

## Glucosamine and chondroitin effective for knee osteoarthritis

*Richy F, Bruyere O, Cucherat M, Henrotin Y, Reginster JY. Structural and symptomatic efficacy of glucosamine and chondroitin in knee osteoarthritis. Arch Intern Med 2003; 163:1514-1522.*

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### ■ PRACTICE RECOMMENDATIONS

Clinicians should consider glucosamine and chondroitin as viable first-line treatment options to reduce the symptoms of knee osteoarthritis. These agents are especially useful for patients who cannot tolerate non-steroidal anti-inflammatory drugs (NSAIDs) or for whom NSAIDs are either contraindicated or ineffective. Neither glucosamine nor chondroitin should be used for the sole purpose of slowing the progression of knee osteoarthritis, as their value for this remains uncertain.

### ■ BACKGROUND

Osteoarthritis causes functional impairment and symptoms that worsen quality of life more than chronic cardiovascular, respiratory, or gastrointestinal disorders. Because the prevalence of osteoarthritis increases with age and NSAID use may cause gastropathy, clinicians desire additional therapeutic options. The latest American College of Rheumatology guidelines do not yet advocate glucosamine or chondroitin use in knee osteoarthritis. A definitive study, the National Institutes of Health Glucosamine/Chondroitin Arthritis Intervention Trial (GAIT), is ongoing.

### ■ POPULATION STUDIED

This analysis included 1775 patients from 15 clinical trials. Although the investigators stated that the groups had similar demographic profiles, they did not specifically describe the baseline characteristics of the subjects.

### ■ STUDY DESIGN AND VALIDITY

The authors of this meta-analysis included 15 prospective, randomized, double-blind, placebo-controlled, parallel group trials with glucosamine or chondroitin for knee or hip osteoarthritis. The authors identified studies by conducting a comprehensive electronic and manual literature search. They also contacted pharmaceutical manufacturers and leading experts in the field to obtain additional data. To be included, the trials must have measured joint space narrowing or used a validated tool to assess pain and mobility, such as the Lequesne Index, Western Ontario McMaster University Osteoarthritis Index (WOMAC), or a visual analog scale. Two blinded, independent authors reviewed each study, abstracted the data, and assessed it for heterogeneity.

The meta-analysis was appropriately conducted. Its results are limited because only 2 trials

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assessed the primary endpoint of joint space narrowing. Additionally, joint space narrowing does not reliably predict disease progression or the eventual need for joint replacement. Although statistically significant, the minuscule reduction in joint space narrowing is not likely clinically significant.

The authors deemed the chondroitin studies to be of low quality. The combination, which may be more or less effective, has not been evaluated. Importantly, the studies did not specifically assess either global or osteoarthritis-specific quality of life but only the symptoms of pain and mobility assessments.

### ■ OUTCOMES MEASURED

The primary outcome was to assess the impact of glucosamine or chondroitin on joint space narrowing for knee osteoarthritis. Secondly, the investigators assessed pain, function, drug safety, and treatment response.

### ■ RESULTS

The studies were relatively homogeneous. Patients taking glucosamine 1500 mg/d for 3 years demonstrated 0.27 mm less joint space narrowing (95% confidence interval [CI], 0.13–0.41 mm) than those taking placebo. Patients taking either glucosamine (1500 mg/d) or chondroitin (at doses ranging from 200–2000 mg/d) experienced less pain and greater mobility than those taking placebo at 4 weeks.

Combined outcomes in the Lequesne Index revealed a global effect size of 0.43 (95% CI, 0.32–0.54); the WOMAC revealed a common effect size of 0.30 (95% CI, 0.11–0.49). The effect sizes for visual analog scale pain (0.45; 95% CI, 0.33–0.57) and mobility (0.59; 95% CI, 0.25–0.92) also demonstrated improvement.

The responder rate was favorable for active treatment (relative risk=1.60; 95% CI, 1.39–1.83) and yielded a number needed to treat of 5. Participants taking glucosamine or chondroitin did not experience more adverse reactions compared with placebo.

## Therapeutic knee taping decreases pain from knee osteoarthritis

*Hinman R, Crossley K, McConnell J, Bennell K. Efficacy of knee tape in the management of osteoarthritis of the knee: blinded randomised controlled trial. BMJ 2003; 327:135–138.*

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### ■ PRACTICE RECOMMENDATIONS

Therapeutic knee taping decreases pain and disability in patients with knee osteoarthritis who are not extremely overweight (body mass index [BMI] <38). The patients with therapeutic knee taping were 7 times more likely to report reduced pain, and 1 patient would receive benefit for every 2 treated. Therapeutic taping provides an additional way to help patients control pain and maintain function.

### ■ BACKGROUND

The American College of Rheumatology has recommended knee taping as a therapy for osteoarthritis, but there are only small, limited studies of its benefit. This study attempts to determine if 3 weeks of knee taping will decrease pain and disability during therapy as well as provide relief after taping is stopped.

