ClinicalEvidence

Sore throat

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ABSTRACT

INTRODUCTION: About 10–30% of people present to primary healthcare services with sore throat each year. The causative organisms of sore throat may be bacteria (most commonly Streptococcus) or viruses (typically rhinovirus), although it is difficult to distinguish bacterial from viral infections clinically. METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical questions: What are the effects of interventions to reduce symptoms of acute infective sore throat? What are the effects of interventions to prevent complications of acute infective sore throat? We searched: Medline, Embase, The Cochrane Library and other important databases up to May 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 eight 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: antibiotics, corticosteroids, non-steroidal anti-inflammatory drugs, paracetamol, and probiotics.

QUESTIONS

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What are the effects of interventions to prevent complications of acute infective sore throat? 7

INTERVENTIONS

TREATING SYMPTOMS

Likely to be beneficial

NSAIDs 3

Paracetamol (acetaminophen) 3

Trade off between benefits and harms

Antibiotics 4

Corticosteroids 4

Unknown effectiveness

Probiotics 6

PREVENTING COMPLICATIONS

Trade off between benefits and harms

Antibiotics 7

Covered elsewhere in Clinical Evidence

Acute bronchitis

Acute otitis media

Acute sinusitis

Common cold

Tonsillitis

Key points

- Sore throat is an acute upper respiratory tract infection that affects the respiratory mucosa of the throat.
- About 10% of people present to primary healthcare services with sore throat each year.

  The causative organisms of sore throat may be bacteria (most commonly *Streptococcus*) or viruses (typically rhinovirus), but it is difficult to distinguish bacterial from viral infections clinically.
- NSAIDs may reduce the pain of sore throat at 24 hours or less, and at 2−5 days.

  NSAIDs are associated with gastrointestinal and renal adverse effects.
- Paracetamol seems to effectively reduce the pain of acute infective sore throat after a single dose, or regular doses over 2 days.
- Antibiotics can reduce the proportion of people with symptoms associated with sore throat at 3 days.

  Reduction in symptoms seems greater for people with positive throat swabs for *Streptococcus* than for people with negative swabs.

  Antibiotics are generally associated with adverse effects such as nausea, rash, vaginitis, and headache, and widespread usage may lead to bacterial resistance.
- Antibiotics may also reduce suppurative and non-suppurative complications of group A beta haemolytic streptococcal pharyngitis, although non-suppurative complications are rare in industrialised countries.
- Corticosteroids added to antibiotics may reduce the severity of pain from sore throat in children and adults compared with antibiotics alone.

  Most studies used a single dose of corticosteroid.

  However, data from other disorders suggest that long term use of corticosteroids is associated with serious adverse effects.

- Super-colonisation with *Streptococcus* isolated from healthy individuals apparently resistant to infections from *Streptococcus* may reduce recurrence of sore throat, although there is currently no evidence to suggest it may treat symptoms of acute sore throat.

DEFINITION

Sore throat is an acute upper respiratory tract infection that affects the respiratory mucosa of the throat. Since infections can affect any part of the mucosa, it is often arbitrary whether an acute upper respiratory tract infection is called "sore throat" ("pharyngitis" or "tonsillitis"), "common cold", "sinusitis", "otitis media", or "bronchitis" (see figure 1, p 9). Sometimes, all areas are affected (simultaneously or at different times) in one illness. In this review, we aim to cover people whose principal presenting symptom is sore throat. This may be associated with headache, fever, and general malaise. Suppurative complications include acute otitis media (most commonly), acute sinusitis, and peritonsillar abscess (quinsy). Non-suppurative complications include acute rheumatic fever and acute glomerulonephritis.

INCIDENCE/ PREVALENCE

There is little seasonal fluctuation in sore throat. About 10% of the Australian population present to primary healthcare services annually with an upper respiratory tract infection consisting predominantly of sore throat. [1] This reflects about a fifth of the overall annual incidence. [1] However, it is difficult to distinguish between the different types of upper respiratory tract infection. [2] A Scottish mail survey found that 31% of adult respondents reported a severe sore throat in the previous year, for which 38% of these people visited a doctor. [3]

AETIOLOGY/ RISK FACTORS

The causative organisms of sore throat may be bacteria (*Streptococcus*, most commonly group A beta haemolytic, but sometimes *Haemophilus influenzae*, *Moraxella catarrhalis*, and others) or viruses (typically rhinovirus, but also coronavirus, respiratory syncytial virus, metapneumovirus, Epstein–Barr, and others). It is difficult to distinguish bacterial from viral infections clinically. Features thought to indicate *Streptococcus* infection are: fever greater than 38.5 °C; exudate on the tonsils; anterior neck lymphadenopathy; and absence of cough. [4] Sore throat can be caused by processes other than primary infections, including GORD, physical or chemical irritation (e.g. from nasogastric tubes, or smoke), and occasionally hay fever. However, we consider only primary infections in this review.

