needed.

PID. The isolation of *N. gonorrhoeae* or *C. trachomatis* from the cervix of a woman with suspected pelvic inflammatory disease (PID) is highly predictive of a confirmation of clinically diagnosed salpingitis if there is a subsequent laparoscopy (52). Other organisms, such as *M. hominis* and enteric and anaerobic bacteria, also play a role in some cases of PID.

A single case of successful treatment of gonococcal salpingitis with ciprofloxacin was reported (31). High doses of ciprofloxacin (1 g twice daily) given for 5 to 11 days (21) produced clinical cures in 16 of 21 patients (76%) with salpingitis of uncertain etiology (negative cervical cultures for *N. gonorrhoeae* and no chlamydial cultures) diagnosed by laparoscopy or on clinical grounds. The lack of activity of many fluoroquinolones against anaerobes in vitro and chlamydiae in vivo suggests that the current group of these agents will have limited use for many cases of PID if used alone. Other fluoroquinolones, such as tosufloxacin (16) and PD 127,391 (65), with enhanced activity against anaerobes and chlamydiae, however, offer the prospect of a future role for these agents in the therapy of PID.

TABLE 2. Use of fluoroquinolones in the treatment of *C. trachomatis* genital infections

Reference	Agent	Daily dose[a] (mg)	Duration (days)	No. cured/total no. treated (%) for the following site of infection:	
				Urethra	Cervix
10	Norfloxacin	800	10	4/25 (16)	
17	Ciprofloxacin	1,500	7	10/22 (46)[b]	
	Doxycycline	200	7	15/20 (75)[b]	
19	Ofloxacin	400	9	11/11 (100)	9/10 (90)
	Doxycycline	200[c]	10	12/12 (100)	7/7 (100)
5	Ofloxacin	400	5	18/20 (90)	
36	Ofloxacin	400	7	11/11 (100)[d]	17/17 (100)
42	Ofloxacin	400	7	27/27 (100)[e]	32/32 (100)[e]
40	Fleroxacin	800	7	10/10 (100)	
		800[c]	7	5/5 (100)	
		400[c]	7	5/5 (100)	

[a] Divided twice daily unless otherwise indicated.
[b] $P = 0.04$.
[c] Given as a single daily dose.
[d] Of an additional 19 men with NGU and negative *C. trachomatis* cultures, all had resolution of their symptoms after the completion of ofloxacin therapy.
[e] Eight patients had additional follow-up chlamydial antigen tests, all of which were negative.

Chancroid. Fluoroquinolones are potent in vitro against *Haemophilus ducreyi*, the agent of chancroid (66). The genital ulcers and inguinal adenopathy of chancroid responded to therapy with ciprofloxacin (7, 35, 57) and enoxacin (32, 34) (Table 3). In the only double-blind comparative study (35), ciprofloxacin given at 500 mg twice daily for 3 days or as a single dose eradicated *H. ducreyi* (93 to 95%) at rates similar to those for trimethoprim-sulfamethoxazole (TMP-SMX) given for 3 days. Failure of the ulcers to heal by 21 days and the necessity to aspirate buboes occurred only in the groups given TMP-SMX or a single dose of ciprofloxacin. In two other open studies of ciprofloxacin therapy of chancroid with one or two 500-mg doses (7, 57), bacteriologic efficacy was high (98 to 100%) (7), and ulcer healing occurred in 87 to 96% of patients. Six patients with persisting ulcers subsequently responded to ceftriaxone (250 mg given intramuscularly) (7). In a randomized trial of 169 men with chancroid, enoxacin (400 mg every 12 h for 1.5 days) was comparable to a single dose of TMP-SMX in healing (81 to 89%) and sterilization (91 to 93%) of the genital ulcers (34). Buboes responded equivalently to each regimen. A longer course of enoxacin (400 mg twice daily for 7 to 12 days) resulted in healing of chancroidal ulcers in seven of seven men (32). Thus, ciprofloxacin and possibly enoxacin may be useful alternatives for the treatment of chancroid, particularly in areas in which resistance to ampicillin, sulfonamides, and tetracycline is common.

Syphilis. Lesions developing after intradermal or intratesticular inoculation of rabbits with *Treponema pallidum* appeared to be unaffected by high doses of ofloxacin (58, 61). Although no data are available for humans, it seems unlikely that the fluoroquinolones will be active against incubating syphilis.

