Evidence-based answer

Steroid injection is effective for both short- and long-term relief of symptoms in patients with carpal tunnel syndrome, while oral steroids are effective only for short-term relief (strength of recommendation [SOR]: A, based on meta-analyses). Wrist splinting is also associated with reduced symptoms at a 2- to 6-week follow-up (SOR: B, based on small clinical trials). Ultrasound is not effective at 2 weeks, but may reduce symptoms by 7 weeks (SOR: B, based on small clinical trials).

Evidence summary

Local steroid injections

A Cochrane review included 2 well-done randomized controlled trials (RCTs) with 141 patients that compared steroid injection (methylprednisolone 40 mg or betamethasone 6 mg) with saline placebo. At 1 month, 73% of patients receiving a steroid injection improved, compared with only 28% of patients receiving placebo (relative risk [RR]=2.6; 95% confidence interval [CI], 1.7–3.9; number needed to treat=2).1

One study compared injection placement at the wrist crease with placement 4 cm proximal to the crease and found no difference in clinical outcomes. Two steroid injections separated by 8 weeks, compared with 1 injection, did not confer additional benefit.1
Oral steroids
A Cochrane review of pooled data from 3 RCTs of oral steroids (prednisone 20–25 mg daily) for 10 to 14 days versus placebo demonstrated a significant improvement in symptoms. The mean difference for symptom improvement on a 50-point scale was −7.2 (95% CI, −10 to −4.1). Oral steroids and local steroid injection have equal efficacy at 2 weeks, but at 12 weeks on a 50-point symptom scale the injection was more efficacious: −7.1 (95% CI, −12 to −2.5).

Splinting
A systematic review of nonsurgical treatment of carpal tunnel syndrome included 3 studies that evaluated the short-term use of splints. One study of 80 patients compared nocturnal splints with no treatment and found that after 4 weeks, splinted patients were 4 times more likely to have improved symptoms (RR=4; 95% CI, 2.3–6.8). A second study of 24 patients compared nocturnal with full-time splinting, and found no difference in symptoms or hand function after 6 weeks. A third study randomized 59 patients to neutral wrist splinting versus splinting at 20 degrees. Neutral splinting was more likely to be associated with overall symptom improvement (RR=2.4; 95% CI, 1.1–5.3) and nocturnal symptom improvement (RR=2.1; 95% CI, 0.99–4.7) at 2 weeks. These 3 studies suffered from bias due to inadequate blinding of subjects and clinicians.

Ultrasound
Two RCTs with a total of 63 patients who had carpal tunnel syndrome treated solely with ultrasound versus placebo showed no improvement after 2 weeks of treatment. One of the studies showed significant improvement in symptom scores on a 0–10 visual analog scale after 7 weeks of ultrasound that was sustained at 6 months (weighted mean difference 1.9 points; 95% CI, 2.7 to −1.1). No improvement was noted in function or nerve conduction with ultrasound treatment.

Other nonsurgical treatments
Studies that evaluated nonsteroidal anti-inflammatory drugs, pyridoxine, diuretic agents, chiropractic manipulation, magnets, and laser found these therapies provided no treatment benefit for patients with carpal tunnel syndrome. One small study with a high bias found yoga provided short-term improvement that was similar to that associated with wrist splinting.

Recommendations from others
The American Academy of Orthopedic Surgeons issued a clinical practice guideline for carpal tunnel syndrome, which advocates a local steroid injection or splinting before considering surgery. Oral steroids and ultrasound are also mentioned as options.

The guideline suggests a stepwise approach to evaluation and treatment of carpal tunnel syndrome. They recommend steroid injection over oral steroids, citing better long-term relief of symptoms. The guidelines state there is insufficient evidence to recommend physical therapy and nonsteroidal medications.

REFERENCES
2. O’Connor D, Marshall S, Massy-Westropp N. Non-surgical treatment (other than steroid injection) for carpal tunnel syndrome. Cochrane Database Syst Rev. 2003; (1):CD003219. (LOE 1a)
From the Editor

Trending toward fullness

Dear EBP Readers,

Given the state of the economy, I can easily imagine myself at an interview for a new job. I picture a lady from some human resources department producing a glass of water and asking the inevitable question: “Is the glass half empty or half full?” I enjoy considering what would happen if I got creative all of a sudden, avoided the two expected responses, and answered emphatically that the glass was “trending toward fullness!”

Surely she would sit back in her chair and smile at my wisdom. She would know immediately that I do not accept half measures. She would understand that I am a super-optimist—betting on hidden trends in favor of increasing abundance and against the forces of evaporation. She would see perhaps that I am cut out for a position of leadership.

Or, she might conclude that I am delusional. In that case, I would be sent packing—fast. Indeed, a quick boot out the door is exactly what I would expect from a quality organization. There is no reason to accept someone claiming to see a trend when one does not actually exist. A firm grasp on reality is a reasonable qualification for most jobs.

But strangely, we seem blind to these sorts of wishful pronouncements about favorable trends when they appear in medical writing. We’ve all seen manuscripts with sentences such as: “There was a trend that approached, but did not achieve, statistical significance (RR=1.15; 95% CI, 0.099–1.2; P=.054).” But what trend are the authors talking about? I hope they are not claiming to be able to see into the future, divining what effect more subjects would have on the confidence interval. That’s the proper work of meta-analysis, not super-optimists.

So let’s not claim to see trends that aren’t there. Research outcomes do not trend toward significance any more than the water glass trends toward full. If we would all just demonstrate some greater objectivity here, there’s less chance that any of us will be interviewing with the human resources lady any time soon.

