

Gonorrhoea

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John Moran

ABSTRACT

INTRODUCTION: In the UK, diagnoses rates for gonorrhoea in 2005 were 196/100,000 for 20–24 year old men, and 133/100,000 for 16–19 year old women. Co-infection with *Chlamydia trachomatis* is reported in 10–40% of people with gonorrhoea in the USA and UK. **METHODS AND OUTCOMES:** We conducted a systematic review and aimed to answer the following clinical questions: What are the effects of treatments for uncomplicated infections in men and non-pregnant women; and in pregnant women? What are the effects of treatments for disseminated gonococcal infection? What are the effects of dual treatment for gonorrhoea and chlamydia infection? We searched: Medline, Embase, The Cochrane Library and other important databases up to July 2006 (BMJ Clinical Evidence reviews are updated periodically, please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). **RESULTS:** We found 21 systematic reviews, RCTs, or observational studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions. **CONCLUSIONS:** In this systematic review we present information relating to the effectiveness and safety of the following interventions: antibiotic regimens (dual treatment, multiple dose, single dose).

QUESTIONS	
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INTERVENTIONS	
TREATMENT IN MEN AND NON-PREGNANT WOMEN	GONORRHOEA AND CHLAMYDIA
<p> Beneficial</p> <p>Single dose antibiotic regimens* 3</p>	<p> Unknown effectiveness</p> <p>Dual antibiotic treatment 5</p>
TREATMENT IN PREGNANCY	Footnote
<p> Beneficial</p> <p>Single dose antibiotic regimens 4</p>	<p>*Based on results in individual arms of RCTs and observational studies.</p> <p>†Based on non-RCT evidence and consensus.</p>
DISSEMINATED GONORRHOEA	
<p> Likely to be beneficial</p> <p>Multidose antibiotic regimens† 4</p>	

Key points

- Gonorrhoea is caused by infection with *Neisseria gonorrhoeae*. In men, uncomplicated urethritis is the most common manifestation while in women only about half of cases produce symptoms (such as vaginal discharge and dyspareunia).
 - In the UK, diagnoses rates for gonorrhoea were 196/100 000 for 20–24 year old men and 133/100 000 for 16–19 year old women in 2005.
 - Co-infection with *Chlamydia trachomatis* is reported in 10–40% of people with gonorrhoea in the USA and UK.
- **Single dose antibiotic regimens** have achieved cure rates of 95% or higher in men and non-pregnant women with urogenital or rectal gonorrhoea. However, resistance to many widely available antibiotics (e.g. penicillins, tetracyclines, fluoroquinolones) continues to spread, making it necessary to consider local *N gonorrhoeae* susceptibility patterns when choosing a treatment regimen.
 - Single dose antibiotics** are also effective for curing gonorrhoea in pregnant women.
- In people with disseminated gonococcal infection, there is consensus that **multidose regimens** using injectable cephalosporins or fluoroquinolones (when the infecting organism is known to be susceptible) are the most effective treatments, although evidence supporting this is somewhat sparse.
- We did not find any sufficient evidence to judge the best treatment for people with both gonorrhoea and chlamydia, although theory, expert opinion, and clinical experience suggest a **combination of antimicrobials** active against both *N gonorrhoeae* and *C trachomatis* are effective.

DEFINITION Gonorrhoea is caused by infection with *Neisseria gonorrhoeae*. In men, uncomplicated urethritis is the most common manifestation, with dysuria and urethral discharge. Less typically, signs and symptoms are mild and indistinguishable from those of chlamydial urethritis. In women, the most

common site of infection is the uterine cervix where infection results in symptoms such as vaginal discharge, lower abdominal discomfort, and dyspareunia in only half of cases. People with gonorrhoea may also have co-infection with *C trachomatis*.