### ■ POPULATION STUDIED

Participants for this study were drawn from volunteers in an Australian community who responded to advertisements in local papers. The researchers included people who met criteria of the American College of Rheumatology (presence of osteophytes on x-ray, age >50 years, and pain in the knee). They excluded people with joint replacement; possible other causes for knee pain; BMI >38; rheumatoid arthritis; physical therapy, steroid injections, or surgery in the past 6 months; or a history of knee taping. The patients

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in this study are similar to a primary care population based on age, BMI, and severity of osteoarthritis. The population studied may be slightly different from the general population because they responded to an advertisement; the racial make-up was not reported.

### ■ STUDY DESIGN AND VALIDITY

This was a randomized, single-blinded controlled trial with 3 treatment arms: therapeutic taping, control taping, and no taping. Randomization was performed by blocks of 3, stratified by sex. The treatment group had rigid taping applied to provide medial glide, medial tilt, and anteroposterior lift to the patella. The tape was applied once a week for 3 weeks. Twelve physical therapists—4 in a university setting and 8 in private practice—applied the tape. Having different therapists apply the tape added to the generalizability of the study. The control group had soft tape applied once a week for 3 weeks. All patients had assessments of pain and disability performed by a blinded evaluator at baseline, 3 weeks, and 6 weeks.

The study was well done. Allocation to treatment group was concealed from the enrolling investigator. The researcher evaluating the results was blinded to treatment. The authors chose reliable and valid measures of their outcomes.

### ■ OUTCOMES MEASURED

The outcomes measured in the study were change in pain, average pain in the previous week, and degree of disability. To assess pain they used an 11-cm, 10-point visual analog scale; patients also rated the average severity of knee pain over the previous week using a Likert scale. Disability was measured using a visual analog scale and the Short Form-36. Secondary measures were made with the Western Ontario and McMaster Universities Osteoarthritis Index. Analysis was on-treatment rather than intention-to-treat.

### ■ RESULTS

A total of 87 people were randomized into the 3 groups. Only 1 patient in the control group with-

**The therapeutic taping group had a significant reduction in pain and disability**

drew from treatment. At 3 and 6 weeks, the therapeutic-taping group had a significant reduction in pain and disability, both from baseline and as compared with the control-taping and no-taping groups. The mean reduction in pain on the analog scale was 2.1/10 (95% confidence interval [CI], 1.3–2.8) for the therapeutic-taping group, compared with a 0.1 (95% CI, –0.8 to 0.9) increase in the control group. Most (73%) of the therapeutic-taping group reported reduced pain at 3 weeks, compared with 10% of the control group (number needed to treat=1.8; 95% CI, 1.8–2.2). The control-taping group had some decrease in symptoms, but it was significantly less than the therapeutic-tape groups. Similar results were found on the secondary outcome measures as well.

## Aspirin prevents preeclampsia and complications

*Coomarasamy A, Honest H, Papaioannou S, Gee H, Khan KS. Aspirin for prevention of preeclampsia in women with historical risk factors: a systematic review. Obstet Gynecol 2003; 101:1319–1332.*

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### ■ PRACTICE RECOMMENDATIONS

This meta-analysis shows that the use of aspirin in pregnant women predisposed to preeclampsia significantly reduces the rates of preeclampsia and perinatal death, without evidence of harm. A recent Cochrane review showed similar results.<sup>1</sup> It is reasonable to recommend low-dose aspirin therapy to women who have 1 or more risk factors for preeclampsia.

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**Spontaneous preterm birth decreased and mean birth weights increased with aspirin therapy**

**■ BACKGROUND**

Diabetes, renal disease, hypertension, and a personal or family history of preeclampsia confer a high risk of preeclampsia. Early identification and treatment of women prone to preeclampsia could reduce its risk and associated sequelae. Randomized trials evaluating aspirin's effectiveness for treating preeclampsia show a trend towards benefit, but most of these studies have been small.

**■ POPULATION STUDIED**

This systematic review represents a total of 12,416 high-risk women. The studies included in this analysis represent women of various ages and used different criteria for defining women as high-risk.

**■ STUDY DESIGN AND VALIDITY**

This was a meta-analysis of randomized trials that assessed aspirin's therapeutic benefit in women with historical risk factors for preeclampsia. The authors searched multiple electronic scientific databases (MEDLINE, EMBASE, Cochrane Library, National Research Register, SCISEARCH, and conference proceedings) and reference lists from primary and review articles to identify an exhaustive list of pertinent research. They contacted researchers to find unpublished studies.

After 729 citations were initially identified, 2 independent reviewers eliminated citations through screening of titles, abstracts, and manuscripts. Agreement was high between the 2 reviewers, but if necessary, a third independent reviewer resolved any disparity. Fourteen primary articles are included in this systematic review. A funnel plot demonstrated that publication or a related bias was unlikely.

