Drugs 1999 May; 57 (5): 743-750
0012-6667/99/0005-0743/$08.00/0

Practical Recommendations for the Drug Treatment of Bacterial Infections of the Male Genital Tract Including Urethritis, Epididymitis and Prostatitis

Marie-Laure Joly-Guillou and *Serge Lasry*

Microbiology Department, Louis Mourier University Hospital, Colombes, France

Contents

Abstract

Bacterial infections of the male genital tract in young men (<35 years old) are primarily caused by sexually transmissible bacteria like *Chlamydia trachomatis*, *Neisseria gonorrhoeae* but also *Mycoplasma* or *Haemophilus* spp. In men aged over 35 years, Enterobacteriaceae are more frequently involved in urethritis, epididymitis and prostatitis. The traditional treatments suggested like tetracyclines or erythromycin are less effective since bacterial resistance is increasingly frequent, particularly in *N. gonorrhoeae*. Moreover, patient compliance with these drug treatments are frequently not well observed. New therapies including short term therapy with fluoroquinolones or azalides (e.g. azithromycin) are very effective and easy to use and thus eliminate any problem of compliance. However, we have to be vigilant for the emergence of resistant strains to these agents.

Infections of the male genital tract are prevalent among young, sexually active persons. The profile of sexually transmitted diseases (STDs) has changed during the last 10 years because of a rapid increase of nongonococcal urethritis (NGU).[1] Gonorrhoea and NGU are endemic at high levels in most regions of the world despite effective methods of diagnosis and treatment. *Chlamydia trachomatis* is the most common pathogen involved in urethritis and epididymitis in young males and is widely spread in most regions of the world.

In spite of the importance which it represents in male urethritis in the world, there has been little epidemiological investigation. The aim of this article is to summarise the most recent elements in the treatment of male genital infections, focusing on urethritis and complications. The general recommendations concerning the treatment of infections

of the male genital tract thus relate to prevalence (*C. trachomatis*), modification of the antibiotic susceptibility profile (*Neisseria gonorrhoeae*) or emergence due to new diagnostic tools (*Mycoplasma genitalium*).

1. Current Recommendations

The division of Sexually Transmitted Disease of the US Centers for Disease Control proposed guidelines for the treatment of STDs in 1993 (updated 1998).[2] The treatment presently recommended for NGU is: doxycycline 100mg orally twice a day for 7 days; or erythromycin (base) 500mg 4 times daily for 7 days as an alternative regimen. For uncomplicated genital tract infections with *C. trachomatis*, doxycycline 100mg orally twice a day for 7 days or a single dose of azithromycin 1g orally are proposed. Ofloxacin 300mg twice daily or erythromycin (base) 500mg 4 times daily for a 7-day course are alternative regimens.

Treatments recommended for uncomplicated gonococcal infections are: a single dose of intramuscular (IM) ceftriaxone 125mg, or cefixime 400mg orally, ciprofloxacin 500mg orally or ofloxacin 400mg orally. Because of frequent coinfection with *C. trachomatis*, a regimen effective against *C. trachomatis* should be given.

2. Pathogenesis and Aetiology

Urethritis is an infection or inflammation of the anterior urethra characterised by the discharge of mucoid or purulent material and by burning during urination, most commonly caused by *C. trachomatis* or *N. gonorrhoeae* in men younger than 35 years old. Asymptomatic infections are common. Complications of chlamydial urethritis include epididymitis. Complications of gonococcal urethritis include disseminated infection, urethra stricture and epididymitis, and may occur at any age.

If diagnostic tools are unavailable, diagnosis is made according to symptoms, and treatment initiated accordingly. If diagnostic tools are available, urethritis has to be confirmed microscopically with the identification of more than 5 polymorphonuclear cells per high powered field together with the identification of the causal pathogen. The goals of early diagnosis and identification are to interrupt the chain of transmission in the community and to prevent sequelae.[3]

Culture on agar plate and identification of the pathogen remain the reference methods for the laboratory diagnostic of classical bacteria such as *N. gonorrhoeae*, *Mycoplasma hominis*, *Ureaplasma urealyticum*, *Haemophilus* spp. or Enterobacteriaceae. Cell culture for *C. trachomatis* has been the traditional method for laboratory diagnosis, but has been replaced by antigen detection methods such as direct fluorescence assay and enzyme immunoassay methods. These tests lack sensitivity as screening assays, especially for asymptomatic men. Nucleic acid amplification tests based on polymerase chain reaction (PCR) or ligase chain reaction and transcription mediated amplification show the best specificity (>99%) and sensitivity as a screening method.[3] Moreover, these tests are done on noninvasive specimens such as urine.

