CME

Evidence-Based Practice

A Peer-Reviewed Publication of the Family Physicians Inquiries Network VOLUME 15 NUMBER 10 OCTOBER 2012

FPIN
Family Physicians Inquiries Network

IN-DEPTH

How accurate are troponin levels in evaluating ACS in patients with renal disease?

Evidence-Based Answer

In patients with elevated troponin levels and symptoms of acute coronary syndrome (ACS), troponin levels should be considered prognostic regardless of creatinine clearance (CrCl) (SOR: **A**, RCT). Troponin assays, however, do have reduced accuracy in patients on dialysis (SOR: **B**, retrospective cohort study).

An RCT (n=7,033) of patients with suspected ACS analyzed the effects of renal dysfunction and short-term risk of death.[1] Patients were enrolled if they had either unstable angina and ST segment depression or positive troponin T levels (>0.1 ng/mL). Patients with CrCl >25th percentile with abnormal troponin T levels had an increased risk of myocardial infarction (MI) or death compared with patients with similar CrCl and normal troponins (7% vs 5%; OR 1.6; 95% CI, 1.2–2; *P*<.001). Likewise, when CrCl was ≤25th percentile with abnormal troponin T, the risk of MI or death was increased compared with patients with similar CrCl and normal troponins (20% vs 9%; OR 2.5; 95% CI, 1.9–3.3; *P*<.001). The authors of this trial concluded elevated troponin T levels are prognostic regardless of CrCl levels.

A retrospective study evaluated the accuracy of troponin I levels in the diagnosis of ACS in 108 African American patients presenting with chest pain to the emergency department with renal disease (defined as creatinine ≥1.2 mg/dL).[2] Troponin I levels were drawn on admission, at 8 hours, and at 16 hours, and considered positive if >0.1 ng/mL. All patients underwent a diagnostic coronary angiogram. In the 76 patients on dialysis, elevated troponin I had a sensitivity of 60% and specificity of 71% (positive likelihood ratio [+LR] 2.1, –LR 0.56) for acute infarct. In the 32 patients with renal insufficiency but not on dialysis, troponin I had a sensitivity of 73% and specificity of 83% (+LR 4.3, –LR 0.3).

Tammy Mantzouris, MD
Robert L. Gauer, MD
Womack FMR Clinic, Fort Bragg, NC

The views expressed herein are those of the authors and do not reflect the official policy of the Department of the Army, Department of Defense, or the US Government.

1. Aviles RJ, et al. *N Engl J Med*. 2002; 346(26):2047–2052. **[LOE 1b]**
2. Balamuthusamy S, et al. *Am J Ther*. 2007; 14(4):356–360. **[LOE 2b]**

How accurate are noninvasive myocardial perfusion studies?

Evidence-Based Answer

In general, stress echocardiography (SE) has a higher sensitivity than myocardial perfusion imaging (MPI) (SOR: **A**, meta-analysis). Myocardial contrast echocardiography (MCE) is also an accurate noninvasive test that may be used for the diagnosis of coronary artery disease (CAD) (SOR: **A**, meta-analysis). Combining perfusion and echo studies may increase overall sensitivity, but will reduce specificity (SOR: **B**, cohort study).

A 2010 meta-analysis included 23 RCTs comparing 2,310 patients undergoing MPI with 1,403 patients undergoing SE, all with left main coronary (>50% stenosis) or triple vessel coronary disease seen on prior coronary angiography.[1] Summary receiver-operative characteristic (SROC) curves for each modality revealed significantly higher area under curve (AUC) for SE (0.82) than for MPI (0.72) (*P*=.01). The negative likelihood ratio (–LR) was significantly lower with SE than MPI, indicating that SE is a better test for ruling out disease (**TABLE 1**).

A 2008 meta-analysis reviewed 13 RCTs including 627 patients undergoing quantitative MCE, a bedside technique for assessing myocardial perfusion using microbubbles similar in flow to red blood cells.[2] It compared myocardial capillary blood volume (MCBV), microbubble velocity (MV), and myocardial blood flow (MBF; the product of MCBV and MV) to the references of either coronary angiography (10 studies) or nuclear imaging (SPECT or PET; 1 study), or both (2 studies). MCBV, MV, and MBF were all significantly reduced in subjects with CAD compared with subjects without CAD as identified on the reference test. Data are summarized in **TABLE 2**.

A 2009 prospective study evaluated the effectiveness of adding MPI to standard wall motion (WM) criteria of dipyridamole-atropine stress echocardiography (DASE).[3] Four hundred consecutive patients presenting to a chest pain unit in whom acute coronary syndromes had been ruled out underwent DASE and MPI. Of these, 116 then underwent quantitative coronary angiography, based on either positive results on DASE or high clinical suspicion despite negative DASE results. Angiography detected >50% stenosis in 73 patients. Of these 73 patients, 46 had WM abnormalities seen on DASE and 71 had abnormalities seen on MPI. DASE had a 63% sensitivity with a 91% specificity (+LR 7, –LR 0.4) while DASE plus MPI had a 97% sensitivity with a 74% specificity (+LR 3.7, –LR 0.04). EBP

Daniel Herleth, MD
Sarah Cole, DO
Mercy FMR
St. Louis, MO

1. Mahajan N, et al. *Heart.* 2010; 96(12):956–966. **[LOE 1a]**
2. Abdelmoneim SS, et al. *Eur J Echocardiogr.* 2009; 10(7):813–825. **[LOE 1a]**
3. Gaibazzi N, et al. *J Am Soc Echocardiogr.* 2009; 22(4):404–410. **[LOE 2b]**

TABLE 1
Comparison of SE and MPI for diagnosing left main and triple vessel disease[1]

Imaging type	Sensitivity	Specificity	Positive likelihood ratio	Negative likelihood ratio
Stress echocardiography (SE)	94%	40%	1.57	0.15[a]
Myocardial perfusion imaging (MPI)	75%	48%	1.44	0.52

[a]*P*<.001 vs MPI.

TABLE 2
MCE reserve parameters for diagnosing coronary artery disease[2]

Reserve parameter	Sensitivity	Specificity	Positive likelihood ratio	Negative likelihood ratio
Myocardial blood volume (MCBV)	67%	52%	1.4	0.63
Microbubble velocity (MBV)	81%	77%	3.5	0.25
Myocardial blood flow (MBF)	80%	81%	4.2	0.25

MCE=myocardial contrast echocardiography.

Evidence-Based Practice

EDITOR-IN-CHIEF
Jon O. Neher, MD, FAAFP
University of Washington

EXECUTIVE EDITOR
John Saultz, MD, FAAFP
Oregon Health & Science University

FOUNDING EDITOR-IN-CHIEF
Bernard Ewigman, MD, MSPH, FAAFP
The University of Chicago

DEPUTY EDITORS

Clinical Inquiries
Gary Kelsberg, MD, FAAFP
University of Washington

Clinical Inquiries
E. Chris Vincent, MD
University of Washington

Clinical Inquiries
Rick Guthmann, MD, MPH
University of Illinois

HelpDesk Answers
Corey Lyon, DO
University of Colorado

eMedRef
Robert Marshall, MD, MPH
Madigan Army Medical Center

Diving for PURLs
Goutham Rao, MD
Kate Rowland, MD
The University of Chicago

SECTION EDITORS

Behavioral Health Matters
Vanessa Rollins, PhD
University of Colorado

Integrative Medicine
David Rakel, MD, FAAFP
University of Wisconsin

Musculoskeletal Health
Andrew W. Gottschalk, MD
Cleveland Clinic

EBM on the Wards
Jennifer Kelley, MD
Research FMR

Maternity Care
Lee Dresang, MD
University of Wisconsin

Pharmacy HDAs
Connie Kraus, PharmD, BCPS
University of Wisconsin

PRODUCTION

Medical Copy Editor
Melissa L. Bogen, ELS
Chester, NY

Managing Editor
Lindsay DuCharme, MJ
Columbia, MO
lindsay@fpin.org

Layout and Design
Robert Thatcher
New York, NY

Statement of Purpose
Evidence-Based Practice (EBP) addresses important patient care questions asked by practicing family physicians, using the best sources of evidence in a brief, clinically useful format. Our goal is to instruct our authors on how to write peer-reviewed scholarly research for the medical and scientific community.

