How does electronic fetal heart rate monitoring affect labor and delivery outcomes?

Evidence-based answer

Continuous electronic fetal monitoring (EFM) reduces the risk of neonatal seizure by 50% compared with intermittent auscultation (IA) (strength of recommendation [SOR]: A, systematic review of randomized controlled trials [RCTs]). EFM increases the incidence of cesarean section by 66% and the incidence of operative vaginal delivery by 16% (SOR: A, systematic review of RCTs). It has no effect on the rates of cerebral palsy or neonatal mortality (SOR: A, systematic review of RCTs). An estimate from a Cochrane meta-analysis suggests that a cohort of 628 women receiving EFM could expect to experience 1 less neonatal seizure and 11 more cesarean sections compared with IA controls.

Evidence summary

Continuous EFM is designed to detect early fetal hypoxia and thereby decrease neonatal morbidity and mortality compared with IA. IA is defined as auscultation of the fetal heart rate for at least 60 seconds every 15 minutes during the first stage of labor and every 5 minutes during the second stage of labor.

A decrease in seizures, but not deaths or cerebral palsy

A 2006 Cochrane systematic review examined 12 RCTs (with >37,000 women) that compared continuous EFM with IA. Continuous EFM reduced the risk of neonatal seizure by 50% (relative risk [RR]=0.50; 95% confidence interval [CI], 0.31–0.80), but had no effect on the rate of neonatal death (RR=0.85; 95% CI, 0.59–1.23) or development of cerebral palsy (RR=1.74; 95% CI, 0.97–3.11).

Reduction of seizures was consistent across all trials. However, a subgroup analysis of high-risk pregnancies (advanced maternal age, diabetes mellitus, chronic hypertension, renal disease, preeclampsia, cardiac disease, renal disease, previous delivery of a low-birth-weight infant) did not find a statistically significant decrease in seizures.

This article was previously published online with the November 2010 issue of The Journal of Family Practice (www.jfponline.com).
Cesarean deliveries rise, regardless of patient risk status
Continuous EFM raised the rates of cesarean delivery (RR=1.66; 95% CI, 1.30–2.13) and instrumental vaginal deliveries (RR=1.16; 95% CI, 1.01–1.32). The increased rate of cesarean section in the EFM group was consistent regardless of clinical risk status (low- vs high-risk women). One additional cesarean section was performed for every 58 women monitored continuously. For “high-risk” women, 1 additional cesarean section was performed for every 12 women monitored continuously.¹

Cesarean section rates varied widely among the individual trials (2.3%–35%). Analysis suggested that studies with higher baseline rates showed the greatest increases with continuous EFM. The rate for all studies combined was just 4.3%; 69% of patients included in the meta-analysis were contributed by the Dublin trial, which had an average cesarean rate of 2.3%.¹ By comparison, the US Division of Vital Statistics reported a cesarean rate of 32.3% in 2008.²

EFM reduces death from fetal hypoxia
A 1995 meta-analysis, including 9 of the Cochrane review studies with a total of 18,561 women, evaluated the additional outcome of death resulting from fetal hypoxia.³ Compared with IA, EFM was associated with a 59% reduction in death from fetal hypoxia (RR=0.41; 95% CI, 0.17–0.98). Continuous EFM prevented 1 perinatal death per 1,000 births. The reduction in perinatal mortality was offset by a 53% increase in cesarean deliveries and a 23% increase in operative vaginal deliveries.³

Recommendations
The American College of Obstetricians and Gynecologists (ACOG) does not recommend for or against continuous fetal heart rate monitoring in uncomplicated labor, recognizing either EFM or IA as acceptable in uncomplicated patients.⁴ ACOG does recommend continuous EFM for women with high-risk conditions (suspected fetal growth restriction, preeclampsia, and type 1 diabetes mellitus).

The US Preventive Services Task Force does not support routine intrapartum EFM for low-risk women. The Task Force found insufficient evidence for using EFM in high-risk pregnancies.⁵

The Royal College of Obstetricians and Gynaecologists and the Royal Australian and New Zealand College of Obstetricians and Gynaecologists both recommend continuous EFM for high-risk women and IA for low-risk patients.⁶⁷

REFERENCES

GLOSSARY
ARR=absolute risk reduction
CDC=Centers for Disease Control and Prevention
CI=confidence interval
CT=computed tomography
FDA=US Food and Drug Administration
HR=hazard ratio
LOE=level of evidence
MRI=magnetic resonance imaging
NNH=number needed to harm
NNT=number needed to treat
OR=odds ratio
RCT=randomized controlled trial
RR=relative risk
SOR=strength of recommendation
From the Editor

Great journal clubs start with PuRls

Dear EBP Readers,

So there you are—a hard-working junior faculty member. You are eager to use all that excellent training you received at your recent fellowship and you are dedicated to improving the academic rigor of your new program. Because of your obvious enthusiasm, you have been put in charge of running the residency's Journal Club.

Having run a Journal Club myself for years, I know this can be a real challenge. In fact, there are 3 challenges. The first is finding a great article, the second is figuring out how to get the residents to read the article, and the third is running an engaging seminar.

The last 2 of these challenges are beyond the scope of this letter.

So let’s talk about finding a great article. The ongoing task is to identify an article that is new, has immediate clinical utility, and is of relatively high quality. This challenge is something I have struggled with month in and month out, and I’ve changed my approach many times.

