Heat or ice for acute ankle sprain?

**EVIDENCE-BASED ANSWER**

For grade 3 and 4 ankle sprains, ice works better than heat to speed recovery (return to play) (strength of recommendation [SOR]: B, based on a single retrospective cohort study). No studies support faster return to play with the application of heat at any time after injury (SOR: B, based on head-to-head randomized trials). Ice therapy also reduces edema, but the clinical significance of this finding is unclear.

**EVIDENCE SUMMARY**

Studies of ankle sprain use variable diagnostic criteria for sprain and definition of recovery (return to play). They often report indirect outcomes such as edema. The effect of decreased edema on recovery time is not addressed.

Only 1 study has directly compared heat vs ice therapy and recovery time for ankle sprains. A retrospective cohort study of 32 patients in a sports medicine clinic demonstrated that early cryotherapy (within 36 hours of injury) for grades 3 and 4 ankle sprains, when compared with early heat therapy, resulted in earlier return to activity, as defined by ability to walk, climb stairs, run, and jump without pain. Grade 3 sprains treated with ice recovered in 11.0 days vs 14.8 days with heat. Grade 4 sprains treated with ice recovered in 13.2 days vs 30.4 days with heat. This study also showed that early application of ice (within 36 hours) decreased time to recovery compared with late application of ice.

However, evidence is heterogeneous about the effect of ice on return to play. In 2 of 3 randomized controlled trials, early application of ice vs placebo did not significantly speed return to play.

One randomized controlled trial compared ice therapy (in the form of a cooling anklet applied upon presentation) with placebo in 143 patients presenting within 24 hours of injury to a university emergency department in England. All patients received high-dose nonsteroidal anti-inflammatory agents. Though a trend was found in favor of ice therapy, no statistically significant difference was found in recovery time, as defined by pain relief and ability to bear weight. The grade of sprain was not specifically accounted for in this study.

Another randomized controlled trial compared ice with placebo in 30 patients with grade 3 and 4 sprains referred to a physiotherapy department within 2 days of ankle injury. No statistical difference was found in recovery time, defined as ability to bear weight with only mild to moderate pain.

However, a randomized controlled trial of 60 patients with acute ankle sprains of all grades presenting to an emergency department compared cryogel plus bandaging with bandaging

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**What is a Clinical Inquiry?**

Clinical Inquiries answer real questions that family physicians submit to the Family Practice Inquiries Network (FPIN), a national, not-for-profit consortium of family practice departments, residency programs, academic health sciences libraries, primary care practice-based research networks, and individuals with particular expertise.

Questions chosen for Clinical Inquiries are those considered most important, according to results of web-based voting by family physicians across the U.S.

Answers are developed by a specific method:
- First, extensive literature searches are conducted by medical librarians.
- Clinicians then review the evidence and write the answers, which are then peer reviewed.
- Finally, a practicing family physician writes a commentary.
alone (cooling vs no cooling). This study found the mean time to recovery—defined as decreased pain—was reduced from 14.8 days to 9.7 days with constant cooling for the first 48 hours.4

The application of ice—but not heat—within 24 to 48 hours of acute ankle sprain also reduced edema. Several studies looked at reduction of edema with cooling. One study measured edema in 30 patients with grade 1 and 2 sprains treated with cold, heat, or contrast baths during the third, fourth, and fifth days.5 Only ice therapy alone significantly reduced edema.

**RECOMMENDATIONS FROM OTHERS**
The American Academy of Orthopaedic Surgeons recommends initial treatment of stable ankle sprains with rest, ice, gentle compression, and elevation (RICE).6 These guidelines are echoed by the American Academy of Family Physicians. In addition, the Institute for Clinical Systems Improvement and the National Guidelines Clearinghouse recommend PRICE, where protecting the ankle is explicitly added to RICE therapy.7

**REFERENCES**

How should patients with mitral regurgitation be followed?