Disclosure
It is the policy of the University of Colorado School of Medicine to require the disclosure of the existence of any relevant financial interest or any other relationship a faculty member or a provider has with the manufacturer(s) of any commercial product(s) discussed in an educational presentation. In meeting the requirements of full disclosure and in compliance with the ACCME Essentials, Standards for Commercial Support, and Guidelines, the following information has been provided by the editors regarding potential conflicts of interest: Jon O. Neher, M.D. and John Saultz, M.D. have disclosed no relationships with commercial supporters.

The PURLs Surveillance System is supported in part by Grant Number UL1RR024999 from the National Center for Research Resources, a Clinical Translational Science Award to the University of Chicago. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Center for Research Resources or the National Institutes of Health.

EBP CME
Evidence-Based Practice (ISSN 1095-4120) is published monthly to family clinicians by the Family Physicians Inquiries Network, Inc. FPIN is a nonprofit 501(C)3 educational and research consortium.

Accreditation Statement
This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education through the joint sponsorship of the University of Colorado School of Medicine and Family Physicians Inquiries Network. The University of Colorado School of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

Credit Designation
The University of Colorado School of Medicine designates this enduring material for a maximum of 48 *AMA PRA Category 1 Credits*™ (4 *AMA PRA Category 1 Credits*™ per issue). Physicians should only claim credit commensurate with the extent of their participation in the activity. Credit must be claimed by March 31, 2013.

2013 Subscription Rates

Personal Subscriptions:	
FPIN Member (includes 48 AMA PRA Category 1 Credits™)	$59
Non-member (includes 48 AMA PRA Category 1 Credits™)	$119
International (outside of the US or Canada)	$179
Institutional Subscriptions:	
US and Canadian Institutions (without CME)	$209
International Institutions (without CME)	$259
EBP Electronic Archives	$500

Third Class postage paid at Columbia, MO 65202. The GST number for Canadian subscribers is 124002536. Postmaster: Send address changes to FPIN, Inc., 409 W. Vandiver Drive, Bldg 4, Suite 202, Columbia, MO 65202; Attn: Lindsay DuCharme. Lindsay@fpin.org. 573-256-2066.

From the Editor

What goes around

Dear EBP Readers,

Editors are human beings just like everyone else. But by golly, editors have standards. That is the whole point of the job.

Nevertheless, I always feel pangs of guilt when I hear from a staff member at the office of *Evidence-Based Practice* (EBP) that my editorial comments have made some budding young author angry or, worse yet, reduced someone to tears of frustration. Naturally I regret causing anyone distress, but I console myself that editors have to stand up for:

- strong declarative sentences
- appropriate application of strength of recommendations (SORs)
- the inclusion of user-friendly statistics
- standardized bibliographies

However, I don't always wear my EBP editor hat. Sometimes, I find myself authoring FPIN Clinical Inquiries (CIs) with residents at the program where I teach. CIs are managed by a different department in the FPIN organization from EBP, and my CI manuscripts are subjected to the same battery of independent editorial review that all CI manuscripts receive. But consider my surprise when I received these editorial comments on the first draft of my most recent CI effort:

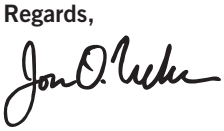
- please use strong declarative sentences
- reconsider the SORs you have chosen
- include user-friendly statistics
- write the bibliography in standard format

I was absolutely flabbergasted. How could I be accused of making these basic mistakes? Once I had my emotions under control, however, I reviewed the manuscript and found that the editor was absolutely correct on all counts.

This just reinforces my often-stated belief that professional writing is a team sport. Editorial review is required to challenge our assumptions, hone our writing clarity, and remove our idiosyncratic language. As an author, I try very hard to be thankful when editors have taken the time to review my writing and have worked with me to create a product that is truly worthy of the FPIN community.

I'd always rather revise than embarrass myself in print. I do that enough as it is.

Regards,



Jon O. Neher, MD

PURLs Criteria
Relevant: Is the topic relevant to family medicine?
Valid: Are the findings scientifically valid?
Change in practice: Would this change practice?
Medical care setting: Is this implementable in clinic, etc?
Implementable: Can we implement this immediately?
Clinically meaningful: Are results clinically meaningful?

Optimal DXA interval less frequent than currently recommended

Gourlay ML, Fine JP, Preisser JS, et al; Study of Osteoporotic Fractures Research Group. Bone-density testing interval and transition to osteoporosis in older women. *N Engl J Med.* 2012;366(3):225–233.

This was a secondary analysis of the Study of Osteoporotic Fractures trial (1986–2004). The study consisted mostly of women who had at least 2 dual x-ray absorptiometry (DXA) scans with normal bone mineral density (BMD) or osteopenia on the first scan. Women who had only 1 DXA scan but had data regarding osteoporotic medications or fractures were also included, for a total of more than 4,500 mostly Caucasian women. Mean follow-up time was 8.2 years, with a maximum of 15 years. Investigators designated the time for 10% of patients to develop osteoporosis as the optimal interval over which to repeat a DXA scan.

This time was 16.8 years for patients with normal baseline BMD (T score above –1.0), 17.3 years for patients with mild osteopenia (T score –1 to –1.5), 4.7 years for patients with moderate osteopenia (T score –1.5 to –2), and 1.1 years for patients with advanced osteopenia (baseline T score –2 to –2.5). Screening intervals were similar when thresholds were changed to time for 20% of patients to progress to osteoporosis (8.5 years for patients with moderate osteoporosis and 2.0 years for patients with advanced osteoporosis). Use of yet another threshold, the development of fragility fractures in 2% of patients, led to intervals of >15 years in those with normal BMD or mild osteopenia and 5 years in those with moderate-advanced osteopenia.

Relevant	Yes	**Medical care setting**	Yes
Valid	Yes	**Implementable**	Yes
Change in practice	Yes	**Clinically meaningful**	Yes

Bottom line: This study supports less frequent intervals for DXA testing than almost all recommending bodies currently advise. The 10% and 20% thresholds were derived from clinical judgment, as there is no prior evidence to guide the proper interval time, and this approach seemed reasonable to us. Furthermore, all analyses supported a longer screening interval—an interval around 15 years in those with normal BMD or mild osteopenia, 5 years in those with moderate osteopenia, and 1 year in those with advanced osteopenia. The population was overwhelmingly Caucasian (>99%), so it should be noted that the applicability of this recommendation to other races is not known.

Article Reviewer and Summary Author: Umang Sharma, MD, The University of Chicago, Department of Family Medicine, Chicago, IL

Antibiotics are minimally effective for acute infective conjunctivitis

Jefferis J, Perera R, Everitt H, et al. Acute infective conjunctivitis in primary care: who needs antibiotics? An individual patient data meta-analysis. *Br J Gen Pract.* 2011;61(590):e542–e548.

This meta-analysis compared antibiotic treatment versus placebo in 2 trials and antibiotics versus no treatment in 1 other trial for acute infective conjunctivitis. Data from 622 individual primary care patients were analyzed. Either chloramphenicol or fusidic acid was used for treatment. The primary outcome was cure at day 7.

Cure was achieved in 80% of antibiotic treatment patients compared with 74% in the placebo group (absolute risk reduction 0.08; 95% CI, 0.01–0.14; NNT 13). However, no significant difference was found between antibiotics and control when only the 2 RCTs that used a placebo as comparison were analyzed.

Relevant	No	**Medical care setting**	Yes
Valid	Yes	**Implementable**	Yes
Change in practice	No	**Clinically meaningful**	Yes

Bottom line: Chloramphenicol and fusidic acid are rarely prescribed for acute conjunctivitis in the United States. Nevertheless, the study is consistent with recommendations that discourage antibiotic use because of the limited benefit. EBP

Article Reviewer and Summary Author: Mari Egan, MD, The University of Chicago, Department of Family Medicine, Chicago, IL

In patients with cytologic abnormalities on Pap smear, what are the indications for HPV DNA testing?

