Interventions for chronic suppurative otitis media

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A substantive amendment to this systematic review was last made on 12 February 1998. Cochrane reviews are regularly checked and updated if necessary.

Background: Chronic suppurative otitis media (CSOM) is a serious bacterial infection of the middle ear that can follow untreated acute otitis media.

Objectives: To assess the effects of different treatments for CSOM.

Search strategy: We searched Medline from 1966 to 1996 and a bibliographic collection of the Hearing Impairment Research Group in Liverpool, UK. We handsearched two otolaryngology journals and contacted members of an international hearing network.

Selection criteria: Randomized trials of any method of management for patients with eardrum perforation and persistent otorrhea.

Data collection and analysis: Three reviewers independently assessed eligibility and trial quality. One reviewer extracted data. We contacted investigators for clarifications.

Main results: Twenty-four trials involving 1660 people were included. Clinical definitions and severity of CSOM varied, methodological quality was generally low and follow-up was short. Treatment with antibiotics or antiseptics accompanied by aural toilet was more effective in resolving otorrhea than no treatment (two trials, odds ratio 0.37, 95% confidence interval 0.24 to 0.57) or aural toilet alone (six trials, odds ratio 0.31, 95% confidence interval 0.23 to 0.43). Topical treatment with antibiotics or antiseptics was more effective than systemic antibiotics (six trials, odds ratio 0.46, 95% confidence interval 0.30 to 0.69). Combining topical and systemic antibiotics was not more effective than topical antibiotics. Topical quinolones were more effective than non-quinolones (five trials, odds ratio 0.26, 95% confidence interval 0.16 to 0.41). No difference in the effectiveness of topical antibiotics and topical antiseptics was found (three studies, odds ratio 1.34, 95% confidence interval 0.64 to 2.81). Some topical antibiotic combinations may be more effective than others in resolving otorrhea. Rates of adverse drug events were low and equal between groups.

Reviewers' conclusions: Treatment of CSOM with aural toilet and topical antibiotics, particularly quinolones, is effective in resolving otorrhea and eradicating bacteria from the middle ear. Longterm outcomes such as preventing recurrences, closure of tympanic perforation and hearing improvement need to be further evaluated.

Background
Chronic suppurative otitis media (CSOM) is an unpleasant and particularly serious bacterial infection of the middle ear. It follows untreated acute otitis media, usually in the first five years of life, and is associated with poor socioeconomic conditions (Wintermeyer 1994). Its natural history, without treatment, is continuous or intermittent purulent ear discharge for months or even years with destruction of the bones of the middle ear and increasing hearing impairment (Jung 1991). Occasionally it may lead to serious infective complications such as chronic mastoiditis, meningitis and cerebral abscess. When it occurs during the first two years of life, the consequent hearing loss is likely to have serious effects on the critical period of a young child's language development, and later it can cause significant delays in school progress (Kempthorne 1991).
The condition occurs throughout the world and the problems of management are similar. In developed countries, since the advent of anti-microbial therapy and more frequent and active interventions, the incidence and prevalence of CSOM has markedly decreased, and that of otitis media with effusion has increased. However, in developing countries and among various disadvantaged indigenous population groups in developed countries, it remains a major cause of ear pathology (Bluestone 1997). In children and young people in these populations it is the commonest cause of persistent mild to moderate hearing impairment (WHO 1986).

The methods of management of CSOM are regular aural toilet, such as dry mopping (‘wicking’) and/or syringing, insufflation of topical antiseptics, administration of topical and/or systemic antibiotics (usually given following ear toilet), and tympanoplasty if the drum fails to heal. All these have been advocated and some are in use in developed and developing countries. The results have been generally disappointing because of inadequately drained middle ear inflammatory exudates, poor antibiotic penetration of the middle ear mucosa and low antibiotic effectivity against the organisms that are frequently cultivated (Shenoi 1987). Because of the common occurrence of CSOM, parents and patients may not appreciate its seriousness and fail to obtain treatment. In addition, in many developing countries, adequate coverage with appropriate treatment is not available; mobile ‘ear camps’ have attempted to bring treatment, including tympanoplasty, to the people, but this approach has so far generally failed because of high costs, poor coverage, and inadequate follow-up (Wintermeyer 1994).