I tried scanning the New England Journal of Medicine and found articles that were new and high quality, but they were often of little utility. I scanned the Internet medical news sites and found articles that were new, but often lacked both quality and utility. I scanned the Internet medical news sites and found articles that were new and high quality, but they were often of little utility. I scanned the Internet medical news sites and found articles that were new, but often lacked quality and utility. I scanned my own dusty article files and found absolutely nothing new. In fact, there was nothing more recent than 1986.

So a few months ago I was pondering other ways I might find newer, high-quality, priority updates from the research literature that I could use for my Journal Club. Then it hit me. The Family Physicians Inquiries Network (FPIN) is already doing that work—Priority Updates from the Research Literature, also known as PuRls®. There is a new PuRl highlighted every month and published in The Journal of Family Practice. Now all I do is read the PuRl and get the article! Step one for creating a great monthly Journal Club experience is done in record time.

Now if I could only figure out how to get the residents to actually read the articles.

Regards,

Jon O. Neher, MD
New mineralocorticoid antagonist beneficial in milder CHF


This multicenter RCT studied the use of a mineralocorticoid antagonist, eplerenone, in ~2,700 patients older than 55 years with class II congestive heart failure (CHF; mild fatigue/dyspnea with activity) and an ejection fraction <35%. Eplerenone 100 mg/d was compared with placebo, with each group also receiving standard care, such as angiotensin-converting enzyme inhibitors and beta-blockers. Median length of treatment was 21 months.

Patients in the treatment group had significantly lower rates of death from cardiovascular causes, death from any cause, CHF-related hospitalizations, and hospitalizations from any cause, leading to early discontinuation of the trial. All-cause mortality was 12.5% in the treatment group and 15.5% in the placebo group (HR 0.76; 95% CI, 0.62–0.93; P=.008). The NNT to prevent a cardiovascular death or CHF hospitalization per year of follow-up was 19, and NNT to postpone 1 death per year of follow-up was 51. Patients in the eplerenone group did experience more episodes of hyperkalemia, although no difference was noted in hospitalizations for adverse effects.

### Bottom line:
Mineralocorticoid antagonists are recommended for class III/IV heart failure, but their benefit in patients with milder degree of CHF is new. It is unclear if this is a class effect, such that this benefit would also be seen with the less expensive drug, spironolactone. Most patients in the study were white men, so the applicability of the results to other populations is not known. Despite these caveats, this information is important because it is the first demonstration of benefit in patients with this stage of CHF.

*Article Reviewer: Sarah-Anne Schumann, MD*

*Summary Author: Umang Sharma, MD*

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Intensive glucose control increases mortality


This arm of the ACCORD study included ~10,000 adults aged 40–79 years with type 2 diabetes and evidence of prior cardiovascular (CV) disease or additional risk factors for CV disease. Patients were randomized to either intensive glucose control (goal glycosylated hemoglobin [A1c] <6.0%) or standard therapy (goal A1c 7%–7.9%). Patients in the intensive group required more medications, and 45% of the intensive group were on rosiglitazone compared with 25% in the standard group.

The trial was discontinued after 3.5 years when all-cause mortality was noted to be significantly higher in the intensive arm group (1.4%) than the standard group (1.2%; P=.03; HR 1.21; 95% CI, 1.02–1.44; NNH=384). Deaths from CV causes were also more frequent in the intensive therapy group, but nonfatal myocardial infarctions were less likely in the intensive group (HR 0.79; 95% CI, 0.66–0.95).

This update described results through 5 years, or another 1.5 years after discontinuation of the intensive treatment. Results were similar to the preliminary data.

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<tr>
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<th>Yes</th>
<th>Medical care setting</th>
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<tr>
<td>Valid</td>
<td>No</td>
<td>Implementable</td>
<td>Yes</td>
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<tr>
<td>Change in practice</td>
<td>No</td>
<td>Clinically meaningful</td>
<td>Yes</td>
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**Bottom line:** More patients in the intensive arm were taking rosiglitazone, a medication now known to increase mortality. This may account for the higher overall and CV mortality in the treatment group. Although we do not question the validity of these findings per se, the greater use of rosiglitazone in the intensive group precludes attribution of increased mortality to the intensive glucose lowering.

We also believe that current practice in family medicine is not to aim for a treatment A1c goal less than 6.0%. Therefore, even if we were to conclude that intensive control (and not rosiglitazone) accounted for the increased mortality, we do not think this would be a change from current practice.

*Article Reviewer: Debra Stulberg, MD, and Dionna Brown, MD*

*Summary Author: Umang Sharma, MD*
A prior Women's Health Initiative (WHI) randomized placebo-controlled trial found no significant increase in cardiovascular risk associated with supplemental calcium (1 g/d) and vitamin D (400 IU/d) over 7 years in postmenopausal women. However, more than half of study participants were already using personal calcium supplements upon randomization. The investigators reanalyzed WHI results according to personal use of calcium.

Among ~16,000 women not taking calcium supplements, risk of clinical myocardial infarction or stroke associated with calcium and vitamin D supplementation was increased (HR 1.16; 95% CI, 1.00–1.35), as was risk of myocardial infarction or revascularization (HR 1.16; 95% CI, 1.01–1.34). In the women already taking personal calcium supplements, cardiovascular risk did not alter with allocation to calcium. The NNH by causing myocardial infarction or stroke was 178. The NNT to prevent 1 osteoporotic fracture was 302. When data from patients not taking calcium supplements were pooled with data from previous studies of effects of calcium, vitamin D, or both on cardiovascular events, the pooled evidence confirmed an increase in the incidence of myocardial infarction and stroke.