PROGNOSIS

The untreated symptoms of sore throat disappear by 3 days in about 40% of people, and untreated fevers in about 85%. [5] By 1 week, 85% of people are symptom free. This natural history is similar in *Streptococcus*-positive, -negative, and untested people,

AIMS OF INTERVENTION

To relieve symptoms and to prevent suppurative and non-suppurative complications of sore throat.

OUTCOMES

Reduction in severity and duration of symptoms (sore throat pain, general malaise, headache, and fever); reduction in suppurative complications (acute otitis media, acute sinusitis, and quinsy) and non-suppurative complications (acute rheumatic fever, and acute glomerulonephritis); time off work or school; patient satisfaction; healthcare utilisation; adverse effects of treatments.

METHODS

BMJ Clinical Evidence search and appraisal May 2007. The following databases were used to identify studies for this systematic review: Medline 1966 to May 2007, Embase 1980 to May 2007, and The Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Clinical Trials 2007, Issue 2. Additional searches were carried out using these websites: NHS Centre for Reviews and Dissemination (CRD) — for Database of Abstracts of Reviews of Effects (DARE) and Health Technology Assessment (HTA), Turning Research into Practice (TRIP), and National Institute for Health and Clinical Excellence (NICE). We also searched for retractions of studies included in the review. Abstracts of the studies retrieved from the initial search were assessed by an information specialist. Selected studies were then sent to the author for additional assessment, using pre-determined criteria to identify relevant studies. Study design criteria included: systematic reviews and RCTs. Open trials were included if the outcomes were objective (otherwise all studies described as "open", "open label", or "non-blinded" were excluded). The minimum number of individuals in each trial was 20. Size of follow-up was 80% or more. There was no minimum length of follow-up. 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 added to the reviews as required. We excluded RCTs that only provided data about bacteriological studies of the throat, because bacteriological cure is not a clinically useful outcome for spontaneously remitting illness. We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 10).

QUESTION **What are the effects of interventions to reduce symptoms of acute infective sore throat?**

OPTION ANALGESICS TO REDUCE SYMPTOMS OF ACUTE INFECTIVE SORE THROAT

Symptom severity
Compared with placebo Paracetamol is more effective than placebo at reducing sore throat pain (moderate-quality evidence).

Note
We found no direct information about other analgesics in the treatment of people with sore throat.

For GRADE evaluation of interventions for sore throat, see table, p 10 .

Benefits: We found one systematic review (search date 1999, 3 RCTs, 312 people with acute moderate to severe sore throat for up to 4 days) comparing paracetamol (acetaminophen) versus placebo. [6] All of the RCTs found that paracetamol significantly reduced sore throat pain compared with placebo. Two RCTs (81 adults, 77 children) identified by the review found that a single dose of paracetamol significantly reduced mean sore throat pain score at 2–3 hours compared with placebo (50% greater reduction than placebo in 1 RCT; P less than 0.01; 31% greater reduction than placebo in the other; P less than 0.05). The third RCT (154 children) identified by the review found that paracetamol three times daily significantly reduced sore throat pain score after 2 days (34% greater reduction than placebo; P less than 0.01). One subsequent RCT (241 adults with throat pain score of 7 or more measured on a 0–10 scale) compared a single dose of paracetamol versus placebo. [7] Pain reduction was measured on an 8-point scale (where 0 = no relief to 7 = complete relief). The RCT found that, compared with placebo, paracetamol significantly reduced pain from 15 minutes to 6 hours post dose (15 minutes: results presented graphically, P less than 0.03; 6 hours: total pain relief scores, 793 with paracetamol v 631 with placebo, P less than 0.05). It did not report outcomes beyond 6 hours. [7] We found no RCTs of other analgesics.

Harms: The review gave no information on adverse effects. [6] The subsequent RCT stated that there were no serious adverse events reported, and that no adverse events were assessed as being related to study treatment. [7]

Comment: An update of the review [6] is underway. [8]

OPTION NSAIDS TO REDUCE SYMPTOMS OF ACUTE INFECTIVE SORE THROAT

Symptom severity
Compared with placebo NSAIDs are more effective than placebo at reducing sore throat symptoms at 24 hours to 5 days (moderate-quality evidence).

Adverse effects
NSAIDs are associated with gastrointestinal and renal adverse effects.

For GRADE evaluation of interventions for sore throat, see table, p 10 .