Evidence-Based Answer

Screening for high-risk human papilloma virus (HPV) can be helpful in addition to cytology in women age >30, for triage in women age >20 with atypical squamous cells of undetermined significance (ASCUS), and for follow-up of a negative colposcopy in women with atypical squamous cells–cannot rule out high grade (ASC-H) (SOR: **A**, RCTs and evidence-based guidelines). HPV testing in ASCUS increases the detection of cervical intraepithelial neoplasia (CIN) 2 and 3 (SOR: **B**, prospective case-control study).

A 2003 RCT assigned women age ≥18 with ASCUS (n=3,488) to immediate colposcopy, high-risk HPV screening, or repeat cytology semiannually.[1] All women had Pap smears at enrollment and semiannually for 2 years, then underwent colposcopy at exit. Patients also had colposcopy if they were HPV-positive at any time during the study. The study endpoint was 2-year cumulative diagnosis of CIN3. In women with ASCUS, HPV screening detected 92% (95% CI, 89-95) of individuals ultimately detected to have CIN3 while referring only 53% (95% CI, 52–55) of the ASCUS group to colposcopy. The authors concluded that HPV screening in ASCUS was as effective as immediate colposcopy.

A similar RCT assigned women with LSIL (n=1,572) to groups receiving surveillance protocols similar to those in the prior study.[2] Study design and endpoints were the same as above. In women with LSIL, HPV screening detected 95% (95% CI, 92–98) of individuals ultimately detected to have CIN3; however a high percentage, 84% (95% CI, 82–86), were referred to colposcopy for positive HPV. Thus, the HPV arm of the LSIL study closed early. The authors concluded that HPV screening in LSIL was not beneficial and recommended immediate colposcopy.

A 2009 prospective case-control study performed Pap smear and HPV-DNA analysis in 197 women ages 21–60 with known ASCUS to determine if HPV testing assisted in the detection of CIN2 or CIN3.[3] Colposcopy was performed if patients were (1) ASCUS+/HPV+, (2) ASCUS–/HPV+, or (3) ASCUS+/HPV– based on repeat Pap at study entrance. All women were re-examined after 3 years. CIN2 or CIN3 was detected in 41% of cytology+/HPV+, in 20% of cytology–/HPV+ women, and in none of the cytology+/HPV– groups. The addition of HPV testing in secondary screening of ASCUS-positive women increases the detection of CIN2 or CIN3 by 33% (*P*=.01) when compared with repeat cytology.

The 2006 evidence-based guidelines for the management of women with abnormal cervical cancer screening tests are based on a systematic review of the literature available at the time.[4] The guidelines recommend HPV testing as a follow-up for ASCUS in patients aged >20 (**TABLE**). The guidelines advised

TABLE

Indications for HPV screening based on age and Pap smear findings[4]

Patient group	Screening recommendation		
<20 years	HPV screening is inappropriate regardless of cytologic findings (EII)		
>20 years with cytologic abnormalities	ASCUS: • Reflex HPV screening recommended (AI) • If positive, proceed with colposcopy (AII)	ASC-H & LSIL: • Reflex HPV testing is inappropriate (EII) • Proceed to immediate colposcopy (AII) • If colposcopy is negative, repeat pap at 6 and 12 months or repeat HPV at 12 months (CIII)	HSIL: • HPV screening is inappropriate (EII) • Proceed to immediate colposcopy (BII)

ASC-H=atypical squamous cells–cannot rule out high grade; ASCUS=atypical squamous cells of undetermined significance; HPV=human papilloma virus; HSIL=high-grade squamous intraepithelial lesion; LSIL=low-grade squamous intraepithelial lesion.

AI: Good evidence of clinical benefit, based on at least 1 RCT.

AII: Good evidence of clinical benefit, based on 1 clinical trial, cohort study, or case-control trial.

BII: Limited clinical benefit, based on 1 clinical trial, cohort study, or case-control trial.

CIII: Evidence is insufficient to support a recommendation for or against use, based on expert opinion.

EII: Good evidence for adverse outcome, based on 1 clinical trial, cohort study, or case-control trial.

against HPV testing as a sole screening method. In 2012, the USPSTF stated that, for women aged 30–65 years who wanted to lengthen their sampling interval, a combination of Pap cytology and HPV testing every 5 years was acceptable.[5]

Sandra Minchow-Proffitt, MD
Jessica Miller, MD
Mercy Family Medicine
St. Louis, MO

1. ALTS Group. *Am J Obstet Gynecol*. 2003; 188(6):1383–1392. **[LOE 1b]**
2. ALTS Group. *Am J Obstet Gynecol*. 2003; 188(6):1393–1400. **[LOE 1b]**
3. Silverloo I, et al. *Acta Obstet Gynecol Scand*. 2009; 88(9):1006–1010. **[LOE 2b]**
4. Wright TC Jr, et al. *Am J Obstet Gynecol*. 2007; 197(4):346–355. **[LOE 1a]**
5. Moyer VA, on behalf of the USPSTF. *Ann Intern Med*. 2012; 156(12):880–891. **[LOE 1a]**

Under what circumstances should a patient with an anterior cruciate ligament tear undergo surgical repair?

Evidence-Based Answer

Candidates for surgical repair of a torn anterior cruciate ligament (ACL) include those who have a high activity level, are skeletally immature, or have a concomitant repairable meniscus injury. Candidates for conservative management are skeletally mature patients who do not anticipate engaging in high-risk activities (SOR: **C**, systematic reviews of case series and expert opinion).

A 2005 Cochrane review of surgical versus conservative interventions for ACL rupture found 2 poorly randomized trials conducted in the early 1980s.[1] These 2 studies (N=324) demonstrated no difference between patients managed with surgery and those treated conservatively in their ability to return to their pre-injury sport. In 1 study (N=157) participants treated conservatively had more rapid recovery after injury (mean difference 4 weeks; 95% CI, 0.44–7.56), but this difference was not sustained at 13 months. Patients treated with surgery had less knee instability and less need for future operations (the review did not combine the data). This review concluded "there is insufficient evidence to determine whether surgery or conservative management was best for ACL injury in the 1980s, and no evidence to inform current practice."

In a 2011 nonsystematic review of the literature on treatment of ACL tears, the reviewers identified 10 studies (N not stated) that examined criteria for selecting patients for surgical versus conservative treatment.[2] The authors concluded there were no evidence-based criteria to recommend surgical over nonsurgical treatments. They noted many patients who had high levels of physical activity before injury and treated conservatively were satisfied with their outcome. They also noted that patients generally could return to non-competitive sports with attention to avoiding twisting motions of the knees.

A 2011 systematic review of 55 uncontrolled case-series reports (935 young patients, mean age 13 years) examined outcomes of operative treatment after ACL rupture in children and adolescents who were skeletally immature.[3] In a meta-regression analysis of the results, 84% (95% CI, 76–93) had good to excellent function after repair.

The International Olympic Committee Concepts Statement from 2008 stated that any decision to undergo surgical ACL repair should be individualized in the absence of high-quality evidence.[4] The statement supported the choice of surgery for patients with high levels of activity, skeletal immaturity or concomitant meniscus injury.

Elizabeth Hutchinson, MD
Swedish First Hill FMR
Seattle WA

Jarret Sands, DO
Madigan Army Medical Center FMR
Tacoma, WA

The views expressed herein are those of the authors and do not reflect the official policy of the Department of the Army, Department of Defense, or the US Government.

1. Linko E, et al. Cochrane *Database Syst Rev*. 2005; (2):CD001356. **[LOE 1a]**
2. Delincé P, et al. *Knee Surg Sports Traumatol Arthrosc*. Epub 20 July 2011. **[LOE 5]**
3. Frosch KH, et al. *Arthroscopy*. 2010; 26(11):1539–1550. **[LOE 4]**
4. Renstrom P, et al. *Br J Sports Med*. 2008; 42(6):394–412. **[LOE 5]**

Does weight loss decrease pain in obese patients with osteoarthritis of the knee?