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<td>Clinically meaningful</td>
<td>Yes</td>
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**Bottom line:** Calcium supplementation should not be recommended for menopausal women at high risk of cardiovascular disease. However, the question of which women can benefit most from calcium supplementation and which women are harmed remains unanswered.

*Article Reviewer and Summary Author: Goutham Rao, MD*

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This Danish study used a nationwide birth registry over a 12-year period to assess the risk of birth defects with fetal exposure to newer-generation antiepileptic drugs. When mothers had filled an antiepileptic prescription during the first trimester, rate of major birth defects was 3.2% (49/1,532), compared with 2.4% (19,911/836,263) in those not exposed. Adjusted pooled odds ratio was 0.99 (95% 0.72–1.36). Individually, lamotrigine, oxcarbazepine, and topiramate all had adjusted odds ratios with 95% confidence intervals indicating no difference between exposed and unexposed fetuses in frequency of birth defects.

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**Bottom line:** Birth defects were rare, as expected, and the sample size may have been too small to detect a small but significant increase in risk. The impact of newer antiepileptics may have been underestimated, because the investigators did not account for birth defects leading to terminations. Finally, it is possible there was misclassification regarding medication use, as filled prescriptions may have overestimated actual medication use.

These concerns about the validity of the study lead us to conclude that this study does not definitely prove the safety of these drugs during pregnancy. Nonetheless, these findings support current recommendations for the use of newer antiepileptics during pregnancy by adding evidence that they are safer than first-generation antiepileptics for use during pregnancy.

*Article Reviewer: Nina Rogers, MD*

*Summary Author: Umang Sharma, MD*
What is the most common pattern of hearing loss associated with acoustic neuroma?

**Evidence-Based Answer**

Asymmetric sensorineural hearing loss (ASHL) >15 dB at 3,000 Hz is a fairly strong predictor of acoustic neuroma (AN). A more restrictive protocol intended to reduce MRI scans further requires a >20-dB difference if the pure-tone threshold in the better hearing ear is reduced (>30 dB). (SOR: B, based on retrospective cohort studies.)

A retrospective cohort analysis compared 74 patients with known AN (48% women, mean age=52 years) with 48 control patients (71% women, mean age=41 years) to determine the best audiometric criteria for referral for MRI evaluation. ASHL >15 dB at 3,000 Hz (OR 6.6; 95% CI, 2.5–17; \( P < .001 \)) and absence of vertigo (OR 6.2; 95% CI, 2.2–17; \( P = .001 \)) were highly predictive for AN. A vestibular deficit >25% by electronystagmography and caloric testing was also associated with AN, but did not significantly contribute to the predictive probability for AN. The symptoms of tinnitus and dizziness were not linked to AN. When the cutoff for a positive test (asymmetric ASHL >15 dB at 3,000 Hz) was assigned a 50% probability, the receiver operating characteristic curve showed 73% sensitivity and 76% specificity for AN, and the area under the curve was 0.826.\(^1\)

A retrospective review of 500 patients (>15 years of age) with ASHL >15 dB (all of whom had undergone MRI evaluation) attempted to assess the prevalence of tumor associated with each configuration of the pure-tone audiogram. The overall prevalence of AN among these patients was 2.6% (13 of 500). No specific audiometric configuration was identified that predicted AN.\(^2\)

A retrospective cohort study of 392 MRI scans analyzed 4 published protocols, as well as guidelines published by the United Kingdom Ministry of Health and the American Academy of Otolaryngology-Head and Neck Surgery, to attempt optimum identification of patients with ASHL most appropriate for MRI evaluation to exclude AN. In this cohort, 36 patients with AN were identified; 32 patients had ASHL, 19 also had tinnitus and 11 had dizziness.\(^3\)

The optimal combination of sensitivity (97%) and specificity (49%) was produced using a criterion of >15-dB difference at 2 adjacent frequencies if the mean threshold in the better hearing ear was ≤30 dB and a 20-dB difference if the mean threshold in the better hearing ear was >30 dB. Application of this protocol would have saved 174 MRI scans in this cohort.\(^3\)

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Do antiangiogenic injections slow or reverse vision loss in patients with wet macular degeneration?

**Evidence-Based Answer**

Intravitreal injections of antiangiogenesis medications reduce the risk of further vision loss in patients diagnosed with wet macular degeneration. There is also evidence that these injections can sometimes improve vision in these patients. (SOR: A, based on a systematic review.)

Age-related macular degeneration (AMD) is the leading cause of irreversible vision loss in the United States. Traditional treatments to prevent vision loss have been ineffective. In wet AMD, choroidal neovascularization leads to hemorrhage, leakage of fluid, and eventual scarring in the retina.\(^1\) Intravitreal injection of antiangiogenic factors targeting vascular endothelial growth factor (VEGF) has emerged as a relatively new therapy for wet AMD.\(^2\)

A meta-analysis reported the outcomes of 5 RCTs, which included 2,484 patients at least 50 years of age with wet AMD. All RCTs were double-blinded and examined the effects of drug injections every 4 to 6 weeks compared with sham injections. Injections of pegaptanib (a small-molecule inhibitor of VEGF) were continued for 48 weeks, while injections of ranibizumab (an anti-VEGF monoclonal antibody) were continued for 96 weeks. Follow-up was at least 1 year. The endpoint was reduction of moderate visual acuity loss, defined as the proportion of patients who lost fewer than 15 letters of visual acuity (3 lines on the study eye chart).\(^2\)

