Antibiotics for acute laryngitis in adults (Review)

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ABSTRACT

Background
Acute laryngitis is a common illness worldwide. Diagnosis is often made by case history alone and treatment is often directed towards controlling symptoms.

Objectives
The aim of this review was to assess the effectiveness of different antibiotic therapies in adults suffering acute laryngitis. A secondary objective was to report the rates of adverse events associated with these treatments.

Search strategy
We systematically screened the following electronic databases: the Cochrane Central Register of Controlled Trials (The Cochrane Library Issue 4, 2006); MEDLINE (January 1966 to December Week 2 2006); and EMBASE (1974 to June 2006), LILACS (from 1982 to December 2006) and BIOSIS (1980 to June 2002). Other strategies included hand searching relevant journals, searching ongoing trial databases and general databases such as Google scholar.

Selection criteria
Randomized controlled trials comparing any antibiotic therapy with placebo in acute laryngitis. The main outcome measurement was objective voice scores.

Data collection and analysis
Data were independently extracted by two review authors and then descriptively synthesized.

Main results
Only two trials met study inclusion criteria after extensive literature searches. One hundred participants were randomly selected to receive either penicillin V (800 mg twice a day for five days), or an identical placebo, in a study of penicillin V in acute laryngitis in adults. A tape recording of each patient reading a standardized text was obtained during the first visit, subsequently during re-examination after one and two weeks, and at follow up after two to six months. No significant differences were found between the groups. The trial also measured symptoms reported by participants and found no significant differences.

The second trial investigated erythromycin for treating acute laryngitis in 106 adults. The mean objective voice scores measured at the first visit, at re-examination after one and two weeks, and at follow up after two to six months did not significantly differ between control and intervention groups. At one week there were significant beneficial differences in the severity of reported vocal symptoms as judged by the participants (P = 0.042). Comparing the erythromycin and placebo groups on subjective voice scores the a priori relative risk (RR) was 0.7 (95% confidence interval (CI) 0.51 to 0.96, P = 0.034) and the number needed to treat (NNT) was 4.5.

Authors’ conclusions
Antibiotics appear to have no benefit in treating acute laryngitis. Erythromycin could reduce voice disturbance at one week and cough at two weeks when measured subjectively. We consider that these outcomes are not relevant in clinical practice. The implications for practice are that prescribing antibiotics should not be done in the first instance as they will not objectively improve symptoms.
Available data suggests that antibiotics (penicillin V and erythromycin) are of limited use for most adults with acute laryngitis.

Acute laryngitis is an inflammation of the larynx. The most common symptoms are hoarseness, fever, sore throat, postnasal discharge and difficulty in swallowing. This review found that penicillin V and erythromycin appear to have no benefit in treating acute laryngitis. Erythromycin could reduce voice disturbance at one week and cough at two weeks when measured subjectively. We consider these outcomes are not relevant in clinical practice as the modest benefits from antibiotics may not outweigh their cost, adverse effects, or negative consequences on antibiotic resistance patterns.

**BACKGROUND**

Upper respiratory tract infection (URTI) is the most common acute illness worldwide and is usually self-diagnosed and self-treated at home (Cherry 2003; McAvoy 1994). In 1995, URTI was the most frequent reason for seeking ambulatory care in the United States, resulting in more than 37 million visits to physician practitioners and emergency departments (Gonzales 2001a). It is also the most common reason for absence from work in the United States. Losses in income for employed persons, costs to employers with time lost from work, and costs of medical treatment amounted to $112 billion in 1997 (Birnbaum 2002).

Laryngeal inflammation may be due to many causes, such as viral infection, acid reflux, voice abuse, toxic inhalation, caustic ingestion, irritation from purulent sinus drainage, hypersensitivity reactions, immune disorders, or from coughing due to any cause (Koufman 1996).

Acute laryngitis is one of the most common pathologies identified in the larynx and can be defined as an inflammation of the larynx and vocal fold mucosa, lasting less than three weeks. Episodes are usually self-limiting and are influenced by weather conditions (Danielides 2002; Vaughan 1982). Symptoms of acute laryngitis include a lowering of the normal pitch of the voice and hoarseness which usually persist from three to eight days. Patients with laryngitis also may experience symptoms of a URTI such as sore throat, odynophagia, rhinorrhea, dyspnea, postnasal discharge and congestion (Postma 1998; Schalen 1988; Spiegel 2000). Direct examination with a flexible nasolaryngoscope usually reveals secretions, erythema and edema of the vocal folds.