Consensus based on good evidence for the most effective and appropriate method of management is lacking (Nelson 1988). The studies that have been conducted suggest that ear toilet improves the natural history of the disease (Browning 1984; Jahn 1984; Kimmelman 1992). Whether antibiotics have any additional benefit is unclear. The numbers investigated were generally small, follow-up times were short, and the effects on hearing impairment were usually not ascertained.

Objectives
To determine the effectiveness of different methods of managing active CSOM. Any method of management such as aural toilet, topical antiseptics, topical and/or systemic antibiotics and tympanoplasty was considered.

Criteria for considering studies for this review

Types of studies
Any randomized controlled trial was included that compared the different methods of management outlined below with each other and/or with a control group receiving no specific treatment.

Types of participants
Patients with CSOM, as defined by the World Health Organisation (WHO). This includes the presence of uni- or bilateral tympanic perforation associated with otitis present continuously for at least two weeks preceding the start of the intervention.

Types of intervention
Outcomes were compared based on:
1. Any form of treatment versus no treatment
2. Aural toilet alone versus no treatment
3. Antibiotic treatment with aural toilet versus aural toilet alone
4. Topical antibiotics versus systemic antibiotics
5. Combined topical and systemic antibiotics versus topical antibiotics
6. Topical antiseptics versus topical antibiotics
7. Topical/systemic quinolones versus topical/systemic non-quinolones
8. Other treatments/treatment combinations used
9. Tympanoplasty
Aural toilet will be taken to mean dry mopping and/or syringing (by either self or caregiver) or suctioning with or without instillation of cleaning solutions.

Types of outcome measures
The outcome measures sought were:
1. Cessation of ear discharge
2. Normalization of middle ear mucosa as evidenced by otoscopic improvement of its color, texture and thickness
3. Prevention of recurrence
4. Healing or closure of perforation
5. Eradication of pathogenic middle ear bacteria as determined by cultures
6. Improvement in hearing by audiometry
7. Any adverse drug reactions

**Search strategy for identification of studies**

See: Collaborative Review Group search strategy

All publications describing (or which might describe) randomized trials of management of CSOM were sought by:

1. Searching Medline from 1966 to December 1996, using the following search terms: 'chronic suppurative otitis media', 'chronic otitis media', 'mastoiditis' and 'otorrhea';
2. Searching the Hearing Network database consisting of a bibliographic collection developed by the Hearing Impairment Research Group in Liverpool over the last ten years, and containing over 2000 published and unpublished articles and a database of over 14000 references on ear disease and hearing impairment. This database was searched for randomized trials using IdeaSoft software and by hand, with the following search terms: 'chronic suppurative otitis media', 'chronic otitis media', 'otorrhea', 'perforation' and 'mastoiditis';
3. Handsearching issues of two journals known frequently to publish clinical trials: Archives of Otolaryngology - Head and Neck Surgery (1975-1995) and Clinical Otolaryngology (1976-1994);
4. Contacting members of the International Hearing Network run by the Hearing Impairment Research Group in Liverpool. The Hearing Network consists of over 230 members from 49 countries who are conducting, or have been involved in, research on hearing impairment and ear disease;
5. Reviewing the proceedings of the 1993 and 1995 World Congresses in Otolaryngology - Head and Neck Surgery for other unpublished trials.

We also contacted authors by mail and sought clarifications from them whenever needed.

**Methods of the review**

The quality of trials included in this systematic review was assessed in a standard way using the following dimensions and criteria, adopted with modifications from Chalmers et al (Chalmers 1990), and the Cochrane Handbook (1996).