The authors included studies in the meta-analysis if they were randomized trials. They compared low-dose aspirin (any definition) with placebo or

no drug treatment, and the participants were women with risk factors for preeclampsia.

**■ OUTCOMES MEASURED**

The primary outcomes in the majority of included studies were preeclampsia and perinatal death. Some studies reported other clinically relevant maternal or perinatal sequelae, such as preterm birth, birth weight, and antenatal bleeding or placental abruption.

**■ RESULTS**

Treatment with aspirin, in doses ranging from 50 mg to 150 mg, started no earlier than at 12 weeks of pregnancy and continued, in most cases, until delivery. Fifty percent of the trials analyzed data based on an intention-to-treat protocol; the other trials failed to report this information. Follow-up for all 14 trials was >90%.

Pooled results from the studies demonstrated a significant reduction in both primary outcomes with aspirin usage. Odds ratios (OR) were 0.86 (95% confidence interval [CI], 0.76–0.96) and 0.79 (95% CI, 0.64–0.96) for preeclampsia and perinatal death, respectively. Analysis of other clinically relevant outcomes also proved the benefits of aspirin therapy. Spontaneous preterm births decreased (OR=0.86; 95% CI, 0.79–0.95) and the mean birth weight increased by a mean of 215 grams (95% CI, 90–341). Number of placental abruptions (OR=0.98; 95% CI, 0.79–1.21) and antepartum bleeding were similar with aspirin compared with placebo or no drug treatment.

**REFERENCE**

1. Knight M, Duley L, Henderson-Smart DJ, King JF. Antiplatelet agents for preventing and treating preeclampsia [systematic review]. *Cochrane Database of Systematic Reviews* 1, 2003.

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## Spinal manipulation effective for low back pain

Assendelft WJJ, Morton SC, Yu EI, Sutorp MJ, Shekelle PG. Spinal manipulative therapy for low back pain. A meta-analysis of effectiveness relative to other therapies. *Ann Intern Med* 2003; 138:871-881.

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### ■ PRACTICE RECOMMENDATIONS

Spinal manipulation, usual care with analgesics, physical therapy, exercises, and “back school” all provide similar results when used for treatment of both acute and chronic low back pain. Clinicians may wish to treat patients with low back pain themselves or refer them for chiropractic care, physical therapy, or back schools. This decision should be based on patient preferences after reviewing relative risks and benefits.

A recent systematic review of alternative therapies for low back pain reported similar effects from spinal manipulation and massage therapy. The effectiveness of acupuncture in the management of low back pain remains unclear.<sup>1</sup>

### ■ BACKGROUND

While a number of treatments have been used for low back pain, none has shown dramatic benefit. Spinal manipulation has been studied widely, and several systematic reviews of this therapy have yielded conflicting results. The goal of this analysis was to determine the relative benefit of spinal manipulation (ie, chiropractic) compared with other approaches.

### ■ POPULATION STUDIED

For inclusion, studies of adults with low back pain had to compare spinal manipulation with another therapy for low back pain or control, and measure at least 1 clinically relevant outcome after follow-up of at least 1 day.

Treatment of low back pain should be based on patient preferences after reviewing risks and benefits

### ■ STUDY DESIGN AND VALIDITY

This study was a meta-analysis in which the results of all identified studies meeting eligibility criteria were analyzed for overall treatment effect. Using the Cochrane Collaboration search strategy, 1 reviewer searched MEDLINE, EMBASE, and CINAHL for all relevant randomized controlled trials. This reviewer also searched for systematic reviews and screened all references for additional articles. The reviewer then evaluated all abstracts for inclusion.

In unclear cases, both authors read the full text and reached consensus. Articles were not blinded for authors, journal, or year of publication. The 2 reviewers independently assessed included articles for methodologic quality using 3 scoring systems. These same authors abstracted the data independently, and 2 additional authors checked for accuracy.

Comparison therapies were grouped into categories according to presumed effectiveness: sham, conventional general practitioner care and analgesics, physical therapy and exercises, back school, and a group of treatments without evidence of benefit, including traction and bed rest.

The validity of the study would have been strengthened had more than 1 author performed a search and decided eligibility. The comprehensive search strategy used, however, is not likely to have missed relevant literature. A flow diagram clearly illustrates appropriate reasons for exclusion of trials.

Sensitivity analyses were performed to assess a number of potential confounders, including the contribution of outlying effect sizes. In addition, publication bias was assessed using standard techniques. An additional, though not unanticipated, challenge to the overall validity of results in this case is the relatively low quality of the included trials. Averages for each of 3 quality scores were less than half of the total possible score.