Etiology is not established in routine practice and the diagnosis can often be made by history alone. Unfortunately, there are no clinically useful criteria that help to distinguish between bacterial and viral infections (Vaughan 1982). Acute infectious laryngitis is usually caused by a viral infection. Respiratory viruses like parainfluenza, rhinovirus, influenza and adenovirus have been etiologically associated with laryngitis (Higgins 1974; Postma 1998). However, bacterial pathogens such as *Moraxella catarrhalis* (M. catarrhalis), *Haemophilus influenzae* (H. influenzae) and *Streptococcus pneumoniae* (S. pneumoniae) have been frequently isolated from the nasopharynx in adults with acute laryngitis (Hol 1996; Schalen 1980; Schalen 1988; Verduin 2002); another related pathogen is *Chlamydia pneumoniae* (C. pneumoniae) (Hashiguchi 1992).

URTIs represent one of the most common causes of antimicrobial use and a frequent reason for prescribing antibiotics in ambulatory practice and primary care (Gonzales 2001a; McAvoy 1994; McGregor 1995; Steinman 2003a). In adults with acute laryngitis, treatment is usually directed to the control of symptoms with voice rest, analgesic therapy and humidification. Macrolides, cephalosporins, a combination of penicillins with beta-lactamase inhibitors, and extended spectrum penicillins are also frequently prescribed (McGregor 1995; Steinman 2003a). In an observational study of the antibiotic prescribing behaviour of general practitioners in managing URTIs, 14.9% of antibiotic treatment courses were prescribed for treating laryngitis or tracheitis (Mazzaglia 1998). A retrospective analysis for a 5-year period of 9.6 million osteopathic physician office visits by patients with URTIs found that antibiotics were prescribed in more 50% of visits (Sun 2006).

Reasons for over-prescribing antibiotics are varied but they often involve physician's and patient's attitudes and expectations (Bertino 2002; Mazzaglia 1998; Steinman 2003a). A Cochrane systematic review evaluated the effectiveness of professional interventions in improving antibiotic prescriptions by healthcare providers in outpatient settings as well as the impact of these interventions on reducing the incidence of antimicrobial resistant pathogens. Reviewers concluded that a multi-faceted intervention, with educational interventions occurring at many levels, including repeated media campaigns, implementation of guidelines, and feedback to the profession on antibiotic prescribing data and resistance, may improve antibiotic prescribing behavior and stop the increase in the prevalence of resistant pneumococci, *H. influenzae* and other microorganisms (Arnold 2005; Malmvall 2007).

Excessive use of antibiotics in ambulatory practice has contributed to the emergence and spread of antibiotic resistant bacteria in the community, at a substantial cost to the health care system (Gonzales 2001a; Gonzales 2001b; Steinman 2003b). As the cost of medical treatment for laryngitis is high and there is increasing concern over the resistance of common bacteria to commonly used antibiotics, there is a need to investigate the role of antibiotic drugs in acute laryngitis.
OBJECTIVES

The aim of this review was to assess the effectiveness of different antibiotic therapies in adults with acute laryngitis. A secondary objective was to report the rates of adverse events associated with these treatments.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

Randomized controlled trials (RCTs) comparing antibiotic therapy with placebo or another antibiotic in the treatment of acute laryngitis.

Types of participants

Adults with acute laryngitis, defined by the International Classification of Health Problems in Primary Care (ICHPPC) as hoarseness associated with other symptoms of URTI. Exclusion criteria comprised of the inclusion of participants with chronic relevant underlying diseases, symptoms of laryngitis for more than three weeks (chronic laryngitis), and antibiotic therapy within the preceding two weeks before diagnosis.

Types of intervention

Trials comparing antibiotics with placebo or antibiotics of a different class for acute laryngitis.

Types of outcome measures

The following outcome measures were considered:

Clinical improvement
Symptom improvement at presentation (hoarseness/subjective voice score, pharyngitis, cough, sore throat and rhinorrhea/nasal congestion) and after the period of time considered in each trial, as assessed by the investigators or the patient. Improvement in recorded voice score assessed by an expert panel at presentation and after the period of time considered in each trial (usually one and/or two weeks). As a standard, trials used the patient's normal voice, recorded weeks later.