Regards,

Jon O. Neher, MD
How do we pick PURLs?
We scour sources that cover 500 journals daily for useful research evidence, and meet weekly to critically appraise and discuss studies that meet our criteria.

Here are our criteria:

Relevant: Is the topic relevant to family medicine?
Valid: Are the findings scientifically valid?
Change in practice: Would our conclusions change practice?
Medical care setting: Is this implementable in a medical care setting?
Implementable: Can we implement this immediately?
Clinically meaningful: Are the results discussed clinically meaningful?

How much medication is in a teaspoon?

This study evaluated the accuracy of the volume of teaspoons and tablespoons collected in 25 Greek homes. Researchers filled each spoon to “full” and then compared the volume with a calibrated syringe. Of the 71 teaspoons, mean and median volumes were both 4.4 mL, ranging from 2.5 to 7.3 mL. Of the 49 tablespoons, the mean volume was 10.4 mL, the median was 10.3 mL, and the range was 6.7–13.4 mL.

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Bottom line: Pharmacists already recommend that patients use standardized measuring devices for liquid formulations. This study had a very small, highly selected sample, and it is not clear that the variations in volume demonstrated would actually harm anyone. Nonetheless, this simple study reminds us to continue to recommend against using household spoons to measure medication volumes and to recommend using standardized measuring devices.

Intensive weight loss regimen may decrease hot flushes

This RCT was designed to study an intensive behavioral weight loss program for urinary incontinence. This report focuses on the program’s effects on the 154 study participants experiencing hot flushes. Patients in the intervention arm went through a 6-month intensive weight loss program that included weekly hour-long group sessions with counseling on behavior change, physical activity (goal 200 min/wk), and diet (goal 1,200–1,500 kcal/d with meal modeling and vouchers for nutritional replacements). The control group received monthly hour-long educational sessions. Each participant rated her hot flush severity on a 5-point Likert scale.

The intervention group had greater improvement in bothersome hot flushes; the odds ratio of improvement by at least 1 point was 2.25 (32% intervention group vs 24% control group; 95% CI, 1.20–4.21). NNT was 11 to improve by at least 1 point on the Likert scale. Participants in the intervention group also achieved more weight loss, lower body mass index, and lower abdominal circumference.

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Bottom line: Here is yet more evidence in favor of the ubiquitous benefits of exercise and weight loss. The main barrier we perceive is that, like many intensive behavioral programs, this program would be difficult for most patients to implement in its entirety.

Article Reviewer: Nina Rogers, MD
Summary Author: Umang Sharma, MD

Additional information can be found at:
www.fpin.org/page/purlsoverview
Probiotics useful to prevent recurrent bacterial vaginosis


This RCT assigned 120 Chinese women with recurrent bacterial vaginosis to a probiotic intravaginal capsule (Probaclac Vaginal) (n=58) or placebo capsule (n=62). The regimen was 1 week on, 1 week off, 1 week on, then off for the remainder of the study. Probaclac Vaginal contains Lactobacillus rhamnosus, Lactobacillus acidophilus, and Streptococcus thermophilus, with lactobacilli concentrations 80 times greater than the dose usually recommended to maintain vaginal flora.

The primary outcome of bacterial vaginosis diagnosis within 2 months occurred in 15.8% of patients in the treatment arm and 45% of the control arm (odds ratio [OR] 0.23; 95% CI, 0.10–0.55; P<.001, NNT to prevent 1 recurrence of bacterial vaginosis=3). Presence of bacterial vaginosis at 11 months was 11% in the treatment group, compared with 28% in the control group (OR 0.31; 95% CI, 0.11–0.93; P=.04; NNT=6). No significant adverse events occurred in either arm.

Bottom line: The low NNT and the complete lack of adverse effects make probiotics a useful option for recurrent bacterial vaginosis. We found the formulation used in this study online at a reasonable price.

A useful technique for weaning bottle-fed infants


This well-done RCT examined a new technique for weaning bottle-fed infants. Prolonged bottle use (ie, at 2 years) has shown to be associated with (and likely causes) iron deficiency and dental caries. Parents of 9-month-old infants received either an educational intervention and home materials or usual care at the well-child check. The intervention consisted of provision of a Sippy cup for the family, information regarding health effects of prolonged bottle use, and a stepwise protocol to use at home to help with weaning.

The primary outcome, low ferritin levels, was not significantly different in the 2 groups (12% vs 17%; P=.42). Other outcomes included excessive milk consumption, which was not significantly different, but infants in the intervention group did successfully transition to cup 3 months earlier (9 vs 12 months; P=.001) and were less likely to be using a bottle at 2 years (15% vs 40%; P=.004, NNT=4).

Bottom line: This technique appears useful for weaning infants from the bottle, but was not associated with any clear patient-oriented outcomes. The intervention was not shown to reduce iron deficiency anemia or the rate of dental caries, possibly because the study was too small and not long enough.

Summary Authors: Umang Sharma, MD, and Debbie Stulberg, MD

Article Reviewer: Debbie Stulberg, MD

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

Diving for PURLS Team

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Does the non-pneumatic anti-shock garment (NASG) have a role in the management of postpartum hemorrhage?

**Bottom line**

Two studies suggest that the NASG may ameliorate obstetrical hemorrhage when standard methods fail or are unavailable. More research is needed before NASG use can be routinely recommended.