INCIDENCE/ PREVALENCE Between 1975 and 1997, the reported incidence of gonorrhoea in the USA fell by 74%, reaching a low point of 120/100 000 people. After a small increase in 1998, the rate of new gonorrhoeal infection declined steadily to an incidence of 112/100 000 people in 2004, then increased slightly to 116/100 000 in 2005.^[1] Rates are highest in younger people. In 2005, incidence was highest in women aged 15–19 years (625/100 000) and men aged 20–24 years (437/100 000). In UK genitourinary medicine clinics, diagnoses figures for 2002 were 269/100 000 for 20–24 year old men, and 195/100 000 for 16–19 year old women.^[2] By 2005, diagnoses of gonorrhoea had fallen to 196/100 000 for 20–24 year old men and 133/100 000 for 16–19 year old women.^[2] Recent studies in the USA and UK found concurrent *Chlamydia trachomatis* in 7–14% of homosexual men with gonorrhoea, in 20–30% of heterosexual men, and in 40–50% of women.^{[3] [4] [5]} Overall, co-infection with *C trachomatis* is reported in 10–40% of people with gonorrhoea.^{[3] [4] [5] [6] [7]}

AETIOLOGY/ RISK FACTORS Most gonococcal infections result from penile–vaginal, penile–rectal, or penile–pharyngeal contact. An important minority of infections are transmitted from mother to child during birth, which can cause a sight threatening purulent conjunctivitis (ophthalmia neonatorum). Less common are ocular infections in older children and adults as a result of sexual exposure, poor hygiene, or the medicinal use of urine.

PROGNOSIS The natural history of untreated gonococcal infection is spontaneous resolution and microbiological clearance after weeks or months of unpleasant symptoms.^[8] During this time, there is a substantial likelihood of transmission to others and of complications developing in the infected individual.^[8] In many women, the lack of readily discernible signs or symptoms of cervicitis means that infections go unrecognised and untreated. An unknown proportion of untreated infections causes local complications, including lymphangitis, periurethral abscess, Bartholinitis, and urethral stricture; epididymitis in men; and in women involvement of the uterus, fallopian tubes, or ovaries causing pelvic inflammatory disease (see pelvic inflammatory disease). One review found *N gonorrhoeae* was cultured from 8–32% of women with acute pelvic inflammatory disease in 11 European studies and from 27–80% of women in eight US studies.^[9] The proportion of *N gonorrhoeae* infections in women that lead to pelvic inflammatory disease has not been well studied. However, one study of 26 women exposed to men with gonorrhoea found that 19 women were culture positive and, of these, five women had pelvic inflammatory disease and another four had uterine adnexal tenderness.^[10] Pelvic inflammatory disease may lead to infertility (see pelvic inflammatory disease). In some people, localised gonococcal infection may disseminate. A US study estimated the risk of dissemination to be 0.6–1.1% among women, whereas a European study estimated it to be 2.3–3.0%.^[11]^[12] The same European study found a lower risk in men, estimated to be 0.4–0.7%.^[12] When gonococci disseminate, they cause petechial or pustular skin lesions; asymmetrical arthropathies, tenosynovitis, or septic arthritis; and rarely, meningitis or endocarditis.

AIMS OF INTERVENTION To relieve symptoms; avoid complications; and prevent further transmission, with minimal adverse effects of treatment.

OUTCOMES Microbiological cure rates (number of infected people or infected sites culture negative 1–14 days after treatment, divided by number of infected people or infected sites cultured 1–14 days after treatment), quality of life, and adverse effects of treatment.

METHODS *BMJ Clinical Evidence* search and appraisal July 2006. The following databases were used to identify studies for this review: Medline (1966 to July 2006), Embase (1980 to July 2006), and The Cochrane Library, Issue 2, 2006. Additional searches were carried out using these websites: NHS Centre for Reviews and Dissemination (CRD), Database of Abstracts of Reviews of Effects (DARE), Health Technology Assessment (HTA), Turning Research into Practice (TRIP), and National Institute for Health and Clinical Excellence (NICE) clinical guidelines. Abstracts of the studies retrieved were assessed independently by two information specialists using predetermined criteria to identify relevant studies. Study design criteria for inclusion in this chapter were: published systematic reviews, RCTs, and cohorts in any language, and containing any number of individuals. There was no minimum length of follow up required to include studies. We evaluated all studies described as “blinded” and also included “open”, “open label”, or not blinded. In addition, we use a regular surveillance protocol to capture harms alerts from organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA), which are continually added to the chapter as required. The contributor did an additional search of Pubmed in December 2006, using the keywords gonorrhoea and *N gonorrhoeae* infections, plus a hand search of references of key articles and books. Non-randomised comparative studies and