Bacteriological findings (evaluated at the acute and the follow up visits).

Adverse reactions following antibiotic therapy
Serious adverse events, i.e. serious enough to require withdrawal from the treatment group.
Minor adverse events reported by participants and not requiring withdrawal from treatment group (gastrointestinal side effects such as diarrhea, dyspepsia, abdominal pain and rash).

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: Cochrane Acute Respiratory Infections Group methods used in reviews.

We systematically screened the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library Issue 4, 2006), MEDLINE (January 1966 to December, Week 2, 2006) (using PUBMED for the 2004 to 2006 update); EMBASE (1974 to June 2006) using the SilverPlatter platform; LILACS (from 1982 to December 2006) (Castro 1997) and BIOSIS (1980 to June 2002). Other strategies included handsearching relevant journals, searching ongoing trial databases and general databases such as Google scholar. There were no language restrictions.

MEDLINE was searched using the following keywords and MeSH terms in conjunction with the highly sensitive search strategy designed by the Cochrane Collaboration for identifying RCTs (Dickersin 1994). The same strategy was used to search CENTRAL and adapted to search EMBASE, LILACS and BIOSIS.

MEDLINE search strategy (OVID)
1 randomized controlled trial.pt.
2 randomized controlled trials/
3 random allocation/
4 controlled clinical trial.pt.
5 double-blind method/
6 single-blind method/
7 or/1-6
8 Animal/ not Human/
9 7 not 8
10 clinical trial.pt.
11 exp clinical trials/
12 (singl$ or doubl$ or trebl$ or tripl$) adj (blind$ or mask$)).tw.
13 (blind$ or placebos/ or random$).tw.
14 research design/
15 (latin adj square).tw.
16 or/14-15
17 (clinical adj trial$).tw.
18 or/10-17
19 16 not 8
20 18 not 9
21 comparative study/
22 exp evaluation studies/
23 follow-up studies/
24 prospective studies/
25 control$ or volunteer$.tw.
26 or/21-25
27 20 not 8
28 26 not 20
29 28 not 9 or 20
30 29 or 20 or 28

Antibiotics for acute laryngitis in adults (Review)
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Other strategies were employed to include in the search references of review articles; books related to infections of respiratory tract; and hand searches of the journals such as Journal of Infectious Diseases, Clinical Infectious Diseases, Journal of Antimicrobial Chemotherapy, Head and Neck, Otorhinolaryngology, Annals of Otolaryngology and Laryngology, and Scandinavian Journal of Infectious Diseases.

A search was made for adverse effects or side effects (combined with the disease terms). The Master List of handsearched journals by the Cochrane Collaboration was reviewed to avoid repeating hand searching several volumes of these journals.

We also consulted local and international experts in the field and searched databases of ongoing trials registers such as www.controlled-trials.com (meta Register of Controlled Trials) and www.clinicaltrials.com and www.latinrec.org. Additional electronic searches were designed for general search engines like AltaVista and Google scholar. This strategy included all languages.

Grey literature such as conference abstracts/proceedings, published lists of theses and dissertations worldwide (dissertation abstract database), letters, government documents (CDC database) and other literature outside of the main journal literature were searched where possible (McAuley 2000).

Some pharmaceutical companies were contacted to obtain unpublished trial data. Leading researchers involved in the field were contacted by e-mail to obtain information on additional published and unpublished data and trials.

### METHODS OF THE REVIEW

Eligibility of the retrieved articles was assessed independently by two review authors (LR and AC) from the title and abstracts. The full text of all studies identified as possibly relevant was obtained and independently assessed by three review authors (LR, AF and EO). There was no blinding of the review authors as to the origin, or conclusions of the article during eligibility assessment, data extraction or quality assessment (Berlin 1997).

#### Data extraction

Data extraction was carried out independently by two review authors on a previously designed form to ensure validity, and discrepancies were solved by an open discussion between all investigators. The differences in the study participants, interventions and outcomes among the included trials were presented in the study tables.

#### Quality assessment

Methodological quality of included studies was assessed according to the following aspects.