N. gonorrhoeae has been by far the most common organism responsible for urethritis, but its prevalence has declined and represents about 20% of the bacteria isolated in urethritis in recent studies.[4,5] *C. trachomatis* is today the most common agent responsible for urethritis and a major public health problem. Its prevalence in the US was 52.1 per 100 000 in 1995,[3] and is involved now in 25 to 40% of cases of bacterial urethritis.[4,5] The increasing role of *C. trachomatis* observed these last years as a cause of urethritis could be related to the routinely developing detection methods of this pathogen.

Mycoplasma infections of the male genital tract are mainly associated with other organisms such as *C. trachomatis* or *N. gonorrhoeae*. Trichomoniasis has been suggested to increase colonisation by *M. hominis*. Genital candidiasis is not common in men. There is an evidence for an aetiological role of *U. urealyticum* in acute NGU and particularly chronic NGU in men.

There is some support for the role of *M. genitalium* in NGU but its prevalence has not been well

studied. Jensen et al.[6] reported that *M. genitalium* could be present in 17% of urethral swabs, significantly present in those of patients with urethritis and more often than not in *C. trachomatis* negative NGU. Numerous laboratories do not look for this species. Indeed, its diagnosis requires a PCR assay and there are no commercial kits for PCR. *M. genitalium* has been involved in urethritis, generally in association with other organisms such as *N. gonorrhoeae*. A study of 45 male patients with gonococcal urethritis showed that *M. genitalium* was present in 4.4% of these patients, while *C. trachomatis* was present in 26.7%.[7] Two studies report the significant frequency of occurrence of *M. pneumoniae*, detected by PCR assay, in the urogenital tract of men.[8]

The role of *Haemophilus* spp. in urethritis varies in the different studies of the literature. A French study carried out in 1994-1995 in 7 laboratories showed that *Haemophilus* (*influenzae, parainfluenzae, aphrophilus*) spp. represented 20% of bacteria isolated in male urethritis and ranked immediately after *N. gonorrhoeae*, *Chlamydia* and *Mycoplasma*.[5] In 2 other studies this bacterium was responsible for 1.2 and 9.3%, respectively, of urethritis in men.[9,10] It was suggested that *Haemophilus* spp. could be responsible for infection when isolated from urethra as the sole pathogen.

In men over 35 years of age, Enterobacteriaceae, particularly *Escherichia coli*, are responsible for epididymitis or prostatitis in more than 80% of cases. The responsibility of *C. trachomatis* or mycoplasma is dubious in prostatitis.

3. Activity of Antibiotics Against Bacterial Strains Isolated in the Male Genital Tract

Selection of treatment regimen for bacterial infections requires consideration of the site of infection, pharmacokinetic parameters and resistance of the organisms to antimicrobials. A French *in vitro* multicentre study[5] carried out in 1994-1995 on 189 strains isolated from patients with urethritis classified antibiotics according to their individual activity to identify those suitable for empiric therapy. An activity score was defined and calculated: percentage of susceptibility to each antibiotic weighted by the frequencies of each isolate in urethritis.

This study pointed out that the best empiric activity scores in urethritis were, in decreasing order, doxycycline (90.4), ofloxacin (88.1) and erythromycin (50.2). About 14% of *N. gonorrhoeae* isolates were resistant to amoxicillin and 28% to doxycycline. Third generation cephalosporins (ceftriaxone) were highly active against *N. gonorrhoeae*. No ceftriaxone-resistant strains have been reported in this study. Recently one ceftriaxone-resistant strain has been observed.[11] Van de Laar[12] noted that penicillin resistant *N. gonorrhoeae* were less susceptible to ceftriaxone (increased MICs) than susceptible penicillin strains. This regimen also may abort incubating syphilis, a concern when *N. gonorrhoeae* treatment is not accompanied by a 7-day course of doxycycline or erythromycin for the presumptive treatment of chlamydial infection.