**EVIDENCE-BASED ANSWER**
Patients with mild to moderate mitral regurgitation should be assessed periodically for a worsening condition; those with severe mitral regurgitation should be monitored for development of congestive heart failure, atrial fibrillation, and decline in left ventricular ejection fraction or increase in left ventricular end-diastolic diameter (strength of recommendation [SOR]=B).1–3

Cardiologists and general internists perform equally well in identifying severe mitral regurgitation among patients with known mitral regurgitation.4 Grade I or II murmurs indicate mild or moderate mitral regurgitation; grade IV or greater murmurs indicate severe mitral regurgitation, and grade III murmurs are indeterminate (SOR=B).4

The optimal frequency of evaluation is uncertain. Patients with severe regurgitation should be followed more frequently, with a combination of physical examination and echocardiography (SOR=B).
Patients with mild mitral regurgitation should undergo annual physical examination

**EVIDENCE SUMMARY**

A well-done, prospective cohort study enrolled 229 patients (mean age, 66; 70% male) diagnosed with severe mitral regurgitation. Overall 10-year mortality was 43%. Older patients, those with New York Heart Association (NYHA) class III or IV heart failure, or those with left ventricular ejection fraction <60% had higher mortality. Eighty-two percent of patients had surgery within 10 years. Mortality among patients undergoing surgery was equivalent to that of the age-matched US population and significantly less than patients managed without surgery.¹

A second report from the same cohort compared the outcomes of patients undergoing early surgery (within 1 month of diagnosis) with those initially treated medically. Eight patients were excluded from this study because they were unsuitable candidates for surgery. The remaining 221 patients were followed based on their original group assignment of early surgery (63 patients) or medical management (158 patients).

Patients undergoing early surgery were more likely to have symptoms at enrollment than those managed medically. Patients in the early surgery group had better 5-year (89% vs 78%) and 10-year (78% vs 65%; P<.05 for both comparisons) survival and were less likely to develop congestive heart failure or atrial fibrillation. These differences remained significant after multivariate adjustment for potential confounders.²

Another cohort study of patients undergoing surgery for severe mitral regurgitation compared the outcomes of 199 patients with NYHA class I/II symptoms with those of 279 patients with NYHA class III/IV symptoms. Patients with NYHA class I/II had better operative outcomes (0.5% vs 5.4%) and better 5-year (90% vs 73%) and 10-year (76% vs 48%) survival than patients with more severe symptoms. In multivariate analysis, NYHA functional class remained inversely associated with survival.³

In a prospective study testing the ability of physical examination to identify severe mitral regurgitation, 170 consecutive patients with mitral regurgitation assessed by echocardiography underwent a clinical examination by internists or cardiologists blinded to the echocardiogram findings. The negative predictive value for absence of severe mitral regurgitation with a murmur less than grade III ranged from 88% to 100%. Murmurs greater than grade III had a predictive value of 91% for severe mitral regurgitation. Grade III murmurs were not predictive of severity.⁴

This study found no difference in the performance of internists and cardiologists. A systematic review found that cardiologists were able to accurately determine the presence or absence of mitral regurgitation by physical exam, but that trainees (internal medicine house staff and students) were much less accurate in their assessment.⁵

**RECOMMENDATIONS FROM OTHERS**

The American College of Cardiology and the American Heart Association recommend that patients with murmurs consistent with mitral regurgitation (holosystolic or late systolic murmurs) undergo echocardiography. Severity of regurgitation determined echocardiographically should dictate subsequent follow-up.