**Evidence summary**

The NASG is a neoprene and Velcro™ device that wraps around a woman’s abdomen, pelvis, and legs, and is currently being studied for use in controlling obstetric hemorrhage. It is similar to a pneumatic anti-shock garment (PASG), also known as MAST trousers (military anti-shock trousers).

Six case reports document the effects of the PASG in US women with obstetrical hemorrhage. All studies showed stabilization and a decrease in blood loss with the PASG.1

PASGs are rarely used in the US since RCTs have shown no improvement in outcome when used for trauma patients; however, most subjects in those studies had penetrating upper body injuries.

**NASG**

A 2010 cohort study enrolled 854 women in Egypt and Nigeria with postpartum hemorrhage >750 mL and signs of shock. An initial group received standard therapy. A second group had the NASG applied in addition to standard therapy.2

NASG use decreased subsequent blood loss by >50% (P<.0001) and decreased mortality from 9% to 3.1% (RR=0.35; 95% CI, 0.19–0.62). In addition, severe morbidity was decreased from 4.2% to 1% (RR=0.24; 95% CI, 0.09–0.67), and combination “adverse outcomes” decreased from 13% to 4.1% (RR=0.32; 95% CI, 0.19–0.53).3

Another cohort study in Egypt reported on NASG use in women with an estimated blood loss >750 mL and a heart rate >100 bpm or systolic blood pressure <100 mmHg. A preintervention phase group of 158 was studied initially, gathering data on blood loss and time to recovery from shock with only routine treatment. The intervention group of 206 women received the NASG in addition to routine treatment.4

Blood loss decreased by 50% with use of the NASG (P<.001).4 In secondary analysis, NASG use also led to decreased recovery time from shock in the subset of women with uterine atony, after controlling for oxytocin dosage.4

**Mechanism of action**

Basic research has shown that the PASG decreases distal aortic blood flow by up to 90%.5 A study on healthy adults showed a decrease in distal aortic blood flow (from a baseline of 2 L/min) by 0.65 L/min for the NASG (95% CI, 0.03–1.3; P=.04) and by 1.1 L/min for an improvised PASG (95% CI, 0.64–1.6; P=.0003).6

PASGs redistribute only about 7% of the blood volume into the upper body, and have no effect on cardiac output.7 Because NASGs generate less pressure than PASGs, it is likely that they have even less of an effect on blood redistribution. They can be expected to aid in hemorrhage control below their upper level of placement, near the umbilicus.

**Recommendation**

Short-term use of a PASG or NASG is relatively benign and is probably appropriate to treat patients with severe postpartum hemorrhage during preparation for more aggressive measures. However, better quality data from RCTs and clear guidelines for appropriate use are needed before the NASG or PASG can be routinely recommended.

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**REFERENCES**

**Can breathing exercises lower blood pressure?**

**Bottom line**
Yes. Small RCTs have shown that daily slow-breathing exercises lower blood pressure (BP), with effects lasting up to 6 months. Due to low cost, lack of adverse effects, and relative ease in performing the exercises, patients and physicians may consider slow-breathing exercises as a primary and adjunct therapy for elevated BP. The effects of breathing exercises on outcomes such as stroke and mortality, however, have not been studied.

**Review of the evidence**
A double-blind RCT of 65 adults with hypertension compared the effects of music-guided slow breathing (intervention) using a target respiratory rate of less than 10 breaths per minute with quiet music alone (control). Weekly BPs were monitored while participants completed 10 minutes of daily treatment.1

After 8 weeks, decreases in diastolic BP (DBP) and mean arterial pressure (MAP) in the intervention group were significantly greater than in the control group (DBP −10.0 mmHg, *P* = .008; MAP −11.7 mmHg, *P* = .03), although differences in systolic BP (SBP −15.2 mmHg, *P* = .14) were not. Six-month voluntary follow-up in 43 subjects demonstrated continued statistically significant reduction in DBP between groups (DBP −9.0 mmHg, *P* = .001).

A multicenter “before and after” study evaluated the effects of breathing on 17 participants with resistant hypertension, defined as elevated BP despite use of a 3-drug regimen. After recording baseline BP, subjects participated in daily 15-minute sessions of device-guided breathing exercises for 8 weeks to slow respiratory rate. The target respiratory rate was not reported. Blood pressures were obtained during office visits at weeks 4 and 8, in addition to daily morning BPs at home.2

Significant reductions were noted in both office BP (−12.9/−6.9 mmHg, *P* < .001 for both) and home BP (−6.4/−2.6 mmHg, *P* < .01/*P* < .05), showing that device-guided breathing can benefit resistant hypertension. There was no long-term follow-up beyond the end of 8 weeks.2

More recent research has sought to distinguish the effects of slow breathing versus relaxation on BP. A small RCT compared the effects of slow breathing using a respiratory rate of 4 to 6 breaths per minute with relaxation on BP over time. Eighty-six participants were randomized into 3 treatment groups: music-guided slow breathing, relaxation by listening to the same slow music, or relaxation by reading. Subjects completed their assigned treatment for 30 minutes daily over 6 months.3

Slow breathing resulted in a significant reduction of 24-hour SBP (−5.4 mmHg, *P* = .001) and nighttime SBP (−7.5 mmHg, *P* < .001). At 6 months, the greatest reduction in SBP was in the slow-breathing group: −4.6 mmHg compared with relaxation by music and −4.1 mmHg compared with relaxation by reading (*P* < .001 for both comparisons). The authors concluded that slow breathing is superior to relaxation for lowering BP.3