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## ■ OUTCOMES MEASURED

The studies evaluated the effect of treatment on short-term pain, long-term pain, short-term function, and long-term function. Studies were grouped according to the duration of pain prior to therapy (acute, chronic, and mixed or indeterminate). Effect sizes were calculated to allow comparison of outcomes among the studies. The authors then back-translated the estimated effect sizes using the 100-mm visual analog scale for pain and the Roland Disability Questionnaire (RDQ) for function. Clinical relevance was defined as a 10-mm difference on the visual analog scale and a 2-point difference on the RDQ.

## ■ RESULTS

Thirty-nine trials met the inclusion criteria for this study; 29 trials assessed spinal manipulative therapy in patients with acute pain, 29 studies evaluated patients with chronic pain, and 14 studies included patients with mixed or indeterminate durations of pain.

For patients with acute low back pain, the only reported clinically significant improvement in short-term pain occurred among patients receiving spinal manipulation as compared with sham therapy (10-mm difference in pain by visual analog scale [95% confidence interval, 2–17 mm]).

In comparisons with all other conventionally advocated therapies, spinal manipulation showed no statistical or clinical difference among patients with acute low back pain. Similarly, among patients with chronic low back pain, the only clinically significant findings exist in comparison with the sham therapy or “ineffective therapies” groups. No differences were found for the outcomes of short-term or long-term function.

## REFERENCE

1. Cherkin DC, Sherman KJ, Deyo RA, Shekelle PG. A review of the evidence for the effectiveness, safety, and cost of acupuncture, massage therapy, and spinal manipulation for back pain. *Ann Intern Med* 2003; 138:898–906.

## What is the best method of diagnosing onychomycosis?

Weinberg JM, Koestenblatt EK, Tutrone WD, Tishler HR, Najarian L. Comparison of diagnostic methods in the evaluation of onychomycosis. *J Am Acad Dermatol* 2003; 49:193–197.

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## ■ PRACTICE RECOMMENDATIONS

Nail plate biopsy followed by periodic acid–Schiff staining is the most accurate method for diagnosing onychomycosis. The positive predictive value (PV+) of periodic acid–Schiff staining was equal to both potassium hydroxide (KOH) preparation and fungal culture, with a greater negative predictive value (PV–) due to superior sensitivity.

However, availability of periodic acid–Schiff staining may vary geographically, and the cost of the diagnostic tests is not addressed in this study. Thus, it makes clinical sense to start with the most accessible test, using periodic acid–Schiff staining if other methods are negative and clinical suspicion is high.

## ■ BACKGROUND

Treatment of onychomycosis requires long-term and expensive therapy with potential negative side effects. Diagnosis based on clinical findings tends to overestimate fungal disease, as only 50% of dystrophic nails have a fungal cause. Traditional diagnostic methods have shown inconsistent sensitivity.

## ■ POPULATION STUDIED

The study evaluated 105 patients with suspected onychomycosis presenting to an outpatient dermatology clinic. No information was provided on patient demographics or exclusion criteria. Seventy-two percent of patients had onychomycosis.

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## ■ STUDY DESIGN AND VALIDITY

The investigators evaluated 105 patients with suspected onychomycosis via 4 diagnostic methods. For periodic acid–Schiff staining, nails were clipped with standard nail clippers at the distal free edge of the nail plate, including any attached subungual debris, and placed in a 10% formalin solution for evaluation by a pathologist. Subungual curettage was then used to obtain material that was evenly divided for KOH preparation, fungal culture, and calcofluor white staining.

The KOH preparations used 20% KOH with the specimen placed on a slide and heated briefly prior to microscopic examination for fungal elements. Fungal cultures used Sabouraud's dextrose agar and mycosel agar, and were checked periodically over 4 weeks. Specimens stained with calcofluor white were examined using fluorescent microscopy. The authors chose calcofluor white as their reference standard for statistical analysis because of its published sensitivity and specificity of up to 95%.

The authors do not provide information on how participants were recruited into the study. Additionally, they do not state if those interpreting the test results were blinded to the results of the other tests. The KOH and fungal culture preparations are readily available for most family physicians. The availability of periodic acid–Schiff staining may vary geographically.

## ■ OUTCOMES MEASURED

The authors calculated the sensitivity, specificity, PV+, and PV– of KOH preparation, fungal culture, and periodic acid–Schiff staining using calcofluor white as the reference standard.

## ■ RESULTS

Overall, 93/105 patients tested positive with at least 1 of the diagnostic methods. A total of 76 (72%) samples were positive by calcofluor white, the reference standard. The sensitivities of the other techniques were as follows: periodic acid–Schiff staining, 92%; KOH preparation, 80%; fungal culture, 59%. Periodic acid–Schiff staining

was significantly more sensitive than KOH preparation ( $P=.03$ ) and both periodic acid–Schiff staining and KOH preparation were significantly more sensitive than culture ( $P=.00002$ ). The specificity of fungal culture was 82% vs 72% for both periodic acid–Schiff staining and KOH preparation. This difference was not statistically significant.