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1. Age-related macular degeneration (AMD) is the leading cause of irreversible vision loss in the United States. Traditional treatments to prevent vision loss have been ineffective. In wet AMD, choroidal neovascularization leads to hemorrhage, leakage of fluid, and eventual scarring in the retina.\(^1\) Intravitreal injection of antiangiogenic factors targeting vascular endothelial growth factor (VEGF) has emerged as a relatively new therapy for wet AMD.\(^2\)
Pegaptanib 0.3 mg reduced the risk of moderate visual acuity loss (RR=0.71; 95% CI, 0.61–0.84; NNT=6.7). Ranibizumab 0.3 mg also resulted in fewer patients losing 15 or more letters visual acuity (RR=0.14; 95% CI, 0.1–0.22; NNT=3.1). In addition, a greater proportion of patients gained visual acuity, defined as a gain of 15 or more letters, using ranibizumab versus placebo (RR=5.81; 95% CI, 3.29–10.26).²

The cost of these antiangiogenic medications might be of concern to patients. One study out of the United Kingdom developed a model to evaluate the cost-effectiveness of ranibizumab and pegaptanib.³ While the authors concluded that all AMD patients benefit from these antiangiogenic treatment compared with sham or photodynamic therapy, 1 year of treatment was estimated at £4,626 for pegaptanib and £9,134 for ranibizumab, roughly $7,495 and $14,800, respectively. Head-to-head comparisons of effectiveness are lacking.

A frequency-matched case-control study of 343 cases and 334 controls showed the 20% of individuals with the highest reported sunlight exposure had an increased chance of having a nuclear cataract (OR 3.68; 95% CI, 1.50–9.01; P=.01). This study did not find a statistically significant relationship between sun exposure and cortical cataract.²

A Japanese case-control study of 661 people (330 with cataract and 331 controls) found an increased chance of having both cortical and nuclear cataract with increased ultraviolet (UV) B exposure at almost all age ranges. The association was strongest for nuclear cataract, and it was also stronger for women than for men. For women, an adjusted OR of 2.3 (95% CI, 1.3–4.5) was found for the association between nuclear opacity and lifetime cumulative UVB exposure.³

Sunglasses may afford some protection by shielding the lens from UV radiation. A case-control study compared 195 cases with 159 controls in the same region. Fifteen percent of patients with cataracts reported sometimes wearing sunglasses from ages 20 through 29, while 27% of persons without cataracts reported the same (OR 2.77; 95% CI, 1.3–5.8; P=.01). This protective effect was not found to be statistically significant at other ages.

Due to the association between long hours in the sun and cataracts,⁴ the American Academy of Ophthalmology recommends wearing 99% and above UV-absorbent sunglasses at all times when outdoors. In particular, they should be worn during the summer, when at the beach or in the water, when participating in winter sports (especially at high altitudes), and when using medications that can cause photosensitivity.⁵

Evidence-Based Answer

Probably. A patient’s sun exposure history is positively associated with the development of cataracts. (SOR: C, based on heterogeneous case-control studies.) Wearing sunglasses to decrease exposure likely reduces the risk of cataract formation and is recommended. (SOR: C, based on a case-control study and expert guidelines.)

A case-control study of 2,520 patients, aged 65 to 84 years with sun exposure since age 30, showed the risk of a cortical cataract increased with increased exposure history. The quartile of patients with the highest sun exposure history (>0.024 Maryland sun-years [MSY], 75.9 J/cm²) had an age-adjusted OR of 1.14 (95% CI, 1.04–2.38; P=.03) for cortical cataract when compared with the quartile who had the lowest sun exposure (≤0.004 MSY).¹
What are the risks and benefits of long-acting anticholinergics in patients with asthma?

**Evidenced-Based Answer**

Long-acting anticholinergics (LA Achs) have been demonstrated to improve peak expiratory flow (PEF) and forced expiratory volume over 1 second (FEV1) in patients with asthma. (SOR: C, based on disease-oriented outcomes.) They produce a small improvement in symptoms when added to inhaled steroid therapy, similar to that achieved by adding a long-acting beta-agonist. (SOR: B, based on a single RCT.) However, long-term safety is unclear.

LA Achs such as tiotropium are approved by the US Food and Drug Administration for managing chronic obstructive pulmonary disease (COPD), but not for asthma. Nevertheless, evidence suggests severe refractory asthma leads to distal airway destruction similar to COPD. Acetylcholine is critical to this process, and LA Achs may slow the progression of airway remodeling.

A randomized, triple-crossover trial of 210 adults with asthma poorly controlled on background therapy of beclomethasone 80 mcg twice daily compared the addition of either the long-acting beta agonist (LABA) salmeterol 50 mcg twice daily or the LA Ach tiotropium 18 mcg/d to doubling the beclomethasone dose.¹

Both tiotropium and salmeterol improved morning and evening PEF and mean daily symptom scores (MDSS) more than high-dose inhaled corticosteroid. Daily symptom scores were evaluated on a 0 to 3 scale, with higher numbers indicating worsened asthma (baseline MDSS for all patients=0.46). Tiotropium improved prebronchodilator FEV1, but did not reduce rescue inhaler use (TABLE 1). Compared with salmeterol, tiotropium improved preand postbronchodilator FEV1, but did not improve any other clinical markers (TABLE 2). There were no safety endpoints.¹

Data regarding the long- and short-term risks of LA Achs are relatively lacking, especially in patients with asthma. A meta-analysis of 17 clinical trials of both long- and short-acting anticholinergics used for COPD demonstrated increased risk of combined