A cohort study compared slow breathing with mental relaxation in same-day BP measurements before and after intervention. One hundred participants with essential hypertension rested for 15 minutes before baseline BP was measured. Repeat pressures were collected after participating for 10 minutes in either slow breathing (taking deep breaths to decrease respiratory rate to 6 breaths per minute by mental counting) or mental relaxation (lying comfortably and thinking of a pleasant thought).4

Slow breathing resulted in a significant immediate decrease in SBP (−8.98 mmHg, *P* < .001) and DBP (−3.53 mmHg, *P* < .05) from pre-intervention levels. Blood pressure changes from mental relaxation were significant only in systolic readings (SBP −5.67 mmHg, *P* systolic < .02; DBP −11.1 mmHg, *P* diastolic > .2). The difference in BP reductions between slow breathing and mental relaxation were statistically significant (*P* systolic < .05, *P* diastolic < .01).4

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**REFERENCES**


Are antibiotics effective for acute flares of chronic asthma?

Evidence-Based Answer
Perhaps, but any effect is probably small. Early clinical trials with beta-lactam antibiotics showed no effect. However, one subsequent trial with a macrolide showed improvement in asthma symptom scores (but not forced vital capacity [FVC]) in a population in which infection with Chlamydia pneumoniae or Mycoplasma pneumoniae was a common asthma trigger. (SOR: B, based on a single RCT.)

Authors of a 2001 Cochrane review concluded that evidence was insufficient to assess whether antibiotic use in the treatment of acute asthma was effective. It identified only 2 RCTs with a total of 97 patients who presented to an emergency department with acute asthma. One RCT with 60 patients compared amoxicillin with placebo. Outcome measures were forced expiratory volume in 1 second (FEV1), peak expiratory flow rate, FVC, and number of days needed for participants to achieve 50% overall improvement. There were no significant differences between the 2 groups for any of the outcomes.

The second study in the Cochrane review compared hetacillin versus placebo in 37 children (with 44 exacerbations). The mean FEV1 at 24 hours was 62% of predicted in the antibiotic group and 52% of predicted for the placebo group (mean difference 9.8; 95% CI, –3.6 to 23). The mean FVC at 24 hours was 73% of predicted in the antibiotic group versus 66% for placebo (mean difference 7.0; 95% CI, –0.46 to 20). Mean length of stay in the antibiotic group was shorter than in the placebo group; however, 1 participant from the control group suffered a respiratory arrest and was hospitalized for 9 days.

In a 2006 double-blind RCT, 278 adults with an acute asthma exacerbation were randomized to treatment with either telithromycin or placebo in addition to usual care. Exclusion criteria included a known lower respiratory tract disease or an overt infection requiring specific antibiotic treatment. The primary endpoint was improvement in asthma symptoms during the 10-day treatment period based on symptom scores and peak expiratory flows. Patients rated the frequency and severity of their symptoms on a 7-point scale.² Patients in the telithromycin group had significantly greater improvement in asthma symptoms than those in the placebo group (40% reduction vs 26% reduction, respectively; mean difference –14 points; 95% CI, –23 to –4.3; P = .005). No significant differences were observed in peak flow rates. Sixty-one of the 278 patients had positive serologies for either C pneumoniae, M pneumoniae, or both. There was not a clear relationship between bacterial infection and response to asthma treatment. Limitations of this study included lack of accurate standardized laboratory testing to diagnose C pneumoniae and M pneumoniae infection.²

The National Asthma Education and Prevention Program (NAEPP) Expert Panel Report 2007 does not recommend the use of antibiotics in chronic asthma due to insufficient evidence and does not comment about their use in acute asthma.³


What are the adverse effects of aggressive glucose control in type 2 diabetes?

Evidence-Based Answer
Although maintaining a 10-year median A1c of 7.0% significantly decreases the rate of overall mortality and myocardial infarction (MI) over long-term follow-up (compared with a median A1c of 7.9%), more aggressive glucose control with a median achieved A1c of 6.4% has no known benefit and may increase mortality. (SOR: B, based on conflicting RCTs.)

The UK Prospective Diabetes Study trial compared mortality and cardiovascular outcomes in patients with newly diagnosed type 2 diabetes randomized to receive either conventional dietary therapy or pharmacological therapy with insulin, sulfonylureas, or metformin (the
last for overweight patients only.\textsuperscript{1–3} The achieved A1c levels with medication ranged from 7.0% to 7.4%, while the dietary therapy arms had A1c levels of 7.9% to 8.0%.

After interventions were discontinued, patients were followed an additional 10 years under the care of individual providers. The sulfonylurea-insulin arm failed to show any significant MI or mortality benefits over standard therapy at treatment termination,\textsuperscript{2} but had a 15% lower risk of MI (RR=0.85; 95% CI, 0.74–0.97; \(P=0.01\)) and a 13% lower risk of all-cause mortality (RR=0.87; 95% CI, 0.79–0.96; \(P=0.007\)) at 10-year follow-up.\textsuperscript{3} In contrast, metformin treatment was associated with a 39% lower MI risk than standard therapy (RR=0.61; 95% CI, 0.41–0.89; \(P=0.01\)) and a 36% lower all-cause mortality risk (RR=0.64; 95% CI, 0.45–0.91; \(P=0.011\)) at treatment termination.\textsuperscript{3} At 10-year follow-up, the metformin arm had maintained a 33% lower MI risk (RR=0.67; 95% CI, 0.51–0.89; \(P=0.005\)) and a 27% lower risk of all-cause mortality (RR=0.73; 95% CI, 0.59–0.89; \(P=0.002\)).\textsuperscript{3}