Bacterial vaginosis. The etiology of bacterial vaginosis remains uncertain, but current understanding suggests a role

TABLE 3. Treatment of chancroid with fluoroquinolones

Reference	Agent	Daily dose[a] (mg)	Duration (days)	No. with the following response/no. of patients treated (%):				
				Bacteriologic response			Clinical response[b]	
				Eradication	Persistence	Recurrence	Ulcer healing	Bubo healing
35	Ciprofloxacin	1,000	3	40/43 (93)	0/43 (0)	3/43 (7)	13/16[c] (81)	9/9 (100)
		500[d]		41/44 (93)	2/44 (5)	1/44 (2)	13/16[e] (81)	10/12 (83)[f]
	TMP-SMX	320/1,600	3	41/45 (91)	2/45 (4)	2/45 (4)	12/17[g] (71)	11/12 (93)[f]
7	Ciprofloxacin	1,000	1	44/44 (100)	0/44 (0)	0/44 (0)	89/92[h] (97)	35/38 (92)[f]
		500[d]		43/43 (100)	0/43 (0)	0/43 (0)	85/88[i] (97)	20/20 (100)
57	Ciprofloxacin	500[d]				—[j]	21/24[k] (88)	—[l]
34	Enoxacin	800	1.5[m]	72/77 (93)	5/77 (6)	0/77 (0)	41/73 (56)	20/23 (87)
	TMP-SMX	320/1,600[d]		67/74 (91)	7/74 (9)	0/74 (0)	31/70 (44)	18/22 (82)
32	Enoxacin	800	7–12	7/7 (100)	0/7 (0)	0/7 (0)	7/7 (100)	3/4 (75)[n]

[a] Divided twice daily unless otherwise indicated.
[b] Cumulative clinical responses as assessed at 28 (34), 21 (35), 20 (57), 14 (7), and 12 (32) days after entry in the respective studies.
[c] One relapse and two reinfections.
[d] Given as a single dose.
[e] Two failures and one relapse.
[f] Unresolved buboes required aspiration for complete healing.
[g] Three failures and two reinfections.
[h] One of 44 ulcers with positive *H. ducreyi* cultures and 2 of 48 ulcers with negative cultures failed to heal. All three failures responded to ceftriaxone (250 mg) given as a single intramuscular dose.
[i] Three of 45 ulcers with negative *H. ducreyi* cultures failed to heal; failures responded to ceftriaxone.
[j] All 25 patients had initial cultures positive for *H. ducreyi*, but follow-up culturing was not done.
[k] Three patients did not complete follow-up, but each had reduced ulcer sizes at follow-up at 4 or 7 days.
[l] All buboes were said to have returned to normal by day 7, but the number of patients with buboes was not given.
[m] Three 400-mg doses.
[n] One bubo persisting at day 7 resolved with an increase in the enoxacin dose to 600 mg twice daily for an additional 5 days.

for bacterial overgrowth in which a variety of bacteria, including *Gardnerella vaginalis*, *Mobiluncus* spp., and anaerobes, replace lactobacilli in the vagina (52). Norfloxacin, ciprofloxacin, and ofloxacin have relatively poor activity against these overgrowing organisms (66).

In a single open study (13) of 22 women with bacterial vaginosis given ciprofloxacin (500 mg twice daily for 7 days), clinical cure occurred in 77% of patients and improvement occurred in an additional 18%. Responses to metronidazole, the current agent of choice for bacterial vaginosis, were similar in other studies (52). Comparative studies with larger numbers of patients are needed.

Miscellaneous genital infections. A single case of *Salmonella hadar* epididymo-orchitis relapse after prolonged courses of ampicillin and TMP-SMX was cured with ciprofloxacin (1 g daily) given for 28 days (37). Ofloxacin (200 mg twice daily) given for 14 days (63) was used to treat seven older patients with urologic infections and with acute epididymitis associated with *Escherichia coli* (six patients) and *Pseudomonas aeruginosa* (one patient) bacteriuria. Although bacteriuria was eradicated in all patients, local painful swelling persisted in six (86%) at the completion of therapy. Five additional patients with acute epididymitis and negative cultures had a similarly limited clinical response. Additional studies are needed.

ADVERSE EFFECTS

Frequency of clinical adverse effects. Because of the high concentrations of many fluoroquinolones achieved in urine, the doses used to treat urinary tract infections have been generally lower than the doses used to treat many infections outside the urinary tract. In addition, single doses have been used in many studies of genital infections. A lower frequency of adverse effects might be expected in such studies than in those with higher doses, more prolonged therapy, or both. This supposition is supported by a comparison of the adverse effects in studies of genitourinary infections (Table 4) with the adverse effects in studies of infections at other sites (24). Excluding studies with norfloxacin, which seldom varied in dose and were limited predominantly to infections of the genitourinary tract, clinical adverse effects occurred in 245 (6.5%) of 3,769 patients with genitourinary tract infections and 238 (10.5%) of 2,269 patients with other infections ($P < 0.001$; χ^2). A similar analysis of ciprofloxacin studies also showed a highly significant difference (data not shown).