1. Allocation concealment
   - A - Adequate measures taken to conceal allocation such as central randomisation; serially numbered, opaque, sealed envelopes; or other descriptions that contained elements convincing of concealment
   - B - Unclearly concealed trials, in which the authors did not report an allocation concealment approach at all, or reported an approach that did not fall into one of the categories in A
   - C - Inadequately concealed trials using methods of allocation such as alternation methods or use of case record numbers

2. Generation of allocation sequence
   - A - Adequate sequence generation reported using random number tables, computerised random number generation, coin tossing, or shuffling
   - B - No report of one of the adequate methods in A but mentioned randomization method
   - C - Other methods of allocation that appeared to be unbiased

3. Inclusion of all randomized participants
   - A - Trials where an intention-to-treat analysis was possible and few losses to follow-up
   - B - Trials which reported exclusions as listed in A but exclusions were less than 10%
   - C - No reporting on exclusions, or exclusions greater than 10%, or large differences in exclusions between groups

4. Blinding of outcome assessors
   - A - Adequate blinding of investigators assessing outcomes
   - B - Unclearly blinded trials in which investigators might have used but did not report any
standard blinding method

C - Inadequately blinded trials or trials in which blinding was clearly not performed

The selection criteria were applied by two authors on all trials identified by the literature search. This was followed by critical appraisal of the 24 included trials. The authors were not blinded to study authorship, origin or conclusions. Data extraction was performed by the primary author. All differences in assessment were resolved in open discussion between the three reviewers.

For each study, univariate analysis of dichotomous outcomes was expressed using an odds ratio. In studies which reported outcomes at several time points we chose the last reported result. In those which enrolled subjects with otitis externa or draining surgical cavities as well, we included only the results for CSOM patients. The weighted odds ratios were combined into an overall estimate expressed as an adjusted Peto odds ratio and its 95% confidence limit. Tests for heterogeneity were performed and a random effects model was used whenever these tests were significant.

Description of studies

The initial Medline search yielded 980 citations while the Idealist search of the Hearing Network database yielded 138 citations. 45 of these dealt with treatments for CSOM and were reviewed in full. Upon application of the inclusion criteria, these were trimmed down to 23 randomized trials. One more trial (Clayton 1990) was identified by hand-searching ‘Clinical Otolaryngology’ and was included in the meta-analysis.

Another trial was found in the proceedings of the 1993 World Congress in Otolaryngology - Head and Neck Surgery and is awaiting assessment pending response from its author (Kobayashi 1993). One non-English trial (Baba 1989) is being translated. These may be included in future updates.

One trial was excluded (Sugiyama 1981) because it did not randomize patients into treatment groups. Another trial (Sabater 1996) was excluded because it was part of a larger trial we included (Llorente 1995).

No additional trials were identified by hand-searching ‘Archives of Otolaryngology-Head and Neck Surgery’. Contacting members of the International Hearing Network likewise did not yield additional studies.

Of the 24 studies that were identified, two (Smith 1996; Eason 1986) were field trials of schoolchildren in Kenya and the Solomon Islands respectively. The rest were hospital-based studies. Three (Picozzi 1983; Picozzi 1984; Browning 1988A) were placebo-controlled. The clinical definition of active CSOM varied among the included studies. While we adopted the WHO definition of persistent ear discharge through a perforated eardrum for more than two weeks, the patients enrolled in the studies had durations of otorrhea ranging from two weeks (Smith 1996) to 45 years (Rotimi 1990). Eleven studies specified duration of otorrhea (Gyde 1982; Eason 1986; Lildholdt 1986; Browning 1988A; Papastavros 1989; Fliss 1990; Rotimi 1990; Legent 1994; Llorente 1995; Tutkun 1995; Smith 1996). However, two frequently noted characteristics support the notion that these patients actually had chronic infection and not simply reactive otorrhea: first, detailed otoscopic evidence of mucosal inflammation in four studies (Browning 1988A; Papastavros 1989; Clayton 1990; Rotimi 1990); secondly, isolation of pathogenic bacteria from the ear discharge in 13 studies (P. aeruginosa, S. aureus and gram-negative coliforms) (Gyde 1976; Gyde 1981; Gyde 1982; Lildholdt 1986; Papastavros 1989; Esposito 1990; Rotimi 1990; Esposito 1992; Legent 1994; Yuen 1994; Povedano 1995; Tutkun 1995; Tong 1996). Picozzi (Picozzi 1983; Picozzi 1984) and Gyde (Gyde 1976; Gyde 1981; Gyde 1982) insisted on the presence of both active otorrhea and positive middle ear cultures before patient enrolment.