The ACCORD trial (see TABLE for trial design features) compared cardiovascular outcomes in patients receiving either standard dietary/pharmacological therapy targeting an A1c of 7.0% to 7.9% or aggressive pharmacological therapy targeting an A1c of <6.0%. The aggressive arm was stopped prematurely after showing higher rates of cardiovascular-related mortality (2.6% vs 1.8%; HR 1.35; 95% CI, 1.04–1.76; \(P=0.02\)) and all-cause mortality (5% vs 4%; HR 1.22; 95% CI, 1.01–1.46; \(P=0.04\)).\textsuperscript{4}

The ADVANCE trial compared micro- and macrovascular outcomes in patients receiving either standard pharmacological therapy that met existing local A1c guidelines or intensive therapy with gliclazide and other drugs that targeted an A1c of ≤6.5%. No significant differences were noted in rates of macrovascular events, cardiovascular-related mortality, or all-cause mortality between the 2 approaches. It is unclear why the mortality effects of achieved HbA1c in the 6.4% to 6.5% range differed in the ADVANCE and ACCORD trial.\textsuperscript{5}

The VADT trial compared cardiovascular outcomes in veterans with long-standing type 2 diabetes who received either maximal pharmacological therapy targeting an A1c of <6% or standard therapy on half-maximal doses. As in the ADVANCE trial, no significant differences were noted in rates of cardiovascular-related mortality or all-cause mortality. However, the mean achieved A1c in the VADT trial was 6.9%.\textsuperscript{6}

Importantly, in all 3 studies aggressive glucose control was associated with statistically significant increases in hypoglycemic events, hospitalizations, serious adverse events (nonhypoglycemic), and weight gain.

\[\text{TABLE 1}\]

| Study design of trials to assess effectiveness of aggressive or standard hemoglobin A1c targets in patients with type 2 diabetes\textsuperscript{4–6} |
|-----------------|-----------------|-----------------|-----------------|
| n | 10,251 | 11,140 | 1,791 |
| Mean age (y) | 62 | 66 | 60 |
| Median follow-up (y) | 3.5\textsuperscript{a} | 5 | 5.6 |
| Baseline A1c | 8.1% | 7.2% | 9.4% |
| Mediated achieved A1c | Aggr | Std | Aggr | Std | Aggr | Std |
| | 6.4% | 7.5% | 6.3% | 7.0% | 6.9% | 8.5% |

\textsuperscript{a}Aggressive arm discontinued early because of safety reasons.

ACCORD=Action to Control Cardiovascular Risk in Diabetes; ADVANCE=Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation; Aggr=aggressive therapy; Std=standard therapy; VADT=Veterans Affairs Diabetes Trial.

How safe and effective are meningococcal vaccines?

Evidence-Based Answer
The meningococcal conjugate vaccines are safe (SOR: \textit{A}, based on systematic review and multiple RCTs) and immunogenic. The conjugate vaccines provide a superior immune response—particularly in younger populations—compared with the older polysaccharide vaccines. Efficacy data are lacking because the disease is rare.

Meningococcal disease is a devastating disease worldwide, with case fatality rates as high as 22.5% in patients aged 15 to 24 years.\textsuperscript{1} The overall low incidence makes it difficult to perform RCTs to prove vaccine efficacy.

A Cochrane review addressed the meningococcal serogroup type C vaccines. It included 22 studies with 14 RCTs (including 6,679 patients) and 4 observational studies (including >30,000 patients) addressing efficacy and nasopharyngeal carriage. Adverse events were common (up to 58%–75% within 7 days), but in general self-limited, including both local (redness, swelling, induration, pain) and systemic reactions (fever, anorexia, diarrhea, drowsiness, fussiness). An immune response presumed to be protective (statistically significant increase of serum or mucosal antibodies) was measured in all studies, although data were not compiled due to variations in the compounding, dosage, and schedule of the vaccines.\textsuperscript{2}

One large head-to-head trial compared Menactra (Sanofi Pasteur, FDA approved for use in children 2–18 years of age) with Menveo (Novartis, approved for 11–18 years of age) in healthy persons 11 to 55 years of age, with separate publications addressing different ages. The first publication involved 2,180 healthy 11- to 18-year-olds in a randomized, observer-blind fashion.\textsuperscript{3} Immunogenicity at baseline and 1 month post-vaccination—as measured by titers of serogroup-specific serum bactericidal activity (hSBA) utilizing human complement—were comparable. The adverse reactions included pain, erythema, and induration, most of which were mild. Only 1% reported fever, and other serious adverse events were rare (<1%) and were considered to be not attributable to the study vaccines, although this conclusion was not further elaborated.

Another comparison was made in adults aged 19 to 55 years and included 1,359 participants,\textsuperscript{4} again showing no significant difference in immunogenicity (measured by hSBA methods) between the 2 vaccines. Side effects were fewer than in the adolescent group, and no severe adverse events were reported.

Current US immunization recommendations supported by these data include Menactra or Menveo for aged 11 to 18 years and Menactra for high-risk patients aged 2 to 55 years.\textsuperscript{4} Menomune (meningococcal polysaccharide vaccine) is recommended for high-risk adults aged >55 years.

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Does stopping a proton pump inhibitor cause a clinically important rebound phenomenon?

