9 Depoortere E, Checchi F, Broillet F, et al. Violence and mortality in West Dafur, Sudan (2003–04): epidemiological evidence from four surveys. *Lancet* 2004; **364:** 1315–20.

10 Coghlan B, Brennan RJ, Ngoy P, et al. Mortality in the Democratic Republic of Congo: a nationwide survey. *Lancet* 2006; **367:** 44–57.

11 White J. Warner downbeat after Iraq trip. *Washington Post* Oct 6, 2006: A3.

12 Horton R. Public health as a counterterrorist measure. *Lancet* 2001; **358:** 1112–13.

13 Fidler DP, Drager N. Health and foreign policy. *Bull World Health Organ* 2006; **84:** 687.

14 Horton R. The next Director-General of WHO. *Lancet* 2006; **368:** 1213–14.

Antibiotics in childhood acute otitis media

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In today's *Lancet*, Maroeska Rovers and colleagues[1] analyse the effectiveness of antibiotics in childhood acute otitis media. Their analysis is of great importance to the family doctor, because acute otitis media is one of the leading reasons for paediatric consultations.[2]

Acute otitis media is the most common reason to prescribe antibiotics in children, even though the effect of such treatment is surprisingly restricted.[3] In many children, acute otitis media often resolves spontaneously.[4] These factors led to the policy of not prescribing antibiotics on the first visit but rather to treat the child with adequate pain relief and start watchful waiting. The main problem has been to identify those children who will most likely benefit from antibiotics.

To address this question, Rovers and colleagues[1] did a meta-analysis of individual patients' data, combining the data from six randomised trials that assessed the effectiveness of antibiotics in acute otitis media. 1643 children aged 6 months to 12 years with acute otitis media were included. Such analysis allowed the identification of subgroups that would benefit most from treatment. The large sample size enabled interaction analysis in multivariate models, reducing the possibility of false-positive results in the identification of subgroups of relevance.[5]

The result seems straightforward. Antibiotics were most beneficial in children younger than 2 years with bilateral acute otitis media, and in children with acute otitis media and a draining ear. An observational policy would be justified for most other children, which would be more than half the children studied. Implementing the results of this meta-analysis in current practice guidelines would suggest that more than half of the children with acute otitis media could be treated with watchful waiting. The resulting reduction in the use of antibiotics in acute otitis media would have vast financial implications and would considerably reduce the adverse effects of antibiotic use, such as diarrhoea and the generation of antibiotic resistance.

Acute otitis media can present with mild inflammation in the middle ear and indolent symptoms, but also with marked inflammation, swelling, bulging, and doughnut appearance of the tympanic membrane with substantial pain and distress to the patient and family. Severity scoring of acute otitis media was done in only one of the six studies[6] in Rovers and colleagues' meta-analysis. Inclusion of severity scoring in forthcoming studies and guidelines of acute otitis media might help the clinician to decide when to prescribe antibiotics and when to start watchful waiting. The scoring methods should include a detailed description of symptoms and general signs such as fever, because the assessment of middle-ear inflammation alone might not suffice.[7] Acute otitis media can also recur frequently. Rovers' meta-analysis was not specifically designed to assess the treatment of recurrent episodes of acute otitis media, which remains a task for future evidence-based analyses.

Reducing the use of antibiotics in acute otitis media has raised concerns about increasing the risk of mastoiditis, a rare purulent complication of acute otitis media in the temporal bone. Among the 1643 children included in Rovers and colleagues' meta-analysis, none developed mastoiditis. It is extremely important to remember that a diagnosis of acute otitis media in a febrile child does not exclude other bacterial diseases, such as pneumonia, sepsis, or meningitis. These diseases in some populations might be more prevalent than mastoiditis in the child with acute otitis media. Although many children presenting with acute otitis media might be treated without antibiotics on the first call, watchful waiting with pain relief must include the exclusion of other bacterial infections, with proper parental education and easy access to follow-up care.

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I declare that I have no conflict of interest.

1 Rovers MM, Glasziou P, Appelman CL, et al. Antibiotics for acute otitis media: a meta-analysis with individual patient data. *Lancet* 2006; **368:** 1429–35.
2 Freid VM, Makuc DM, Rooks RN. Ambulatory health care visits by children: principal diagnosis and place of visit. *Vital Health Stat* 1998; **13:** 1–23.
3 Glasziou PP, Del Mar CB, Sanders SL, Hayem M. Antibiotics for acute otitis media. *Cochrane Database Syst Rev* 2004; **1:** CD000219.
4 Rovers MM, Schilder AG, Zielhuis GA, Rosenfeld RM. Otitis media. *Lancet* 2004; **363:** 465–73.
5 Brookes ST, Whitely E, Egger M, Smith GD, Mulheran PA, Peters TJ. Subgroup analyses in randomized trials: risks of subgroup-specific analyses; power and sample size for the interaction test. *J Clin Epidemiol* 2004; **57:** 229–36.
6 McCormick DP, Chonmaitree T, Pittman C, et al. Nonsevere acute otitis media: a clinical trial comparing outcomes of watchful waiting versus immediate antibiotic treatment. *Pediatrics* 2005; **115:** 1455–65.
7 Appelman CL, Claessen JQ, Touw-Otten FW, Hordijk GJ, de Melker RA. Severity of inflammation of tympanic membrane as predictor of clinical course of recurrent acute otitis media. *BMJ* 1993; **306:** 895.