1. **Generation of the allocation sequence**: adequate (table of random numbers, computer generated random numbers, or similar), unclear (not reported), or inadequate (alternation, date of birth, or similar).
2. **Allocation concealment**: adequate (central randomization, serially numbered opaque sealed envelopes, or similar), unclear (not reported), or inadequate (open table or similar).
3. **Who was blinded/not blinded**: participants, clinicians, outcome assessors.
4. **Follow up**: whether numbers and reasons for dropouts and withdrawals was clearly described (yes or no).

We also reported if the investigators used an intention-to-treat analysis.

In addition, we graded studies using the five point Jadad 1996 study quality score.
Was the study described as randomised? Yes = 1; No = 0.
Was the study described as double blind? Yes = 1; No = 0.
Was there a description of the withdrawals and dropouts? Yes = 1; No = 0.

Was the method of randomization well described and appropriate? Yes = 1; No = 0.
Was the method of double blinding well described and appropriate? Yes = 1; No = 0.
Deduct one point if methods for randomization or blinding were inappropriate.

The maximum score is five. Studies scoring three or more points were considered high quality. The points achieved for each of the above three items are listed in order for each study in the table describing the 'Characteristics of included studies' (for example, for a trial getting full points on each item, the score would be 2-2-1) (Jadad 1996).

DESCRIPTION OF STUDIES

From the results of the extensive literature search 3610 citations were initially identified as potentially relevant. An updated search was performed from June 2004 to December 2006 resulting in an additional similar number of citations. Manual culling reduced this to three reports of possibly eligible trials. Only two trials fulfilled the criteria for inclusion in the review (Schalén 1985; Schalén 1993) and a duplicated trial was excluded (Schalén 1992). Both studies were conducted by the same group of researchers in Sweden. Complementary strategies to identify other relevant studies or unpublished data were not effective; no ongoing trials have been identified.

In a study of penicillin V in acute laryngitis in adults (Schalén 1985), 100 participants over 18 years of age were examined and recruited at the otolaryngology department of the University of Lund, Sweden and randomized to receive either penicillin V (800 mg two times a day for five days) or an identical placebo. No participants were reported to have dropped out or as lost to follow up. Exclusion criteria included participants with relevant underlying diseases like chronic bronchitis, pregnancy, antibiotic treatment within the preceding two weeks, and a history of penicillin allergy.

In the penicillin V study (Schalén 1985) methods to generate the sequence of randomization and allocation concealment were not reported. Furthermore, no description of the sample size or power calculation was recorded. Both the participants and treating physicians were blinded; however, the characteristics of this blinding were not described. No dropouts or withdrawals were reported.

Information was given regarding baseline characteristics including gender, age, voice demand or abuse, smoker condition and previous laryngitis (three or more episodes during the preceding five years) making it easy to ascertain that the groups were sufficiently similar at the start of the trial. There were no statistically significant differences between the two groups in symptoms and clinical findings at the acute visits (in terms of preceding URTI, presence of rhinitis, cough and sore throat, abnormal findings like redness and edema in the larynx, pharynx and epipharynx, mean voice score and bacterial pathogen isolated from the nasopharynx).

The mean interval between the start of vocal symptoms and the first evaluation was 3.6 days. However, the interval was longer for participants receiving antibiotics (3.8 ± 3.3) compared to the placebo (3.4 ± 3.0). All data were evaluated using a cross-tabulated chi-square test or Student's test and a probability level of 0.01 was considered significant. The Jadad (Jadad 1996) study quality score was two, for both review authors (AC and LR).

The erythromycin study publication (Schalén 1993) stated that the trial was randomized and participants and physicians were
blinded by using identical placebo tablets. A power calculation and intention-to-treat analysis were not reported. Seven of 106 participants dropped out or withdrew from the study for specific reasons and were not accounted for in the trial analysis. Baseline characteristics of the participants appeared to be broadly similar between groups and included the same variables as the penicillin V study. As they were not described, we calculated P values for any differences in the population characteristics and the symptoms and signs at presentation and found no significant difference between the two groups.

The erythromycin group had a higher and more significant number of bacterial pathogens and M. catarrhalis was isolated from the nasopharynx in this group (P = 0.045 and P = 0.012, Fisher’s exact test), respectively. The mean interval between the start of vocal symptoms and the first evaluation was not reported. Non-parametric tests were used for statistical analysis. Fisher’s exact probability test was used to compare bacterial elimination rates between the two groups and the Mann-Whitney U test with adjusted z was used for all other comparisons. A probability level of 5% was considered significant. The Jadad study quality score was three.