Patients with mild mitral regurgitation should undergo annual physical examination. Patients with moderate mitral regurgitation should undergo annual clinical evaluation and echocardiographic examination. Asymptomatic patients with severe mitral regurgitation should have a clinical and echocardiographic evaluation every 6 to 12 months. Patients with symptoms of heart failure or with mild left ventricular dysfunction (ejection fraction 50%–60% or end-diastolic dimension 45–50 mm) should be referred for surgery. Surgery should be considered in patients with severe mitral regurgitation and atrial fibrillation (SOR=D).⁶

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This question is best answered with the following assumptions:

- The mitral regurgitation is not acute (e.g., following acute ischemia or frank myocardial infarction) and does not require immediate intervention
- If no other associated valve disease is found, care should be individualized
- Mitral regurgitation is clearly differentiated from mitral valve prolapse (although in reality they may lie on a continuum).

Given these assumptions, stratifying patients into mild, moderate, and severe categories makes the most sense. These recommendations accurately reflect a literature that has few randomized controlled trials to guide us.

As echocardiography and other technology for assessing the cardiovascular system have become readily available, physicians’ ability to accurately auscultate the heart has diminished. Given this, echocardiograms are an increasingly important way to identify and follow patients with all stages of mitral regurgitation.

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REFERENCES

Does glucosamine relieve arthritis joint pain?

EVIDENCE-BASED ANSWER
Glucosamine may provide some pain relief. Studies have shown varied results, ranging from glucosamine being superior or equivalent to other agents, to no difference between glucosamine and placebo. However, most of these studies have small sample sizes, short duration, and often other significant flaws. Meta-analyses of available studies suggest a trend toward benefit from glucosamine (strength of recommendation: B).

Glucosamine may help osteoarthritis pain, but it is premature to recommend it universally until better studies are done. Even if glucosamine is effective, this sector of the market is currently unregulated, and products may not contain the amount or kind of glucosamine material advertised on their labels.

EVIDENCE SUMMARY
Multiple methodological flaws have characterized studies trying to answer this question over the past 30 to 35 years. The companies manufacturing glucosamine have funded most studies. The overwhelming proportion of positive but marginal results raises the possibility of a publication bias (the tendency to publish only positive or supportive results), and the funding sources for the positive studies make that bias plausible.

Identified flaws in the studies include small sample size, inconsistent diagnostic criteria, variable disease sites, differing routes of administration, inconsistent doses, compositions and forms of glucosamine, the brief durations of studies, and poorly defined endpoints.1 Those problems account for the relatively low quality scores of the studies used in meta-analyses, particularly in earlier ones. Quality scores range from 12% to 52% of optimal and make any definitive conclusions suspect.2
The magnitude of the treatment effect is variable. Meta-analyses demonstrate aggregate treatment effects ranging from 0.36 to 1.02—where a small effect is 0.2, a moderate effect is 0.5, and a large effect is 0.8.\(^2\)

When more recent, higher-quality studies are analyzed, trends toward benefit and the effect sizes for glucosamine diminish but remain at aggregate values ranging from 0.26 to 0.44.\(^2-4\) Statistically significant differences exist in some subgroup analyses and secondary endpoints.\(^5\) Typical trends suggest that glucosamine is superior to placebo for pain relief, and less effective but safer than nonsteroidal anti-inflammatory agents.\(^6\)

Statements about safety are speculative given the brief duration of available trials, most of which lasted <10 weeks.\(^6\) Reported adverse effects are few. Mild gastrointestinal, skin, and constitutional symptoms predominate, but seldom at rates much higher than placebo.\(^3-4\) Pain relief may require as much as 4 to 6 weeks of therapy, and short studies may not demonstrate these benefits. The possibility of site-specific benefits or a difference in effect from a different dose or form is impossible to determine based on the current literature.

**RECOMMENDATIONS FROM OTHERS**

The American College of Rheumatology Subcommittee on Osteoarthritis believes that it is too early to issue recommendations for use of glucosamine sulfate or chondroitin sulfate for treatment of osteoarthritis.\(^7\)

The National Institutes of Health Glucosamine/Chondroitin Arthritis Intervention Trial (GAIT) began recruiting in May 2002. The design of this study is specifically directed at addressing the flaws of previous studies. This study will enroll 1588 patients at 13 study sites, and will use standardized products and doses with a single route of administration in a double-blinded, placebo-controlled fashion.