The combination of sulbactam 500mg and ampicillin 1g in a single dose plus probenecid 1g has been proposed for the treatment of gonorrhoea.[13] Cure rates were obtained in 97.2% of men who received treatment and for 98.4% of patients with non–penicillinase-producing *N. gonorrhoeae*. This regimen was equally effective against gonococcal urethritis as amoxicillin-clavulanate, but had little effect on frequent concomitant chlamydial infection. The practice of combining amoxicillin with probenecid is not recommended because of the increasing rate of penicillinase-producing strains of *N. gonorrhoeae*.

Some of the newer fluoroquinolones may be suitable agents for the treatment of *C. trachomatis* infections and nongonococcal infections. Some studies have shown that these drugs achieve a cure rate of 85 to 95% for urethritis caused by *C. trachomatis*. Fleroxacin and ofloxacin were more effective than ciprofloxacin and were comparable to doxycycline.[14-17] *In vitro* susceptibility differences were reported for minimum inhibitory concentration (MIC) values of ofloxacin against

C. trachomatis. They ranged from 0.0012 mg/L to 1 mg/L.[5,17] MIC_{90} values of ofloxacin, fleroxacin and lomefloxacin reported in several studies ranged between 1 and 4 mg/L. Sparfloxacin and trovafloxacin were the most active fluoroquinolones, with an MIC_{90} of 0.06 mg/L. The susceptibility differences observed between the various studies were probably related to the lack of standardised methods for susceptibility testing rather than a possible serotype susceptibility difference.

Tetracyclines are highly effective against *C. trachomatis*, nevertheless, a few resistant strains have been described.[14,18] Against *N. gonorrhoeae*, ofloxacin and fleroxacin were efficacious with a good *in vitro* bactericidal effect (MIC values of 0.003 to 0.06 mg/L). Strains with decreased susceptibility to some fluoroquinolones were first described in Asia and have been reported in North America since 1991.[19,20] The prevalence of gonococci with decreased susceptibility to ciprofloxacin increased in the US from 2% in 1991 to 16% in 1994.[21]

Treatment failure after quinolone therapy in gonococcal urethritis was first described in 1995.[20] The development of resistance after a single dose quinolone treatment (rufloxacin 400mg) for gonococcal urethritis has been described recently during a phase III clinical trial which included 7 patients. Resistance also occurred to tetracycline and to other members of the quinolone family by means of Gyr-A single amino acid substitution.[22,23]

The susceptibility of *M. hominis* and *U. urealyticum* to the newer quinolones is similar to the susceptibility of Gram-positive organisms (staphylococci or streptococci). In several *in vitro* studies, fluoroquinolones seemed to be more active against *M. hominis* (range for ofloxacin: 0.12 to 1 mg/L) than *U. urealyticum* (0.5 to 8 mg/L).[5,24] *In vivo* studies have shown that fluoroquinolones were efficacious in eradicating *M. hominis* but failed to eradicate *U. urealyticum*.[25] Tetracyclines and macrolides exhibited a good activity against about 60 to 80% of *N. gonorrhoeae* and mycoplasmas.

Tetracyclines are effective as treatment for genital chlamydial infections, including those affecting the accessory glands. A few isolates have demonstrated heterotypic resistance to tetracycline and erythromycin. This observed resistance is a rare characteristic of this organism which may be a factor in some treatment failures.[14]

Macrolides such as erythromycin, clarithromycin or azithromycin, exhibit good activity against *C. trachomatis* and are clinically effective for the treatment of chlamydial urethritis. Azithromycin is different from erythromycin and clarithromycin in terms of pharmacokinetic and pharmacodynamic properties. This drug concentrates extensively within cells and has a tissue half-life of approximately 60 hours. Azithromycin concentrations in human tissues after a single 500mg dose may exceed the MIC of *C. trachomatis* 10-fold for as long as 5 days. A study performed on 200 men with confirmed NGU showed that there were no significant differences in efficacy between a standard duration therapy course of tetracycline (7 days)

Table I. Treatment of urethritis: syndromic diagnosis

Indications	Suspected pathogens	Treatment	Adverse effects
Urethritis with purulent material	*Neisseria gonorrhoeae* (20-50%) + associated *Chlamydia* (30%)	Ceftriaxone 125 **or** 250mg single dose IM; or cefixime 400mg SD PO; or ofloxacin 400mg SD PO; or ciprofloxacin 500mg SD PO + doxycyclin 100mg bid × 7 days; or azithromycin 1g SD PO	β-Lactams: allergy Fluoroquinolones: tendinitis, photosensitivity, G6PD deficit Doxycycline: photosensitivity
Urethritis without purulent material	*C. trachomatis* (40%), *Mycoplasma* (*Ureaplasma urealyticum*, *M. genitalium*), others: *Haemophilus influenzae*	Doxycycline 100mg bid × 7 days	Doxycycline: photosensitivity

bid = twice daily; **G6PD** = glucose-6-phosphate-dehydrogenase; **IM** = intramuscular; **SD PO** = single oral dose.