Using a typical prevalence of 50% in primary care, the positive predictive values were similar among the 3 diagnostic methods: periodic acid–Schiff staining (77%), KOH (74%), and fungal culture (76%). However, fungal culture had the highest false-negative rates (PV+ for periodic acid–Schiff staining=90%; KOH=78%; culture=67%).

## Amoxicillin-clavulanate ineffective for suspected acute sinusitis

*Bucher HC, Tschudi P, Young J, et al. Effect of amoxicillin-clavulanate in clinically diagnosed acute rhinosinusitis: a placebo-controlled, double-blind, randomized trial in general practice. Arch Intern Med 2003; 163:1793–1798.*

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## ■ PRACTICE RECOMMENDATIONS

Amoxicillin-clavulanate was no more effective than placebo in quickly relieving symptoms in patients diagnosed clinically with acute sinusitis in a general practice setting. It was, however, much more likely to cause diarrhea. Because most patients will improve spontaneously, antibiotics should be reserved for patients with prolonged symptoms. An inexpensive, narrow-spectrum drug such as amoxicillin is a good initial choice.

## ■ BACKGROUND

Fifty percent of patients with acute sinusitis will have a viral infection and will not benefit from antibiotic therapy. This study evaluated the effect

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## Cure rates for amoxicillin-clavulanate and placebo were similar at 1 and 2 weeks

of a broad-spectrum antibiotic on adults with acute sinusitis diagnosed clinically in general practice.

### ■ POPULATION STUDIED

The investigators enrolled 252 adult patients over 4 winter seasons, recruited from general practices and the internal medicine and otolaryngology outpatient clinics of a university hospital in Basel, Switzerland. Clinical diagnosis was based on a history of repeated purulent nasal discharge and maxillary or frontal sinus pain for at least 48 hours but less than 1 month. Presence of pus under rhinoscopy was an initial inclusion criterion, but was dropped after the first winter season. After randomization, treatment groups were relatively well-matched for characteristics that would affect the outcomes of interest.

Patients were excluded if they were aged <18 years, pregnant, breastfeeding, immunosuppressed, allergic to amoxicillin-clavulanate, had an upper respiratory tract infection or used antibiotics for any reason within 4 weeks, or had malformation of the nasal cavities or pharynx.

### ■ STUDY DESIGN AND VALIDITY

Eligible patients were consecutively enrolled and randomly assigned (with concealed allocation) to receive amoxicillin 875 mg/clavulanic acid 125 mg or matching placebo twice daily for 6 days. Patients also received a topical nasal decongestant and acetaminophen, and were allowed to use steam inhalation. Central randomization was stratified by treatment site in blocks of 6.

At baseline and day 7, physicians performed a focused clinical exam and recorded sinusitis-related symptoms and the number of days during which sinusitis restricted activities at home or work. At these times, patients also completed a questionnaire on their symptoms and any adverse effects from antibiotics. Patients also rated sever-

ity of symptoms on a 10-point Likert scale. A study nurse interviewed patients by telephone on days 14 and 28, asking about sinusitis-related symptoms and adverse effects as well as visits to other physicians.

Overall the methodology was good: it included triple-blinding (physician, study nurse, and patient) with concealed allocation (determined centrally by a statistician not involved with the analysis) and intention-to-treat analysis. The study was adequately powered to detect a 50% increase in cure rate at day 7 after making assumptions about spontaneous cure rates for patients with and without bacterial sinusitis. Weaknesses included dropping "pus under rhinoscopy" as an inclusion criterion after the first year and the need for 2 definitions of the primary outcome.

### ■ OUTCOMES MEASURED

The primary outcome was time to cure, defined as no days since the previous visit or interview during which symptoms restricted activity at home or work. Because 10% of recruited patients reported no restriction on activities, analysis of time to cure was repeated using a 10-point visual analog scale to describe degree of restriction on activity. Secondary outcomes included number of days during which symptoms restricted activity and frequency of adverse effects of antibiotics.

### ■ RESULTS

Using either definition of cure, there was no difference in the primary outcome (time to cure) between treatment groups. Cure rates for amoxicillin-clavulanate and placebo at 1 week (29.8% and 30.7%) and 2 weeks (76.6% and 74.0%) were similar for the 2 groups. The time to cure was also similar between antibiotic-treated and placebo-treated patients. There was no significant difference between the 2 treatment groups in the secondary outcome of number of days of restricted activity. However, at 1 week patients who took amoxicillin-clavulanate were almost 4 times more likely to have diarrhea (odds ratio=3.89; 95% confidence interval, 2.09–7.25).



## Discontinuing aspirin or warfarin optional before cataract surgery

Katz J, Feldman MA, Bass EB, et al. Risks and benefits of anticoagulant and antiplatelet medication use before cataract surgery. *Ophthalmology* 2003; 110:1784–1788.