The trials imposed a treatment-free period of one to four weeks before starting intervention and excluded patients with cholesteatoma or other supplicative complications of otitis media. Participants were usually adults, with only four trials dealing mainly with children (Eason 1986; Fliss 1990; Rotimi 1990; Smith 1996). In nine studies (Gyde 1976; Gyde 1981; Gyde 1982; Browning 1983; Lildholdt 1986; Browning 1988A; Clayton 1990; Crowther 1991; Legent 1994) post-mastoidectomy patients with draining cavities were included amongst the participants, indicating the importance of this surgical complication. However, only Gyde (Gyde 1976; Gyde 1981; Gyde 1982) and Clayton (Clayton 1990) performed separate analyses for mastoidectomies.

Nineteen of the 22 studies compared various topical treatments with each other or with systemic treatments. The topical antibiotics included aminoglycosides (e.g. gentamycin and neomycin) and polypeptides (e.g. polymyxin and colistin), which are active against
gram-negative bacteria, as well as chloramphenicol and trimethoprim-sulpha, which are active against both gram-negative and gram-positive bacteria. A newer class of antibiotics, the quinolones, is specific against Pseudomonas aeruginosa and has aroused interest because it may be particularly effective against CSOM. Quinolones were studied in eight trials (Esposito 1990; Esposito 1992; Legent 1994; Yuen 1994; Llorente 1995; Povedano 1995; Tutkun 1995; Tong 1996). Three studies compared systemic antibiotics with each other (Fliss 1990; Rotimi 1990; Legent 1994). Only one study compared ear surgery plus prophylactic systemic antibiotic with ear surgery alone (Lildholdt 1986).

The primary outcome used by all studies was ‘dry ear’ as assessed by the investigator either immediately or several weeks after treatment. Seven studies (Eason 1986; Browning 1988A; Papastavros 1989; Clayton 1990; Rotimi 1990; Legent 1994; Smith 1996), went further by defining cure as absence of mucosal inflammation and/or healing of perforation. Thirteen studies (Gyde 1976; Gyde 1981; Gyde 1982; Lildholdt 1986; Papastavros 1989; Esposito 1990; Rotimi 1990; Esposito 1992; Legent 1994; Yuen 1994; Povedano 1995; Tutkun 1995; Tong 1996) included negative cultures of middle ear aspirates in the definition of cure. The Crowther study (1991) used a scoring system with cutoff values to determine clinical improvement. Wilde (Wilde 1995) also used a scoring system and was the only author who measured effectiveness with mean resolution scores.

While some studies differentiated between treatment success, improvement and failure, our a priori decision to dichotomize the outcomes led us to combine improvement and failure for simplicity and consistency. This is also more stringent and rightfully underestimates any treatment effect on a disorder in which symptoms wax and wane.

Methodological quality
The quality of studies was generally low. Methods for generating and concealing the allocation sequence and for blinding those who assessed the outcomes were often not reported. Whether patients dropped out after randomization was often not reported either, and those who excluded potential subjects for noncompliance did not state the exact number.

With respect to allocation concealment, only seven of the 24 included studies (Gyde 1981; Browning 1988A; Clayton 1990; Yuen 1994; Wilde 1995; Smith 1996; Tong 1996) offered evidence that the investigators were unaware of the allocation sequence prior to randomization and thus obtained a score of ‘A’. Only three studies (Gyde 1981; Lildholdt 1986; Smith 1996) stated the use of random numbers. These merited a score of ‘A’ for adequacy of the method of generating the allocation sequence. The rest scored ‘B’. With regard to completeness of follow-up, only three studies (Eason 1986; Lildholdt 1986; Legent 1994) appeared to have achieved near complete follow-ups and could be analyzed by intention-to-treat. Three studies scored ‘B’ by reporting less than 10% exclusions. The rest scored ‘C’ because of the absence of any statement on the number of exclusions.