Benefits: We found one systematic review (search date 1999, 12 RCTs, 1189 people with acute sore throat for up to 5 days, severity unclear) comparing NSAIDs versus placebo. [6] The review did not perform a meta-analysis. Seven RCTs (492 people) identified by the review assessed the effects of NSAIDs (including 1 RCT of oral aspirin and 1 RCT of aspirin gum) over 24 hours or less. All of the RCTs found that NSAIDs significantly reduced throat pain compared with placebo. The range of significant improvements in throat pain compared with placebo ranged from 25% to 75% (P less than 0.05 in all RCTs). Six RCTs (697 people) identified by the review assessed the effects of NSAIDs over more than 24 hours. All of the RCTs found that NSAIDs significantly reduced symptoms (primarily throat pain) over 2–5 days. The range of significant improvements in symptoms compared with placebo ranged from 33% to 93% (P less than 0.05 in all RCTs). In the RCTs pain was assessed using a variety of visual analogue and scoring systems. [6]

Harms: The review gave no information on adverse effects. [6] However, data from systematic reviews in people with other disorders suggested that NSAIDs were associated with gastrointestinal and renal adverse effects (see review on NSAIDs).

Comment: An update of the review [6] is underway. [8]

Clinical guide:
NSAIDs seem effective, but have potential for adverse effects. Aspirin is best avoided in children under 15 years of age owing to the rare risk of Reye's syndrome.

OPTION ANTIBIOTICS TO REDUCE SYMPTOMS OF ACUTE INFECTIVE SORE THROAT

Symptom severity
Compared with placebo Antibiotics are more effective at 3 days than placebo at reducing sore throat and headache, particularly in people with positive throat swabs for Streptococcus (moderate-quality evidence).

Antibiotics plus corticosteroids compared with placebo Antibiotics plus corticosteroids may be more effective at improving short-term pain relief in children, adolescents, and adults with sore throat, compared with placebo (very-low quality evidence).

Note
We found no direct information about the effects of antibiotics in reducing the severity of sore-throat symptoms. Antibiotics may increase the risk of nausea, vomiting, rash, headache, and vaginitis. Widespread antibiotic use may lead to bacterial resistance to antibiotics.

For GRADE evaluation of interventions for sore throat, see table, p 10 .

Benefits: We found one systematic review (search date 2006, 27 randomised or quasi-randomised trials, 12,835 people with sore throat, severity unclear) comparing antibiotics versus placebo. [5] The review found that antibiotics significantly reduced the proportion of people with symptoms of sore throat at 3 days compared with placebo (15 trials; 1006/2066 [49%] with antibiotics *v* 1031/1555 [66%] with placebo; RR 0.68, 95% CI 0.59 to 0.79). [5] The reduction in the proportion of people with symptoms of sore throat with antibiotics compared with placebo remained significant at 6–8 days (13 trials; 246/1839 [13%] with antibiotics *v* 206/1135 [18%] with placebo; RR 0.49, 95% CI 0.32 to 0.76). The review estimated that this represents an average shortening of symptoms of sore throat by about 16 hours for the first week. [5] The review found no significant difference between antibiotics and placebo in the proportion of people with fever at 3 days (7 trials, 1334 people, RR 0.71, 95% CI 0.45 to 1.10). It found that antibiotics significantly reduced the proportion of people with headache at 3 days compared with placebo (3 trials; 122/552 [22%] with antibiotics *v* 147/359 [41%] with placebo; RR 0.47, 95% CI 0.38 to 0.58). The review found limited evidence from indirect comparisons that, in people with throat swabs positive for *Streptococcus*, the absolute and relative reduction in the proportion of people with sore throat symptoms at 3 days was greater than in people with negative swabs (positive swabs: 11 trials; 471/1073 [44%] with antibiotics *v* 544/766 [71%] with placebo; RR 0.58, 95% CI 0.48 to 0.71; negative swabs: 6 trials; 262/458 [57%] with antibiotics *v*202/278 [73%] with placebo; RR 0.78, 95% CI 0.63 to 0.97). The review also assessed the incidence of streptococcal complications (see benefits of antibiotics for prevention of complications of acute sore throat, p 7). We found no systematic review or RCTs that assessed severity of sore throat symptoms.

Harms: The systematic review gave no information on the adverse effects associated with antibiotic use. [5] However, data from systematic reviews in people with other disorders suggested that antibiotics were associated with nausea, vomiting, headache, skin rash, and vaginitis (see reviews on acute bronchitis, and acute otitis media in children).

Comment: Severely unwell people were not included in the RCTs included in the systematic review. [5] Consequently, these findings may not apply to those people.

Clinical guide:
Widespread antibiotic use may lead to bacterial resistance to antibiotics (see review on acute bronchitis).

OPTION CORTICOSTEROIDS TO REDUCE SYMPTOMS OF ACUTE INFECTIVE SORE THROAT

Symptom severity
Compared with placebo Oral dexamethasone is more effective than placebo at reducing time to initial pain relief, and duration of throat pain, in children and adolescents with moderate to severe sore throat, but without group A beta haemolytic streptococcal infection (moderate-quality evidence).

