taking more than 7 tablets of regular strength (325 mg) acetaminophen per week should be monitored closely for any rise in INR levels. Patients taking warfarin who experience a sudden jump in their INR levels should be queried regarding recent acetaminophen use. Steady intake of foods containing vitamin K and moderate alcohol consumption (up to 2 drinks per day) may protect patients from INR elevations.

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Warming Bupivacaine for Intradermal Anesthesia

Jones JS, Plzak C, Wynn BN, Martin S. Effect of temperature and pH adjustment of bupivacaine for intradermal anesthesia. Am J Emerg Med 1998;16:117-120.

Clinical question What effect does the warming and buffering of bupivacaine (Marcaine) have on the pain associated with intradermal injection and the onset of anesthesia?

Background Despite bupivacaine's long duration of action, other local anesthetics are more often used for intradermal anesthesia because of bupivacaine's tendency to cause burning with injection and to have a prolonged onset of anesthesia. Buffering the bupivacaine has been shown to decrease the pain of infiltration. Whether warming bupivacaine to body temperature can reduce injection-associated pain and the duration of onset of anesthesia is unknown.

Population studied The population studied included 40 healthy adult volunteers from the medical and nursing staff at Butterworth Hospital in Grand Rapids, Michigan. There were no reported dropouts and no biographical data were given.

Study design and validity This 3-part randomized, double-blind study compared bilateral forearm injection of room temperature 0.5% bupivacaine buffered to a pH of 7.1 with 8.4% sodium bicarbonate with each of the following three solutions: buffered bupivacaine warmed to 37°C; unbuffered bupivacaine at 37°C; and unbuffered bupivacaine at room temperature. Comparison injections occurred over a 1-month time period. Volunteers rated their pain at the site of injection on a scale of 0 to 100. Participants were given guidelines for the pain scale to create some consistency in rating. Duration of onset of anesthesia in a 1-cm diameter was timed with a stopwatch. The methods for warming and buffering the solution were carefully defined.

Outcomes measured Mean injection pain scores and the duration of onset of anesthesia were compared between buffered room temperature bupivacaine and the other three solutions.

Results Warming buffered bupivacaine significantly reduced the pain of injection by a mean score of 12.1 mm (95% CI, 6.9 - 16.4). Warming also reduced the time of onset of anesthesia by 12.1 seconds from a mean latency time of 83.7 seconds to 71.6 seconds ($P = 0.03$; 95% CI, 0.6 - 23.6). Buffering room temperature bupivacaine reduced the mean pain score compared with an unbuffered solution by 12.8 mm (95% CI, 7.7 - 17.0). Buffering did not, however, affect the duration of onset of anesthesia (95% CI, -13.4 to 10.4 sec). Warming had more of an effect on pain than buffering, but both appeared to have a cumulative effect.

Recommendations for clinical practice **Warming and buffering bupivacaine decreases the pain of injection on intact nontraumatized skin. Although it is feasible to buffer bupivacaine in most clinical settings, it may be difficult to warm the solution as was done in this study. Warming bupivacaine reduced the time of onset of anesthesia statistically, but this difference is unlikely to be clinically significant. Before adopting the practice of warming bupivacaine, which may be more technically challenging than buffering, further studies should be performed on traumatized tissue to see if the results are consistent. A recent study has shown that slower rates of lidocaine infusion can reduce the pain of injection.[1] Thus, paying attention to the speed of injection of bupivicaine may also be important.**

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Lack of Efficacy of Cisapride and Nizatidine in Dyspepsia

Hansen JM, Bytzer P, Schaffalitzky de Muckadell OB. Placebo-controlled trial of cisapride and nizatidine in unselected patients with functional dyspepsia. Am J Gastroenterol 1998; 93:368-74.

Clinical question **Are cisapride or nizatidine useful for the treatment of nonulcer dyspepsia in primary care patients?**

Background While many physicians empirically treat nonulcer dyspepsia with an H_2-antagonist, several small trials have not shown these agents to be effective. Others believe that nonulcer dyspepsia is a motility dis-

order, and recommend prokinetic agents. Unfortunately, there has been no large randomized controlled trial to answer these questions. In addition, most previous trials have been conducted with patients referred for endoscopy, which raises questions of referral bias and generalizability of the results to all primary care patients.

