

What is the evidence supporting antibiotic prophylaxis in meningococcal disease outbreaks?

Primary Reviewers: Anastasia Chew¹

Secondary Reviewer: Mike Levin²

¹ Edinburgh University, Scotland

² St Mary's Hospital, London

The World Health Organization has produced guidelines for the management of common illnesses in hospitals with limited resources. This series reviews the scientific evidence behind WHO's recommendations. The WHO guidelines, and more reviews are available at: http://www.who.int/child-adolescent-health/publications/CHILD_HEALTH/PB.htm

This review addresses the question: *What is the evidence supporting antibiotic prophylaxis in meningococcal disease outbreaks?*

The **WHO Pocketbook of Hospital Care for Children** recommends that in meningococcal disease outbreaks advise families of the possibility of secondary cases within the household so that they report for treatment promptly. (Pocketbook chapter 6.3, page 153).

Introduction:

Meningococcal meningitis is a contagious bacterial disease spread by respiratory droplets. The causative bacterium is *Neisseria meningitidis*, which is found as a commensal in the nasopharynx in large proportions of human populations (rates vary from 10% in random samples to 95% during epidemics of meningococcal disease). Chemoprophylaxis aims to prevent secondary cases after contact with an infected individual by eradication of nasopharyngeal carriage, as most new cases are acquired through contact with asymptomatic carriers.

In the African "meningitis belt" (from Ethiopia to Senegal, with an estimated population of 300 million) meningitis is endemic, with serotypes A, C and W135 being responsible for the majority of cases. Several factors result in this endemic state; the climate, social habits and housing. Crowded,

poorly ventilated homes and frequent upper respiratory tract infections increase people's susceptibility to the disease. Pilgrimages and markets also cause large population movements, which contribute to the spread of *N.meningitidis*.

Some African communities have reported disease rates as high as 1000 per 100,000 during outbreaks. Endemic attack rates are highest in young children, but during epidemics all ages are affected. The 1995–1996 epidemic season was the most serious, with a total of 201 000 cases and 14 500 deaths. Unfortunately, it seems that the meningitis belt is spreading south, with the potential to affect a far greater number of people.

Methodology

The Cochrane library was searched for relevant articles:

[http://www.mrw.interscience.wiley.com/cochrane/cochrane_search_fs.html]

One Cochrane review was found [1]:

The paper gives detailed information about the how studies were selected for the review, including inclusion and exclusion criteria. Findings are presented in sections outlining the outcome being assessed, with tables for further clarification. The limitations of each study are made clear in the review of all data.

Results and Discussion

Assuming that eradication of nasopharyngeal carriage of *N. meningitidis* reduces the risk of meningococcal infection [2] which has been a key control measure for many decades [3], several antibiotics were identified by this systematic review as being effective.

There were no cases of meningococcal disease following treatment with antibiotic or placebo therefore the efficacy cannot be directly assessed.

All results are therefore not based on clinical outcomes of disease.

After one week ciprofloxacin (relative risk (RR) 0.04; 95% CI 0.01 to 0.12), rifampicin (RR 0.17; 95% CI 0.12 to 0.24), minocycline (RR = 0.30; 95% CI 0.19 to 0.45) and ampicillin (RR 0.41; 95% CI 0.25 to 0.66) all successfully eradicated *N.meningitidis* when compared to placebo. However, with a longer follow-up (one to two weeks) only rifampicin (RR 0.20; 95% CI 0.14 to 0.29) and ciprofloxacin (RR 0.03; 95% CI 0.00 to 0.42) proved effective although this was based on one study. [4] In one study ceftriaxone was also found to be more effective when compared to rifampicin (RR 5.93; 95% CI 1.22 to 28.68), but no placebo was included. [5]

Rifampicin has good tissue penetration, achieving the necessary therapeutic levels in mucosa. Efficacy for longer than 2 weeks was reported for rifampicin, however, resistant isolates were also found. Six trials assessed resistance development to rifampicin (increased MICs were described in 3 of 6 studies analysing pre and post treatment rifampicin susceptibilities). [6-11] Hence rifampicin use may be associated with the appearance of resistant isolates.

Chemoprophylaxis should only be considered for those with close contact with people with meningococcal infection. This can be further quantified; for those living in the same household as the case for the first seven days post onset [12].

Summary

- There is no direct clinical evidence of chemoprophylaxis preventing meningococcal disease. Decreased nasopharyngeal carriage rates are used as a proxy for effectiveness of prevention.
- Ceftriaxone, rifampicin and ciprofloxacin are the most effective antibiotics to eradicate nasopharyngeal carriage of *N. meningitidis*.
- Rifampicin has more unwanted side effects and important contraindications, but is cheaper and more widely available in many developing countries. There is documentation of resistant strains emerging in persistent isolates.

- Ceftriaxone ensures adherence as it is given in a single IM dose, and is suitable for young children and pregnant women.
- Ciprofloxacin is effective as a single oral dose, but is contraindicated in pregnancy.
- Resistance has not yet been reported to ciprofloxacin and ceftriaxone.

References

1. Fraser A, Gafter-Gvili A, Paul M, Leibovici L. Antibiotics for preventing meningococcal infections. *Cochrane Database Syst Rev* 2005(1):CD004785.
2. Mandell GD, JE Dolin, Reisser Lima AAP. Mandell, Douglas, and Bennett's Principles & Practice of Infectious Diseases Principles and Practice of Infectious Diseases. 5th Edition ed: Churchill Livingstone; 2000.
3. Samuelsson S. Meningococcal disease--still a major challenge. *Commun Dis Public Health* 2002;5(3):178-80.
4. Pugsley MP, Dworzack DL, Horowitz EA, Cuevas TA, Sanders WE, Jr., Sanders CC. Efficacy of ciprofloxacin in the treatment of nasopharyngeal carriers of *Neisseria meningitidis*. *J Infect Dis* 1987;156(1):211-3.
5. Schwartz B, Al-Tobaiqi A, Al-Ruwais A, Fontaine RE, A'Ashi J, Hightower AW, et al. Comparative efficacy of ceftriaxone and rifampicin in eradicating pharyngeal carriage of group A *Neisseria meningitidis*. *Lancet* 1988;1(8597):1239-42.
6. Blakebrough IS, Gilles HM. The effect of rifampicin on meningococcal carriage in family contacts in northern Nigeria. *J Infect* 1980;2(2):137-43.
7. Deal WB, Sanders E. Efficacy of rifampin in treatment of meningococcal carriers. *N Engl J Med* 1969;281(12):641-5.
8. Guttler RB, Counts GW, Avent CK, Beaty HN. Effect of rifampin and minocycline on meningococcal carrier rates. *J Infect Dis* 1971;124(2):199-205.
9. Kaiser AB, Hennekens CH, Saslaw MS, Hayes PS, Bennett JV. Seroepidemiology and chemoprophylaxis disease due to sulfonamide-resistant *Neisseria meningitidis* in a civilian population. *J Infect Dis* 1974;130(3):217-24.
10. Munford RS, Sussuarana de Vasconcelos ZJ, Phillips CJ, Gelli DS, Gorman GW, Risi JB, et al. Eradication of carriage of *Neisseria meningitidis* in families: a study in Brazil. *J Infect Dis* 1974;129(6):644-9.
11. Simmons G, Jones N, Calder L. Equivalence of ceftriaxone and rifampicin in eliminating nasopharyngeal carriage of serogroup B *Neisseria meningitidis*. *J Antimicrob Chemother* 2000;45(6):909-11.
12. Hall RG. The control of meningococcal disease. *Med J Aust* 2002;176(12):573-4.