Evidence-Based Answer
After at least 4 weeks of therapy, cessation of proton pump inhibitors (PPIs) may cause a clinically significant increase in dyspepsia. (SOR: \textit{A}, based on 2 double-blind RCTs.)

A systematic review from 2007 found 8 studies regarding rebound acid hypersecretion (RAHS) after PPI withdrawal. These studies measured the acid level in the stomach to determine RAHS. The sample sizes varied from 6 to 32, with a total of 138 patients involved in the review. The studies were heterogeneous in the brand of PPI given, duration of therapy, type of gastric acid measurement, timing of the test, and type of participants. The authors concluded the evidence was not strong for RAHS after PPI treatment, because only 3 of the 8 studies showed hypersecretion.\textsuperscript{1}

Whether hypersecretion has a clinical impact on patients has only recently been studied. Two double-blind RCTs in healthy volunteers from 2009 and
2010 used clinical symptom rating scales in addition to gastric acid levels to determine the significance of RAHS.\(^2,3\)

In the 2009 trial, 120 patients filled out the Gastrointestinal Symptom Rating Scale (GSRS) weekly for 8 weeks during treatment with either esomeprazole 40 mg or placebo, and for 4 weeks after cessation. Fasting blood samples for plasma levels of gastrin and chromogranin A were taken at weeks 0, 4, 8, and 12 to determine acid hypersecretion.\(^2\)

During cessation, the proportion reporting dyspepsia, heartburn, or acid regurgitation in the PPI group was 26 of 59 (44%), compared with only 9 of 59 (15%) in the placebo group (calculated NNH=3.5). Hyperacidity symptoms lasted for the entire 4-week cessation period. The measures of increased acid secretion were significantly correlated with the GSRS score in the PPI group and not in the placebo group ($r=0.34$, $P=0.01$).\(^2\)

The trial from 2010 followed the Glasgow dyspepsia score on a daily basis throughout the study. Forty-eight healthy patients had a 2 week run-in, 4 weeks of treatment with either pantoprazole 40 mg or placebo, and then had 6 weeks of follow-up.\(^3\)

A total of 11 of 25 (44%) patients in the PPI group developed dyspepsia after withdrawal, compared with only 2 of 23 (9%) in the placebo group (calculated NNH=2.8). The peak dyspepsia score was during the first week after cessation in the PPI group, but after that the score was not statistically different from placebo.\(^3\)

Of note, 47 of the 84 (56%) patients taking PPIs in these 2 trials had no rebound symptoms. The length of RAHS symptoms also differed between the 2 trials: 4 weeks versus 1 week. Another limitation of these studies was that only healthy individuals were studied—patients taking PPIs with diagnosed gastrointestinal diseases were not included.

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**Evidence-Based Answer**

Available evidence does not indicate a single best dressing for healing of partial thickness (second-degree) burns. Products that have shown faster wound healing compared with conventional dressings include hydrocolloids, hydrogels, polyurethane dressings, silicon-coated dressings, biosynthetic dressings, antimicrobial dressings, aloe vera, and honey. (SOR: B, based on systematic reviews of RCTs with inconsistent results.) Products that promote moist wound healing are recommended. (SOR: C, based on expert opinion.)

Three systematic reviews have examined the evidence for various products. The first evaluated aloe vera for burn wound healing. Four studies were found, but only 2 studies with 127 patients using the outcome time to wound healing were included in a meta-analysis.\(^1\)

In these studies the aloe vera was applied saturated in gauze or as a cream and compared with Vaseline gauze or antibiotic cream. The weighted mean difference (WMD) in healing time was 8.8 days shorter in the aloe vera group than in the control group (95% CI, 2.5–15 days; $P=0.006$). The authors noted the studies had quality concerns with blinding, allocation concealment, and dropouts. One of the studies was not an RCT, but each patient received both treatments on different areas.\(^1\)

The next systematic review identified RCTs that evaluated the effect of various newer dressings on partial thickness burns. Meta-analysis was not performed. Hydrocolloids, hydrogels, silicon-coated dressings, biosynthetic dressings, and antimicrobial dressings all showed faster healing compared with silver sulfadiazine, with a range of 2 to 17 days. Each comparison included 1 to 6 studies.\(^2\)

Studies comparing hydrogels and polyurethane dressings with paraffin gauze or chlorhexidine-impregnated gauze were less consistent, with some showing faster healing by 2 to 4 days and others showing no significant difference. Each comparison included only 1 or 2 studies.\(^2\)

Few studies have compared the newer dressings with each other, but 1 study showed no difference in healing time between biosynthetic dressings and hydrocolloids. The studies were small (most <100 patients).
How effective is rate control compared with rhythm control in preventing adverse outcomes in patients with atrial fibrillation?

Evidence-Based Answer
In the treatment of atrial fibrillation, rate control is associated with fewer adverse outcomes compared with rhythm control, with no difference in overall mortality. (SOR: A, based on consistent RCTs.)