Results from the trials were not aggregated as there was significant heterogeneity between them with different drugs and definitions of some outcomes.

RESULTS

Primary outcomes
(1) Clinical improvement

In the penicillin V trial (Schalén 1985) the mean objective voice scores at the first visit and at re-examination after one and two weeks, as well as at follow up after two to six months, did not differ significantly between the penicillin V and the placebo groups. Significant improvement was reported in the severity of reported vocal symptoms, nasal congestion/rhinorrhea, throat symptoms, cough, and laryngeal abnormalities evaluated by indirect laryngoscopy at the follow up examinations in the control and intervention groups, as judged by the participants. Significant improvement measured by higher mean voice scores were found at the acute visits among participants with M. catarrhalis, H. influenzae or S. pneumoniae (26 ± 8) isolated from the nasopharynx, compared to results obtained for those with negative cultures (20 ± 10) (Student’s t test; P < 0.05). However, the subjective voice scores at the acute visits did not differ between the participants harboring the three mentioned pathogen isolates and those without the organisms. This study used parametric measures.

In the erythromycin trial (Schalén 1993) the mean objective voice scores at the first visit, at re-examination after one and two weeks, and at follow up after two to six months did not differ significantly between control and intervention groups. Thirty randomly selected voice samples recorded at presentation were evaluated and the Kendall coefficient of concordance between listeners for the voice qualities ranged from 0.45 to 0.91. (The Kendall’s coefficient of concordance is a measure of the agreement among several judges who are assessing a given set of objects). After one week, the mean scores were clearly reduced and the voice profiles were essentially normalized in both groups.

At one week there were significant improvements in the severity of reported vocal symptoms, comparing erythromycin and placebo groups (P = 0.042), as judged by the participants. At two weeks, significantly fewer complaints of cough were reported by the erythromycin group compared to the placebo group (P = 0.031). The trialists compared signs of laryngitis, pharyngitis and rhinitis, evaluated by mirror endoscopy or direct inspection and found no statistical differences between the two groups. This study used non-parametric statistics.

Secondary outcomes
(1) Bacteriological findings

In the penicillin V trial (Schalén 1985) M. catarrhalis, H. influenzae and S. pneumoniae were isolated from 50%, 15% and 1% of the participants respectively, at the first evaluation. The isolation rates of each of the mentioned pathogens at the acute and at the follow up visits did not differ significantly between the two intervention groups.

In the erythromycin trial (Schalén 1993) M. catarrhalis was isolated from the nasopharynx in 50% of participants, H. influenzae in 20% of participants and S. pneumoniae in 5% of participants at the acute visit. After one week, M. catarrhalis was eliminated in 83% of the participants in the erythromycin group as compared with 31.6% in the placebo group (P < 0.00038, Fisher’s exact test). However, there was no difference between the two groups in the recovery rate of M. catarrhalis at two weeks.

(2) Adverse drug reactions

No deaths were reported in either the penicillin V trial (Schalén 1985) or the erythromycin study (Schalén 1993). No adverse drug reactions were reported in the penicillin V trial (Schalén 1985) although it was unclear which potential toxic effects were monitored for. Only one patient was reported to present with an exanthema, on the second day of erythromycin treatment.

DISCUSSION

Antibiotics appear to have no benefit in treating acute laryngitis; no differences were found in the so-called “objective outcome”. Erythromycin could reduce voice disturbance at one week and cough at two weeks when measured subjectively. We consider that these outcomes are sufficient to justify the use of antibiotics in clinical practice. Treating laryngitis with conservative measures in the first instance is reasonable as it remains unclear that antibiotics are worthy and beneficial to individuals or populations.

Benefits of treatment
The effectiveness of antibiotic treatment for the common cold and for sore throat is covered in other Cochrane reviews (Arroll 2002; Del Mar 2004). Trials identified in these reviews included some participants with symptoms of acute laryngitis; conditions that affect the upper respiratory tract are not a single entity. As mentioned by Arroll et al, the review authors had to accept the clinical judgement of the trialists as to which participants were included in their URTI clinical trials (Arroll 2002).