Eight studies scored ‘A’ for adequacy of blinding of outcome assessors. Eleven other studies scored ‘B’ for probably having blinded their assessments and the rest scored ‘C’.

The point at which outcomes were assessed varied from last treatment day in Fliss' study (1990) to the 16th week after treatment in Smith's study (1996). These variations presented problems in that the first option might represent too early a point in time for treatment effects to achieve clinical importance. On the other hand, the second option, while allowing for treatment to alter the natural course of CSOM, might fail to measure other important factors that influence long-term middle ear integrity such as continued patient compliance to ear care and freedom from respiratory infections. The two studies by Esposito (1990;1992) represent the moderate view of measuring outcomes at two and three weeks after cessation of treatment. Studies that measure outcomes at short but regular intervals on a long-term basis are needed.

Studies that randomized patients but analyzed according to number of dry ears (Gyde 1976; Gyde 1982; Eason 1986; Papastavros 1989; Tong 1996) also presented a problem because of the expected concordance between ears of the same subject. However, since no detailed data were provided, we could not correct for this.

Results
Twenty-four randomized trials involving 1660 patients with eardrum perforations and otorrhea persisting for two weeks to several years were included in the meta-analysis.

The pharmacological treatments used in the studies identified were:

ANTIBIOTICS:
1. Topical: chloramphenicol, ciprofloxacin (quinolone), colistin, gentamicin, neomycin,
1. Antibiotics/antiseptics with aural toilet were better than no treatment in resolving otorrhea (odds ratio 0.37, 95% confidence interval 0.24 to 0.57). This was based on two studies (Eason 1986; Smith 1996). These were field trials on children in developing countries, the Solomon Islands and Kenya, in which CSOM was highly prevalent. Eason and co-workers employed increasing combinations of borate, Sofradex (framycetin, gramicidin and dexamethasone), and oral clindamycin. They assessed their subjects after 3 and 6 weeks of therapy. Smith and co-workers used Sofradex plus oral amoxicillin and followed up their patients 4, 8, 12 and 16 weeks after start of treatment. Both groups did not appear to have blinded their outcome assessors. Eason et al. seemed to have followed up all of their patients and reported proportions of dry ears at 6 weeks. Smith et al. had varying proportions of absent schoolchildren at each follow-up. They reported mean proportions of children with dry ears for each treatment group weighted according to the number of children available for evaluation at each time point.

2. Aural toilet alone was no better in resolving otorrhea than no treatment in the two studies mentioned in 1 (Eason 1986; Smith 1996). Aural toilet in both studies consisted of dry mopping with cotton wool wisps on orange sticks four times per day and was performed by either parents or by schoolmates and teachers. Both studies found that proportions of healed perforations were small and similar in all treatment groups.

3. Antibiotics/antiseptics with aural toilet were better than aural toilet alone in resolving otorrhea (odds ratio 0.31, 95% confidence interval 0.23 to 0.43). Six studies (Picozzi 1983; Eason 1986; Browning 1988A; Fliss 1990; Rotimi 1990; Smith 1996) used the following active treatments: topical gentamicin/hydrocortisone, intravenous mezlocillin or ceftazidime, intramuscular gentamicin with oral clindamycin or metronidazole or lincomycin and the previously mentioned antibiotics in Smith's study. Outcomes were reported at varying time points from the first week to the fourth month after treatment. Three of the six studies noted that effectiveness varied directly with the degree of compliance. One study found no evidence of ototoxicity of gentamicin.