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**TABLE 1**

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Adding tiotropium (95% CI)</th>
<th>P</th>
<th>Doubling glucocorticoid (95% CI)</th>
<th>P</th>
<th>Adding salmeterol (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morning PEF (L/min)</td>
<td>24.4 (16.0 to 32.7)</td>
<td>&lt;.001</td>
<td>1.4 (–8.4 to 5.6)</td>
<td>.69</td>
<td>18.0 (11.5 to 24.5)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Evening PEF (L/min)</td>
<td>29.6 (21.9 to 37.3)</td>
<td>&lt;.001</td>
<td>–5.7 (–12.3 to 0.9)</td>
<td>.09</td>
<td>19.0 (11.7 to 26.3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Mean daily symptom score</td>
<td>–0.09 (–0.12 to –0.05)</td>
<td>&lt;.001</td>
<td>0.03 (–0.01 to 0.06)</td>
<td>.11</td>
<td>–0.04 (–0.08 to –0.01)</td>
<td>.02</td>
</tr>
<tr>
<td>Prebronchodilator FEV1 (L)</td>
<td>0.12 (0.07 to 0.17)</td>
<td>&lt;.001</td>
<td>0.02 (–0.03 to 0.07)</td>
<td>.47</td>
<td>0.01 (–0.04 to 0.06)</td>
<td>.60</td>
</tr>
<tr>
<td>Albuterol rescue use (puffs/day)</td>
<td>–0.11 (–0.26 to 0.03)</td>
<td>.12</td>
<td>–0.07 (–0.19 to 0.06)</td>
<td>.30</td>
<td>–0.16 (–0.28 to –0.03)</td>
<td>.01</td>
</tr>
</tbody>
</table>

FEV1=forced expiratory volume in 1 second; PEF=peak expiratory flow.

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**TABLE 2**

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Tiotropium vs salmeterol (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morning PEF (L/min)</td>
<td>6.4 (–4.8 to 17.5)</td>
<td>.26</td>
</tr>
<tr>
<td>Evening PEF (L/min)</td>
<td>10.6 (–0.1 to 21.3)</td>
<td>.05</td>
</tr>
<tr>
<td>Mean daily symptom score</td>
<td>–0.04 (–0.09 to 0.01)</td>
<td>.10</td>
</tr>
<tr>
<td>Prebronchodilator FEV1 (L)</td>
<td>0.11 (0.04 to 0.18)</td>
<td>.003</td>
</tr>
<tr>
<td>FEV1 after 4 puffs of albuterol (L)</td>
<td>0.07 (0.05 to 0.10)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

FEV1=forced expiratory volume in 1 second; PEF=peak expiratory flow.
cardiovascular death and myocardial infarction (absolute risk increase=0.6%, NNH=166). Increased cardiovascular risk, including an additional stroke risk, may be associated with therapy longer than 6 months.

However, a randomized, double-blind, placebo-controlled trial comparing tiotropium 18 mcg/d with placebo in patients older than 40 years of age with COPD demonstrated that after 4 years treatment, tiotropium was associated with decreased risk of all-cause mortality (ARR=1.9%; NNT=52). Mortality benefits were not maintained 30 days after discontinuation of tiotropium. According to the package insert, less significant adverse effects, such as dry mouth, upper respiratory infection, sinusitis, and pharyngitis, are commonly associated with LAAch use.

Recurrent intussusception occurred in patients aged 9 to 71 months, with no significant sex difference between this group and overall initial intussusceptions. None of the patients who underwent operative reduction during the first episode experienced recurrence, but 9 of 62 (14.5%) patients who underwent hydrostatic reduction experienced recurrence. Of the 9 recurrences, 2 occurred within 3 days, 3 within 3 months, and 4 more than 3 months after the initial episode.

A retrospective cohort study of 258 patients with intussusception from 1980 to 1995 at Montreal Children’s Hospital found a recurrence rate of 10.8%. Thirty percent reoccurred within 24 hours, and 74% occurred within the first 6 months after the first episode. Intussusception reoccurred in 8 of 97 patients (8.2%) after surgical repair and in 20 of 160 (12.5%) after hydrostatic reduction.

A literature review of intussusception from 1974 found a 1% to 3% recurrence rate after operative repair and 10% to 15% after hydrostatic reduction. Underlying conditions (polyps, tumors, and Meckel's diverticulum) increased the risk of recurrence. For comparison, the incidence of initial intussusception in North America is 0.05% to 0.23%.

What is the recurrence rate of intussusception in children?

Evidence-Based Answer

The recurrence rate of intussusception in children is 10% to 11%. Approximately one-quarter reoccur in the first 24 to 72 hours and three-quarters reoccur within the first 6 months after the initial episode. Recurrence appears to be more common after hydrostatic repair (12.5%–14.5%) than after operative repair (0%–8.2%). (SOR: A, based on cohort studies.)

A prospective cohort study from National Taiwan University Hospital followed 89 cases of intussusceptions diagnosed in an emergency room setting from April 1994 to May 1998 and found an overall repeat intussusception rate of 10.1%.1

Lindsey Eimore, PharmD
Kevin Johnson, MD
New Hanover Regional Medical Center
Wilmington, NC

How do the rapid strep antigen tests and throat culture compare when testing for strep?

Evidence-Based Answer

Rapid strep tests have higher specificity than sensitivity. (SOR: B, based on cohort studies.) A negative rapid antigen diagnostic test (RADT) should be backed up by a throat culture in children. A RADT can be used as a stand-alone test in adults, or if previously validated as having comparable sensitivity and specificity with a throat culture. (SOR: C, based on expert guidelines.)

