who were treated with 2 mg of estradiol. Thus, smoking may affect drugs metabolized by CYP1A2, with various consequences on target organs (Table 1).

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1. Wilkinson GR. Drug metabolism and variability among patients in drug response. N Engl J Med 2005;352:2211-21.
2. Drug interactions. (Accessed August 11, 2005, at http://www.drug-interactions.com.)
3. Jensen J, Christiansen C, Rødbro P. Cigarette smoking, serum estrogens, and bone loss during hormone-replacement therapy early after menopause. N Engl J Med 1985;313:973-5.
4. Bjarnason NH, Christiansen C. The influence of thinness and smoking on bone loss and response to hormone replacement therapy in early postmenopausal women. J Clin Endocrinol Metab 2000;85:590-6.
5. Bjarnason NH, Jørgensen C, Kremmer H, Alexandersen P, Christiansen C. Smoking reduces breast tenderness during oral estrogen-progestogen therapy. Climacteric 2004;7:390-6.

DR. WILKINSON REPLIES: It is well established that cigarette smoking may lead to the induction of drug metabolism and reduced effects when the usual dosages of certain drugs are administered.[1] This effect occurs through a mechanism involving the polycyclic aromatic hydrocarbons inhaled in tobacco smoke and the hepatic aryl hydrocarbon receptor, leading to transcriptional up-regulation of CYP1A2.[2] Other environmental factors can also induce CYP1A2, including the ingestion of cruciferous vegetables and charcoal-broiled meat.[3] Moreover, CYP1A2 may be inhibited by commonly used drugs, including fluvoxamine, most fluoroquinolones, and oral contraceptives.[4] However, the number of drugs with which such interactions are clinically important (estradiol, theophylline, clozapine, olanzapine, and tacrine) is relatively small. Dr. Bjarnason's comment, therefore, further emphasizes that drug metabolism and responsiveness may vary markedly among patients, often for reasons that are not immediately apparent to the prescriber. Consequently, drug dosages need to be individualized to each patient and responses routinely monitored for unexpected changes.

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1. Zevin S, Benowitz NL. Drug interactions with tobacco smoking: an update. Clin Pharmacokinet 1999;36:425-38.
2. Ma Q, Lu AY. Origins of individual variability in P4501A induction. Chem Res Toxicol 2003;16:249-60.
3. Harris RZ, Jang GR, Tsunoda S. Dietary effects on drug metabolism and transport. Clin Pharmacokinet 2003;42:1071-88.
4. Drug interactions. (Accessed August 11, 2005, at http://www.drug-interactions.com.)

Persistent Low Back Pain

TO THE EDITOR: Carragee (May 5 issue)[1] states that "radiofrequency ablation . . . was ineffective in one randomized trial" but does not discuss flaws in the methods and procedures of that study.[2] In his comments on a double-blind, randomized trial reported by van Kleef and colleagues, Carragee notes that radiofrequency "showed a moderate effect . . . which lasted only four weeks" but does not mention that, as compared with the placebo group, the group treated with zygapophyseal joint denervation showed statistically significant improvement at 3, 6, and 12 months.[3]

Our opinion of minimally invasive treatment options (injections and neuroablation procedures) differs from Carragee's. The potential advantages of these treatments include low risk–benefit ratios and relatively low costs. We fully acknowledge that more clinical studies are needed to support this new and promising approach for low back pain.

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1. Carragee EJ. Persistent low back pain. N Engl J Med 2005;352:1891-8.
2. Dreyfuss P, Baker R, Leclaire R, et al. Radiofrequency facet joint denervation in the treatment of low back pain: a placebo-controlled clinical trial to assess efficacy. Spine 2002;27:556-7.
3. van Kleef M, Barendse GA, Kessels A, Voets HM, Weber WE, de Lange S. Randomized trial of radiofrequency lumbar facet denervation for chronic low back pain. Spine 1999;24:1937-42.

TO THE EDITOR: In his review article on low back pain, Carragee advocates the use of amitriptyline but does not mention anything about weight loss. A significant reduction in disability related to low back pain has been noted with reduction of weight in obese patients, from a group mean of 132 kg to 92 kg.[1] Though not mentioned as an adverse effect in Table 1 of the article, amitriptyline causes weight gain. Cyclobenzaprine is an effective treatment for insomnia and nocturnal pain from paraspinal muscle spasm in the low back.[2]

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1. Melissas J, Kontakis G, Volakakis E, Tsepetis T, Alegakis A, Hadjipavlou A. The effect of surgical weight reduction on functional status in morbidly obese patients with low back pain. Obes Surg 2005;15:378-81.
2. Toth PP, Urtis J. Commonly used muscle relaxant therapies for acute low back pain: a review of carisoprodol, cyclobenzaprine hydrochloride, and metaxalone. Clin Ther 2004;26:1355-67.

DR. CARRAGEE REPLIES: Dr. Singla and colleagues note that although one randomized trial showed no benefit, a second blinded, randomized trial, by van Kleef et al., showed increased improvement in the group treated with radiofrequency ablation for supposed facet-joint pain.[1] Unfortunately, the randomization in that study failed to distribute confounding factors evenly because of very small numbers (only 31 subjects were recruited), and the sham-treatment group had pain that lasted two years longer than that in the radiofrequency-ablation group and had worse functional disability (representing a difference of 7 points, at baseline, on the Oswestry Disability Index). Despite these baseline biases predisposing to better results in the treatment group, by eight weeks there was no difference in function according to the Waddell method and a minimal difference in mean scores (less than 2 points). More recently, in a much larger, multicenter, randomized trial, van Wijk et al. failed to show even these small differences between radiofrequency ablation and sham treatment.[2] In both of these studies, the diagnosis of facet-joint pain was made on the basis of pain relief with an anesthetic injection at the facet joint. It is possible that this screening method resulted in the inclusion of subjects who did not have true facet-joint pain and thus might account for the lack of efficacy. However, it may be that the procedure is relatively ineffective even in subjects with true facet-joint pain.

Dr. Meyer notes that an uncontrolled clinical trial showed that morbidly obese subjects who lost 40 kg after bariatric surgery had a decrease in functional disability. Even in the absence of higher levels of evidence, weight loss in this setting seems a prudent recommendation. Whether small weight-control differences that are hypothetically achieved by avoiding amitriptyline will have any effect is unknown. To my knowledge, there are no randomized trials comparing cyclobenzaprine and amitriptyline. Both agents appear to have moderate efficacy in chronic low back pain.

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1. van Kleef M, Barendse GA, Kessels A, Voets HM, Weber WE, de Lange S. Randomized trial of radiofrequency lumbar facet denervation for chronic low back pain. Spine 1999;24:1937-42.
2. van Wijk RM, Geurts JW, Wynne HJ, et al. Radiofrequency denervation of lumbar facet joints in the treatment of chronic low back pain: a randomized, double-blind, sham lesion-controlled trial. Clin J Pain 2005;21:335-44.

Americans as Survivors

TO THE EDITOR: Dr. Lifton writes in his thought-provoking article (June 2 issue) that "physicians have always been concerned with how people survive trauma," arguing that survivors of mass trauma, such as the Vietnam and Iraq wars and the attacks on September 11, 2001, had "collective psychological responses" and that their "psyches have often been decimated."[1] This proposition is not supported by studies that were conducted after these events or by data on similar events in other countries. Studies aimed at documenting the consequences of mass trauma suggest that most exposed persons manifest impressive resilience or quick recovery from their initial responses to the trauma. Post-traumatic stress disorder (PTSD) developed in only a minority of those exposed to combat in Vietnam,[2] Iraq, and