4. Topical antibiotics or antiseptics were better than systemic antibiotics in resolving otorrhea (odds ratio 0.46, 95% confidence interval 0.30 to 0.68). Six studies (Browning 1983; Papastavros 1989; Esposito 1990; Esposito 1992; Yuen 1994; Povedano 1995) used the following topical antibiotics: gentamicin, chloramphenicol, ofloxacin, and ciprofloxacin; the topical antiseptics used were hydrogen peroxide, boric acid and iodine powder. The systemic antibiotics were cephalexin, flucloxacillin, cloxacillin, amoxycillin, co-amoxiclav, erythromycin, metronidazole, piperacillin, ciprofloxacin, azactam, trimethoprim-sulfamethoxazole, ofloxacin, and intramuscular gentamicin. An alternative analysis that excluded two less rigorous trials decreased heterogeneity and further showed benefit in favor of topical treatment (odds ratio 0.19, 95% confidence interval 0.11 to 0.32).

Treatment durations varied from as long as 4 weeks in the Browning trial to as short as 1 week in the Yuen study. Success or cure was defined as resolution of otorrhea in five of the six studies. Five studies classified patients as cured, improved or failed treatment. In addition, 'cure' was defined as negative middle ear cultures in five of the six studies and as the absence of middle ear granulations or edema and the return of the pink color of the mucosa in Papastavros' study. None of the studies reported healing of perforation, improvement in hearing, recurrence rates or patient compliance rates. Only one study followed up the patients beyond the last day of treatment.

In terms of eradicating bacteria, three of the six studies also favored topical ofloxacin and ciprofloxacin over their oral counterparts and gentamicin (odds ratio 0.14, 99% confidence interval 0.07-0.28).

5. There was no significant difference in effectiveness between topical antibiotics alone and topical plus systemic antibiotics in terms of otorrhea resolution (odds ratio 1.71, 95% confidence interval 0.88-3.34) and bacterial eradication (odds ratio 2.95, 95% confidence interval 0.38-22.72). Three studies (Picozzi 1984; Eason 1986; Esposito 1990) combined oral clindamycin with topical Sofradex, oral ofloxacin with topical ofloxacin and oral metronidazole with topical gentamicin/hydrocortisone.
6. There was no difference in effectiveness between topical antiseptics and topical antibiotics (odds ratio 1.34, 95% confidence interval 0.64 to 2.81). Three studies (Browning 1983; Eason 1986; Clayton 1990) compared borax and iodine powder versus chloramphenicol, aluminium acetate versus gentamicin, and boric acid versus Sofradex. Treatments were given for 3 to 6 weeks. Patients were comparable across studies except for one that included draining mastoidectomy cavities.

7. Topical and oral quinolones were more effective than non-quinolones. Five studies (Esposito 1992; Yuen 1994; Llorente 1995; Tutkun 1995; Tong 1996) found that topical ofloxacin or ciprofloxacin was more effective than intramuscular gentamicin, topical gentamicin, topical neomycin-polymyxin, and oral co-amoxiclav in resolving otorrhea (odds ratio 0.26, 95% confidence interval 0.16 to 0.41) and in eradicating bacteria (odds ratio 0.30, 95% confidence interval 0.17 to 0.52). Legent found that oral ciprofloxacin was slightly better than oral co-amoxiclav in resolving otorrhea (odds ratio 0.41, 95% confidence interval 0.16 to 1.00). Treatments were administered for 5 to 10 days. Outcomes were assessed at cessation of treatment and 3 to 4 weeks afterwards. Patients were comparable except for Legent's study (1994) which included patients with draining mastoidectomy cavities.

We excluded oral drugs and compared topical quinolones with topical non-quinolones and found that the former were still more effective in resolving otorrhea and eradicating middle ear bacteria.

8. Other topical treatments compared were gentamicin/betamethasone versus betamethasone (Crowther 1991), trimethoprim-sulfacetamide-polymyxin B versus trimethoprim-polymyxin B (Gyde 1981), trimethoprim-sulfacetamide-polymyxin B versus gentamicin (Gyde 1976), gentamicin versus colistin-neomycin-hydrocortisone (Gyde 1982), and neomycin-gramicidin-triamcinolone ointment on gauze versus the same ointment instilled into the ear (Wilde 1995). Crowther's study found that the addition of gentamicin significantly increased the effectiveness of betamethasone. The three double-blind studies of Gyde and the trial by Wilde found no difference in effectiveness between the drugs that they compared but this may be partly due to small numbers.