Table II. Treatment of urethritis: laboratory confirmed infection

Indications	Pathogens	Treatment	Adverse effects
Urethritis with purulent material *(>5 polymorphonuclear cells per high power field)*			
Direct examination: Gram-negative diplococci; positive culture on agar plate/PCR	*Neisseria gonorrhoeae* (20-50%) + associate *Chlamydia trachomatis* (30%)	Ceftriaxone 125 **or** 250mg SD IM; or cefixime 400mg SD PO; or ofloxacin 400mg SD PO; or ciprofloxacin 500mg SD PO + doxycycline 100mg bid × 7 days; or azithromycin 1g SD PO	β-Lactams: allergy Fluoroquinolones: tendinitis, photosensitivity, G6PD deficit Doxycycline: photosensitivity
Direct examination and culture: Gram-negative bacilli, positive culture on agar plate	*Haemophilus* spp.	Ceftriaxone 125/250mg SD IM; or cefixime 400mg SD PO; or ofloxacin 400mg SD PO; or ciprofloxacin 500mg SD PO	β-lactams: allergy Fluoroquinolones: tendinitis, photosensitivity, G6PD deficit
Urethritis without purulent material *(≤ 5 polymorphonuclear cells per high power field)*			
Chlamydial urethritis with microbiological documentation	*C. trachomatis*	Azithromycin 1g SD PO; or doxycycline 100mg bid × 7 days; or ofloxacin 400mg SD PO; or erythromycine 500mg qid PO × 7 days	Macrolides: allergy, photosensitivity
Mycoplasma urethritis with microbiological documentation: positive culture or PCR (*Mycoplasma genitalium*)	*Ureaplasma urealyticum*, *M. hominis*, *M. genitalium*	Doxycycline 100mg bid × 7 days	Photosensitivity

bid = twice daily; **G6PD** = glucose-6-phosphate-dehydrogenase; **IM** = intramuscular; **PCR** = polymerase chain reaction; **PO** = oral; **qid** = 4 times daily; **SD** = single dose.

and a single 1g oral dose of azithromycin.[26] Numerous studies have shown the comparable efficacy of azithromycin versus doxycyline in the treatment of uncomplicated male genital chlamydial infections, showing that if a single oral dose of antibiotic would ensure adequate therapy, it would also eliminate the compliance problem.[18,26-31]

Azithromycin is now licensed for the treatment of uncomplicated genital chlamydial infection, but has not, as yet, a product license for the treatment of NGU in France and other world markets.

4. Practical Recommendations

Tables I, II and III give the details for recommendations and doses in the treatment of infections the male genital tract.

4.1 When to Treat Urethritis

Direct examination is a sensitive and specific test for the diagnosis of *N. gonorrhoeae* from urethral samples. Treatment is administered after the result of the direct examination when possible. If there is no possibility of microbiological documentation, *N. gonorrhoeae* should be taken into account in the treatment of purulent urethritis. Then, the first-line therapy could be tailored to local sensitivity pattern.

In countries where fluoroquinolones are used as an empiric therapy, the susceptibility of the quinolones decreases. Thus, the first recommendation for the treatment of gonococcal urethritis should be ceftriaxone 125 or 250mg in a single dose, or cefixime 400mg orally. In these countries, fluoroquinolones could be recommended as second line therapy (ciprofloxacin 500mg or ofloxacin 400mg orally as a single dose). In all cases, treatment for associate chlamydial infection should be administered.

Tetracyclines are a highly effective treatment for genital chlamydial infections. Since azithromycin and doxycycline have comparable cure rates and both treatments are well tolerated, azithromycin 1g in a single dose appears to be a good recommendation for the treatment of a documented chlamydial infection.