observational studies from these results were included; in these studies, participant selections were not biased, diagnoses were reliably established, and treatment outcomes were well described. Studies were excluded if they defined possible treatment failures as “reinfections”, if they did not use end points based on microbiological cure, or if they were based on drug regimens unlikely to be of general use (e.g. those using antibiotic regimens that are toxic or to which resistance is now widespread).^[13] The contributor did not search for, or include, studies published before 1981 as the susceptibility of *N gonorrhoea* changes over time. The results of particularly old clinical trials may be misleading because of intervening changes in susceptibility. The contributor updated his own systematic review^[13] using the original methods. We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 8).

QUESTION What are the effects of treatments for uncomplicated infections in men and non-pregnant women?

OPTION SINGLE DOSE ANTIBIOTIC REGIMENS

Cure rates

Single-dose antibiotic regimens compared with each other Single-dose antibiotics may be equally effective when compared with each other in achieving cure rates of more than 95% in urogenital or rectal infection and about 80% in pharyngeal infections (low-quality evidence).

Note

Resistance to penicillins, tetracyclines, and sulphonamides is now widespread, and resistance to fluoroquinolones has become common in some geographic areas.

For GRADE evaluation of interventions for gonorrhoea, see table, p 8 .

Benefits:

Uncomplicated urogenital, rectal, and pharyngeal infections:

We found one systematic review (search date 1993).^[13] The results were updated to 2004 by the contributor of the review using the original methods (see table 1, p 7)^{[13] [14] [15]} (Moran JS, personal communication, 2004). The original review identified studies (both RCTs and other clinical trials) published from 1981 to 1993 that used a single dose regimen based on an antimicrobial other than a beta-lactamase sensitive penicillin or a tetracycline.^[13] The search retrieved studies with a total of 24 383 evaluable people or infected sites. Combining results across individual arms of trials, 97% were cured on the basis of culture results. Sites of infection, when specified, included the cervix, urethra, rectum, and pharynx. Comparison of cure rates by site of infection found that cure rates were over 95% for all sites except the pharynx, for which they were about 80% (see table 1, p 7).^[16]

Eye infections:

We found no systematic review or RCTs (see comment below).

Harms:

Single dose regimens using fluoroquinolones, third generation and extended spectrum cephalosporins, or spectinomycin are generally safe and well tolerated. The most important adverse effects are rare hypersensitivity reactions. Minor adverse effects are most troublesome for the cefixime 800 mg regimen^{[17] [18]} and the azithromycin 2 g regimen;^[19] both cause frequent gastrointestinal upset. All the other effective doses are associated with a low incidence of adverse outcomes. One large observational cohort study of azithromycin, cefixime, ciprofloxacin, and ofloxacin “in everyday use” found few serious adverse effects.^[20] Quinolones may cause arthropathy in animals. One systematic review of harms (search date 2000) found no irreversible fluoroquinolone induced cartilage pathology after 0.3–10.0 months of follow up in 201 adolescents treated for between 7 and 270 days.^[21]

Comment:

Clinical guide:

There is good agreement between assessments of antigenococcal activity of antimicrobials *in vitro* and their efficacy in clinical trials. A large number of people were evaluated in a range of settings, suggesting that the results can be generalised. However, comparative results from different settings were not reported. Single dose regimens may make adherence more likely. The ceftriaxone and spectinomycin regimens require intramuscular injection. Resistance is now widespread for all penicillins, sulphonamides, and tetracyclines, and is becoming common for fluoroquinolones in many parts of the world.^{[2] [22] [23] [24]} Resistance to third generation and extended spectrum cephalosporins or spectinomycin is rarely reported (see table 2, p 7).^{[22] [23] [24] [25] [26] [27]}

Eye infections:

We found two small cohort studies of single dose ceftriaxone for gonococcal eye infections.^{[28] [29]} In the first study (12 adults with conjunctivitis), all people responded well to a single 1 g dose

of ceftriaxone.^[28] In the second study (21 neonates with gonococcal ophthalmia), eye swabs from all neonates were negative 24 hours after a single intramuscular 62.5 mg dose of ceftriaxone.^[29] Further RCTs are unlikely.