The GAIT study will measure change in joint space width (baseline to 2 years) and consists of 4 arms: glucosamine vs placebo, chondroitin vs placebo, glucosamine and chondroitin vs placebo, and celecoxib vs placebo. It is likely that the National Institute of Arthritis, Musculoskeletal and Skin Diseases, in collaboration with the National Center for Complementary and Alternative Medicine, will issue recommendations regarding the efficacy of glucosamine when the study is complete in 2005 or 2006. Updates are available at http://nccam.nih.gov/clinicaltrials/glucosamine.htm.

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**CLINICAL COMMENTARY**

Patients frequently ask me if glucosamine, in combination with chondroitin or methylsulfonylmethane (MSM), reduces or prevents arthritis pain. It appears that glucosamine is safe and offers some promise.

I think a 6-week trial in patients with osteoarthritis is reasonable, preferably using glucosamine—a type that complies with the United States Pharmacopia/National Formulary standards—500 mg orally 3 times daily, once it becomes widely available. In my experience, very few patients who give glucosamine an enthusiastic and adequate trial of therapy continue the course for more than a few months. Those who use it longer often acknowledge only modest relief but continue with the hope of preventing further joint degeneration and increased pain, another currently unsubstantiated expectation.

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ment on insufflation, or by abnormal tympanometry, all in the absence of acute inflammation. OME is defined as chronic when the effusion has been present for at least 3 months.

The natural course of OME was observed in a longitudinal cohort study of 1439 children aged 2 years in the Netherlands. Single or recurrent flat screening tympanograms were noted in 20% and remitted spontaneously at a rate of 50% every 3 months. This prevalence and spontaneous resolution rate is consistent with other studies.

Three randomized controlled trials published in English tested intranasal steroids for OME (Table).

- The Lilholdt study enrolled children through a private ear, nose, and throat clinic over autumn, winter, and spring with a primary or new bout of OME.
- The Shapiro study enrolled children who had documented allergic rhinitis and OME with failure to respond to 4 weeks of oral antihistamine and decongestant therapy at time of entry. This was the only study with short-term follow-up comparing intranasal steroids with control. The odds ratio for OME persisting after 3 weeks was 2.12 (95% confidence interval [CI], 0.65–6.90).
- The Tracy study enrolled children with chronic OME referred to a chronic ear clinic from October to June. Inclusion criteria included 3 episodes of acute otitis media in the prior 6 months or 4 episodes in the prior 12 months. This was a randomized comparison study with 3 treatment arms: an active nasal spray group and 2 control groups. The odds ratio for OME persisting after short-term follow-up was 0.79 (95% CI, 0.20–3.19); after intermediate follow-up the odds ratio was 0.72 (95% CI, 0.21–2.44).

This study, which included a symptom score after 3 months, favored treatment, with a weighted mean difference of −4.5, but with wide 95% CI of −10.28 to 1.28. An effect was demonstrated on clearing effusions in the short term, but the advantage appeared to vanish for the most part by 3 months. The study did not evaluate improvements in hearing.

Are nasal steroid sprays effective for otitis media with effusion?

**Evidence-Based Answer**

Treatment of otitis media with effusion (OME) with nasal steroids is not recommended (strength of recommendation [SOR]=A, based on systematic review).

Limited evidence exists that shows nasal steroids may increase the rate of resolution of OME in the short term, alone or in combination with antibiotics (SOR: A, based on randomized controlled trials). However, within 3 to 12 weeks, resolution of OME with nasal steroids is no better than placebo. No evidence exists that treatment with nasal steroids has any effect on decreasing potential complications of OME, such as hearing loss and delayed language development.