A 2007 retrospective study of more than 18,000 pediatric patients being evaluated for pharyngitis used 2 different second-generation RADTs. Of this cohort, 4,342 (24%) of the RADTs were positive. Negative RADTs (about 14,000) were followed by a throat culture; of these, 968 (6.8%) were positive. The sensitivity of the RADTs was calculated to be 82% and specificity to be 99.2%. The likelihood ratio of a positive test (LR+) was 102, and of a negative test (LR–) was 0.18.¹ A major weakness of the study was that not all patients were cultured, and some numbers provided were author estimates.

A prospective cohort study, done in 2003 in a pediatric emergency department setting, included 213 children with a clinical diagnosis of pharyngitis. All participants were tested with a RADT. Cultures were obtained for children with negative RADTs. A final diagnosis of group A strep pharyngitis was obtained in 33 patients. The RADT was positive in 21 of these patients. Eleven samples were negative on RADT but positive on follow-up throat culture. One weakly positive RADT was negative at culture follow-up. With the prevalence of streptococcal pharyngitis at 15.9% in the study population, the sensitivity of the RADT was 21 of 32 or 65.6% and the specificity was 168 of 169 or 99.4% (LR+ 109.3 and LR– 0.346).² A major weakness of this study was that cultures were not obtained from all participants. Patients with a positive RADT were assumed to be true cases. One weakly positive RADT was followed up with a negative culture and was counted as a true negative.

A 2010 prospective study evaluated 100 consecutive adult patients (aged 18–64 years) with symptoms of acute pharyngitis at an emergency department. Both RADTs and cultures were done. RADTs were found to have a sensitivity of 68.2% and a specificity of 89.7% (LR+ 6.43 and LR– 0.36).³ A previous RCT also compared the sensitivity, specificity, and cost-effectiveness of a RADT with throat culture in adults. Three hundred seventy-two adult patients with a clinical diagnosis of pharyngitis had both throat culture and RADT performed. Compared with throat culture, the RADT achieved a global sensitivity of 91.4% and a specificity of 95.3% (LR+ 19 and LR– 0.09). The positive predictive value was 92% and negative predictive value was 95%. After comparing the costs of testing and treatment with the appropriateness of treatment, systematic RADT without culture back-up was found to be more cost-effective than routine throat culture.⁴

The Infectious Diseases Society of America and the American Academy of Pediatrics recommends using a throat culture as back-up for a RADT in children and adolescents with negative tests.⁵ RADTs may be used as a stand-alone test in adults, or in children if the test has been previously validated by a culture.⁶

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“Evidence based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. The practice of evidence based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research.”
Hypertensive urgencies and emergencies

Hypertensive emergency
Acute, life-threatening blood pressure (BP) elevations, usually >180/120 mmHg, with evidence of end-organ damage. Includes 2 clinical syndromes:
- Malignant hypertension (HTN): retinal manifestations, renal nephrosclerosis
- Hypertensive encephalopathy: cerebral hyperperfusion and edema

Severe asymptomatic HTN
Severe BP elevation not accompanied by end-organ damage. Includes 2 clinical syndromes:
- Hypertensive urgency: risk factors for impending end-organ dysfunction
- Severe uncontrolled HTN: no risk factors

Incidence, prevalence
- In the United States, 33% adults have HTN, and 5% patients presenting to the emergency department have severe HTN
- Approximately 25% of patients with diastolic BP >110 mmHg are asymptomatic (including 8% with hypertensive emergency)

Diagnostics
Presentation
- Hypertensive emergencies present with headache and/or visual changes (75%), nausea or vomiting (40%), chest pain (27%), dyspnea (22%), and neurologic deficit (21%)
- Hypertensive urgencies present with headache (22%), epistaxis (17%), and faintness (10%). Majority of cases are asymptomatic

Diagnostic “criteria”
- Absolute BP less important than rate and acuity of BP increase and presence or absence of end-organ damage
- End-organ damage uncommon with diastolic BP <130 mmHg (except children and pregnant women)

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Meconium aspiration syndrome
Fetal aspiration of meconium-stained amniotic fluid during antepartum or intrapartum period. Refers to newborn respiratory distress secondary to presence of meconium in tracheobronchial airways.

Pathophysiology
- Postterm delivery
  - Occurs more often after 40 or 41 weeks
  - Decline in meconium aspiration syndrome from 5.8% to 1.5% from 1990 to 1997 was attributed to a 33% reduction in births after 41 weeks’ gestation
- Thick meconium and APGAR scores less than 7 at 1 and 5 minutes associated with 80% probability of meconium aspiration syndrome
- Non-Hispanic black race associated with 80% higher risk of meconium-stained amniotic fluid and 67% higher risk of meconium aspiration syndrome compared with non-Hispanic white race, but no difference in mortality

Prognosis
Generally recover without clinical sequelae
- May develop childhood asthma, obstructive airway disease, alveolar hyperinflation, and airway hyperreactivity to exercise at rates of 30% to 40% vs 10% to 12% in general population, but develop normal aerobic capacity
- Significantly higher rates of acute otitis media and tympanostomy during first 4 years of life
- Higher risk for cerebral palsy and neonatal seizures

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Magnesium sulfate for fetal neuroprotection in preterm birth

**Bottom line**

RCTs looking at the magnesium sulfate for neuroprotection in women with imminent preterm labor found no difference in primary outcomes. However, in a meta-analysis of secondary outcomes, rates of cerebral palsy (CP) and gross motor dysfunction were reduced. Based on this evidence, the American Congress of Obstetricians and Gynecologists (ACOG) recommends magnesium sulfate for neuroprophylaxis when preterm delivery seems likely.