QUESTION What are the effects of treatments for uncomplicated infections in pregnant women?

OPTION SINGLE DOSE ANTIBIOTIC REGIMENS

Cure rates

Single-dose antibiotic regimens compared with each other Single doses of antibiotics (amoxicillin plus probenecid, spectinomycin, ceftriaxone, cefixime) may be equally effective when compared with each other in curing gonorrhoea at 14 days in pregnant women (*low-quality evidence*).

For GRADE evaluation of interventions for gonorrhoea, see table, p 8 .

Benefits: We found one systematic review (search date 2001, 2 RCTs^[30] ^[31]) of treatments of gonococcal infection during pregnancy.^[32] The first RCT identified by the review compared amoxicillin 3 g plus probenecid 1 g versus spectinomycin 2 g versus ceftriaxone 250 mg. Overall, it found no significant difference between regimens in cure rate at 14 days (267 pregnant women with positive cultures for gonorrhoea; failure to achieve cure: 9/84 [10.7%] with amoxicillin plus probenecid v 4/84 [4.8%] with spectinomycin; RR 2.25, 95% CI 0.72 to 7.02; 9/84 [10.7%] with amoxicillin plus probenecid v 4/84 [4.8%] with ceftriaxone; RR 2.25, 95% CI 0.72 to 7.02). However, the study may have lacked the power to detect clinically important effects. By site of infection, amoxicillin plus probenecid cured 91% of cervical infections, 85% of rectal infections, and 80% of pharyngeal infections; ceftriaxone cured 95% of rectal and cervical infections and 100% of pharyngeal infections; spectinomycin cured 97% of rectal and cervical infections and 83% of pharyngeal infections at 14 days.^[30] The second RCT compared a single dose of ceftriaxone intramuscularly 125 mg versus a single dose of cefixime orally 400 mg.^[31] It found that eradication rates were similar in the two groups (95 women with positive cultures for gonorrhoea; eradication rates: 96.8%, 95% CI 89.0% to 99.6% of cervical and rectal infections and 100.0%, 95% CI 47.8% to 100.0% of pharyngeal infections with intramuscular ceftriaxone v 96.0%, 95% CI 88.8% to 99.6% of cervical and rectal infections and 100.0%, 95% CI 54.1% to 100.0% of pharyngeal infections with oral cefixime; reported as not significant; figures not reported).

Harms: The systematic review reported vomiting after treatment in 1/267 (0.4%) women included in one trial.^[32] The second RCT reported soreness at the injection site among women receiving ceftriaxone and some "minor" malformations among their children, generally cosmetic (e.g. nevus, café au lait spots, skin tag: 10/60 [16.7%] with ceftriaxone v 7/62 [11.3%] with cefixime).^[31] Because quinolones cause arthropathy in animals, their use is not recommended in pregnancy, although we found no reports of adverse effects of quinolones on pregnancy outcome in humans. One multicentre, prospective, controlled study (200 exposed women) found no evidence of adverse effects.^[33] We found no evidence that the non-quinolone regimens listed above are less safe or less well tolerated by pregnant women than by men or non-pregnant women.

Comment: None.

QUESTION What are the effects of treatments for disseminated gonococcal infection?

OPTION MULTIDOSE ANTIBIOTIC REGIMENS

We found no direct information about multidose antibiotics regimens in the treatment of people with disseminated gonococcal infections. Consensus is that multidose antibiotic regimens are effective in disseminated gonococcal infection.

For GRADE evaluation of interventions for gonorrhoea, see table, p 8 .