Corticosteroids plus antibiotics compared with placebo Corticosteroids plus antibiotics may be more effective than placebo at improving short-term pain relief in children, adolescents, and adults with sore throat (very low-quality evidence).

Note

We found no direct information about adverse effects of corticosteroids in people with sore throat. Corticosteroids have been associated with serious adverse effects (although possibly only after long-term use).

For GRADE evaluation of interventions for sore throat, see table, p 10 .

Benefits:

Corticosteroids versus placebo:

We found one systematic review (search date 1999), which identified no RCTs of corticosteroids alone in people with sore throat. [6] We found one subsequent RCT, which randomised children and adolescents with moderate to severe sore throat (defined as odynophagia or dysphagia, plus pharyngeal erythema or swelling, plus a score at least 0.75 on a pain scale ranging from 0 = no pain to 1 = maximum pain) to either oral dexamethasone (0.6 mg/kg up to 10 mg daily) or placebo. [9] People who were subsequently found to be group A beta haemolytic streptococci (GABHS) positive received antibiotics and were analysed separately (see corticosteroids plus antibiotics, below). In GABHS-negative people, dexamethasone significantly reduced time to initial and complete pain relief compared with placebo (55 GABHS-negative children aged 5–18 years with moderate to severe sore throat; time to initial pain relief: 8.7 hours with dexamethasone *v* 24.0 hours with placebo; mean difference 15.3 hours, 95% CI 6.4 hours to 24.1 hours; P = 0.001; time to complete pain relief: 37.9 hours with dexamethasone *v* 70.8 hours with placebo; mean difference 32.9 hours, 95% CI 11.3 hours to 54.4 hours; P = 0.006).

Corticosteroids plus antibiotics versus antibiotics alone:

We found one systematic review (search date 1999, 1 RCT), [6] one additional RCT [10] and three subsequent RCTs. [9] [11] [12] The review [6] identified one RCT (51 adults with severe sore throat infection) comparing adding corticosteroid injection (dexamethasone 10 mg) to antibiotics versus adding placebo over 24 hours. [13] It found that adding dexamethasone significantly reduced sore throat pain at 24 hours (mean improvement in pain measured on a 6-point visual analogue scale: 1.8 with adding dexamethasone *v* 1.2 with adding placebo; P less than 0.05). It also found limited evidence that, compared with placebo, adding dexamethasone significantly reduced the duration of throat pain (completer analysis in 50% of people followed up for 7 days; mean time to being pain free reduced from 35 hours to 15 hours; P less than 0.02). The additional RCT (92 people aged 14–65 years) compared a single dose of intramuscular betamethasone plus antibiotics versus intramuscular placebo plus antibiotics. [10] Pain scores were measured by a visual analogue scale (0–10 cm). Follow-up at 24 hours and 48 hours was by telephone. The RCT found that betamethasone plus antibiotics significantly reduced pain compared with antibiotics alone at 1 day (decrease in pain score from baseline: 5.5 with betamethasone plus antibiotics *v* 3.9 with antibiotics alone; P = 0.004), and found no significant difference between groups at 2 days (decrease in pain score from baseline: 6.8 *v* 6.2; P = 0.28). [10] Scores were similar in those with and without GABHS. However, the number of participants in each subgroup was small. The RCT found no significant difference between groups in the number of days of school or work missed (0.4 days with betamethasone plus antibiotics *v* 0.7 days with placebo, P = 0.19). The RCT did not report clinical symptoms other than pain. However, participants were allowed to take additional pain medication (for example, ibuprofen, paracetamol) and the use of this pain medication was not recorded, which may have confounded the results. The first subsequent RCT found that, in children with moderate to severe sore throat (see above for details) who tested positive for GABHS, oral dexamethasone plus antibiotics (penicillin, amoxicillin, or azithromycin) significantly reduced the time to initial pain relief compared with placebo plus antibiotics (70 GABHS-positive children aged 5–18 years with moderate to severe sore throat; time to initial pain relief: 9.7 hours with dexamethasone *v* 14.8 hours with placebo; mean difference 5.1 hours, 95% CI 0.5 hours to 10.8 hours; P value not reported). [9] However, it found no significant difference between treatments in time to complete pain relief (21.9 hours with dexamethasone *v* 28.2 hours with placebo; mean difference +6.3 hours, 95% CI –6.7 hours to +19.4 hours; P value not reported). The second subsequent RCT (118 people aged 15–57 years) compared a single dose of intramuscular dexamethasone, a single oral dose of dexamethasone, and placebo. [11] All participants also received antibiotics. Pain was assessed by visual analogue scale score (0 = no pain to 10 = worst pain imaginable). Follow-up was by telephone. The RCT found that both preparations of dexamethasone significantly reduced pain at 12 hours compared with placebo (median change in pain from baseline: 4 with intramuscular dexamethasone *v* 3 with oral dexamethasone *v* 2 with placebo; intramuscular dexamethasone *v* placebo, P less than 0.001, oral dexamethasone *v* placebo, P = 0.002), but found no significant difference in pain among groups at 24 hours (median change: 5 *v* 5 *v* 4; between-group analysis, P = 0.097). [11] The third subsequent RCT (90 people age 4–21 years, all with GABHS) compared a single oral dose of dexamethasone, a single oral dose of dexamethasone daily for 3 days, and placebo. [12] All participants had antibiotics. Symptoms were assessed with a validated visual tool which used a 6-point scale, and the primary outcomes were: time to improvement or resolution in throat pain (score 0 or 1 on the 6 point scale); return to general health; and return to normal activity. Follow-up was by telephone. The RCT found a significant difference among groups in days to improvement of throat pain, general condition, and activity level (median time to improvement; throat pain: 2 days with single dose of dexamethasone *v* 1 day with 3 day regimen of dexamethasone *v* 2 days with