Acute laryngitis may result from direct infection of the larynx, from irritation of the larynx due to coughing or to contact with infected secretions. Hence the supposition that acute laryngitis, along with other conditions that affect the upper respiratory tract, may not be related to one particular cause. Acute laryngitis is a self-limiting condition that usually varies in duration from three to eight days. Considering that the time taken from the start of hoarseness to the visit reported in the penicillin V trial was 3.6 (± 3.2) days, most of the first re-examinations would have been done five to seven days later, when symptoms were likely to have disappeared.

Other outcomes, like reduction of illness time and absolute reduction averaged over the whole illness, were not estimated in the present trials. These clinically important outcomes and other outcomes such as re-attendance or time off school or work are probably at least as important as those that were used. It is important to state that the use of the voice score attempts to qualify different signs in a quantitative manner. This implies some subjectivity in assessing each score. Furthermore, the trial authors assumed that any difference from zero to one, or from one to two, was equally relevant, and that the 10 (or 12) signs analysed were also considered equally important (Altman 1999).

Erythromycin is apparently effective at reducing voice disturbances as measured by participants after one week and cough after two weeks. The authors considered that these findings suggested the usefulness of antibiotics in a special subgroup of people for whom voice function was essential to their professional or social activities, but their use appeared to be discretionary rather than mandatory. We calculated the relative risk (RR) of 0.7 (95% CI 0.51 to 0.96, \( P = 0.034 \)) with a number needed to treat (NNT) of 4.5 for the subjective voice scores, considering total improvement as score ‘0’ and partial or no improvement as the sum of scores 1, 2 and 3; for the cough after two weeks the relative risk (RR) was 0.38 (95% CI 0.15 to 1, \( P = 0.058 \)).

The trials included only people with laryngitis who were admitted to the ear, nose and throat department, which may have lead to selection bias that favored participants with severe symptoms. People with this condition will often not go to hospital or consult a primary care practitioner (Cherry 2003; McAvoy 1994). Another concern was information not collected by the trial authors, such as the concomitant use of other medications that may alter the course of illness, for example, decongestants, heated or humidified air, voice rest, etc.

**Adverse effects of treatment**

Reporting on adverse effects of antibiotic use was irregular. Other studies described rare but severe adverse reactions, for example, hepatotoxicity, transient deafness and allergic reactions. Gastrointestinal symptoms represented the most frequent disturbance, occurring in 15% to 20% of participants on erythromycin. A significant number of drug interactions have also been reported (FDA 2004; Periti 1993).

**Natural history and microbiological findings**

Natural history and microbiological findings also supports the non-use of antimicrobials. Almost 20 years ago bacterial pathogens such as *M. catarrhalis* and *H. influenzae* were implicated in the genesis of upper respiratory tract infection (URT) and acute laryngitis. This conclusion was based on studies that confirmed that carriage of these pathogens is an uncommon feature in healthy adults (DiGiovanni 1987; Ejlertsen 1994; Schalen 1980).

The high nasopharyngeal isolation rates of *M. catarrhalis* (50% in both studies) and *H. influenzae* (15% in the penicillin V trial and 20% in the erythromycin trial) were apparently consistent with the use of antibiotics for this condition. However, after one week the voice profiles appeared to be essentially normalized in both antibiotic and placebo groups in both trials; no relevant differences were found in clinical symptoms assessed by the participants apart from the above described. These findings support the conclusion that the disorder is generally self-limiting, and maybe the majority of participants in the studies were suffering from viral URTIs.

Isolates of *M. catarrhalis* as reported by Schalen et al. in both trials were obtained from swabs placed in hematin agar tubes and inoculated onto hematin agar plates in 6% CO\(_2\) atmosphere as well as on to blood agar plates incubated anaerobically. *M. catarrhalis*, considered to be the principal bacterial pathogen related to acute laryngitis by the authors, was confirmed by fermentation reactions and by testing for species specific protein antigen. If no growth was found, the swabs kept in the hematin agar tubes were streaked and incubated as above.