9. One study found that tympanoplasty with pre-operative administration of ceftazidime (Lildholdt 1986) was more effective than tympanoplasty alone in terms of otorrhea resolution, bacterial eradication and graft take.

10. The 11 studies that monitored ototoxicity (Gyde 1976; Gyde 1982; Browning 1988A; Esposito 1990; Fliss 1990; Esposito 1992; Yuen 1994; Llorente 1995; Tutkun 1995; Smith 1996; Tong 1996) found negligible or no changes in hearing levels after topical treatments. Equally negligible to absent adverse drug events were noted by 11 studies (Gyde 1976; Gyde 1982; Lildholdt 1986; Esposito 1990; Crowther 1991; Esposito 1992; Legent 1994; Yuen 1994; Llorente 1995; Tutkun 1995; Tong 1996). These side effects included Candida infections, dizziness, local pain for topical treatments, and headache, nausea and allergic reaction to systemic treatments.

Summary of analyses

MetaView: Tables and Figures

Discussion

Surgical closure of the tympanic perforation is frequently necessary to cure CSOM permanently. But since this is neither feasible in nor available to all patients with draining ears, conservative medical treatment plays an important role in controlling otorrhea both as an alternative to and as a preparation for tympanoplasty.

The randomized trials that were included in this review offered direct comparisons between two or more treatment alternatives in controlled settings but were often marked by uneven methodologic quality and inadequate reporting of outcomes. In addition, most studies fell short of following up patients at regular intervals and for durations that would better document real changes in the natural course of the disease. Information on patients not complying with treatment was generally unreported but these problems were occasionally serious enough to warrant exclusion of randomized patients from analysis.

Because the clinical definitions of CSOM varied from study to study it is also possible that subjects differed in terms of chronicity and activity of infection. Although many trials obtained positive bacterial cultures, none offered detailed description of the conditions of the middle ear or the size of perforation which can further support the chronicity of the infection or the likelihood of the antibiotics being able to enter the middle ear.
Few studies observed patients long enough to report such important outcomes as recurrence of discharge, need for surgical management, healing of perforation, improvement in hearing and long-term stability of the middle ear. The degree of patient adherence to a regimen that includes meticulous and frequent ear cleaning for the treatment of a protracted, recurrent and initially innocuous disorder has also been studied by only a few of these studies.

Heterogeneity among the studies may also be due to the inclusion of patients with draining mastoidectomy cavities in some trials. There were also differences in study settings, in racial and genetic characteristics, and in the intensities of follow-up examinations and co-interventions.

Despite these flaws, we think that the differences in effectiveness were both real and important. Our results corroborate the findings of many case series on treatments for CSOM (Cronin 1974; Gyde 1976; Palva 1978; Browning 1988A; Kenna 1988; Meyerhoff 1988; Pollack 1988; Brownlee 1992; Gehanno 1993). That topical treatment alone dries discharging ears and eradicates bacteria much better than systemic antibiotics supports the CSOM-induced presence of mucosal barriers to antibiotic penetration (Shenoi 1987; Meyerhoff 1988; Pollack 1988).

The effectiveness of topical and oral quinolones is probably due to their activity against Pseudomonas aeruginosa, a commonly isolated pathogen in the studies included in our review. That we did not find any difference in effectiveness between topical antiseptics and topical antibiotics may be due to small numbers and the clinical heterogeneity produced by a significant number of mastoidectomy patients in the three studies included in this comparison. However, this is a potentially useful finding in developing countries where antibiotics may be unavailable or unaffordable. The antimicrobial property of topical antiseptics may be due to their acid pH which is bacteriostatic (Fairbanks 1981).

**Reviewers' conclusions**

**Implications for practice**

In terms of short-term resolution of otorrhea from active CSOM, antibiotic treatment is better than aural toilet alone. Topical antibiotics with aural toilet is the most effective method of treatment. The effect of treatment on healing of the tympanic perforation is small and still insignificant. Quinolones, whether systemic or topical, seem to be more effective than other types of antibiotics in resolving otorrhea and clearing bacteria from the middle ear. Antiseptics may be just as effective as antibiotics.