The 2002 Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) trial was a randomized multicenter comparison of rhythm and pharmacologic rate control over approximately 3.5 years in 4,060 patients with atrial fibrillation. The following adverse outcomes were more common in the rhythm control group: torsade de pointes (0.2% vs 0.8%, \(P<.007\)), cardiac arrest featuring pulseless electrical activity or bradycardia followed by resuscitation (4.2% vs 6.0%, \(P=.001\)), pulmonary events (1.7% vs 7.3%, \(P<.001\)), and prolonged QTc \(>520\) msec (0.3% vs 1.9%, \(P<.001\)). No significant difference was noted in the primary endpoint of death or in the key secondary composite endpoint of death, disabling stroke, disabling anoxic encephalopathy, major bleeding, and cardiac arrest.\(^1\)

The 2008 Japanese Rhythm Management Trial for Atrial Fibrillation (J-RHYTHM) was a randomized, multicenter comparison trial of rhythm and pharmacologic rate control in 823 Japanese patients with paroxysmal atrial fibrillation over an average of 578 days. Rates of primary endpoint occurrence—a composite of death, symptomatic stroke, systemic embolism, major bleeding, heart failure, and physical/psychological disability—were lower in the rhythm group (15.3% vs 22.0%, \(P=.0128\)). Physical/psychological disability represented the vast majority of these outcomes, and was usually the result of the patient’s desire to move to an alternate therapy. No difference was noted in the remaining primary endpoints when that factor was removed (4.3% in rhythm and 5.4% in rate control group, \(P=.26\)). No significant difference was noted in overall mortality (1.0% in rhythm and 0.7% in rate control group).\(^2\)

The 2000 Pharmacologic Intervention in Atrial Fibrillation (PIAF) study was a randomized comparison of rhythm and pharmacologic rate control in 252 patients with symptomatic, persistent atrial fibrillation over a period of 1 year. Patients in the rhythm-control group showed a higher incidence of hospital admission (69% vs 24%, \(P=.001\)) and adverse drug events resulting in a change in therapy (25% vs 14%, \(P=.036\)).\(^3\)

\(^{1}\) Hohnloser SH, Kuck KH, Lilienthal J. Rate or rhythm control in atrial fibrillation—Pharmacologic Intervention in Atrial Fibrillation (PIAF): a randomised trial. Lancet. 2000; 356(9244):1789–1794. [LOE 1b]


Ludwig’s angina

A rapidly progressing submandibular and sublingual necrotizing cellulitis that usually originates from second and third mandibular molar infection.

Therapeutics

Acute treatment
- Requires admission
- Prompt airway management if compromised
- IV antibiotics (immunocompetent patients)
  - Ampicillin/sulbactam 2 g IV q4h, or
  - Penicillin G 2–4 MU IV q4–6h plus metronidazole 500 mg IV q6h
- IV antibiotics (immunocompromised host)
  - Cefotaxime 2 g IV q6h,
  - Ceftizoxime 3 g IV q8h,
  - Imipenem 500 mg IV q6h, or
  - Piperacillin-tazobactam 3.375 g q6h
- Dexamethasone
  - 10 mg IV ×1, then 4 mg q6 h ×48 h
- Nebulized epinephrine
  - 1 mL of 1:1,000 diluted to 5 mL with 0.9% NS

Further management
- Incision and drainage of abscess near caries
- Decompression of submandibular space
- Removal of carious molars

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Herniated disc disease

Extension of the disc material beyond the annulus fibrosus; with or without extension lateral to the posterior longitudinal ligament and spinal column.

May or may not impinge on the nerve roots, thecal sac, or spinal cord.

Background
- Back pain, sciatica, paresthesia, pseudoclaudication (radiating lower-leg pain after walking, relieved by rest)
- Symptoms may worsen with cough, sneezing, Valsalva, prolonged rest
- Frequently pain begins suddenly after an inciting movement

Incidence/prevalence
- 4% of patients with acute low back pain
- 30% of MRIs of asymptomatic patients reveal disc herniations
- Peak incidence between 35 and 45 years of age

Risk factors include family history, trauma, and smoking. Smoking is a risk factor for disc degeneration and herniation.

Prevention
- Preventive measures:
  - Weight loss
  - Regular exercise (SOR: A)
  - Back physical therapy (SOR: B)
  - Smoking cessation
  - Other healthy lifestyle modifications
  - Workplace ergonomics
  - Back school — not recommended (SOR: A)
  - Lumbar supports/back belts — not recommended (SOR: B)

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To review complete topic monograph, visit www.fpin.org/page/ebpemedref
Are alpha-blockers effective for preventing recurrent acute urinary retention in adult men?

Bottom line
Alfuzosin is not effective for the primary prevention of acute urinary retention (AUR) associated with benign prostatic hyperplasia (BPH) in adult men. (SOR: B, based on an RCT.) However, it is effective for secondary prevention for up to 3 months after an initial episode of AUR. (SOR: B, based on an RCT.) Doxazosin does not appear to be effective for preventing AUR. (SOR: C, extrapolated from a single RCT with both primary and secondary prevention as outcomes.)

Evidence summary
Alfuzosin is effective for secondary, not primary, prevention of AUR
An RCT of primary prevention included men aged ≥55 with a ≥6 month history of urinary symptoms related to BPH at risk of BPH progression (worsening symptoms, AUR, decreased urine flow rate) with no prior history of AUR or prostatic surgery. Two years of therapy with 10 mg alfuzosin daily improved lower urinary tract symptoms and quality of life over placebo, but did not reduce the risk of primary AUR compared with placebo among the 1,506 patients who completed the study (2.1% vs 1.8%; P=.82).¹

Phase 2 of a second RCT published in 2005 (n=165) attempted to determine whether 6 months of 10 mg alfuzosin daily could prevent AUR relapse or the need for BPH surgery in men >50 years of age with a first episode of spontaneous AUR related to BPH. Emergency surgery for AUR relapse was necessary in 13.4% of patients receiving alfuzosin, compared with 19.3% receiving placebo. At 1 and 3 months, respectively, AUR relapse occurred in 75% and 97% of patients in the placebo group compared with 36% and 64% in the alfuzosin group. Alfuzosin reduced the risk of AUR relapse requiring emergency surgery at both 1 month (ARR=9.6%, P=.04; NNT=10) and 3 months (ARR=9.5%, P=.04; NNT=10) after the initial AUR event, but the risk reduction at 6 months was no longer significant (ARR=5.9%, P=.20).²