**Evidence Summary**

OME is diagnosed by visualization of an effusion on otoscopy, by limited tympanic membrane movement on insufflation, or by abnormal tympanometry, all in the absence of acute inflammation. OME is defined as chronic when the effusion has been present for at least 3 months.

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No adverse effects of intranasal steroid treatment were seen except for transient drops in cortisol levels in the Shapiro study, which tested dexamethasone. Approximately 8 randomized controlled trials using oral steroids with and without antibiotics for OME and chronic OME mirror a trend for short-term benefit of treatment, spontaneous resolution, and frequent recurrence.

In summary, limited evidence exists for short-term improvement of OME with intranasal steroids plus antibiotics, and no evidence exists for lasting beneficial effect on effusion or OME associated hearing loss.

**RECOMMENDATIONS FROM OTHERS**

The Canadian Task Force on Preventative Health Care found insufficient evidence to recommend screening for OME to prevent delayed language development.6

The Cochrane Ear, Nose and Throat Disorders Group concludes that both oral and topical intranasal steroids alone or in combination with an antibiotic lead to a quicker resolution of OME in the short term, but no long-term benefit is seen from treating OME effusions or associated hearing loss with topical intranasal steroids.6 They separately reviewed antibiotic treatment for OME, noting the short-term benefit above, but cited several drawbacks including cost and increased antibacterial resistance.7

The American Academy of Family Physicians Clinical Recommendation on Otitis Media with Effusion in Young Children does not recommend steroid medications for treatment of OME in a child of any age.8

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**TABLE**

Clinical trials: Intranasal steroids for otitis media with effusion

<table>
<thead>
<tr>
<th>Study</th>
<th>Subjects</th>
<th>Groups</th>
<th>Duration</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lilholdt</td>
<td>n=70</td>
<td>Beclomethasone vs placebo</td>
<td>2 mo</td>
<td>No benefit at end of treatment month or after second month with no treatment by otoscopy, tympanometry, or audiometry. Spontaneous improvement in 25% and resolution in 25%.1</td>
</tr>
<tr>
<td>Shapiro</td>
<td>n=45</td>
<td>Dexamethasone vs placebo</td>
<td>3 wk</td>
<td>Normalization of ear pressure and middle ear gradient at 1 and 2 weeks of treatment group over placebo (P&lt;.05). No significant differences by third week.2</td>
</tr>
<tr>
<td>Tracy 1998</td>
<td>n=61</td>
<td>Beclomethasone + amoxicillin vs placebo + amoxicillin vs amoxicillin alone</td>
<td>12 wk</td>
<td>Beclomethasone group showed a significantly greater frequency of resolution of chronic effusion at 4 and 8 weeks (P&lt;.05) but not at 12 weeks, with improved middle ear pressures: left (P=.004) and right (P=.010) over the 12 weeks.3</td>
</tr>
</tbody>
</table>

OME, otitis media with effusion

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**CLINICAL COMMENTARY**

Management of OME can be challenging and expensive—annual costs are estimated at $5 billion. Antibiotics are often inappropriately prescribed for OME, which may promote bacterial resistance. Commonly, clinicians augment OME treatment with antihistamines, decongestants, and steroids. Yet studies such as those cited above confirm that these treatments offer limited or no benefit. We must avoid the kitchen-sink treatment of OME. Furthermore, randomized controlled trials have shown that 80% to 90% of cases of acute otitis media and OME resolve without any therapy.

However, children with chronic OME, especially those with bilateral disease or possible hearing loss, may benefit from tympanostomy tube placement and adenoidectomy. If the OME doesn’t clear within 3 months, refer to an ear, nose, and throat specialist.

Prevention efforts are valuable. Immunization of infants with pneumococcal conjugate vaccine reduced tympanostomy tube placement by 20% to 39%. Since increased incidence of OME and recurrent acute otitis media are associated with secondhand smoke exposure, motivating parents to quit smoking may further reduce chronic OME.

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**REFERENCES**


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