In urethritis without purulent material and without microbiological documentation, the use of oral

Table III. Treatment of epididymitis and prostatitis

Indications	Pathogens	Therapy
Epididymitis		
Men <35 years old	*Neisseria gonorrhoeae*, *Chlamydia trachomatis*, Enterobacteriaceae (in homosexual men)	Ceftriaxone 500mg SD IM + doxycycline 100mg bid PO × 10-21 days; or ofloxacin 200mg bid PO × 10-21 days
Men >35 years old	Enterobacteriaceae	Ofloxacin 200mg bid PO × 10-21 days; or ciprofloxacin 500mg bid PO × 10-21 days; or ceftriaxone: 1g od IV/IM × 10-21 days; or trimethoprim-sulfamethoxazole 960mg bid × 10-21 days
Prostatitis		
Uncomplicated prostatitis	Enterobacteriaceae (*Escherichia coli*), *N. gonorrhoeae*	Ofloxacin 200mg bid PO × 4-6wk; or ciprofloxacin 500mg bid PO × 4-6wk; or trimethoprim-sulfamethoxazole 960mg bid × 4-6wk
Complicated prostatitis	As above	Ofloxacin or ciprofloxacin or ceftriaxone 1-2g od IV/IM; or cefotaxime 1-2g tid IV/IM until apyrexia + aminoglycoside until apyrexia, followed by fluoroquinolone or trimethoprim-sulfamethoxazole PO × 4-6wk
Chronic prostatitis	As above	Fluoroquinolone or trimethoprim-sulfamethoxazole PO × 3 months

bid = twice daily; **G6PD** = glucose-6-phosphate-dehydrogenase; **IM** = intramuscular; **IV** = intravenous; **od** = once daily; **PO** = oral; **SD** = single dose; **tid** = 3 times daily; **wk** = weeks.

doxycycline 100mg twice daily for 7 days make it possible to treat *C. trachomatis* and mycoplasmas.

In documented NGU, the treatment will be guided by the pathogen isolated:

- *C. trachomatis*: azithromycin 1g as a single dose or alternatively doxycycline 100mg twice daily for 7 days or ofloxacin 200mg twice daily for 7 days or erythromycin 500mg 4 times daily for 7 days
- *Mycoplasma* spp.: doxycycline 100mg twice daily for 7 days.

Patients should be instructed to return for evaluation after treatment. Treatment effectiveness is assessed clinically. Nevertheless, an endourethral swab to check for a microbiological test of cure should be performed routinely for gonococcal infection apart from countries where syndromic management is practised. In all cases, a control test will be carried out in case of clinical failure or recurrence. The regular increase of antibiotic-resistant *N. gonorrhoeae* strains justifies this attitude which is more controversial for chlamydial infections where diagnosis identifies both viable and nonviable organisms. Patients with persistent or recurrent urethritis should be retreated if they failed to comply with their treatment regimen or if they were re-exposed to an untreated sex partner.

The success of a public health control programme is based on the interruption of the chain of transmission in the community. Sex partners should be evaluated and treated. Thus, patients should be instructed to refer sex partners whose contact was within 30 days of onset of symptoms or less than 60 days if asymptomatic. Testing both *N. gonorrhoeae* and *C. trachomatis* is encouraged.

4.2 Prostatitis and Epididymitis

Prostatitis and epididymitis are the most frequent complications of male urethritis in men aged younger than 35 years. Because of the risk of chronic infections or reduction of male fertility, prompt antibiotic treatment should be administered.

In epididymitis in men aged under 35 years, treatment of choice is ceftriaxone 500mg in a single dose plus doxycycline 100mg twice daily for 10 to 21 days; or ofloxacin 200 to 300mg twice daily for 10 to 21 days, particularly if enteric infection is suspected.

Because of limited data on the use of single dose therapy of azithromycin in complicated infections of the male genital tract, studies are needed to determine if these regimens achieve clinical and microbiological cure while preserving fertility and preventing further tissue damage.

In epididymitis in men over 35 years old and in prostatitis, Enterobacteriaceae are predominant pathogens. The combination of amoxicillin plus a β-lactamase inhibitor is not advised because of the frequency of high level penicillinase-producing *E. coli*. Fluoroquinolones like ciprofloxacin 500mg twice daily or ofloxacin 200mg twice daily have good activity against these bacteria and good tissue penetration. These drugs are proposed in the treatment of uncomplicated prostatitis (for 4 to 6 weeks) or epididymitis (10 to 21 days).