Magnesium sulphate for tetanus

Published Online October 4, 2006
DOI:10.1016/S0140-6736(06)69445-2
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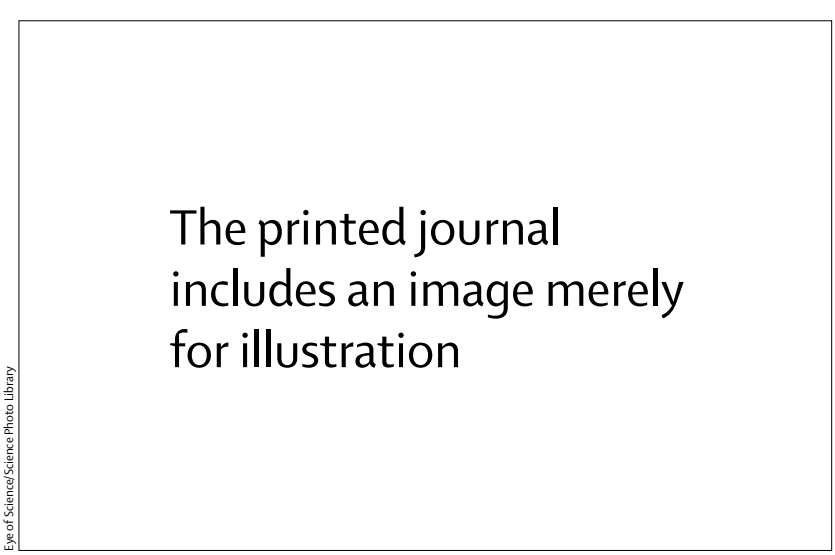
> "Tychon the soldier [was hit by] an arrow in his back…[He] sounded like someone gnashing his teeth in a fury of rage…He was arched back in opisthotonos, his jaws locked together against his will. A friend forced some wine between his teeth, but Tychon could not swallow, and the liquid was expelled in spurts from his nostrils. The following day the iatros arrived. In whispers he said there was little he could do, with the exception of [applying] soothing plasters."
>
> *Hippocrates (c 425 BC)*[1]

Tychon died of tetanus, which is the subject of a report by Louise Thwaites and colleagues[2] in today's *Lancet*. Their research is commendable for various reasons. First, they studied tetanus—a disease frequently forgotten, but certainly not gone,[3] with an estimated global incidence of a million cases a year.[4] Second, they did a randomised trial of a therapeutic intervention for tetanus, which is rare—there have been only nine such trials for tetanus in the past 30 years.[5] Third, they assessed an inexpensive, easily available drug—magnesium sulphate—also a unique feature because too often randomised trials are industry-sponsored research of expensive agents that might be unavailable in some health-care systems. Fourth, they address the controversial issue of magnesium sulphate for tetanus. Fifth, the trial was done in intensive care, an environment in which too few trials are completed. Sixth, the trial was done in a developing country (Ho Chi Minh City, Vietnam), where the resources needed to do a trial are often unavailable.

What does Thwaites and colleagues' report say? In terms of the endpoints, the results are not as promising as hoped: magnesium sulphate neither reduced the need for mechanical ventilation, nor decreased the frequency of death from severe tetanus. So what is their message? Magnesium sulphate is safe, and reduces the need to use other drugs to control tetanic muscle spasms and autonomic dysfunction: fewer courses of the benzodiazepine midazolam (given for severe spasms), of the curare-like drug pipecuronium, and of the calcium-channel blocker verapamil were given to patients allocated continuous infusions of magnesium sulphate than those allocated placebo. No difference was found in diazepam doses given (first-line sedative for less severe muscle spasms).

But let us take a step back. The tetanus treatment unit where Thwaites works admits about one patient with tetanus a day, or about 300 a year—much the same as the number of cases reported in Italy in 3 years.[6] Physicians in developed countries might lack experience in treating tetanus. By contrast, those in developing countries encounter people with tetanus commonly—a difference explained by high immunisation rates in developed countries and sadly low rates in those less well developed.



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Coloured scanning electron micrograph of *Clostridium tetani*