In a separate analysis of the data from genitourinary tract infections, clinical adverse effects were reported in 67 (3.3%) of 2,038 patients given single doses of fluoroquinolones and

TABLE 4. Adverse effects of fluoroquinolones in studies of the treatment of genitourinary tract infections

Drug and type of study[a]	No. of patients	No. (%) of the following adverse experience:			
		Total	Gastrointestinal	Central nervous system	Skin or allergic
Norfloxacin					
UTI	2,869	410 (14.3)	108 (3.8)	59 (2.1)	13 (0.5)
STD	676	49 (7.2)	25 (3.7)	24 (3.6)	0 (0.0)
Ciprofloxacin					
UTI	1,040	78 (7.5)	39 (3.8)	28 (2.7)	11 (1.1)
STD	708	37 (5.2)	26 (3.7)	10 (1.4)	1 (0.1)
Ofloxacin					
UTI	290	7 (2.4)	2 (0.7)	2 (0.7)	3 (1.0)
STD	534	15 (2.8)	7 (1.3)	7 (1.3)	1 (0.2)
Enoxacin					
UTI	174	43 (24.7)	22 (12.6)	20 (11.5)	2 (1.2)
STD	636	23 (3.6)	7 (1.1)	2 (0.3)	1 (0.2)
Pefloxacin, UTI	104	27 (26.0)	17 (16.4)	5 (4.8)	5 (4.8)
Fleroxacin					
UTI	29	2 (6.9)	1 (3.4)	1 (3.4)	0 (0.0)
STD	86	12 (14.0)	3 (3.5)	6 (7.0)	3 (3.5)

[a] UTI, Urinary tract infections; STD, sexually transmitted diseases.

TABLE 5. Adverse effects of fluoroquinolones in comparison with other agents or placebo in double-blind studies of the treatment of genitourinary tract infections[a]

Reference	Quinolone	Daily dose[b] (mg)	Duration (days)	No. of patients with adverse effects/no. treated (%)	Comparative agent	Daily dose[b] (mg)	Duration (days)	No. of patients with adverse effects/no. treated (%)
49	NFX	800	168	5/8 (62)[c]	Placebo		84	0/7 (0)[c]
59	NFX	800	7	125/330 (37.9)[d]	TMP-SMX	320/1,600	7	105/216 (48.6)[d,e]
		400	7	96/328 (29.2)[e]				
17[f]	CFX	1,500	7	14/87 (16)	DOXY	200	7	19/83 (23)
35[f]	CFX	1,000	3	2/47 (4.2)	TMP-SMX	320/1,600	3	0/46 (0)
22	CFX	500	10	3/31 (10)[g]	TMP-SMX	320/1,600	10	10/34 (29)[g]
1	CFX	500	7	1/22 (4.6)[h]	TMP-SMX	320/1,600	7	6/23 (26)[h]
43[f]	CFX	250[i]		2/49 (4.1)	AMP + PBN	3,500 + 1,000[i]		3/51 (5.9)
28	OFX	200	7	2/30 (7)	CFX	500	7	2/31 (6)

[a] Unless otherwise indicated, urinary tract infections were studied. NFX, norfloxacin; CFX, ciprofloxacin; DOXY, doxycycline; AMP + PBN, ampicillin plus probenecid; OFX, ofloxacin.
[b] Divided twice daily unless otherwise indicated.
[c] All patients received norfloxacin for 84 days; those remaining in the study were then randomized to receive either norfloxacin or placebo for a subsequent 84 days. Adverse effects occurring during the second 84-day period differed significantly ($P = 0.018$; Fisher exact test).
[d] $P = 0.017$; χ^2.
[e] $P < 0.001$; χ^2.
[f] Sexually transmitted diseases were studied.
[g] $P = 0.04$; Fisher exact test.
[h] $P = 0.054$; Fisher exact test.
[i] Single dose.

in 607 (10.6%) of 5,723 patients given more than one dose ($P < 0.001$; χ^2). Differences in the groups of patients compared in addition to dose and duration of therapy might also have contributed to the different frequencies of adverse effects. In a large double-blind, randomized study adverse effects were significantly fewer with norfloxacin given in a dose of 200 mg twice daily than with norfloxacin given in a dose of 400 mg twice daily (59) (Table 5), and in another double-blind study (26) significantly fewer central nervous system adverse reactions occurred among patients given norfloxacin (400 mg twice daily) for 3 days as compared with 7 days.