placebo, across-group analysis P = 0.0025; general condition: 1 day with single dose of dexamethasone *v* 1 day with 3-day regimen of dexamethasone *v* 2 days with placebo, across-group analysis P = 0.001; activity level: 1 day with single dose of dexamethasone *v* 1 day with 3-day regimen of dexamethasone *v* 2 days with placebo, across-group analysis P less than 0.001; all results presented graphically). The RCT reported that, after controlling for multiple comparisons, the 3-day regimen of dexamethasone significantly improved sore throat pain compared with placebo (Cox proportional hazards; HR 2.12, 95% CI 1.23 to 3.56), while the single-dose dexamethasone regimen did not reach statistical significance compared with placebo (Cox proportional hazards; HR 1.72, 95% CI 1.0 to 2.98). [12]

Harms:

Corticosteroids versus placebo:
The subsequent RCT gave no information on adverse effects. [9] Potential harms of oral corticosteroids are covered elsewhere in *BMJ Clinical Evidence* (see review on asthma).

Corticosteroids plus antibiotics versus antibiotics alone:
The review gave no information on adverse effects. [6] The additional RCT reported that the most frequently reported complication was pain at the injection site (no numerical data reported). [10] The three subsequent RCTs gave no information on adverse effects. [9] [11] [12] Data from systematic reviews in people with other disorders suggest that corticosteroids may be associated with serious adverse effects, although possibly only after long term use.

Comment:

More RCTs are needed. An update of the review [6] is underway. [8]

Clinical guide:
Based on limited evidence, a single dose of dexamethasone seems to reduce pain earlier than placebo, with or without evidence of streptococcal infection.

OPTION PROBIOTICS TO REDUCE SYMPTOMS OF ACUTE INFECTIVE SORE THROAT

Recurrence
Compared with placebo Super-colonisation with Streptococcus is effective at reducing recurrent sore throats at 2–3 months compared with placebo (moderate-quality evidence).

Note
We found no direct information about other probiotics, or about the effects of probiotics on the symptoms of acute sore throat.

For GRADE evaluation of interventions for sore throat, see table, p 10 .

Benefits:

We found one systematic review [6] (search date 1999, 2 RCTs) [14] [15] and one subsequent RCT [16] comparing super-colonisation with *Streptococcus* grown from a child resistant to infections from *Streptococcus* versus placebo (see comment below). We found no RCTs of other probiotics. The first RCT identified by the review (36 people aged 5–40 years with culture-confirmed recurrence of sore throat, all taking antibiotics) found that super-colonisation with *Streptococcus* significantly reduced the proportion of people who had recurrence of streptococcal sore throat over 3 months compared with placebo (1/17 [6%] with super-colonisation *v* 11/19 [59%] with placebo; P less than 0.001). [14] The second RCT (130 people aged 3–59 years with culture-confirmed recurrence of sore throat, all taking antibiotics) identified by the review found no significant difference between super-colonisation with *Streptococcus* and placebo in the proportion of people who had recurrence of streptococcal sore throat over 8 weeks, although fewer people using bacterial spray with *Streptococcus* had recurrence (22% with super-colonisation *v* 38% with placebo; P = 0.064). [15] The subsequent RCT (342 people, all treated with antibiotics) found that super-colonisation with *Streptococcus* significantly reduced sore throat recurrence over a mean of 3 months compared with placebo (proportion with recurrent sore throat: 36/189 [19%] with super-colonisation *v* 28/93 [30%] with placebo; P = 0.04). [16] We found no RCTs examining the effects of probiotics on the symptoms of acute sore throat.