Benefits: We found no systematic review and no RCTs of the treatment of disseminated gonococcal infection published since 1981.

Harms: We found no reports of adverse effects of multidose regimens using injectable cephalosporins or quinolones in this context.

Comment: **Clinical guide:** More than 100 clinical trials involving over 20 000 people have found that many single dose antimicrobial regimens cure uncomplicated infections more than 90% of the time.^[13] Given the protracted natural history without treatment, this evidence suggests that treatment with these antimicrobial

regimens is beneficial in disseminated disease as well. Which regimens are most beneficial cannot be determined precisely because direct randomised comparisons of the best different regimens have not been performed. However, analysis of available trials supports the consensus that the most effective regimens are those using selected third generation or expanded spectrum cephalosporins and, except where resistance is common, those using selected fluoroquinolones or spectinomycin. Although we found no published data establishing the efficacy of these treatments, we found no reports of treatment failures.

QUESTION What are the effects of dual treatment for gonorrhoea and chlamydia infection?

OPTION DUAL ANTIBIOTIC TREATMENT

Note

We found no direct information about the effects of dual antibiotic treatment in people with gonorrhoea and chlamydia infections.

For GRADE evaluation of interventions for gonorrhoea, see table, p 8 .

Benefits: We found no systematic review or RCTs on the effects of dual antibiotic treatment.

Harms: We found no good evidence on the harms of dual treatment. Treatment for chlamydia can cause mild gastrointestinal distress. Excess antibiotic treatment may lead to spread of resistance in *Neisseria gonorrhoeae* or other bacteria.

Comment: **Clinical guide:**

Routine dual treatment has been advocated and implemented for the treatment of chlamydia in people with gonorrhoea and is believed to have two potential benefits. First, routine dual treatment may retard the spread of resistant gonococcal strains. Second, dual antibiotic treatment is believed to have contributed to the decline in the prevalence of chlamydia infection observed in some populations. However, other factors may also have contributed (including widespread screening for asymptomatic chlamydia infection and changes in sexual behaviour), making it difficult to directly attribute decreases in the prevalence of chlamydia infection to any specific cause. Testing for chlamydia has become more widely available, more affordable, quicker, and more sensitive than it was in the past. However, in spite of routine testing and the use of dual antibiotic treatment, chlamydia is still found in 20–40% of people with gonorrhoea in many clinics. [3] [4] [5] [6] [7]

GLOSSARY

Dual treatment The routine treatment of people with gonorrhoea with an antimicrobial regimen effective against genital *Chlamydia trachomatis* infection in addition to a regimen effective against gonorrhoea (sometimes called dual therapy or co-treatment).

