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Letter to the Editor

A Pilot Study Evaluating Antimicrobial Antagonism in Syphilis/*Chlamydia trachomatis* Co-Infection in Men Who Have Sex with Men

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Penicillins are bactericidal, whereas doxycycline is bacteriostatic; simultaneous use of penicillin and doxycycline has been associated with antimicrobial "antagonism," and treatment failure in clinical cases of pneumococcal meningitis, scarlet fever, and ocular syphilis.[1–4] There have been significant increases in early syphilis and *Chlamydia trachomatis* in men who have sex with men (MSM). Early syphilis is treated with a single injection of Benzathine penicillin (BPG) and chlamydia is treated with 7 days of oral doxycycline 100 mg BID.[5] The summary of product characteristics (SmPC) of both products recommend the avoidance of simultaneous use of BPG and doxycycline (www.medicines.org.uk/emc/product/11044/smpc#gref; www.medicines.org.uk/emc/product/4063/smpc#gref). There is little data on syphilis/chlamydia co-infection or associated antimicrobial antagonism.

We reviewed all cases of syphilis/chlamydia co-infection in MSM in our sexual health clinic in the UK which sees 6,500 attendances by MSM per year. At the time of this study, HIV Prep-exposure prophylaxis (PrEP) was not widely available.

In 2019, 6613 MSM attended for sexually transmitted infection testing and 155 MSM were diagnosed with early syphilis. Fifty-three (34%) were HIV positive, 26 of 102 (25%) HIV negative MSM were using PrEP, the median age was 43 years (interquartile range = 34-53), none had neurological syphilis and all were treated with BPG. Twenty-one (14%, 95% confidence interval = 8.6-20.1) were simultaneously diagnosed with chlamydia (rectal: 17/21 [81%], urethra: 4/21 [19%]). All MSM with rectal chlamydia were tested for Lymphogranuloma venereum: None were positive. MSM with syphilis/chlamydia co-infection were the same age (43 vs 44 years, $P = .426$), had similar baseline Venereal Disease Research Laboratory (VDRL) titers (1:32 vs 1:32, $P = .586$), were diagnosed at similar stages of syphilis, but were more likely to be HIV-positive than MSM diagnosed with syphilis alone (13/21 [62%] vs 40/134 [30%], $P = .004$). Thirteen out of 21 with co-infection were not treated simultaneously because of delays in laboratory results (N = 10) or clinician concerns about antimicrobial antagonism (N = 3). Eight out of 21 MSM were inadvertently treated simultaneously with BPG and doxycycline. There were no treatment failures: Overall 108/155 (70%) attended for at least one follow-up VDRL and all had at least a four-fold reduction in VDRL titer (median 1:1) at a median of 101 days. All eight who were treated simultaneously with BPG/doxycycline returned for follow-up VDRL.

We have shown that 14% of MSM diagnosed with syphilis have syphilis/chlamydia co-infection, mostly rectal chlamydia (81%). It is interesting that living with HIV MSM with syphilis were significantly more likely to have syphilis/chlamydia co-infection than HIV-negative MSM suggesting that their sexual networks remain relatively distinct or that immune responses to chlamydia differ in HIV patients. We treated 8 MSM simultaneously with BPG and doxycycline and there were no apparent treatment failures. There is a lack of guidance on the simultaneous

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treatment of syphilis/chlamydia co-infection with BPG and doxycycline despite concerns about antimicrobial antagonism, apart from the SmPC. Caution is needed with co-prescribing BPG/doxycycline for syphilis until further research is available demonstrating the safety and efficacy of simultaneous treatment. An option is to use 3 weeks of oral doxycycline BID for the treatment of syphilis/chlamydia co-infection; however, more research is needed.

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References

1. Lepper MH, Dowling HP. Treatment of pneumococcic meningitis with penicillin compared with penicillin plus aureomycin: Studies including observations on an apparent antagonism between penicillin and aureomycin. *AMA Arch Intern Med*. 1951;88:489-494. [CrossRef]
2. Olsson RA, Kirby JC, Romansky MJ. Pneumococcal meningitis in the adult. Clinical, therapeutic and prognostic aspects in 43 patients. *Ann Intern Med*. 1961;55:545-549. [CrossRef]
3. Strom J. The question of antagonism between penicillin and chlortetracycline, illustrated by therapeutical experiments in scarlatina. *Antibiotic Med Clin Ther (New York)*. 1955;1:6-12.
4. Smith GT, Goldmeier D, Migdal C. Neurosyphilis with optic neuritis: An update. *Postgrad Med J*. 2006;82:36-39. [CrossRef]
5. BASHH Guidelines. https://www.bashh.org/guidelines/. Accessed August 3, 2021.