Harms:

Two of the RCTs found no adverse effects associated with *Streptococcus* bacteriological spray. [14] [15] The subsequent RCT found no significant difference in adverse-event rates between *Streptococcus* super-colonisation and placebo (36% with super-colonisation *v* 33% with placebo; reported as equally tolerated; P value not reported). [16] However, the authors suggested that the high rates of apparent adverse events found in both study arms were likely to be due to the condition being treated.

Comment:

Super-colonisation with *Streptococcus* isolated from healthy individuals apparently resistant to infections from *Streptococcus* is available only experimentally. An update of the review [6] is underway. [8]

Clinical guide:
Probiotics may yet prove useful to reduce recurrence; there is no suggestion that they will improve current symptoms of acute sore throat.

QUESTION What are the effects of interventions to prevent complications of acute infective sore throat?

OPTION ANTIBIOTICS TO PREVENT COMPLICATIONS OF ACUTE INFECTIVE SORE THROAT

Prevention of complications
Compared with placebo Antibiotics are more effective than placebo at reducing suppurative and non-suppurative complications of group A beta haemolytic streptococcal pharyngitis (high-quality evidence).

Note
In industrialised countries, non-suppurative complications are extremely rare. Antibiotics increase the risk of adverse events, including gastrointestinal upset, rash, and vaginitis. Widespread antibiotic use may lead to bacterial resistance to antibiotics.

For GRADE evaluation of interventions for sore throat, see table, p 10 .

Benefits:

We found one systematic review (search date 2006, 27 randomised or quasi-randomised trials, 12,835 people with sore throat, severity unclear) comparing antibiotics versus placebo to prevent complications of sore throat infection. [5] (see antibiotics to reduce symptoms of acute sore throat, p 4).

Acute otitis media:
The review found that antibiotics significantly reduced acute otitis media at 14 days compared with placebo, although it was a rare complication in the trials identified (11 trials; 11/2325 [0.5%] with antibiotics *v* 28/1435 [2.0%] with placebo; RR 0.30, 95% CI 0.15 to 0.58). [5]

Acute rheumatic fever:
The review found that antibiotics significantly reduced the proportion of people who had developed acute rheumatic fever at 2 months compared with placebo (16 trials: 37/5656 [0.7%] with antibiotics *v* 74/4445 [2%] with placebo; RR 0.27, 95% CI 0.12 to 0.60; see comment below). [5] The incidence of acute rheumatic fever has declined with time. The 111 cases of acute rheumatic fever assessed by the review all occurred in 10 trials undertaken between 1950 and 1961; there were no cases in the remaining five trials undertaken between 1987 and 2000.

Acute glomerulonephritis:
Too few people had acute glomerulonephritis for there to be a detectable possible protective effect of antibiotics (10 trials, 5147 people: 0/2927 [0%] with antibiotics *v* 2/2220 [0.1%] with placebo; RR 0.22, 95% CI 0.02 to 2.08; see comment below).

Acute sinusitis:
The review found no significant difference between antibiotics and placebo in the proportion of people who had developed acute sinusitis at 14 days, but there may have been too few events to detect a clinically important difference (8 trials: 4/1545 [0.3%] with antibiotics *v* 4/842 [0.5%] with placebo; RR 0.48, 95% CI 0.08 to 2.76).

Peritonsillar abscess (quinsy):
The review found that antibiotics significantly reduced peritonsillar abscess at 2 months compared with placebo (8 trials: 2/1438 [0.1%] with antibiotics *v* 23/995 [2.0%] with placebo; RR 0.15, 95% CI 0.05 to 0.47).

Harms:

The systematic review gave no information on adverse effects associated with the use of antibiotics. [5] However, data from systematic reviews in people with other disorders suggested that antibiotics were associated with nausea, vomiting, headache, skin rash, and vaginitis (see reviews on acute bronchitis, and acute otitis media in children).

Comment:

Acute rheumatic fever and acute glomerulonephritis associated with sore throat infection may be related to host antibodies to *Streptococcus* cross-reacting with host tissue in the heart and kidney. See also comment on antibiotics under treatments for sore throat, p 4 . In some populations, rheumatic fever may follow streptococcal skin infections or even non-streptococcal infections. [17] Best practice may be to advise antibiotics to treat sore throats only for those individuals or populations known to be at high absolute risk of rheumatic fever — for example, some Maori children in New Zealand. Widespread antibiotic use may lead to bacterial resistance to antibiotics (see review on acute bronchitis).

Clinical guide:
It seems reasonable to treat suppurative complications only if they arise. Antibiotics seem justified to prevent non-suppurative complications only in communities where the prevalence of non-suppurative complications remains high.

GLOSSARY

High-quality evidence Further research is very unlikely to change our confidence in the estimate of effect
Moderate-quality evidence Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Very low-quality evidence Any estimate of effect is very uncertain.