Low-quality evidence Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

REFERENCES

1. Division of STD Prevention, Centers for Disease Control and Prevention. *Sexually transmitted disease surveillance, 2005*. Atlanta, Georgia: US Department of Health and Human Services, Centers for Disease Control and Prevention, November 2006. Available online at: <http://www.cdc.gov/std/stats> (last accessed 4 January 2007).
2. Health Protection Agency. Diagnoses and rates of selected STIs seen at GUM clinics: 2001–2005. Available online at: http://www.hpa.org.uk/infections/topics_az/hiv_and_sti/epidemiology/2005data/Selected_sti_re-gion_sex_age_grp_2001_2005_AR.pdf (last accessed 4 January 2007).
3. McMillan A, Manavi K, Young H. Concurrent gonococcal and chlamydial infections among men attending a sexually transmitted diseases clinic. *Int J STD AIDS* 2005;16:357–361. [PubMed]
4. Kent CK, Chaw JK, Wong W, et al. Prevalence of rectal, urethral, and pharyngeal chlamydia and gonorrhoea detected in 2 clinical settings among men who have sex with men: San Francisco, California, 2003. *Clin Infect Dis* 2005;41:67–74. [PubMed]
5. Habib AR, Fernando R. Efficacy of azithromycin 1 g single dose in the management of uncomplicated gonorrhoea. *Int J STD AIDS* 2004;15:240–242. [PubMed]
6. Creighton S, Tenant-Flowers M, Taylor CB, et al. Co-infection with gonorrhoea and chlamydia: how much is there and what does it mean? *Int J STD AIDS* 2003;14:109–113. [PubMed]
7. Lyss SB, Kamb ML, Peterman TA, et al. *Chlamydia trachomatis* among patients infected with and treated for *Neisseria gonorrhoeae* in sexually transmitted disease clinics in the United States. *Ann Intern Med* 2003;139:178–185. [PubMed]
8. Hook EW, Handsfield HH. Gonococcal infections in the adult. In: Holmes KK, Mardh PA, Sparling PF, et al, eds. *Sexually transmitted diseases*. 3rd ed. New York: McGraw-Hill, 1999.
9. Cates WC Jr, Rolfs RT, Aral SG. Sexually transmitted diseases, pelvic inflammatory disease, and infertility: an epidemiologic update. *Epidemiol Rev* 1990;12:199–220. [PubMed]
10. Platt R, Rice PA, McCormack WM. Risk of acquiring gonorrhoea and prevalence of abnormal adnexal findings among women recently exposed to gonorrhoea. *JAMA* 1983;250:3205–3209. [PubMed]
11. Holmes KK, Wiesner PJ, Pedersen AHB. The gonococcal arthritis-dermatitis syndrome. *Ann Intern Med* 1971;75:470–471. [PubMed]
12. Barr J, Danielsson D. Septic gonococcal dermatitis. *BMJ* 1971;1:482–485. [PubMed]
13. Moran JS, Levine WC. Drugs of choice for the treatment of uncomplicated gonococcal infections. *Clin Infect Dis* 1995;20(suppl 1):47–65. Search date range 1981–1993; primary sources Medline, reference lists from retrieved articles, abstracts from the annual Interscience Conference on Antimicrobial Agents and Chemotherapy, and meetings of the International Society for Sexually Transmitted Disease Research.
14. Aplasca De Los Reyes MR, Pato-Mesola V, Klausner JD, et al. A randomized trial of ciprofloxacin versus cefixime for treatment of gonorrhoea after rapid emergence of gonococcal ciprofloxacin resistance in the Philippines. *Clin Infect Dis* 2001;32:1313–1318. [PubMed]
15. Rahman M, Alam A, Nessa K, et al. Treatment failure with the use of ciprofloxacin for gonorrhoea correlates with the prevalence of fluoroquinolone-resistant *Neisseria gonorrhoeae* strains in Bangladesh. *Clin Infect Dis* 2001;32:884–889. [PubMed]
16. Moran JS. Treating uncomplicated *Neisseria gonorrhoeae* infections: is the anatomic site of infection important? *Sex Transm Dis* 1995;22:39–47. [PubMed]
17. Handsfield HH, McCormack WM, Hook EW III, et al. The Gonorrhoea Treatment Study Group. A comparison of single-dose cefixime with ceftriaxone as treatment for uncomplicated gonorrhoea. *N Engl J Med* 1991;325:1337–1341. [PubMed]
18. Megran DW, LeFebvre K, Willets V, et al. Single-dose oral cefixime versus amoxicillin plus probenecid for the treatment of uncomplicated gonorrhoea in men. *Antimicrob Agents Chemother* 1990;34:355–357. [PubMed]