Evidence-Based Answer

Weight loss of any magnitude can improve symptoms of knee pain and improve knee function in obese patients with osteoarthritis (SOR: **A**, consistent RCTs).

Obesity is clearly a risk factor for osteoarthritis (OA) of the knee. A meta-analysis of 21 studies (15 cohort studies and 6 case-control studies) with almost 900,000 patients found a 5-unit increase in body mass index (BMI) associated with a 35% increased risk of knee OA (RR 1.4; 95% CI, 1.2–1.5).[1]

TABLE

Comparison of measurements of knee pain and function at 18 months in patients with OA of the knee who lost weight[2]

Study group (at 18 months)	Weight loss (kilograms)	6-minute walk (meters)	Stair climb time (seconds)	Pain score (WOMAC)[b]
Healthy lifestyle (control)	1.1	430	9.4	6.0
Diet + exercise	5.2	478[a]	8.5[a]	5.1[a]

[a]*P*<.05 vs healthy lifestyle.
[b]Score shown is for the 5 questions that evaluated the degree of pain with activities of daily living (each question rated from 0 to 4, total of 20 points).
OA=osteoarthritis; WOMAC=Western Ontario and McMaster Universities Osteoarthritis Index.

Three RCTs have evaluated the impact of weight loss. One 18-month RCT examined the effectiveness of 4 weight loss strategies (either alone or in combination) on physical function and pain in overweight and obese adults (defined as BMI ≥28 kg/m²) with OA.[2] The study randomized 316 participants into 4 groups that achieved weight loss through healthy lifestyle (control), diet only, exercise only (180 min/wk), or a combination of diet and exercise. Weight loss led to significant improvements in knee pain and function compared with control (**TABLE**).

A second RCT examined weight change and pain scores in 96 obese patients (BMI ≥28 kg/m²) with OA.[3] Participants were randomized into a low-calorie diet (1,200 kcal/d) group and a control group. At 12 months, patients in the low-calorie group experienced a weight loss of 11% compared with 4% in the control group (*P*<.05). Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain scores (5 questions, each scored 0–4, measuring the degree of pain with activity, total of 20 points) were significantly improved in the low-calorie group compared with placebo (mean difference [MD] 7.2; 95% CI, 1.0–13; *P*=.022).

A third RCT examined diet and improvement in knee function in 80 obese participants (BMI ≥28 kg/m²) with knee OA who were randomized into low-calorie and control diets.[4] Function was measured through questions addressing severity of joint pain, stiffness, and limitation of physical function (using 24 different 100-point visual analog scales for a worst possible score of 2,400). The low-calorie group participants lost more weight than the control group (–11.0 and –4.4 kg, respectively; MD –6.6 kg; 95% CI, –7.9 to –5.3; *P*<.0001). This greater weight loss was associated with lower composite disability scores in the low-calorie group compared with control (MD –219; 95% CI, –369 to –69; *P*=.005).

Christopher P. Varacallo, DO
Robert B. Kelly, MD, MS
Fairview Hospital/Cleveland Clinic
Cleveland, OH

1. Jiang L, et al. *Joint Bone Spine.* 2012; 79(3):291–297. **[LOE 2a]**
2. Messier SP, et al. *Arthritis Rheum.* 2004; 50(5):1501–1510. **[LOE 1b]**
3. Bliddal H, et al. *Ann Rheum Dis.* 2011; 70(10):1798–1803. **[LOE 1b]**
4. Christensen R, et al. *Osteoarthritis Cartilage.* 2005; 13(1):20–27. **[LOE 1b]**

What treatments are effective for childhood obesity?

Evidence-Based Answer

Medium- to high-intensity weight loss interventions that include a combination of nutritional counseling, physical activity counseling, and behavioral management can reduce the body mass index (BMI) in obese children (SOR: **A**, systematic review). Behavioral counseling alone may also be successful to some degree (SOR: **B**, meta-analysis of lower quality RCTs). Orlistat is effective in reducing BMI in obese children and is FDA-approved for obese adolescents aged 12–16 years, although the effect is small (SOR: **A**, systematic review).

A 2010 US Preventive Services Task Force systematic review examined 11 fair or good-quality studies of 13 comprehensive weight loss interventions in 1,513 overweight and obese children and adolescents. Comprehensive interventions included 3 components: dietary counseling, physical activity, and behavioral management.[1] Interventions were categorized into very low (<10 contact hours during the course of the study), low- (10–25 hours), moderate- (26–75 hours), or high-intensity (>75 hours) interventions. Moderate- or high-intensity interventions resulted in a decrease in BMI at 6 to 12 months, ranging from 1.9 to 3.3 kg/m² compared with controls.

CONTINUED

A 2009 Cochrane review examined 64 fair- or good-quality RCTs studying lifestyle interventions (54 studies, N=3,806) and drug treatment (10 studies, N=1,424) for obesity.[2] Among 301 children <12 years who participated in 4 fair- or good-quality RCTs examining lifestyle counseling, those who received behavioral counseling had a mean difference in BMI of –0.06 (95% CI, –0.12 to –0.01) over 6 months compared with those who did not receive counseling. No differences were found in 264 children from 3 trials studying diet and activity counseling (mean BMI difference 0.04; 95% CI, –0.12 to 0.04). In children >12 years, 173 adolescents in 3 trials randomized to behavioral counseling had a mean decrease in BMI of 0.14 (95% CI, 0.17–0.12).

In 2007, an expert committee of the American Medical Association recommended treatment with a comprehensive multidisciplinary intervention for obese children.[3] This review found evidence of benefit from strategies that involve the family, increased activity, and reduced high-calorie food and beverage intake. They also recommend ongoing support from the physician to maintain weight loss.

The Cochrane review mentioned above also included 10 studies evaluating medication (metformin, orlistat, and sibutramine) and pooled data from 2 RCTs evaluating orlistat (N=579).[2] Children who received orlistat 120 mg TID had a lower BMI than children who received placebo (mean difference –0.76; 95% CI, –1.07 to –0.44). The larger of the 2 studies (N=539 children, aged 12–16 years) found that, over 1 year, children treated with orlistat 120 mg TID decreased BMI by 0.55 whereas children who received placebo gained 0.31 in BMI (P<.001). Mild to moderate gastrointestinal side effects (fatty, oily stool and spotting, fecal urgency, abdominal pain, and flatus with discharge) occurred with orlistat.

Thomas Gavagan, MD, MPH
U of Illinois at Chicago

Amy Swift-Johnson, MD
U of Chicago & NorthShore University Health System

Kate Rowland, MD
U of Chicago and Advocate Illinois Masonic FMR

Susan E. Meadows, MLS
U of Missouri, Columbia

1. Whitlock EP, et al. *Pediatrics.* 2010; 125(2):e396–e418. **[LOE 1a]**
2. Oude Luttikhuis H, et al. *Cochrane Database Syst Rev.* 2009; (1):CD001872. **[LOE 1a]**
3. Barlow SE, et al. *Pediatrics.* 2007; 120(suppl 4):S164–S192. **[LOE 5]**

What are the benefits and harms for chlamydia screening in asymptomatic men and women?

Evidence-Based Answer

Annual *Chlamydia trachomatis* screening in high-risk asymptomatic, nonpregnant women reduces the incidence of pelvic inflammatory disease (PID) (SOR: **B**, systematic review and inconsistent RCTs). Evidence is insufficient to suggest benefit from routine screening of asymptomatic males. Harms appear to be minimal.

An RCT of 2,607 women aged 18–34 years assessed screening high-risk women for chlamydia and its effect on PID.[1] High risk was defined as a score of ≥3 out of the following characteristics; age <25 = 1 point, black race = 2 points, nulligravida = 1 point, douching in the previous 12 months = 1 point, and >2 sexual partners in preceding 12 months = 1 point. Patients were randomly assigned to chlamydia screening once (1,009) or to usual care (1,598). The rate of PID after 1 year was 8/10,000 woman-months in the screed group versus 18/10,000 woman-months in the usual care group (RR 0.44; 95% CI, 0.20–0.90).