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### ■ PRACTICE RECOMMENDATIONS

Neither warfarin nor aspirin need to be stopped before cataract surgery: patients who continue to use warfarin or aspirin are not at increased risk of ocular hemorrhagic events. Conversely, those who discontinue warfarin or aspirin prior to cataract surgery have no increased risk of thromboembolic or cardiovascular events.

### ■ BACKGROUND

There is controversy over whether the risks of adverse events due to stopping anticoagulation and antiplatelet therapy prior to cataract surgery outweigh the benefits of fewer hemorrhagic events. This study compared adverse outcomes related to continued use or discontinuation of anticoagulant and antiplatelet therapy in patients who had cataract surgery.

### ■ POPULATION STUDIED

This study included 19,354 patients undergoing cataract surgery recruited from 9 centers in the United States and Canada: private practices in ambulatory surgery centers, academic centers, and community hospitals.

Patients were excluded if they were aged <50 years, had a history of myocardial infarction in the last 3 months, or if general anesthesia was planned. The average age of the patients was 72 years, and they had high rates of comorbidities. Thus, the patients were similar to many of those undergoing cataract surgery.

Risk of ocular hemorrhage was no higher in those who continued aspirin or warfarin before surgery

### ■ STUDY DESIGN AND VALIDITY

This was a prospective cohort study. Eligible patients were characterized as users and nonusers of aspirin or warfarin. Those who did not use aspirin within 4 days or warfarin within 10 days of surgery were considered nonusers. Overall, 76.7% of patients did not routinely use aspirin, 5.2% discontinued their use of aspirin before surgery, and 18% continued to use aspirin throughout the surgery. Most (96.1%) patients did not routinely use warfarin, 1.1% discontinued their use of warfarin, and 2.8% continued to use it throughout the surgery.

Of 19,354 patients undergoing cataract surgery, 94.1% agreed to participate; 99.8% of these patients gave a telephone interview 7 days after surgery. Medical events reported during these interviews were reviewed in the hospital record by a physician to determine whether they met the study definition for a related event.

### ■ OUTCOMES MEASURED

The intraoperative and postoperative (within 7 days) outcomes assessed were retrobulbar hemorrhage, vitreous or choroidal hemorrhage, hyphema, transient ischemic attack, stroke, deep vein thrombosis, and myocardial infarction or myocardial ischemia.

### ■ RESULTS

There was no increased risk of stroke, transient ischemic attacks, or thromboembolic events in routine users of aspirin or warfarin who discontinued use compared with those who continued. The risk of myocardial events and transient ischemic attacks was higher among routine users of aspirin or warfarin who continued to use. This increase rate probably occurred because these patients had a higher baseline risk of a thromboembolic event. Risk of ocular hemorrhage was no higher in those patients who continued aspirin or warfarin before surgery.

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## Consider early cephalic version for breech presentation

Hutton EK, Kaufman K, Hodnett E, et al. External version beginning at 34 weeks' gestation versus 37 weeks' gestation: A randomized multicenter trial. *Am J Obstet Gynecol* 2003; 189:245-254.

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### ■ PRACTICE RECOMMENDATIONS

Early external cephalic version for breech presentation (at 34 to 36 weeks gestation instead of after 37 weeks) appears to decrease the rate of noncephalic presentation at birth, as well as cesarean sections, without increasing maternal or fetal morbidity or mortality.

This pilot study was not powered to prove whether the 9% absolute reduction in noncephalic presentation and the 7% absolute reduction in the cesarean section rate are valid estimates. A routine policy of early external cephalic version should probably wait for a confirmatory study.

### ■ BACKGROUND

In many areas, clinical practice is to deliver nearly all breech presentations by cesarean section. Since cesarean section remains a major cause of maternal morbidity after childbirth, any intervention that safely decreases the rate of noncephalic presentation at birth would be beneficial.

External cephalic version before labor is one such established method; however, it usually does not result in cephalic birth. This pilot study investigated whether initiating external cephalic version earlier in pregnancy (between 34 and 36 weeks) reduces the likelihood of noncephalic presentation at birth compared with delaying until after 37 weeks.

### ■ POPULATION STUDIED

The study sample consisted of 233 eligible women receiving prenatal care at 25 centers in Canada, Australia, the United States, the United Kingdom, Israel, Egypt, and New Zealand from July 1999 to February 2002. Eligible women presented at a gestational age between 34 weeks and 36 weeks and were nulliparous with any breech presentation or multiparous with a frank breech presentation with a live singleton fetus. These groups typically have the lowest rate of successful version.

Women were excluded when their parity was >4; if there were contraindications for labor, vaginal delivery, external cephalic version, or early external cephalic version; or if the subject planned to move away during the pregnancy. The enrolled population appears similar to that found in most primary care settings.