SUBSTANTIVE CHANGES

Analgesics to reduce symptoms of acute infective sore throat One RCT of paracetamol added; [7] benefits and harms data enhanced, categorisation of paracetamol as Likely to be beneficial unchanged.
Antibiotics to prevent complications of acute infective sore throat One previously included systematic review updated; [5] benefits and harms data enhanced, categorisation unchanged (Trade off between benefits and harms).
Antibiotics to reduce symptoms of acute infective sore throat One previously included systematic review updated; [5] benefits and harms data enhanced, categorisation unchanged (Trade off between benefits and harms).
Corticosteroids to reduce symptoms of acute infective sore throat One additional RCT [10] and two subsequent RCTs added; [12] [11] benefits and harms data enhanced, categorisation unchanged (Trade off between benefits and harms).

REFERENCES

1. Del Mar C, Pincus D. Incidence patterns of respiratory illness in Queensland estimated from sentinel general practice. *Aust Fam Physician* 1995;24:625–9,32.[PubMed]
2. Benediktsdottir B. Upper airway infections in preschool children – frequency and risk factors. *Scand J Prim Health Care* 1993;11:197–201.[PubMed]
3. Hannaford PC, Simpson JA, Bisset AF, et al. The prevalence of ear, nose and throat problems in the community: results from a national cross-sectional postal survey in Scotland. *Fam Pract* 2005;22:227–233.[PubMed]
4. Dagnelie CF, Bartelink ML, van der Graaf Y, et al. Towards a better diagnosis of throat infections (with group A beta-hemolytic streptococcus) in general practice. *Br J Gen Pract* 1998;48:59–62.
5. Del Mar CB, Glasziou PP, Spinks AB. Antibiotics for sore throat. In: The Cochrane Library, Issue 2, 2007. Chichester, UK: John Wiley & Sons, Ltd. Search date 2006; primary sources Medline, The Cochrane Library, and hand searches of reference lists of relevant articles.
6. Thomas M, Del Mar C, Glaziou P. How effective are treatments other than antibiotics for acute sore throat? *Br J Gen Pract* 2000;50:817–820. Search date 1999; primary sources Medline and Cochrane Controlled Trials Registry.[PubMed]
7. Burnett I, Schachtel B, Sanner K, et al. Onset of analgesia of a paracetamol tablet containing sodium bicarbonate: A double-blind, placebo-controlled study in adult patients with acute sore throat. *Clin Ther* 2006;28:1273–1278.
8. Francis D, Del Mar C, Thomas M, et al. Non-antibiotic treatments for sore throat (Protocol for a Cochrane Review). In: The Cochrane Library, Issue 2, 2007. Chichester, UK: John Wiley & Sons, Ltd.
9. Olympia RP, Khine H, Avner JR. Effectiveness of oral dexamethasone in the treatment of moderate to severe pharyngitis in children. *Arch Pediatr Adolesc Med* 2005;159:278–282.[PubMed]
10. Marvez-Valls EG, Ernst AA, Gray J, et al. The role of betamethasone in the treatment of acute exudative pharyngitis. *Acad Emerg Med* 1998;5:567–572.
11. Wei JL, Kasperbauer JL, Weaver AL, et al. Efficacy of single-dose dexamethasone as adjuvant therapy for acute pharyngitis. *Laryngoscope* 2002;112:87–93.
12. Niland ML, Bonsu BK, Nuss KE, et al. A pilot study of 1 versus 3 days of dexamethasone as add-on therapy in children with streptococcal pharyngitis. *Pediatr Infect Dis J* 2006;25:477–481.
13. O'Brien JF, Meade JL, Falk JL. Dexamethasone as adjuvant therapy for severe acute pharyngitis. *Ann Emerg Med* 1993;22:212–215.[PubMed]
14. Roos K, Holm SE, Grahn E, et al. Alpha-streptococci as supplementary treatment of recurrent streptococcal tonsillitis: a randomized placebo-controlled study. *Scand J Infect Dis* 1993;25:31–35.[PubMed]
15. Roos K, Holm SE, Grahn-Hakansson E, et al. Recolonization with selected alpha-streptococci for prophylaxis of recurrent streptococcal pharyngotonsillitis – a randomized placebo-controlled multicentre study. *Scand J Infect Dis* 1996;28:459–462.[PubMed]
16. Falck G, Grahn-Hakansson E, Holm SE, et al. Tolerance and efficacy of interfering alpha streptococci in recurrence of streptococcal pharyngotonsillitis: a placebo-controlled study. *Acta Otolaryngol* 1999;119:944–948.[PubMed]
17. McDonald M, Currie BJ, Carapetis JR. Acute rheumatic fever: a chink in the chain that links the heart to the throat? *Lancet Infect Dis* 2004;4:240–245. [PubMed]