A 2010 RCT utilized a single chlamydia screening of 2,529 sexually active adolescents and young women aged 16–27 years.[2] Patients self-administered vaginal swabs and the samples were randomized to immediate testing and treatment, or analysis at 1 year. Chlamydia prevalence was 5.4% in those screened and 5.9% in controls. The overall incidence of PID in both groups was low and was not statistically different between the screened women (1.3%) and the control (1.9%), with 94% follow-up (RR 0.65; 95% CI, 0.34–1.22). Seventy-nine percent of PID cases diagnosed in 12 months were in those who tested negative for chlamydia at baseline. The authors suggested these infections were likely incident infections and that certain populations may benefit from more frequent testing.

Cost effectiveness of chlamydia screening was assessed in a study of 2,000 males and 2,000 females, aged 16–24 years and entering a job-training program.[3] The combination of universal endocervical nucleic acid amplification testing (NAAT) in females and universal urine NAAT screening in males reduced the incidence of PID, with a total cost savings of $141,000 vs no screening and just treating the sequelae of PID. The utility of the study was limited by a small cohort, recruitment bias, and hypothetical estimations of savings.

In 2007, after a systematic review that included the first RCT above, the US Preventive Services Task Force (USPSTF) recommended that all sexually active women aged ≤25 years, and other asymptomatic women at increased risk for infection be routinely screened for chlamydia infection due to the decrease in incidence of PID (USPSTF A recommendation).[4] Increased risk was defined as any of the following: older sexually active women who are unmarried, are African American, have a history of a sexually transmitted infection, have new or multiple sexual partners, have cervical ectopy, or use barrier contraceptives inconsistently. The review did not find any harms with screening. The review concluded the evidence was insufficient to recommend for or against routinely screening asymptomatic men for chlamydia infection (I recommendation).

Toni A. Williams, MD
Marci Moore-Connelley, MD
Southern Illinois University
Carbondale, IL

1. Scholes D, et al. *N Engl J Med*. 1996; 334(21):1362–1366. **[LOE 1b]**
2. Oakeshott P, et al. *BMJ*. 2010; 340:c1642. **[LOE 1b]**
3. Blake DR, et al. *Sex Transm Dis*. 2008; 35(1):91–101. **[LOE 2b]**
4. Screening for Chlamydial Infection: A Focused Evidence Update for the U.S. Preventive Services Task Force. Evidence Synthesis No. 48. Rockville, MD: Agency for Healthcare Research and Quality; June 2007. AHRQ publication 07-05101-EF-1. http://www.uspreventiveservicestaskforce.org/uspstf07/chlamydia/chlamydiasyn.pdf. Accessed August 28, 2012. **[LOE 1a]**

Is there an association between aluminum and Alzheimer's disease?

Evidence-Based Answer

Evidence linking aluminum intake and Alzheimer's disease is inconsistent. However, it might be prudent to keep intake <0.1 mg/d (SOR: **C**, conflicting observational studies).

A 2008 systematic review found 34 observational studies (N not stated) that examined the association between aluminum exposure and Alzheimer's disease.[1] Sixty-eight percent of the studies showed a relationship between aluminum and Alzheimer's disease, 23.5% of the studies were inconclusive about any relationship, and 8.5% suggested that no relationship existed between aluminum exposure and Alzheimer's disease. A major weakness of the review was that the study quality of each article was not discussed.

Another 2008 systematic review on the etiology and epidemiology of dementia included 6 observational studies (N=4,108) that examined the risk of dementia from exposure to aluminum either in drinking water or at work.[2] Two studies showed a positive association, 1 showed an inverse association, and 3 showed no association between aluminum exposure and the development of dementia. The review authors concluded evidence was insufficient to link aluminum exposure to dementia and Alzheimer's disease. A weakness of this review was that study quality was medium to low.

A subsequent cohort study from 2009 followed 1,677 patients in France for an average of 11.3 years to see who developed dementia and, of those, who had high concentrations of aluminum in their drinking water.[3] This study showed that in patients with higher daily aluminum intake (≥0.1 mg/d), there was a higher risk of dementia (adjusted relative risk 2.3; 95% CI, 1.0–5.1) when compared with aluminum intake <0.1 mg/d. This study was limited by a small number of patients (13) who had high aluminum content in their drinking water. The authors adjusted for the following confounding factors: age, sex, educational level, wine consumption, and bottled water consumption. They acknowledged there may be other confounding factors not accounted for.

Jennifer Cook, MD
FMR of Idaho, Boise

Karlynn Sievers, MD
University of Wyoming, Casper

1. Ferreira PC, et al. *Rev Lat Am Enfermagem*. 2008; 16(1):151–157. **[LOE 3a–]**
2. Swedish Council on Technology Assessment in Health Care (SBU). *Dementia – Etiology and Epidemiology*. Vol 1. Stockholm, Sweden: SBU; June 2008. Report no. 172E/1. http://www.sbu.se/upload/publikationer/content1/1/dementia_vol1.pdf. Accessed August 14, 2012. **[LOE 3a]**
3. Rondeau V, et al. *Am J Epidemiol*. 2009; 169(4):489–496. **[LOE 2b]**

***Evidence-Based Practice* learning objectives**

1. To become knowledgeable about evidence-based solutions to commonly encountered clinical problems.
2. To understand how ground-breaking research is changing the practice of family medicine.
3. To become conversant with balanced appraisals of drugs that are marketed to physicians and consumers.

What is the best medication for migraine prevention?

Evidence-Based Answer

Propranolol is the best medication for migraine prevention, based on its efficacy, tolerability, and the quality of evidence supporting it (SOR: **A**, consistent systematic reviews). Other options include nadolol, amitriptyline, topiramate, and sodium valproate (SOR: **B**, systematic reviews with inconsistent findings).

A 2010 systematic review and meta-analysis of 18 commonly prescribed medications for the prevention of migraines included 59 prospective, double-blind RCTs and one 2006 Cochrane review.[1] The Cochrane review of propranolol vs placebo looked at 26 studies involving 668 patients and showed the relative risk for a 50% decrease in migraine frequency to be 1.9 (95% CI, 1.6–2.4, *P*<.00001). The Cochrane review concluded that propranolol has similar efficacy, safety, and tolerability as other medications.[2] An RCT of 100 patients found amitriptyline more effective than placebo at producing a ≥50% reduction in migraines (OR 2.4; 95% CI, 1.1–5.4; *P*=.03). The review authors rated propranolol, amitriptyline, and nadolol as first-line migraine prophylaxis medications. Although the authors' own meta-analysis of trials comparing topiramate with placebo found topiramate was also associated with a ≥50% decrease in migraine frequency (OR 2.4; 95% CI, 1.8–3.3; *P*<.0001), they noted that topiramate is abandoned in up to 30% of patients because of adverse effects. The authors rated it as a second-line treatment. Sodium valproate, among other drugs, was considered third-line treatment for similar reasons.[1]

In 2008, the Scottish Intercollegiate Guidelines Network (SIGN) conducted a systematic review of the literature to assess diagnosis and management of headaches, including migraines.[3] Medications for prevention were given a recommendation grade (A–D) based on the quantity, quality, and consistency of evidence; the external validity of the studies; and the adverse effects of the medication. Based on the above Cochrane review,[2] propranolol was identified as first-line therapy for migraine prophylaxis (grade A recommendation). Topiramate and sodium valproate were also given grade A recommendations,[3] citing a 2004 Cochrane review (23 RCTs, N=2,927) of anticonvulsants for the prevention of migraines. The Cochrane review showed topiramate (6 RCTs, N=898) increased the number of patients who had a ≥50% decrease in migraine frequency versus placebo (OR 3.3; 95% CI, 2.4–4.7; NNT 4) as well as sodium valproate (4 RCTs, N=574) versus placebo (OR 3.3; 95% CI, 1.5–7.7; NNT 3).[4] SIGN gave amitriptyline a grade B recommendation, citing its favorable ability to decrease headache frequency and severity, but with less high-quality evidence than propranolol, topiramate, or sodium valproate.[3]

Jinsong Wu, DO
Drew C. Baird, MD
C. R. Darnall Army Medical Center
Ft. Hood, TX

The views expressed in this article are those of the authors and do not reflect the official policy or position of the Department of the Army, Department of Defense, or the US Government. Opinions, interpretations, conclusions, and recommendations herein are those of the authors and are not necessarily endorsed by the US Army.