### ■ STUDY DESIGN AND VALIDITY

This study was a randomized controlled trial using concealed allocation. After enrollment, a screening ultrasound was done to obtain baseline fetal information prior to randomization to either early external cephalic version at 34 to 36 weeks or delayed external cephalic version at 37 to 38 weeks. Subjects, clinicians, and investigators were not blind to individual group assignment following randomization.

Clinicians experienced in external cephalic version performed all maneuvers by either a forward or backward somersault technique. Each procedure was limited to 2 attempts within 5 minutes and lasted no longer than 5 minutes of actual manipulation time. After each attempt, investigators confirmed fetal presentation by ultrasound. Repeat external cephalic versions were allowed if the first was unsuccessful or the fetus reverted to a noncephalic position, but not before 5 days.

Women were monitored throughout the study to ensure continued eligibility and fetal well-being. Tocolytics were used in some procedures and, after November 2000, epidural analgesia

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was also allowed. The investigators did not control for other alternative version modalities, such as exercises or homeopathy.

The authors analyzed the data by intention-to-treat and decided a priori that a 15% absolute reduction in noncephalic presentation rates was clinically significant. The authors used a reasonably sound methodology for this type of study.

### ■ OUTCOMES MEASURED

The primary outcome was rate of noncephalic presentation at birth. Other outcomes of interest were cesarean section rate, serious fetal complications, pain, and preterm birth at less than 37 weeks.

### ■ RESULTS

Data were reported for 232 women, with 116 women in each group. One patient was lost to follow-up. The groups had similar baseline characteristics. The overall initial success rate of external cephalic version was 34% in the early group and 23% in the delayed group. There was an absolute difference of 9% in noncephalic presentations at birth (57% in the early group vs 66% in the late group; number needed to treat=11; relative risk [RR]=0.89; 95% confidence interval [CI], 0.70–1.05;  $P=.09$ ). Cesarean section rates were also reduced (65% vs 72%; RR=0.90; 95% CI, 0.76–1.08,  $P=.32$ ).

These results, while not statistically significant, are probably of clinical significance. Approximately 3 external cephalic version procedures were performed for each 1% decrease in cesarean section rate. No statistically significant differences in preterm birth or serious fetal or maternal complications were found between the early and delayed groups. There was 1 intrauterine demise after a spontaneous version in the delayed group. Half of the women attempted alternative methods to induce version, including moxibustion and tilt exercises.

## Tubes for otitis media do not improve developmental outcomes

*Paradise JL, Dollaghan CA, Campbell TF, et al. Otitis media and tympanostomy tube insertion during the first three years of life: Developmental outcomes at the age of four years. Pediatrics 2003; 112:265–277.*

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### ■ PRACTICE RECOMMENDATIONS

In young children with persistent otitis media with middle-ear effusions, the insertion of tympanostomy tubes does not improve cognitive, language, or speech development.

### ■ BACKGROUND

Ear infections are common occurrences in pediatric patients. Children who suffer from frequent bouts of these infections may have developmental delays due to hearing loss associated with the effusion. The insertion of tympanostomy tubes in these children after 3 months of persistent effusion is currently recommended in hopes of preventing such complications. However, there are few data to show these procedures are necessary.

### ■ POPULATION STUDIED

The investigators enrolled 6350 healthy infants aged between 2 and 61 days from urban and rural sites. The children were monitored at least monthly for the first 3 years of life for the presence of middle-ear effusions using otoscopy, supplemented with tympanometry.

The investigators identified 429 children, aged <3 years, who suffered from persistent bilateral middle-ear effusions for 90 days or unilateral middle-ear effusions for 135 days. This group was randomized to immediate tympanostomy tube placement or delayed tube placement for 6 to 9 months. A third group of 211 children who did not qualify for the study served as sociodemographic

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controls. At age 4 years the 3 groups underwent a series of tests to determine developmental progress.

### ■ STUDY DESIGN AND VALIDITY

The investigators conducted a randomized, double-blinded, controlled trial with many strengths. It was likely large enough to find a clinically significant difference if one existed. Throughout the trial, study investigators were regularly assessed for interobserver variability. A series of standardized tests and questionnaires, validated instruments for evaluating pediatric development, were used after the hearing tests.

Diverse populations of urban and rural children were enrolled. The study population was limited to otherwise healthy children. The results, therefore, may not be applicable to children with health problems or difficult social situations, although the results, if anything, probably would be worse in these children.

In subgroup analyses, the investigators examined the data for relationships between age at onset of effusion, degree of hearing loss, and pattern of illness.