Doxazosin alone of no benefit
An RCT published in 2003 (n=3,047) compared 4 years of doxazosin, finasteride, combination therapy, or placebo on the incidence of AUR. Participants were men aged >50 years with American Urological Association symptom scores of 8 to 30 (scores range from 0 [no symptoms] to 35 [severe symptoms]). Patients were excluded if they had prostate surface antigen levels greater than 10 ng/mL or previous medical or surgical intervention for BPH. Participants were randomized to receive 5 mg finasteride daily, 8 mg doxazosin daily, both medications, or placebo.³

Doxazosin was not more effective than placebo at preventing AUR (0.4 vs 0.6 per 100 person-years; P=.23). The risk of AUR was significantly reduced by finasteride (0.2 vs 0.6 per 100 person-years; P<.001) and by combination therapy (0.1 vs 0.6, P<.001) compared with placebo. Combination therapy was not significantly more effective than finasteride alone.³

REFERENCES
1. Roehrborn CG. Alfuzosin 10 mg once daily prevents overall clinical progression of benign prostatic hyperplasia but not acute urinary retention: results of a 2-year placebo controlled study. BJU Int. 2006; 97(4):731–741. [LOE 1b]

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.
1. Which statement best describes rhythm-control therapy when compared with pharmacologic rate control for the treatment of patients with atrial fibrillation?
   - a. There is no difference in morbidity or mortality
   - b. There is no difference in morbidity, but there is decreased mortality
   - c. There is increased morbidity, but no difference in mortality
   - d. There is increased morbidity and mortality

2. Which of the following statements is true regarding the non-pneumatic anti-shock garment (NASG)?
   - a. Redistribution of blood from lower extremities to vital organs completely explains the NASG’s mechanism of action
   - b. Randomized controlled trials show that the NASG increases distal aortic blood flow
   - c. Cohort studies suggest that the NASG can reduce blood loss and stabilize women with severe obstetrical hemorrhage
   - d. The best efficacy data come from Western Europe

3. Which of the following statements regarding aggressive blood glucose control in patients with type 2 diabetes has been shown to be true in recent randomized clinical trials?
   - a. Aggressive blood glucose control improves overall cardiovascular health
   - b. Aggressive blood glucose control is associated with increased frequency of hypoglycemic events
   - c. The initial beneficial clinical outcomes of aggressive blood glucose control are not evident at follow-ups beyond 5 years
   - d. All of the above

4. Conjugate meningococcal vaccines are
   - a. Not licensed for use in any age group
   - b. Recommended for otherwise low-risk infants
   - c. Similarly safe in infant, adolescent, and adult patients
   - d. Proven effective in multiple placebo-controlled trials

5. In which of the following situations would an alpha-blocker be appropriate?
   - a. As a single agent for primary prevention of acute urinary retention (AUR)
   - b. As a single agent for secondary prevention of AUR 1 year after the initial event
   - c. To augment the effect of finasteride for primary prevention of AUR
   - d. None of the above

6. Which of the following dressings is recommended for the treatment of patients with partial thickness (second-degree) burns?
   - a. Hydrocortisone cream
   - b. Open air
   - c. Silver sulfadiazine
   - d. Hydrocolloid dressing

7. Which of the following statements is true about antibiotic use in asthma management?
   - a. Antibiotics have no role in the treatment of acute asthma exacerbation
   - b. Guidelines recommend using antibiotics for all asthma flares
   - c. Macrolides may improve asthma symptom scores, but not forced vital capacity
   - d. Most asthma exacerbations caused by infection are by bacterial agents

8. Which of the following statements is true regarding the effects of slow-breathing exercises on blood pressure?
   - a. Large randomized trials have demonstrated that breathing exercises reduce cardiovascular mortality
   - b. Decreasing respiratory rate to 12 breaths per minute has been proven effective for lowering systolic blood pressure
   - c. Relaxation by reading is superior to slow breathing for lowering blood pressure
   - d. Slow breathing can be achieved through slow music, mental counting, or use of device guides
The Department of Family Medicine at the University of Colorado Denver Health Sciences Center is seeking a full-time ABFM-certified or eligible family physician for our community-based program. The Rose Residency is located at Rose Medical Center, ranked nationally as a top 100 hospital, and is supported by the Colorado Health Foundation, a nonprofit organization dedicated to making Colorado the healthiest state in the nation. Applicants must possess or be eligible for medical licensure in the State of Colorado. Applicants must demonstrate experience and competence in teaching and patient care. This is a full-time position with obstetric skills and hospital call required. Women and minorities encouraged to apply. Detailed job descriptions and qualifications required can be found on jobsatcu.com and the Department's website, http://fammed.ucdenver.edu/home/careers.aspx.

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Required Qualifications:
MD/DO degree, Colorado Medical License, DEA Certificate, Board Certified/Board Eligible in Family Medicine. Practices full spectrum of Family Medicine, including obstetrics and inpatient medicine. Must obtain medical staff privileges within the HealthONE LLC d/b/a Rose Medical Center and obtain medical staff privileges at University of Colorado Hospital.

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