Alternative treatments could be intravenous (IV) or IM ceftriaxone 1 g/day, or trimethoprim-sulfamethoxazole 960mg twice daily for 10 to 21 days in epididymitis and 4 to 6 weeks in uncomplicated, acute prostatitis.

In complicated, acute prostatitis we propose the following treatment:

- ofloxacin or ciprofloxacin IV until apyrexia followed by a switch to oral therapy for a further 4 to 6 weeks; or
- cefotaxime 2g or ceftriaxone 1g IM/IV in combination with aminoglycosides until apyrexia followed by a switch to oral quinolone therapy for a further 4 to 6 weeks; or
- trimethoprim-sulfamethoxazole 960mg twice daily (orally) for 4 to 6 weeks.

In chronic prostatitis, trimethoprim-sulfamethoxazole or fluoroquinolones are recommended for treatment for 3 months.

Although the epidemiology of HIV is related more closely to genital ulceration, HIV investigation is recommended in the presence of urethritis or epididymitis. Moreover, urethritis may facilitate HIV transmission. Patients who have urethritis and are also infected with HIV should receive the same treatment as those who are HIV negative.[2]

5. Conclusion

In summary, new approaches to the treatment of urethritis and other male genital infections include classical therapy with tetracyclines and β-lactams, but now also azalides and fluoroquinolones. The aim of the diversification of the compounds is to offer the best bactericidal activity, to limit recurrence and emergence of resistance. Azithromycin offers an important advance in the management of sexually transmitted diseases by elimination of compliance problems, particularly in the control of chlamydial infection. Whereas, the cost of treatment could be prohibitive for resource limited settings, selective use in persons with a history of non-compliance may prove cost effective.

References

1. Meria P, Janier M, Desgrandchamps F, et al. Sexually transmitted disease in men. Prog Urol 1996; 6 (3): 447-54
2. Centers for Disease Control. 1998 Sexually transmitted diseases treatment guidelines. MMWR Morb Mortal Wkly Rep 1997; RR1: 47
3. Centers for Disease Control. *Chlamydia trachomatis* genital infections in United States: 1995. MMWR Morb Mortal Wkly Rep 1997; 46 (9): 193-7
4. Janier M, Lassau F, Casin I, et al. Male urethritis with and without discharge: a clinical and microbiological study. Sex Transm Dis 1995; 22 (4): 244-52
5. Joly-Guillou ML, Judlin P, Lefévre JC, et al. Bactéries isolées en 1994-1995 au cours des infections gynécologiques hautes et des urethrites masculines: distribution et sensibilité aux antibiotiques. Presse Medicale 1996; 25 (8): 342-8
6. Jensen JS, Orsum R, Dohn B, et al. *Mycoplasma genitalium*: a cause of male urethritis? Genitourin Med 1993; 69 (4): 265-9
7. Uno M, Deguchi T, Komeda H, et al. Prevalence of *Mycoplasma genitalium* in men with gonococcal urethritis. Int J STD AIDS 1996; 7 (6): 443-4
8. Sharma S, Brousseau R, Kasatiya S. Detection and confirmation of *Mycoplasma pneumoniae* in urogenital specimens by PCR. J Clin Microbiol 1998; 36 (1): 277-80
9. Lefevre JC, Lepargneur JP, Bauriaud R, et al. Clinical and microbiologic features of urethritis in men in Toulouse, France. Sex Trans Dis 1991; 18 (2): 76-9
10. Vasquez F, Andres MT, Palacio V, et al. Isolation of *Haemophilus influenzae* and *Haemophilus parainfluenzae* in genitourinary infections: a 4 years review. Enferm Infecc Microbiol Clin 1996; 14 (3): 181-5
11. Bhuiyan B, Rahman M, Miah MRA, et al. Antimicrobial susceptibilities and plamid contents of *Neisseria gonorrhoeae* isolates from commercial sex workers in Dhaka, Bangladesh: emergence of high-level resistance to ciprofloxacin. J Clin Microbiol 1999; 37 (4): 1130-6
12. Van de Laar MJ, Van Duynhoven YT, Dessens M, et al. Surveillance of antibiotic resistance in *Neisseria gonorrhoeae* in the Netherlands 1977-1995. Genitourin Med 1997; 73: 510-7
13. Ngeow YF, Ramachandran S, Cheong YM. Treatment of gonorrhea with sulbactam/ampicillin. Sex Transm Dis 1991; 18 (3): 192-4
14. Jones RB, Van der Pol B, Jonhson RB. Susceptibility of *Chlamydia trachomatis* to trovafloxacin. J Antimicrob Chemother 1997; 39 (B Suppl.): 63-5
15. Moi H, Morel P, Gianotti B, et al. Comparative efficacy and safety of single oral doses of sparfloxacin versus ciprо-