### ■ OUTCOMES MEASURED

The primary endpoint of the trial was developmental progress (cognitive, language, speech, and psychosocial development) determined by a series of tests and parental questionnaires. The tests were the General Cognitive Index of McCarthy Scales of Children's Abilities, the Peabody Picture Vocabulary Test-Revised, the Nonword Repetition Test, the Number of Different Words, the Percentage of Consonants Correct-Revised, the Parenting Stress Index-Short Form, the Mean Length of Utterance in Morphemes, and the Child Behavior Checklist. All 3 groups received the same testing.

The study investigators evaluated sociodemographic variables and their role in developmental delays as the secondary endpoint.

### ■ RESULTS

No significant differences were found in developmental tests between the early- and late-treatment groups. The one exception was a small but significant difference on the Nonword Repetition Test, which favored the late-treatment group (66.3 vs 69.7; 95% confidence interval [CI], -6.2 to -0.7;  $P=.01$ ). Under no circumstances was early treatment favored in the subgroup analyses.

The mean scores on most tests were significantly better in children of higher socioeconomic background, which was determined based on health insurance status and level of maternal education.

## Patients with acute MI should be transferred for angioplasty

*Andersen HR, Nielsen TT, Rasmussen K, et al. A comparison of coronary angioplasty with fibrinolytic therapy in acute myocardial infarction. N Engl J Med 2003; 349:733-742.*

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### ■ PRACTICE RECOMMENDATIONS

Angioplasty within 2 hours of presentation for acute myocardial infarction (MI) is superior to thrombolysis, primarily due to a lower reinfarction rate. This is true whether a patient presents to a healthcare facility with angioplasty capability or one that transfers a patient.

### ■ BACKGROUND

Several studies have demonstrated the superiority of emergent angioplasty over thrombolysis for acute MI, but these studies took place in experienced angioplasty centers. It has not been clear whether transporting a patient with acute MI to another hospital for angioplasty is better than local care with fibrinolysis.

## ■ POPULATION STUDIED

Researchers enrolled 1572 adult patients diagnosed with acute MI, defined as ST segment elevation in the presence of symptoms for 30 minutes to 12 hours. The study, which took place between 1997 and 2001, included 24 referral hospitals (where angioplasty was not available) and 5 invasive treatment centers (where angioplasty was available) in Denmark.

Exclusion criteria were pulseless femoral arteries, a life-threatening arrhythmia, unstable blood pressure, a life expectancy of less than 12 months, contraindication to fibrinolysis, left bundle-branch block, need for mechanical ventilation, previous coronary bypass surgery, renal failure, diabetes treated with metformin, and nonischemic heart disease.

## ■ STUDY DESIGN AND VALIDITY

Patients were randomized at the presenting hospital to receive immediate coronary angioplasty or tissue plasminogen activator. Both groups received aspirin, an intravenous beta-blocker, and heparin. If the patient presented to a referral hospital and was randomized to angioplasty, transfer to the nearest angioplasty center had to be completed within 3 hours; a physician accompanied the patient.

Patients in both groups were similar in age (median 62–64 years), sex (73% male), and cardiac risk. Evaluators who were unaware of treatment group assignment determined endpoints, and analysis was by intention-to-treat. Although this was not a US study, transfer times are probably similar or better in most areas of this country, given our abundance of angioplasty centers.

## ■ OUTCOMES MEASURED

The primary endpoint was a composite of death, clinical reinfarction, or disabling stroke within 30 days. The researchers also analyzed each of these components separately and performed extensive subgroup analysis.

Death, reinfarction, and disabling stroke were lower in the angioplasty group than the thrombolysis group

## ■ RESULTS

The composite endpoint was lower in angioplasty group compared with the thrombolysis group (8.0% vs 13.7%;  $P<.001$ ) regardless of site of enrollment. The difference was more significant for referral hospitals (8.5% vs 14.2%;  $P=.002$ ) than at invasive treatment centers (6.7% vs 12.3%;  $P=.05$ ).

The number needed to treat to avoid 1 death, clinical reinfarction, or disabling stroke was 17 for referral hospitals and 18 for invasive treatment centers. Most of this composite difference was due to a lower reinfarction rate (6.3% vs 1.6%;  $P<.001$ ).

Of the 62 patients with reinfarction, the 30-day mortality was much higher than the other patients with no reinfarction (24.4% vs 6.5%;  $P<.001$ ). While not reaching statistical significance, there was a trend toward lower overall mortality (6.6% vs 7.8%;  $P=.35$ ) or disabling stroke (1.1% vs 2.0%;  $P=.15$ ) in the angioplasty groups at both types of presenting hospitals.

Most (96%) of the transferred patients arrived at an invasive treatment center within 2 hours. No deaths occurred en route. Although the median transfer time was 67 minutes, the median difference of time to angioplasty between referral hospitals and invasive treatment centers was only 36 minutes. This is due to the preparation required for the angioplasty facility, part of which can be done while the patient is in transit. The benefit of angioplasty was consistent across all ranges of duration of symptoms (<2 hours, 2–4 hours, or >4 hours).