These conclusions must be regarded with caution, since they are based on short term outcome measures which may have no relevance to the ultimate resolution of CSOM given its natural course. At best, they offer guidance to the temporary management of CSOM given the lack of better evidence.

Physicians should administer antibiotics while advising patients on the proper care of their draining ears. However, the current WHO/UNICEF initiative for the Integrated Management of Childhood Illness (Gove 1997) does not recommend antibiotic treatment for 'chronic ear infection'. This recommendation is likely to be reviewed.

The cautious use of topical antibiotics instilled into the middle ear while monitoring for adverse effects such as allergic reactions and ototoxicity should be encouraged.

However, medical treatment of chronic draining ears should not delay physicians from operating whenever irreversible disease is present, particularly if it threatens life and well-being.

**Implications for research**

The long term effects of medical treatment on the natural course of CSOM should be investigated. Drying up of discharge, bacterial clearance and other surrogate measures may be better replaced by more clinically important outcomes such as healing of the tympanic perforation, hearing improvement, prevention of suppurative complications, avoidance of surgery and occurrence of treatment complications. The most effective kinds of antibiotics for the treatment of CSOM must be determined. The effectiveness of cheap topical antiseptic powders and solutions must also be studied. Treatment options for patients with draining surgical cavities must be evaluated.

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Characteristics of included studies
Table: Characteristics of included studies

Characteristics of excluded studies
Study: Sabater 1996
Part of a larger trial by Lorente.
Study: Sugiyama 1981
Not randomized.

References
References to studies included in this review
Browning 1983 \{published data only\}

Browning 1988 \{published data only\}

Clayton 1990 \{published data only\}

Crowther 1991 \{published data only\}

Eason 1986 \{published data only\}

Esposito 1990 \{published data only\}

Esposito 1992 \{published data only\}

Fliss 1990 \{published data only\}

Gyde 1978 \{published data only\}
Gyde MC, Randall RF. Etude comparative a double insu de la trimethoprim-sulfacetamide-polymyxine B et de la gentamicine dans le traitement de l'otite media suppurative [Comparative double-blind study of trimethoprim-sulfacetamide-polymyxin B and of gentamicine in the treatment of otitis media]. Annales d'Otolaryngologie et de Chirurgie

Gyde 1981 {published data only}

Gyde 1982 {published data only}

Legent 1994 {published data only}

Lildholdt 1986 {published data only}

Llorente 1995 {published data only}
Llorente J, Sabater F, Maristany M, Jimenez R, Menem J, Vinas J, et al. Estudio multicentrico comparativo de la eficacia y tolerancia de ciprofloxacino topical (0.3%) versus gentamicina topical (0.3%) en el tratamiento de la otitis media crónica sin colecsteatomatosa en fase supurativa [Multicenter comparative study of the effectiveness and tolerability of topical ciprofloxacin (0.3%) versus topical gentamicin (0.3%) in the treatment of chronic suppurative otitis media without cholesteatoma]. Anales Otorrinolaringologicos Iberoamericanos 1995;5:521-33.

Papastavros 1989 {published data only}

Picozzi 1983 {published data only}

Picozzi 1984 {published data only}

Povedano 1995 {published data only}

Rotimi 1990 {published data only}

Smith 1996 {published data only}

**Tong 1996 {published data only}**


**Tutkun 1995 {published data only}**


**Wilde 1995 {published data only}**


**Yuen 1994 {published data only}**


* indicates the major publication for the study

References to studies excluded from this review

**Sabater 1996**


**Sugiyama 1981**


References to studies awaiting assessment

**Baba 1989**


**Kobayashi 1993**


Additional references

**Bluestone 1997**


**Browning 1984**

Browning 1988

Brownlee 1992

Chalmers 1990

Cronin 1974

Fairbanks 1981

Gehanno 1993

Gove 1997

Gyde 1976

Jahn 1984

Jung 1991

Kempthorne 1991

Kenna 1988

Kimmelman 1992

Meyerhoff 1988