**Evidence summary**

Despite advances in obstetric and neonatal care, rates of CP and developmental disorders have increased in premature infants. The risk of developing CP is inversely related to gestational age at birth: only 1 in 1,500 term babies develop CP, versus 4% to 8% of preterm infants (weighing <1,500 g at birth).²

A Cochrane review in 2009 evaluated the effectiveness and safety of magnesium sulfate as a neuroprotective agent for women considered to be at risk of preterm birth. Studies were included if they were RCTs and if the primary aim was to prevent neurological abnormalities in the infant or if long-term neurological outcomes were reported.²

They found a decreased risk of CP in infants of women who received magnesium (RR=0.68; 95% CI, 0.54–0.87; 5 trials with 6,145 infants). The NNT to prevent 1 case of CP was 63 (95% CI, 43–155). They also found a reduced risk of substantial gross motor dysfunction (RR=0.61; 95% CI, 0.44–0.85; 4 trials with 5,980 infants). Furthermore, the authors found no harmful neonatal effects such as pediatric mortality, respiratory depression, or low Apgar scores, although maternal adverse effects such as hypotension and tachycardia were documented.²

Of the 5 RCTs included in the Cochrane review, 2 studies had perinatal death or development of CP as primary outcomes. One of these 2 relevant RCTs randomized 2,241 women at imminent risk of delivery between 24 and 31 weeks to placebo or magnesium (6-g bolus followed by 2 g/h for ≤12 hours) and found no difference in the 2 groups for the primary outcome of a composite of stillbirth or infant death by 1 year of corrected age or moderate or severe CP at ≥2 years of corrected age. In secondary analysis, moderate or severe CP occurred significantly less frequently in the magnesium group (1.9% vs 3.5%; RR=0.55; 95% CI, 0.32–0.95; NNT=62).³

The second relevant RCT randomized 1,062 women prior to 30 weeks’ gestation with delivery expected within 24 hours to placebo or magnesium (4-g bolus followed by 1 g/h for ≤24 hours) and found no difference in the 2 groups for the primary outcomes of infant death or CP or both by 2 years of corrected age. Secondary analysis found infants in the magnesium group had significant reduced gross motor dysfunction (3.4% vs 6.6%; RR=0.51; 95% CI, 0.29–0.91; NNT=31) and combined death or substantial gross motor dysfunction (17.0% vs 22.7%; RR=0.75; 95% CI, 0.59–0.96).⁴

A 2010 ACOG Committee Opinion concluded that magnesium sulfate given before preterm birth reduces the risk of CP in surviving infants. The committee noted that none of the RCTs found that magnesium neuroprophylaxis affected their primary outcome; the benefit was found in secondary analysis, raising some question of its validity. Physicians are encouraged to develop specific guidelines for treatment in accordance with one of the larger RCTs.⁵

**REFERENCES**

Shoe wear and the prevention of ankle sprains

Background

Ankle sprain is the most common trauma among athletes, accounting for 14% of all sports-related injuries.\(^1\) In January 2010, we discussed how semirigid ankle foot orthoses (srAFO, ie, ankle braces that resist inversion and eversion forces) and proprioception physical therapy were effective at preventing reinjury in people with a prior history of ankle sprain.\(^2\)

Unfortunately a stigma exists regarding the use of srAFO in sports, and perhaps with some reason. A 1991 study demonstrated that performance in broad jump, vertical leap, 10-yard shuttle run, and 40-yard sprint were all decreased to varying degrees when both srAFO and ankle taping were compared with performance on unaided ankles. While performance in these activities was never reduced more than 4.6% (\(P<.05\)) with ankle stabilization devices,\(^3\) athletes may be reluctant to use such devices in competition. Subsequently, at least as far back as 1973, authors have been attempting to demonstrate the effectiveness of high-top shoes in the prevention of ankle sprain\(^4\) in an effort to offer protection to athletes without requiring them to wear additional external support.

Review of the evidence

Biomechanically, high-top shoe use makes sense for the prevention of sprains. In 1 study, 20 males were subjected to ankle inversion forces while wearing both high- and low-top shoes. From recorded films of these sudden inversions, the amount and rates of inversion were calculated. The authors found that high-top shoes reduced the amount of inversion by 4.5° (\(P<.001\)).\(^5\)

Although these results were encouraging, a Cochrane meta-analysis of randomized trials of interventions to prevent ankle sprains in athletes was less so. The meta-analysis included 14 trials with a total of 8,279 participants. Interventions included srAFO, air-cast braces, and high-top shoes. Patients using external ankle supports (srAFO and air-cast braces) had a significant reduction in the number of ankle sprains (RR=0.53; 95% CI, 0.40–0.69). This reduction was more pronounced in patients with a prior history of sprain, but still significant if no prior history was present. The authors could not conclusively state that high-top shoes were effective using the existing studies.\(^6\)

Another meta-analysis of trials of interventions for the prevention of lateral ankle sprains identified 8 trials with a total of 7,513 participants. Interventions analyzed included srAFO, ankle taping, and shoe choice. The authors noted that while both srAFO and taping appeared to reduce the incidence of ankle sprains, srAFO seemed to be more protective. As with the Cochrane analysis, the authors noted that shoe choice played an unclear role, but did venture that the “newness” of the shoe was perhaps more protective than its height on the ankle.\(^7\)

Clinical considerations

It has not been shown that high-top athletic shoes reduce the incidence of ankle sprain. Currently, high-top shoes should not be used as a substitute for proven methods of sprain prevention.