1. Pringsheim T, et al. *CMAJ.* 2010; 182(7):E269–E276. **[LOE 1a]**
2. Linde K, et al. *Cochrane Database Syst Rev.* 2004; (2):CD003225. **[LOE 1a]**
3. Diagnosis and management of headache in adults: a national clinical guideline. Edinburgh, Scotland: Scottish Intercollegiate Guidelines Network; November 2008. http://www.sign.ac.uk/pdf/sign107.pdf. Accessed August 27, 2012. **[LOE 1a]**
4. Chronicle E, et al. *Cochrane Database Syst Rev.* 2004; (3):CD003226. **[LOE 1a]**

How effective are leukotriene inhibitors in children with asthma?

Evidence-Based Answer

Leukotriene inhibitors are more effective than placebo in reducing respiratory symptoms in children with intermittent and mild to moderate persistent asthma (SOR: **B**, several RCTs). They do not appear helpful in children with intermittent asthma who present with severe symptoms (SOR: **B**, a single RCT). Also, inhaled corticosteroids (ICS) are more effective than montelukast in preventing asthma exacerbations that require systemic corticosteroids (SOR: **A**, a meta-analysis in adolescents).

A 2008 systematic review of RCTs identified 4 studies that evaluated montelukast as a monotherapy for the treatment of asthma in children.[1] One RCT (n=549) compared montelukast 4 mg/d with placebo for 48 weeks in children 2–5 years old with intermittent asthma. The primary endpoint was number of asthma episodes. Montelukast reduced yearly asthma exacerbations over placebo by 32% (RR 0.7; 95% CI,

0.6–0.8; *P*<.001).

A second RCT included 689 children ages 2–5 years with mild persistent asthma who received either montelukast 4 mg/d or placebo for 12 weeks. The montelukast group showed significant reductions in mean percentage of days with daytime symptoms (59% vs 64%; *P*<.05; NNT=20), days with beta-agonist use (49% vs 55%; *P*<.05; NNT=17), and subjects requiring oral corticosteroids (19% vs 28%; *P*<.05; NNT=11) compared with the placebo group. Montelukast was also associated with more days without asthma symptoms (34% vs 28%; *P*<.05; NNT=17). There was no significant difference in the number of subjects experiencing 1 or more asthma attacks with montelukast or placebo (26% vs 32%, respectively; *P*=.107).[1]

Two additional RCTs included in the systematic review evaluated montelukast efficacy in older children, ages 6–14 years. A multicenter trial (n=336) evaluated 8 weeks of montelukast 5 mg/d versus placebo in subjects with mild to moderate persistent asthma. Concomitant ICS were used by about a third of patients in each group. The primary endpoint, morning FEV1, increased significantly in the montelukast group (mean difference [MD] 4.7%; 95% CI, 1.9–7.4; *P*<.001). The second RCT was a multicenter, 2-period, parallel-group, noninferiority trial (n=949) comparing montelukast 5 mg/d with inhaled fluticasone 200 mcg/d for 12 months in subjects with mild persistent asthma. The primary endpoint was asthma rescue-free days, defined as days which no asthma rescue medication or asthma-related healthcare resource was used. There was an increase from baseline in asthma rescue-free days in the montelukast group (22%) and fluticasone group (25%) over 12 months (no *P* value provided). There were more asthma rescue-free days in the fluticasone group (87%) than in the montelukast group (84%) (MD –2.8%; 95% CI, –4.7% to –0.9%).[1]

A 2011 multicenter, parallel-group, 52-week RCT compared montelukast 4 mg taken daily or intermittently with placebo in 1,771 children 6 months to 5 years old with intermittent asthma presenting with severe symptoms.[2] The intermittent montelukast group took 4 mg/d for 12 days when symptoms consistent with imminent cold or breathing problem began. No significant difference was seen in the number of asthma episodes ending in worsening symptoms between daily (5.3% rate reduction; 95% CI, –11 to 20; *P*=.51) or intermittent montelukast (– 1.2%; 95% CI, –19.2 to 14.0; *P*=.884) when compared with placebo.

A 2010 systematic review 18 RCTs (n=3,757) evaluated the efficacy of ICS versus montelukast in schoolchildren and adolescents with mild to moderate persistent asthma.[3] A meta-analysis of 7 of these RCTs (n=2,429) presented data on asthma exacerbations requiring systemic corticosteroids and demonstrated that ICS significantly reduced the risk of asthma exacerbations requiring systemic corticosteroids compared with montelukast (RR 0.8; 95% CI, 0.7–1.0; NNT=24).

Jeffrey Freund, PharmD
Connie Kraus, PharmD
U of WI School of Pharmacy
Madison, WI

1. Wahn U, et al. *Clin Ther.* 2008; 30(spec no):1026–1035. **[LOE 1a]**
2. Valovirta E, et al. *Ann Allergy Asthma Immunol.* 2011; 106(6):518–526. **[LOE 1b]**
3. Castro-Rodriguez JA, et al. *Arch Dis Child.* 2010; 95(5):365–370. **[LOE 1a]**

Is acupuncture effective for treatment of alcohol, opiate, and cocaine abuse?

Evidence-Based Answer

Acupuncture may be a helpful adjunctive therapy (with an opioid agonist) in reducing narcotic withdrawal symptoms. Acupuncture probably does not improve opiate, cocaine, or alcohol abstinence (SOR: **C**, systematic reviews of low-quality RCTs).

A meta-analysis of 11 unblinded RCTs (n=1,105) of Chinese patients (aged 24–34 years) with heroin dependence compared once- or twice-daily auricular acupuncture (using the National Acupuncture Detoxification Association protocol) combined with opioid agonist (methadone or buprenorphine) versus opioid agonist alone for acute withdrawal.[1] Pooled data from 7 RCTs (n=685) assessed observer-rated opiate withdrawal symptom severity scores measured at baseline to day 10 of treatment (based on the 36-point Himmelsbach scale). Withdrawal scores in the combined treatment group were significantly lower for the first (D1), seventh (D7), and the final 2 days (D9, D10) of treatment compared with opioid agonist alone, but not on other days (weighted mean difference [WMD] for D1, –3.7; 95% CI, –5.8 to –1.5; WMD for D7, –9.5; 95% CI, –18 to –1.1; WMD for

D9, –9.5; 95% CI, –16 to –2.8; WMD for D10, –7.5; 95% CI, –12 to –3.2). Pooled analysis of 4 RCTs (N=524) examining relapse rates at 6 months after discontinuation of acupuncture showed no differences compared with opioid agonist alone (RR 0.60; 95% CI, 0.32–1.1). Limitations of this meta-analysis included lack of sham acupuncture, inconsistent effect (benefit not seen all days), inadequate randomization reporting, and uncertainty of generalizability to US populations.

A Cochrane systematic review examining 7 RCTs (n=1,433 patients, aged 18–51 years) analyzed the effectiveness of auricular acupuncture for cocaine abstinence.[2] There was no difference in urine toxicology-confirmed abstinence after 8 weeks of daily or every other day auricular acupuncture treatment compared with sham acupuncture (1 RCT, N=425; RR 0.98; 95% CI, 0.89–1.1). Likewise, there was no difference with 3 to 8 weeks of daily auricular acupuncture treatments compared with no acupuncture at 6 and 9 month follow-up (2 RCTs, N=522; RR 0.92; 95% CI, 0.84–1.1). Studies were poor quality, with low power and high dropout rates (up to 50%).