Over the years the following criteria have been used to clearly identify *M. catarrhalis* from other bacterial species: gram stain (Verduin 2002); colony morphology; lack of pigmentation of the colony on blood agar; oxidase production; DNAase production; failure to produce acid from glucose, sucrose, fructose, lactose and maltose; growth at 22° C on nutrient agar; failure to grow on modified Thayer-Martin medium; and finally, reduction of nitrite and nitrate. Currently, the identity of this pathogen is best confirmed by positive reactions in at least three of the following tests, since none are 100% sensitive or specific by themselves: positive reaction for DNAase production, reduction of nitrate and nitrite and tributyrin hydrolysis (Catlin 1990). Furthermore, PCR tests are currently considered an unequalled diagnostic assay (Greiner 2003; Post 1995; Post 1996). Modern tests show that the methods used in the present trials to identify *M. catarrhalis* may have
introduced some misclassification in the percentage of isolates of this pathogen in participants with acute laryngitis.

By the years 1980 and 1990, the presence of B-lactamase in isolates of *M. catarrhalis* from the United States was 75% and 80% respectively. By 1990, B-lactamase was in over 90% of isolates from England and Scotland; and by 2003, in 87.4% of isolates from China (Fung 1991; Jorgensen 1990; Wallace 1990; Wang 2003). In a recent study conducted in the United States, most isolates of *M. catarrhalis* were resistant to amoxicillin, cefaclor, cefprozil, and trimethoprim/sulfamethoxazole; among *H. influenzae* isolates, 28.6% were B-lactamase positive (Jacobs 2004). In the present penicillin trial, 18% of *M. catarrhalis* isolated at the acute visit produced B-lactamase.

**Authors’ Conclusions**

Implications for practice

Definitive recommendations cannot be made since evidence is only available from two RCTs. Antibiotics appear to have no benefit in the treatment of acute laryngitis. Even if erythromycin could reduce voice disturbance at one week and cough at two weeks, measured subjectively, we consider these outcomes are not relevant in clinical practice. The implications for practice are that prescription of antibiotics should not be given in the first instance, as they will not objectively improve symptoms. Unnecessary antibiotic prescribing may contribute to increasing rates of antibiotic resistance. Antibiotics may not outweigh their costs or adverse effects. Currently, antibiotics are widely prescribed for patients with URTIs.

**Implications for research**

Although definitive recommendations cannot be made, since evidence is only available from two RCTs, it seems that there is no need of additional trials to examine antibiotics in acute laryngitis.

**Potential Conflict of Interest**

Edgar Ospina has contributed to this systematic review in a personal capacity and during his spare time. Most of his contributions were made before joining Novartis Colombia S.A. He is a medical advisor for this company, but there is no conflict of interest. Novartis Colombia S. A. does not assume responsibility for the statements contained therein.

**Acknowledgements**

Liz Dooley, Keryl Michener, Ruth Foxlee and the Cochrane Acute Respiratory Infections Group for their assistance. We also wish to thank the following people for commenting on this updated draft: Chapen Choprapawon, Rob Ware and Abigail Fraser.

**Sources of Support**

External sources of support

- No sources of support supplied

Internal sources of support

- No sources of support supplied

**References**

References to studies included in this review

Schalén 1985 *(published data only)*


Schalén 1993 *(published data only)*


References to studies excluded from this review

Schalén 1992


Additional references

Altman 1999


Arnold 2005


Arroll 2002


Berlin 1997

Berlin J. University of Pennsylvania Meta-analysis Blinding Study Group. Does blinding readers affect the results of meta-analysis?
McAuley 2000

McAvo 1994

McCaig 1995

McGregor 1995

Periti 1993

Post 1995

Post 1996

Postma 1998

Schalen 1980

Schalen 1988

Spiegel 2000

Steinman 2003a

Steinman 2003b

Sun 2006

Vaughan 1982

Verduin 2002

Wallace 1990

Wang 2003

WHO 2003

References to other published versions of this review
Reveiz 2005

* Indicates the major publication for the study

### TABLES

**Characteristics of included studies**

<table>
<thead>
<tr>
<th>Study</th>
<th>Schalén 1985</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methods</td>
<td>Randomized double blind controlled trial</td>
</tr>
</tbody>
</table>

Antibiotics for acute laryngitis in adults (Review)
Participants      Adult patients aged over eighteen with history of acute laryngitis defined as hoarseness associated with other symptoms of upper respiratory tract infection. Exclusion = patients with chronic relevant underlying diseases, symptoms of laryngitis for more than three weeks (chronic laryngitis) and antibiotic therapy within the preceding two weeks before diagnosis.
N = 100. No dropouts. Penicillin V n = 51
Placebo n = 49