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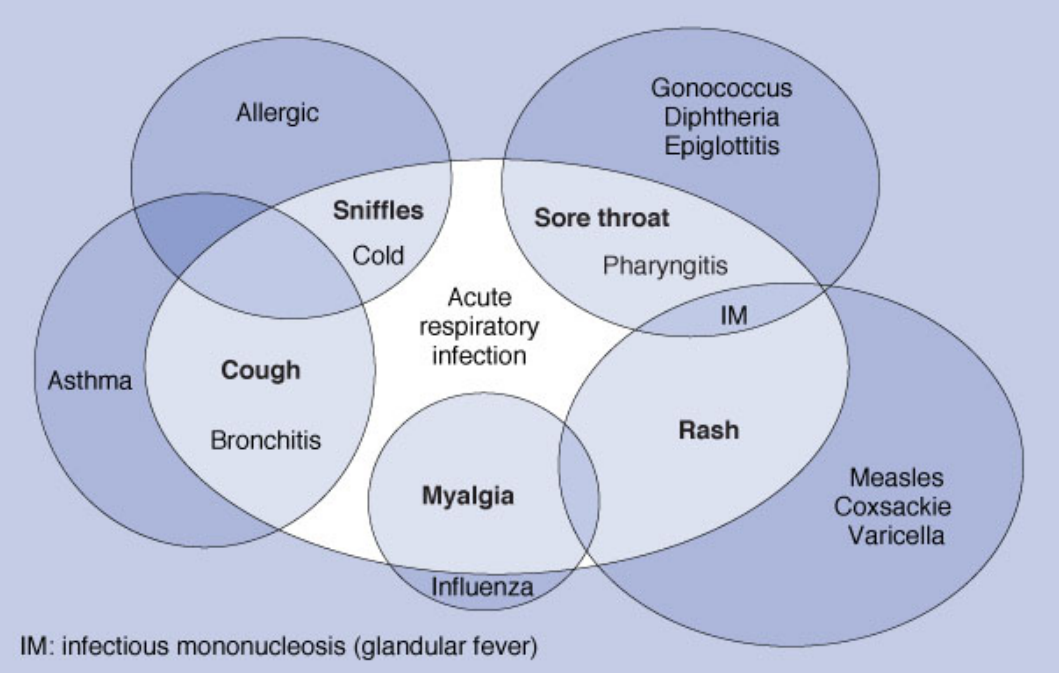

FIGURE 1 **Confusion and overlap in the classification of acute respiratory infections. IM, infectious mononucleosis (glandular fever).**

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TABLE GRADE evaluation of interventions for sore throat

Important outcomes	Symptom severity, recurrence, adverse effects								
Number of studies (participants)	**Outcome**	**Comparison**	**Type of evidence**	**Quality**	**Consistency**	**Directness**	**Effect size**	**GRADE**	**Comment**
What are the effects of interventions to reduce symptoms of acute infective sore throat?									
4 (553) [6] [7]	Symptom severity	Analgesics *v* placebo	4	–1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
13 (1189) [6]	Symptom severity	NSAIDs *v* placebo	4	–1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
27 (12,835) [5]	Symptom severity	Antibiotics *v* placebo	4	0	0	–1	0	Moderate	Directness point deducted for narrow inclusion criteria
1 (55) [6]	Symptom severity	Corticosteroids *v* placebo	4	–1	0	0	0	Moderate	Quality point deducted for sparse data
5 (421) [9] [10] [11] [12] [13]	Symptom severity	Corticosteroids plus antibiotics *v* antibiotics	4	–1	–1	–1	0	Very low	Quality point deducted for incomplete reporting of results. Consistency point deducted for conflicting results. Directness point deducted for inclusion of other drug interventions
3 (448) [14] [15] [16]	Recurrence rates	Probiotics *v* placebo	4	0	–1	0	0	Moderate	Consistency point deducted for conflicting results
What are the effects of interventions to prevent complications of acute infective sore throat?									
11 (3760) [5]	Prevention of complications (AOM)	Antibiotics *v* placebo	4	0	0	0	+1	High	Effect size point added for RR less than 0.5
16 (10,101) [5]	Prevention of complications (acute rheumatic fever)	Antibiotics *v* placebo	4	0	0	0	+1	High	Effect size point added for RR less than 0.5
10 (5147) [5]	Prevention of complications (glomerulonephritis)	Antibiotics *v* placebo	4	0	0	0	0	High	
8 (2387) [5]	Prevention of complications (acute sinusitis)	Antibiotics *v* placebo	4	0	0	0	0	High	
8 (2433) [5]	Prevention of complications (peritonsillar abscess)	Antibiotics *v* placebo	4	0	0	0	+1	High	Effect size point added for RR less than 0.5

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