19. Handsfield HH, Dalu ZA, Martin DH, et al. Azithromycin Gonorrhoea Study Group. Multicenter trial of single-dose azithromycin vs. ceftriaxone in the treatment of uncomplicated gonorrhoea. *Sex Transm Dis* 1994;21:107-111. [PubMed]
20. Wilton LV, Pearce GL, Mann RD. A comparison of ciprofloxacin, norfloxacin, ofloxacin, azithromycin and cefixime examined by observational cohort studies. *Br J Clin Pharmacol* 1996;41:277-284. [PubMed]
21. Burstein GR, Berman SM, Blumer JL, et al. Ciprofloxacin for the treatment of uncomplicated gonorrhoea infection in adolescents: does the benefit outweigh the risk? *Clin Infect Dis* 2002;35(suppl 2):191-199. Search date 2000; primary sources Medline, and citation lists.
22. The WHO Western Pacific Gonococcal Antimicrobial Surveillance Programme. Surveillance of antibiotic resistance in *Neisseria gonorrhoeae* in the WHO Western Pacific Region, 2004. *Commun Dis Intell* 2006;30:129-132. Available online at: [http://www.health.gov.au/internet/wcms/publishing.nsf/Content/cda-cdi3001-pdf-ent.htm/\\$FILE/cdi3001g.pdf](http://www.health.gov.au/internet/wcms/publishing.nsf/Content/cda-cdi3001-pdf-ent.htm/$FILE/cdi3001g.pdf) (last accessed 4 January 2007). [PubMed]
23. Ye S, Su X, Wang Q, et al. Surveillance of antibiotic resistance of *Neisseria gonorrhoeae* isolates in China, 1993-1998. *Sex Transm Dis* 2002;29:242-245. [PubMed]
24. Centers for Disease Control and Prevention. Sexually Transmitted Disease Surveillance 2004 Supplement: Gonococcal Isolate Surveillance Project (GISP) Annual Report 2004. Atlanta, Georgia: US Department of Health and Human Services, December 2005. Available online at: <http://www.cdc.gov/std/GISP2004/> (last accessed 4 January 2007).
25. Dan M, Poch F, Sheinberg B. High prevalence of high-level ciprofloxacin resistance in *Neisseria gonorrhoeae* in Tel Aviv, Israel: correlation with response to therapy. *Antimicrob Agents Chemother* 2002;46:1671-1673. [PubMed]
26. GRASP Steering Group. *The Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP) Year 2005 report*. London: Health Protection Agency, 2006. Available online at: http://www.hpa.org.uk/infections/topics_az/hiv_and_sti/sti-gonorrhoea/publications/GRASP_2005_Annual_Report.pdf (last accessed 4 January 2007).
27. Fiorito S, Galarza P, Pagano I, et al. Emergence of high level ciprofloxacin resistant *Neisseria gonorrhoeae* strain in Buenos Aires, Argentina. *Sex Transm Infect* 2001;77:77.
28. Haimovici R, Roussel TJ. Treatment of gonococcal conjunctivitis with single-dose intramuscular ceftriaxone. *Am J Ophthalmol* 1989;107:511-514. [PubMed]
29. Hoosen AA, Kharsany AB, Ison CA. Single low-dose ceftriaxone for the treatment of gonococcal ophthalmia: implications for the national programme for the syndromic management of sexually transmitted diseases. *S Afr Med J* 2002;92:238-240. [PubMed]
30. Cavenee M, Farris J, Spalding T. Treatment of gonorrhoea in pregnancy. *Obstet Gynaecol* 1993;81:33-38.
31. Ramus RM, Sheffield JS, Mayfield JA, et al. A randomized trial that compared oral cefixime and intramuscular ceftriaxone for the treatment of gonorrhoea in pregnancy. *Am J Obstet Gynecol* 2001;185:629-632. [PubMed]
32. Brocklehurst P. Antibiotics for gonorrhoea in pregnancy. In: *The Cochrane Library*, Issue 1, 2006. Chichester, UK: John Wiley & Sons, Ltd. Search date 2004; primary source Cochrane Pregnancy and Childbirth Group Register.
33. Loebstein R, Addis A, Ho E, et al. Pregnancy outcome following gestational exposure to fluoroquinolones: a multicenter prospective controlled study. *Antimicrob Agents Chemother* 1998;42:1336-1339. [PubMed]

John S Moran

Medical Epidemiologist
Centers for Disease Control and Prevention
Atlanta
USA

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TABLE 1 Effectiveness of selected single dose regimens for treating gonorrhoea; published clinical trials ^[13] updated to 2005 and comparison of cure rates at different sites of infection performed ^[16] (see text, p 3).