Interventions
- Penicillin V 0.8 g b.i.d for five days
- Placebo

Outcomes
- Objective voice scores. No statistical difference were found between the two groups
- Symptoms judged by the patients. No differences were found between the two groups
- Bacteriological findings. The isolation rates of pathogens at the acute and at the follow up visits after one and two weeks, did not differ significantly between the two groups

Notes
Allocation concealment  B – Unclear

Study  Schalén 1993
Methods  Randomized double blind controlled trial
Participants  Adult patients aged over eighteen with history of acute laryngitis defined as hoarseness associated with other symptoms of upper respiratory tract infection. Exclusion = patients with chronic relevant underlying diseases, symptoms of laryngitis for more than two weeks, history of allergy or intolerance to erythromycin, pregnancy and antibiotic therapy within the preceding two weeks before diagnosis
N = 106. 7 dropouts. Penicillin V, n = 51; Placebo n = 49

Interventions
- Erythromycin 500 mg b.i.d for 5 days
- Placebo

Outcomes
- Objective voice scores. No statistical difference were found between the two groups
- Symptoms judged by the patients. At one week there were significant differences in the severity of reported vocal symptoms as judged by the patients, comparing the erythromycin and placebo groups (P = 0.042). At two weeks significantly fewer complaints of cough were reported by the erythromycin group
- Bacteriological findings. There was no difference between the two groups in the recovery rate of pathogens at two weeks

Notes
Allocation concealment  B – Unclear

Characteristics of excluded studies

Study  Schalén 1992
Reason for exclusion  A preliminary report of the erythromycin trial (Schalen 1993)

G R A P H S A N D O T H E R T A B L E S

This review has no analyses.

I N D E X T E R M S

Medical Subject Headings (MeSH)
Acute Disease; Anti-Bacterial Agents [*therapeutic use]; Erythromycin [therapeutic use]; Laryngitis [*drug therapy]; Penicillin V [therapeutic use]; Randomized Controlled Trials
## COVER SHEET

<table>
<thead>
<tr>
<th><strong>Title</strong></th>
<th>Antibiotics for acute laryngitis in adults</th>
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<tbody>
<tr>
<td><strong>Authors</strong></td>
<td>Reveiz L, Cardona AF, Ospina EG</td>
</tr>
<tr>
<td><strong>Contribution of author(s)</strong></td>
<td>Ludovic Reveiz (LR), Andres Cardona (AC) and Edgar Ospina (EO) initiated, designed and conducted the study. Ludovic Reveiz and Andres Cardona provided methodological perspectives and techniques for writing the protocol and the review. Edgar Ospina acted as an ombudsman for planned data extraction and statistical analysis, and revised the protocol and the review. Carlos Granados and Johanna Osorio withdrew from the review because of personal and professional commitments. An update was performed in December 2006. Ludovic Reveiz and Andrés Cardona evaluated the titles and abstracts of the search. All the review authors contributed to manuscript revision.</td>
</tr>
<tr>
<td><strong>Issue protocol first published</strong></td>
<td>2004/2</td>
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<tr>
<td><strong>Review first published</strong></td>
<td>2005/1</td>
</tr>
<tr>
<td><strong>Date of most recent amendment</strong></td>
<td>16 February 2007</td>
</tr>
<tr>
<td><strong>Date of most recent SUBSTANTIVE amendment</strong></td>
<td>31 January 2007</td>
</tr>
<tr>
<td><strong>What's New</strong></td>
<td>We updated the searches in December 2006. There were no new included or excluded trials to add to the review.</td>
</tr>
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<td><strong>Date new studies sought but none found</strong></td>
<td>18 December 2006</td>
</tr>
<tr>
<td><strong>Date new studies found but not yet included/excluded</strong></td>
<td>Information not supplied by author</td>
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<tr>
<td><strong>Date new studies found and included/excluded</strong></td>
<td>24 June 2004</td>
</tr>
<tr>
<td><strong>Date authors’ conclusions section amended</strong></td>
<td>Information not supplied by author</td>
</tr>
</tbody>
</table>
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