Total clinical adverse effects in studies of treatment of genitourinary tract infections with fluoroquinolones ranged from 2.4 to 26% (Table 4). These values can vary depending on the characteristics of the patient population studied and the method of ascertainment. In most double-blind, randomized, comparative studies adverse effects were equivalent (17, 22, 35, 43) or significantly fewer (1, 59) in the fluoroquinolone group in comparison with TMP-SMX or doxycycline (Table 5); ofloxacin and ciprofloxacin also had equivalent side effects in one small study (28). In another double-blind study (49) norfloxacin given for 12 weeks had significantly more side effects than did placebo.

Types of clinical adverse effects. The types of clinical adverse effects (Table 4) were similar to those previously described (23) and were most frequently related to the gastrointestinal tract (nausea, vomiting, abdominal discomfort, diarrhea) or central nervous system (headache, dizziness, sleep disturbance). In two studies, five patients had seizures while receiving enoxacin (18, 25). Rashes were uncommon. Candidal vaginitis following fluoroquinolone therapy was reported in several studies (20, 25, 49, 50, 53).

Laboratory adverse effects. Laboratory abnormalities were reported in 103 (2.2%) of 4,681 patients treated with fluoroquinolones for genitourinary tract infections overall and were usually mild, rarely requiring the cessation of therapy. These abnormalities were most commonly hematologic (transient leukopenia or eosinophilia in 1.2%) or hepatic (transient elevations of transaminases in 0.85%). Elevations in serum creatinine were uncommon (0.11%). Crystalluria has been seen rarely in patients given norfloxacin (45, 54, 62) and ciprofloxacin (2, 12, 47) and has not been associated with elevations in serum creatinine.

Drug-drug interactions. Magnesium- and aluminum-containing antacids or sucralfate given concurrently interfere with the absorption of orally administered fluoroquinolones, but histamine receptor antagonists do not. The elimination of theophylline and caffeine is slowed by enoxacin and ciprofloxacin, but little or no effect occurs with norfloxacin and ofloxacin. Fenbufen, a nonsteroidal anti-inflammatory agent, may potentiate the central nervous system toxicities of enoxacin (24, 64, 67).

Contraindications. Patients with a history of allergic reactions to fluoroquinolones or older agents such as nalidixic acid should not be given fluoroquinolones. Pregnancy should be excluded in women treated with fluoroquinolones because of fetal skeletal abnormalities and wastage seen in animals given high doses. Children whose skeletal growth is incomplete should also not routinely receive fluoroquinolones because of cartilage erosions that developed in the weight-bearing joints of juvenile animals given these agents. Joint toxicities have, however, been rare in the small numbers of children reported to have received nalidixic acid or ciprofloxacin (24, 67).

CONCLUSIONS

For the treatment of uncomplicated cystitis, fluoroquinolones have proved equal in efficacy to TMP-SMX and equal or superior in efficacy to other agents and thus offer alternatives for the therapy of patients unable to receive a drug of choice. For the treatment of uncomplicated pyelonephritis, comparative trials are few but suggest efficacy similar to that of TMP-SMX. For complicated urinary tract infections, fluoroquinolones have also proved equal or superior in efficacy to comparative agents and thus offer oral therapy of infections which otherwise often require parenteral therapy. Limited studies of bacterial prostatitis suggest promise for fluoroquinolones, especially with gram-negative bacillary infections, but more comparative trials are needed.

Single doses of fluoroquinolones are highly effective in the treatment of uncomplicated gonorrhea, including infections

caused by penicillin-resistant strains of *N. gonorrhoeae*. Rectal infections also appear to respond satisfactorily, but some pharyngeal infections do not. Ofloxacin and fleroxacin, in addition, hold promise for the treatment of *C. trachomatis* infections. TMP-SMX and ciprofloxacin produce similar clinical responses in chancroid. Thus, these fluoroquinolones are likely to be effective alternative therapies for these genital infections. Studies comparing fluoroquinolones with ceftriaxone are needed. The roles of fluoroquinolones in the treatment of disseminated gonococcal infections, culture-negative NGU, PID, and bacterial vaginosis remain to be defined. In populations at risk for syphilis, patients given fluoroquinolones should be monitored with serologic tests for syphilis. Pregnancy should be excluded in women treated with fluoroquinolones.

The emergence of bacterial resistance during fluoroquinolone therapy is uncommon but occurs particularly with complicated urinary tract infections and infections with difficult-to-treat pathogens, including *P. aeruginosa*. The extent to which resistance will be a problem is as yet unknown. Monitoring for bacterial resistance and studies of its prevention are needed.

The fluoroquinolones, particularly when used in low or single doses, have generally been tolerated as well as or better than conventional agents used for the treatment of genitourinary tract infections. The central nervous system toxicities of enoxacin require further monitoring. The low risk of nephrotoxicity in patients with complicated urinary tract infections may be especially advantageous.

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