Drug and dose	Pharyngeal infections	Urogenital and rectal infections
	% cured (95% CI)	% cured (95% CI)
Ceftriaxone 250 mg	99.0 (94.4 to 100)	99.2 (98.8 to 99.5)
Ciprofloxacin 500 mg*	97.2 (85.5 to 99.9)	99.8 (98.7 to 100)
Ciprofloxacin 250 mg	88.5 (81.8 to 95.2)	98.7 (98.0 to 99.4)
Ceftriaxone 125 mg	94.1 (85.6 to 98.4)	98.9 (97.9 to 99.8)
Gatifloxacin 600 mg	100 (82.3 to 100)	99.6 (97.7 to 100)
Spectinomycin 2 g	51.8 (38.7 to 64.9)	98.2 (97.6 to 99.9)
Azithromycin 2 g	100 (82.3 to 100)	99.2 (97.2 to 99.9)
Ofloxacin 400 mg	88.7 (68.8 to 97.8)	98.6 (97.8 to 99.4)
Gatifloxacin 400 mg	100 (63.1 to 100)	99.2 (97.1 to 99.9)
Cefixime 800 mg	80.0 (51.9 to 95.7)	98.4 (95.9 to 99.6)
Cefixime 400 mg	92.3 (74.9 to 99.1)	97.4 (95.9 to 98.6)
Cefuroxime axetil 1 g	56.9 (43.3 to 70.5)	96.2 (94.8 to 97.5)
Cepodoxime proxetil 200 mg	78.9 (54.5 to 94.0)	96.5 (94.3 to 98.5)

*Excludes two published clinical trials among people known to be at high risk of harbouring fluoroquinolone resistant strains; ciprofloxacin 500 mg cured only 48/72 (67%) of cervical infections in one trial ^[14] and 41/66 (62%) in the other. ^[15]

TABLE 2 Reported resistance of *N gonorrhoeae* to antimicrobials (see text, p 3).

Drug	Resistance
Sulphonamides	Widespread
Penicillins	Widespread
Tetracyclines	Widespread
Third generation cephalosporins (e.g. ceftriaxone, cefixime)	One report from China ^[23]
Spectinomycin	Rare
Quinolones	Asia: becoming very common, especially in the Far East (e.g. 94% in China, 82% in Japan, 47% in the Philippines); ^[22] few data are from the Middle East, but a high prevalence of resistance (61%) has been reported in Israel. ^[25] USA: in 2003, resistance to ciprofloxacin (MIC greater-than or equal to 1.0 µg/mL) was reported in 4.1% of 6552 isolates. In Hawaii and California, where the use of quinolones for the treatment of gonorrhoea is no longer recommended, 17.9% of isolates were resistant to ciprofloxacin. In the remainder of USA, 1.3% of isolates were resistant overall but only 0.4% of isolates from heterosexuals were resistant. ^[24] UK: among 1030 gonorrhoeae isolates from England and Wales tested in 2004, 22% were fluoroquinolone resistant. ^[26] Australia: 21% and New Zealand 19%. ^[22] South America: one fluoroquinolone resistant isolate reported. ^[27]

TABLE GRADE evaluation of interventions for gonorrhoea

Important outcomes	Cure rates, adverse effects								
Number of studies (participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment
What are the effects of treatments for uncomplicated infections in men and non-pregnant women?									
At least 28383 people ^[13] ^[16]	Cure rates	Single-dose regimens compared with each other	4	-1	0	-1	0	Low	Quality point deducted for inclusion of CCTs. Directness point deducted for no direct comparison of different antibiotics
What are the effects of treatments for uncomplicated infections in pregnant women?									
2 (362) ^[30] ^[31]	Cure rates	Different single-dose regimens compared with each other	4	-1	0	-1	0	Low	Quality point deducted for incomplete reporting of results. Directness point deducted for small number of comparisons

Type of evidence: 4 = RCT; 2 = Observational; 1 = Non-analytical/expert opinion.
 Consistency: similarity of results across studies.
 Directness: generalisability of population or outcomes.
 Effect size: based on relative risk or odds ratio.