floxacin in the treatment of acute gonococcal urethritis in men. J Antimicrob Chemother 1996; 37 (A Suppl.): 115-22
16. Philips I, Dimian C, Barlow D, et al. A comparative study of two different regimens of sparfloxacin versus doxycycline in the treatment of non-gonococcal urethritis in men. J Antimicrob Chemother 1996; 37 (A Suppl.): 123-34
17. Ronald AR, Peeling RW. Chlamydial infections and quinolones. Eur J Clin Microbiol Infect Dis 1991; 10 (4): 351-4
18. Jones RB. New treatments for *Chlamydia trachomatis*. Am J Obstet Gynecol 1991; 164 (6): 1789-93
19. Bogaerts J, Tello WM, Akingeneye J, et al. Effectiveness of norfloxacin and ofloxacin for treatment of gonorrhoeae and decrease susceptibility to quinolones over time in Rwanda. Genitourin Med 1993; 69 (3): 196-200
20. Centers for Disease Control. Fluoroquinolones resistance in *Neisseria gonorrhoeae*: Colorado, Washington 1995. MMWR Morb Mortal Wkly Rep 1995; 44: 761-4
21. Gordon SM, Carlyn CJ, Doyle LJ, et al. The emergence of *Neisseria gonorrhoeae* with decreased susceptibility to ciprofloxacin in Cleveland, Ohio: epidemiology and risk factors. Ann Intern Med 1996; 125: 465-70
22. Deguchi T, Saito I, Tanaka M, et al. Fluoroquinolone treatment failure in gonorrhoea: emergence of a *Neisseria gonorrhoeae* strain with enhanced resistance to fluoroquinolones. Sex Transm Dis 1997; 24 (5): 247-50
23. Vila J, Olmos L, Ballesteros J, et al. Development of *in-vivo* resistance after quinolone treatment of gonococcal urethritis. J Antimicrob Chemother 1997; 39 (6): 841
24. Kenny GE, Hooton TM, Roberts MC, et al. Susceptibilities of genital mycoplasmas to the newer quinolones as determined by the agar dilution method. Antimicrob Agent Chemother 1989; 33 (1): 103-7
25. Nilsson S, Johannisson G, Lycke E. Treatment of complicated infections of the male genital tract, with emphasis on *Chlamydia trachomatis*. Scand J Infect Dis Suppl 1982; 32: 173-6
26. Carlin EM, Barton SE. Azithromycin as the first-line treatment of non-gonococcal urethritis (NGU): a study of follow-up rates, contact attendance and patients treatment preference. Int J STD AIDS 1996; 7 (3): 185-9
27. Lauharanta J, Saarinen K, Mustonen MT, et al. Single-dose oral azithromycin versus seven-day doxycycline in the treatment of non-gonococcal urethritis in males. J Antimicrob Chemother 1993; 31 (E Suppl.): 177-83
28. Lister PJ, Balechandran T, Ridgway GL, et al. Comparison of azithromycin and doxycycline in the treatment of non-gonococcal urethritis in men. J Antimicrob Chemother 1993; 31 (E Suppl.): 185-92
29. Thorpe EM, Stamm WE, Hook EW, et al. Chlamydial cervitis and urethritis: single dose treatment compared with doxycycline for seven days in community based practices. Genitourin Med 1996; 72 (2): 93-7
30. Waugh MA. Azithromycin in sexually transmitted disease: an overview. Int J STD AIDS 1991; 49 (2): 246-7
31. Wendel TD. 1-day azithromycin was as effective as 7-day doxycycline for non gonococcal urethritis syndrome in men. ACP J Club 1996; 125 (3): 82

Correspondence and reprints: Dr *Marie-Laure Joly-Guillou*, Microbiology Department, Louis Mourier University Hospital, 178 rue des Renouillers, 192701 Colombes, France.
E-mail: marie-laure.joly-guillou@lmr.ap-hop-paris.fr