A systematic review of 11 RCTs (n=1,110 patients, aged 32–48 years) assessed the efficacy of acupuncture for the treatment of alcohol dependence.[3] Three RCTs (N=380) measuring alcohol craving (by various self-reported scales) showed no difference between acupuncture and sham acupuncture groups. One RCT (n=54) did show a reduction in cravings in the acupuncture group but had a >70% dropout rate. There was no difference between acupuncture and placebo or sham acupuncture for treatment completion rates. Studies were generally of poor quality.

The World Health Organization consensus recommendation endorses acupuncture as a therapeutic option for alcohol, narcotic, and cocaine dependence, while calling for further quality studies.[4]

Vania Rudolf, MD
Mary Ludwig, MD
Sarah Safranek, MLIS
Janelle Guirguis-Blake, MD
Tacoma FMR
Tacoma, WA

1. Liu TT, et al. *Cell Mol Neurobiol*. 2009; 29(4):449–454. **[LOE 1a–]**
2. Gates S, et al. *Cochrane Database Syst Rev*. 2006; (1):CD005192. **[LOE 1a–]**
3. Cho SH, et al. *Alcohol Clin Exp Res*. 2009; 33(8):1305–1313. **[LOE 1a–]**
4. Acupuncture: review and analysis of reports on controlled clinical trials. Geneva, Switzerland: World Health Organization; 2003. http://apps.who.int/medicinedocs/en/d/Js4926e/. Accessed January 25, 2012. **[LOE 5]**

Is there a proven benefit for chest physiotherapy (CPT) in hospitalized patients with pneumonia?

Evidence-Based Answer

Based on current evidence, CPT is not recommended as a routine adjunctive therapy in patients with pneumonia (SOR: **B**, inconsistent or limited-quality patient-oriented evidence).

As the leading cause of death among infectious diseases, pneumonia is usually treated with antibiotics. CPT is an adjunctive therapy used to help clear the airways. Use of CPT requires a trained practitioner and is often used as adjunctive therapy in patients with cystic fibrosis, chronic obstructive pulmonary disease, or lobar atelectasis, or in postoperative patients.[1]

A 2010 Cochrane systematic review searched multiple databases for RCTs assessing the efficacy of CPT for treating pneumonia in adults.[1] Six studies (N=434) met the inclusion criteria, appraising 4 types of CPT (conventional, osteopathic manipulation, active cycle of breathing, and positive expiratory pressure). Comparison groups were either placebo or routine treatment.

No trials revealed a significant difference in the primary outcomes of mortality and cure rate. Only osteopathic manipulative therapy and positive expiratory pressure showed improvement in the secondary outcomes of duration of hospital treatment of 2.0 days (95% CI, –3.5 to –0.58) and 1.4 days (95% CI, –2.8 to –0.03), respectively. Many methodological problems were noted with the studies, including small sample sizes, lack of blinding, dropout rate >10%, and not using intention-to-treat analysis. Thus, the validity of the findings of the secondary outcomes is questionable. EBP

Rajit Kaushal, MD
Marcia Chesebro, MD, MPH
Huntsville FMRP
Huntsville, AL

1. Yang M, et al. *Cochrane Database Syst Rev*. 2010; (2):CD006338. **[LOE 1a]**

We invite your questions and feedback.
Email us at EBP@fpin.org.

Depression in bipolar I disorder

Trigger case

A 26-year-old woman with a diagnosis of bipolar I disorder presents to her physician with 1 month of depressed mood. She is not currently taking any psychotropic medication, and asks to be put on an SSRI. Would this be an appropriate treatment approach?

Summary

Consensus guidelines recommend against antidepressant monotherapy for bipolar I disorder. Rather, a mood stabilizer with good antidepressant effects should be considered. In addition, several trials of common antidepressants combined with a mood stabilizer have not shown any benefit over an adequately dosed mood stabilizer alone.

The evidence

Over the lifetime of a typical patient with bipolar disorder, depressive episodes will be more frequent and longer lasting than manic episodes.[1] The safety and efficacy of antidepressants for bipolar depression has not been clearly defined. Of possible adjunctive treatments, only paroxetine, bupropion, and imipramine have been studied in large, randomized placebo-controlled trials with mood stabilizer monotherapy for comparison.[2]

Paroxetine and imipramine in combination with lithium were examined in a double-blind placebo-controlled study.[3] A total of 117 patients with bipolar disorder, on lithium and in a depressive episode, were randomly assigned to receive paroxetine (mean dose 32.6 mg, range 20–50 mg), imipramine (mean dose 166.7 mg, range 50–300 mg), or placebo (lithium monotherapy). Secondary analysis was done according to each patient's lithium level (high: >0.8 mEq/L; low: ≤0.8 mEq/L). The Hamilton Depression Scale (HAMD) and Clinical Global Impression–Severity scale (CGI-S) were given at weeks 1–6, 8, and 10.

No significant differences were noted in mean change scores between the combined medication groups on the HAMD or CGI-S. There were also no significant differences in response rates (defined as HAMD ≤7 or CGI-S ≤2) in the primary analysis (56%, 41.8%, and 53.8% achieved response in the paroxetine, imipramine, and placebo groups, respectively). However, in the subset of patients with a low serum lithium level, the paroxetine and imipramine groups showed greater improvement in HAMD (mean change –10.4 and –10.7, respectively, $P<.05$) and CGI-S (mean change –1.47 and –1.58, $P<.04$) scores vs lithium alone (mean change –5.82 and –0.59). No serious adverse events were reported in the paroxetine group, but mania or homicidal ideation occurred in 2 patients (5.1%) in the imipramine group, and mania or increased depression occurred in 4 patients (9.3%) in the placebo group.[3]

An RCT compared the efficacy of bupropion or paroxetine as adjuncts with a mood stabilizer (lithium, valproate, or carbamazepine) to placebo plus a mood stabilizer in patients with bipolar I or II in a current depressive episode.[4] Paroxetine or matching placebo was started at 10 mg and increased to a maximum of 40 mg daily, and bupropion or placebo was started at 150 mg and increased to a maximum of 375 mg daily. Each group received up to 26 weeks of treatment. The primary outcome measure was the percentage of subjects who met the criteria for durable recovery (8 weeks of euthymia). The Clinical Monitoring Form and mood rating scales were administered at baseline and follow-up visits.

Durable recovery was seen in 23.5% of the antidepressant plus mood stabilizer group (n=179) and 27.3% of the placebo plus mood stabilizer group (n=187). No significant differences were noted between the treatment groups. There was also no significant difference between the groups on the secondary outcome variables—transient remission (32% antidepressant/mood stabilizer vs 40% placebo/mood stabilizer), treatment-effectiveness response (58% vs 71%), treatment-emergent affective switch (18% vs 20%), and discontinuation due to adverse event (22% vs 17%).[4]

For patients with bipolar disorder type I presenting with depression, experts recommend consideration of a mood stabilizer with robust antidepressant properties such as quetiapine, olanzapine, olanzapine-fluoxetine, lamotrigine, and lithium plus lamotrigine.[1,2] EBP

William Chisholm, MD
Vanessa Rollins, PhD
Rose FMR
Denver, CO

REFERENCES

1. Ostacher MJ. *J Clin Psychiatry*. 2006; 67(suppl 11):18–21. **[LOE 2a]**
2. Goldberg JF. Antidepressants in bipolar disorder: 7 myths and realities. *Curr Psychiatry*. 2010; 9(5):41–51. **[LOE 2a]**
3. Nemeroff CB, et al. *Am J Psychiatry*. 2001; 158(6):906–912. **[LOE 1b]**
4. Sachs GS, et al. *N Engl J Med*. 2007; 356(17):1711–1722. **[LOE 1b]**

Carpal tunnel syndrome (CTS)

Entrapment neuropathy of median nerve as it courses through carpal tunnel.