Population studied Patients who presented to general practitioners for dyspepsia of greater than 3 days duration were studied. Dyspepsia was defined as epigastric or retrosternal pain or discomfort, with or without other gastrointestinal symptoms. Patients underwent endoscopy within 1 week and were excluded if ulcer, esophagitis, or cancer was found, but not for minor abnormalities such as erythema or erosions. Other exclusion criteria included previously diagnosed ulcer or esophagitis, use of ulcer drugs or nonsteroidal anti-inflammatory drugs in the preceding month, suspected infection or serious disease, chronic disease, drug abuse, pregnancy, lactation, or the need for an interpreter.

Study design and validity This was a well-designed study. The design was a double-blind, randomized clinical trial in which patients were treated for 2 weeks with one of the following three therapies: cisapride 10 mg tid, given 30 minutes before meals; nizatidine 300 mg qhs; or placebo for 2 weeks. Randomization was stratified by four symptom subgroups (ulcer, reflux, dysmotility, and unclassifiable). Baseline characteristics were similar among all three groups.

Of the patients initially referred by 66 general practitioners, 40% were excluded on the basis of endoscopy results. Approximately half of the remaining patients were excluded because of other criteria; 330 patients were ultimately enrolled. Fifty-one patients withdrew, primarily because of noncompliance or adverse events, but they were evenly distributed among the 3 groups. Nine additional patients had incomplete data. The data were analyzed in a variety of ways, including intention-to-treat analysis, but the method of analysis did not alter the results.

Outcomes measured The primary outcome was a global assessment of symptoms on day 14 compared with day 0, and described as resolved, improved, unchanged, or worse. A secondary outcome was the number of symptom-free days in the second week according to a symptom diary.

Results Symptoms resolved or improved for 54% of patients in the nizatidine group and 62% of patients in the cisapride and placebo groups (P= ns). The number of symptom-free days was also not significantly different among groups, and the response to treatment did not vary by symptom subgroup. No drug was superior for improving specific symptoms of epigastric pain, heartburn, acid regurgitation, nausea, fullness, bloating, night pain, or irritable bowel syndrome. Individual symptoms or symptom subgroups were not predictive of the response to a specific drug or placebo. A multivariate analysis did find that certain symptoms predicted a better response to each drug. Patients with fullness, early satiety, pain aggravated by meals, and globulus sensation responded better to cisapride, while those with retrosternal pain, acid regurgitation, diffuse epigastric pain, and alcohol consumption responded better to nizatidine.

Recommendations for clinical practice **Neither an H_2-antagonist nor a prokinetic agent was more effective than placebo in the treatment of nonulcer dyspepsia; these patients tend to feel better after 2 weeks no matter what we do. Using a clinically based classification of symptoms to guide the choice of medication is not particularly helpful, either. It is important to remember that only 30% of the patients referred for the study were actually included in the study, and that patients with esophagitis or ulcer probably do benefit from these drugs.**

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Identifying Cardiac Risk in Patients with Atypical Chest Pain

Colon PJ, Mobarek SK, Milani RV, et al. Prognostic value of stress echocardiography in the evaluation of atypical chest pain patients without known coronary artery disease. Am J Cardiol 1998; 81:545-51.

Clinical question **Is stress echocardiography better than stress electrocardiography for evaluating cardiac risk in patients with atypical chest pain?**

Background Stress electrocardiography (ECG) seeks evidence of ischemia by increasing cardiac load and looking for typical ECG changes. Stress echocardiography is a newer modality that identifies ischemia by detecting wall motion abnormalities under cardiac stress. It has not been extensively tested in patients with atypical chest pain. This article compares stress echocardiography and stress ECG in patients at low risk for heart disease.

Population studied Of the 1998 patients referred for stress echocardiography testing at this New Orleans cardiology department in 1993, 1310 (67%) were exclud-