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REFERENCES


ERRATUM

In the July issue, the HelpDesk Article, “What is the best screening test for past tuberculosis infection?” (EBP 2011; 14(7):10), incorrectly listed the authors’ affiliation. Juliann Gaydos-Gabriel, MD, and Elizabeth Hutchinson, MD, are from Swedish Medical Center FMR in Seattle, WA.
Is colchicine an effective treatment for pericarditis?

**Bottom line**
The addition of colchicine to conventional treatment (aspirin or prednisone) significantly reduces symptoms at 72 hours and the rate of recurrence of pericarditis compared with conventional treatment alone. The effects are seen in patients with either a first episode of pericarditis or a first recurrence of pericarditis. (SOR: B, based on 2 RCTs.)

**Evidence summary**
Pericarditis recurs in 15% to 50% of patients treated with aspirin or corticosteroids.1,2

**Colchicine reduces recurrence rates after a first episode of pericarditis**
A prospective, randomized, open-label trial evaluated 120 patients with a first episode of pericarditis. Patients were randomly assigned to conventional treatment or conventional treatment plus colchicine at 1 to 2 mg for the first day and then 0.5 to 1 mg/d for 3 months. Conventional treatment consisted of either aspirin (800 mg every 6 or 8 hours for 7–10 days then tapered over 3–4 weeks) or prednisone (1–1.5 mg/kg daily for 1 month then tapered) when aspirin was contraindicated.1

The primary endpoint, pericarditis recurrence rate at 18 months, was 23.5% in aspirin group, 8.8% in aspirin plus colchicine group, 86.7% in prednisone group, and 11.1% in prednisone plus colchicine group. Colchicine significantly reduced the recurrence rate (10.7% in those who received colchicine vs 32.3% in those who did not receive colchicine; P=.004; NNT=5).1

**Symptoms clear fast and recurrence intervals increase**
The secondary endpoint, rate of symptom persistence at 72 hours, was reduced in those who received colchicine—11.7%, compared with 36.7% in patients who did not receive colchicine (P=.03). Patients taking colchicine had a longer symptom-free interval (22.9 vs 17.2 months; P=.007). Five (8.3%) colchicine patients withdrew due to diarrhea.1

**Subsequent recurrences of pericarditis are reduced**
A prospective, open-label, parallel-group trial randomized 84 patients to colchicine with conventional therapy or conventional therapy alone for the first recurrence of pericarditis. Colchicine was dosed at 1 to 2 mg the first day then 0.5 to 1 mg/d for 6 months. Conventional treatment was the same as in the above trial. Patients were followed for 8 to 44 months and all received omeprazole 20 mg/d.

Colchicine significantly decreased the primary endpoint, recurrence rate (45% vs 21%; P=.04; NNT=4), and the secondary endpoint, symptom persistence at 72 hours (10% vs 31%, P=.03, NNT=5). In multivariate analysis, previous corticosteroid usage was shown to be an independent risk factor for further recurrences (OR 2.89; 95% CI, 1.10–8.26; P=.04). Three patients discontinued colchicine due to diarrhea and 2 of these relapsed.

**References**
1. In patients with age-related macular degeneration, orbital injections of antiangiogenic therapy:
   a. Slow vision loss in both wet and dry forms of the disease
   b. May help regain some lost vision when using ranibizumab
   c. Have no effect on wet macular degeneration
   d. Must be given weekly to have any effect

2. What is the rate of recurrent intussusception in children?
   a. 90%
   b. 75%
   c. 10%
   d. 1%

3. Which of the following statements is true about sunlight exposure and cataract formation?
   a. A person’s sunlight exposure is positively associated with cataract risk
   b. Cataract formation is not related to sunlight exposure in young adulthood
   c. Filtered sunlight has been shown to be protective against cataracts
   d. All sunglasses are protective against cataracts

4. A fairly strong predictor of acoustic neuroma at initial presentation is:
   a. Asymmetric hearing loss >15 dB at 3,000 Hz
   b. Asymmetric hearing loss >30 dB at 4,000 Hz
   c. Vertigo/dizziness with symmetric loss >30 dB at 3,000 Hz
   d. Aural fullness and any degree of unilateral hearing loss

5. Colchicine added to conventional therapy for pericarditis may:
   a. Reduce symptoms at 72 hours
   b. Increase time to recurrence of pericarditis
   c. Reduce the number of pericarditis recurrences
   d. All of the above

6. High-top athletic shoes have been shown to:
   a. Significantly decrease the risk of ankle sprain in patients with prior sprains
   b. Significantly reduce the amount of ankle inversion during varus stress
   c. Significantly reduce performance compared with semirigid orthotics
   d. Significantly decrease sprains compared with semirigid orthotics

7. Magnesium sulfate used prior to imminent preterm birth decreases the risk of which adverse events in neonates?
   a. Subgaleal hemorrhage and cerebral palsy
   b. Seizures and sepsis
   c. Cerebral palsy and hyperbilirubinemia
   d. Cerebral palsy and gross motor delay

8. Women with which of the following factors have been shown to be at higher risk for venous thrombosis while taking estrogen replacement therapy?
   a. Hip or lower-extremity fractures
   b. History of superficial thrombophlebitis
   c. Age <52 years old at menopause
   d. Nonsurgical hospitalizations >6 months ago
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