- Stage I: Predominantly nocturnal symptoms; numbness/ tingling in fingers/hand over median nerve distribution
- Stage II: Nocturnal and daytime symptoms; hand weakness and/or dropping objects
- Stage III: Less sensory complaints; fine motor skill loss; weakness; thenar muscle atrophy

Pathophysiology

- Pathology
  - Local compressive entrapment: demyelination, nerve block (neurapraxia)
  - If compression persists, local nerve blood flow impeded. Event cascade culminating in axon damage
- Incidence, prevalence
  - 1988 US survey: 1.9% self-reported CTS
  - Highest prevalence: white females
- Risk factors
  - Repetitive bending/twisting of hands/wrists
  - Unclear if keyboard use (>4–6 h/d) is a factor

Diagnostics

- History
  - Symptom onset
  - Provocative factors
  - Occupation
  - Pain localization (median nerve vs whole hand)
  - Alleviating hand maneuvers (shaking out; position changes)
  - Predisposing conditions (diabetes, obesity, pregnancy, polyarthritis)
- Physical examination
  - Tinel's test: little diagnostic value
    - Sensitivity 67%, specificity 68%
  - Phalen's test
    - Static wrist flexion for 60 seconds/symptoms reproduced
    - Sensitivity 85%, specificity 89%
- Diagnostic testing
  - Nerve conduction studies (NCS)
  - Needle electromyography (EMG)
- Diagnostic imaging
  - Ultrasound (NCS more useful for grading severity)
  - MRI (if space-occupying lesion suspected)

Key differential diagnoses

- Cervical radiculopathy
- Diabetic neuropathy
- Rheumatoid arthritis

Therapeutics

- Acute treatment
  - Wrist splints: nighttime use effective
  - NSAIDS: no better than placebo
  - Oral corticosteroids: injected steroids more effective
- Further management (24 h)
  - Corticosteroid injections
    - 40 mg triamcinolone without lidocaine
    - Repeat when symptoms recur
- Treatment during pregnancy
  - Wrist splinting less effective in this population
  - Corticosteroid injections provide significant relief
    - 4 mg dexamethasone in 3rd trimester
- Conservative therapy: most patients - symptom reduction
- Long-term care
  - Surgery: good long-term results; low recurrence rates

Follow-up

Orthopedic surgery referral: conservative methods fail; severe sensory deficit; muscle atrophy

Prevention

- Avoid repetitive wrist movements
- Weight management
- Ergonomic keyboards controversial EBP

Authors: Shannon Haas, MD, and Brice Mohundrom, PharmD, BCACP, Baton Rouge General Medical Center, LA

Editor: Carol Scott, MD, University of Nevada Reno FPRP

REFERENCES

1. Tanaka S, et al. *Am J Public Health.* 1994, 84(11):1846-1848. **[LOE 2c]**
2. Brüske J, et al. *Acta Orthop Belg.* 2002; 68(2):141–145. **[LOE 1b]**
3. Graham RG, et al. *Plast Reconstr Surg.* 2004; 113(2):550–556. **[LOE 1b]**

CME EVIDENCE-BASED PRACTICE

CONTINUING MEDICAL EDUCATION TEST OCTOBER 2012

EBP CME Tests are online at www.fpin.org/cme

Each month CME subscribers may earn up to 4 AMA PRA Category 1 credits™ per test!

For each question, please mark the single best answer by checking the appropriate box.
To receive CME credit, a minimum score of 75% (6 out of 8 correct) is required.

1. **What can be said about the relationship between aluminum intake and the risk of Alzheimer's disease?**
   - ❑ a. There is a definite link between aluminum exposure and Alzheimer's disease regardless of the level of exposure
   - ❑ b. Observational studies consistently fail to note an association between the two
   - ❑ c. Studies seeking an association have had conflicting outcomes
   - ❑ d. Because aluminum is not an essential nutrient, no aluminum intake is safe

2. **Which of the following interventions has been shown to lead to weight loss in obese adolescents over a 6- to 12-month period?**
   - ❑ a. Monthly primary care office visits for weight counseling
   - ❑ b. Moderate- to high-intensity behavioral and lifestyle counseling
   - ❑ c. Educational pamphlets
   - ❑ d. Brief physician counseling

3. **Which patient would be a good candidate for conservative (nonsurgical) management of an anterior cruciate ligament tear?**
   - ❑ a. A 14-year-old skier
   - ❑ b. A 25-year-old professional basketball player
   - ❑ c. A 65-year-old with a concomitant painful meniscus injury
   - ❑ d. A 50-year-old who walks 2 miles a day

4. **Which of the following drugs has efficacy in migraine prevention?**
   - ❑ a. Amitriptyline
   - ❑ b. Propranolol
   - ❑ c. Valproic acid
   - ❑ d. All of the above

5. **Although studies of auricular acupuncture are generally of low quality, the procedure may**
   - ❑ a. Be beneficial as an adjunctive therapy in opiate withdrawal
   - ❑ b. Increase alcohol abstinence rates compared with placebo
   - ❑ c. Increase cocaine abstinence rates compared with sham acupuncture
   - ❑ d. Increase opiate abstinence rates compared with sham acupuncture

6. **Weight loss for obese patients with osteoarthritis of the knee**
   - ❑ a. Is not effective
   - ❑ b. Improves function but not pain scores
   - ❑ c. Improves pain scores but not walking speed
   - ❑ d. Improves both pain and function scores

7. **Chlamydia screening in high-risk, nonpregnant, asymptomatic females is effective for decreasing the rate of pelvic inflammatory disease when provided at least:**
   - ❑ a. Every 6 months
   - ❑ b. Every 12 months
   - ❑ c. Every 2 years
   - ❑ d. Every 3 years

8. **Human papilloma virus screening is useful in which of the following populations?**
   - ❑ a. A teen with cytologic abnormalities on Pap smear
   - ❑ b. A woman age 25 with LSIL (low-grade squamous intraepithelial lesion) on Pap smear
   - ❑ c. A woman age 25 with ASCUS (atypical squamous cells of undetermined significance) on Pap smear
   - ❑ d. A woman age 25 with ASC-H (atypical squamous cells–cannot rule out high grade) on Pap smear

Through joint sponsorship by FPIN and the University of Colorado School of Medicine, CME subscribers in 2012 are eligible to earn 4 AMA PRA Category 1 credits™ per month.

This test must be received by March 31, 2013 to be accepted for credit

Answer Key: 1. c; 2. b; 3. d; 4. d; 5. a; 6. d; 7. b; 8. c

A maximum of 4 AMA PRA Category 1 credits™ per month may be earned by CME subscribers. If you are not a subscriber to 'EBP With CME', please include your check for $15 with each test submitted. Make checks payable to: FPIN

To ensure proper credit for your CME test, please provide the following information:

Name (Please print) _____ Title (MD, DO, etc) _____ SSN (last 4 digits) _____

Address _____

City _____ State _____

Zip Code _____ Daytime Phone Number _____ Ext. _____

Email address (to notify you of credits earned) _____

For CME credit, return this test to: FPIN, 409 W. Vandiver Drive, Bldg. #4, Ste 202, Columbia, MO 65202. If you have questions, please contact LuShawna Romeo (email lushawna@fpin.org or call 573-256-2066).

Renew or Subscribe to EBP at fpin.org or call 573-256-2066

Evidence-Based Practice

Family Physicians Inquiries Network, Inc.
409 West Vandiver Drive
Building 4, Suite 202
Columbia, MO 65202

Change Service Requested

PRESORTED
STANDARD
U.S. POSTAGE
PAID
LINCOLN, NE
PERMIT # 365

Expanding the FPIN INSTITUTE

"The Next Era" 2012-2013

Instant Access to Online Scholarly Success

Whatever your schedule, it's our schedule too.
The FPIN Institute is always in session!

The FPIN Institute..."The Next Era" launched this academic year. Our expanding curricula of online modules are accessible through an easy-to-use advanced learning management system (LMS). **PLUS**, members who subscribe to the Institute will also receive access to the PURLs Journal Club Toolkit.

To learn more, contact support@fpin.org