LETTERS TO THE EDITOR

CHONIC BACK PAIN AND SUBSTANCE ABUSE

To the Editor:

The article "Substance Abuse Among Patients with Chronic Back Pain" by Brown and colleagues (*J Brown RL, Patterson JJ, Rounds LA, Papsouliotis O. J Fam Pract 1996; 43:152-60*) provides some interesting information regarding the prevalence of substance abuse among patients with low back pain. The clinical usefulness of this information appears limited, however, because of important issues not addressed by the authors.

My first concern is the demographic data not included in the patient profiles. It would be helpful to know the number of patients unemployed or on some form of disability for each group as well as the practice as a whole. These numbers should then be compared with community and regional levels. If the center population has a higher level of patients on disability or unemployment due to the interest of the investigators in the treatment of chronic pain, then the study may not be applicable to the general population. Similarly, if patients regularly receiving opioids for chronic low back pain have a higher or even comparable level of disability or unemployment as compared with the community or control population, it would likely affect the enthusiasm for the use of opioids for chronic low back pain. The usefulness of opioids for chronic pain should be based on a measurable improvement in patient function due to the use of these medications. If the use of controlled substances does not result in such improvement, then there is no need to expose the patient to the potential problems of these medications.

My second concern is the conclusion listed in the abstract, which says that "Chronic back pain did not connote special risk for current substance abuse disorders." This appears in conflict with the finding of the authors that ". . .patients with low back pain have a significantly higher prevalence of lifetime substance use disorders than do patients without chronic back pain." This latter statement would appear to justify caution in the use of controlled substances for patients with low back pain. The lack of increased current substance use disorder in this population may simply be due to the substitution of opioids for the previously employed substances of abuse.

The treatment of chronic pain is often frustrating for many health care providers. Further research into the optimal approach to this problem should be encouraged. Caution, however, should be used in the use of controlled substances for the treatment of chronic pain until the use of these substances can be shown to result in a decreased level of disability and improved patient function.

Jerry Ryan, MD
University of Wisconsin–Madison
Madison

The preceding letter was referred to Dr Brown, who responds as follows:

We thank Dr Ryan for raising some important issues about our study.[1] He expresses concern that the patient population of the study site may be representative of other clinics. Dr Ryan is probably correct in this regard. Although we do not have systematic information on our patients' employment status, I believe that our patients do have a higher unemployment rate than those of most other clinics in Madison. This difference, however, is probably related less to our interest in treating chronic pain than to our location near many public housing units. In any case, Dr Ryan is correct in his implication that our study should be repeated in other sites before its conclusions are taken for granted.

Dr Ryan points out that we found a higher prevalence of lifetime substance use disorders among patients with chronic back pain compared with those without chronic pain. The difference, however, was accounted for by differences in the racial and think composition and the education levels of the two samples. Thus, we cannot conclude from our data that lifetime substance abuse is directly linked to chronic pain.

Dr Ryan suggests that the prescription of opioids for some of our subjects could have masked current substance use disorders in our study. This is unlikely, because the instrument we used to measure substance use disorders, which is based on the DSM-III-R criteria, is probably overly sensitive (more formally, not highly specific) in identifying substance use disorders that are related to medications that are prescribed and taken as directed. For example, under DSM-III-R, one could count the physical dependence associated with the described continuous use of opioids as a symptom of opioids dependence, and one could interpret the constipation associated with such opioids use as a symptom of opioids abuse, even for patients who realize a net gain in function from opioids. In our study, despite the potential for overestimating, the prevalence of substance use

The Journal welcomes letters to the editor. If found suitable, they will be published as space allows. Letters should be typed double spaced, should not exceed 400 words, and are subject to abridgment and other editorial changes in accordance with Journal style. All letters that reference a recently published Journal article are sent to the original authors for their reply. If no reply is published, the authors have not responded by date of publication. Send letters to Paul A. Nutting, MD, MSPH, Editor, The Journal of Family Practice, 1650 Pierce St, Denver, CO 80214. Telephone (303) 202-1543, Fax (303) 202-1539, E-mail nuttingp@usa.net

disorders were similar between both groups.

We agree with Dr Ryan that function is a critical guideline in following patients with chronic pain who are treated with opioids. In our experience, and in the published experience of several other clinicians, many patients do exhibit improved function with opioids, and even those patients who exhibit signs of opioid abuse or addiction can be managed by tight enforcement of behavioral contracts.[2]

Dr Ryan speaks of clinicians' frustration in managing chronic pain. We must remain cognizant that our frustration pales in comparison with the frustration and suffering of patients with chronic pain. An evidence-based approach to clinical medicine does not dictate that we await definitive clinical trials before administering treatments. The preponderance of the evidence suggests that opioids are safe and effective for some patients with severe, chronic noncancer pain that has not responded to other modalities. Our duty to such patients who seem to be a low risk for opioid addiction is to inform them in a balanced fashion about the potential advantages and disadvantages of opioids and either to provide them ourselves or to refer them to physicians who will.

Richard L. Brown, MD, MPH
University of Wisconsin–Madison
Madison

REFERENCES

1. Brown RL, Patterson JJ, Rounds LA, Papsouliotis O. Substance abuse among patients with chronic back pain. J Fam Pract 1996; 43:152-60.
2. Brown RL, Fleming MF, Patterson JJ. Chronic opioid analgesic therapy for chronic low back pain. J Am Board of Fam Pract 1996; 9:191-204.

TIMELY MESSAGE FOR FPs PERFORMING CESAREAN SECTIONS

To the Editor:

The November issue could not have been more timely and I thank you. I arrived home late last night to find it in my mailbox after performing an urgent cesarean section on a young woman who had been laboring unsuccessfully at the local free-standing birthing center. This center is run by nurse midwives and backed up by our family practice group. After alerting the local obstetrician on call to precept me (I am newly starting practice and am being monitored for 6 months at the hospital prior to full credentialling) and a pediatrician to assist in newborn resuscitation (since I cannot do surgery and resuscitate at the same time), I performed the cesarean section successfully and baby and mother recovered nicely in the ICUs (the baby was transferred to our tertiary care center).

As mentioned by Dr Deutchman in his wonderfully supportive editorial "Who Ever Heard of Family Physicians Performing Cesarean Sections?" (*J Fam Pract 1996: 43:449-53*), I would note that the OB who assisted me left halfway through the operation, as he was covering two rural hospitals and had other women in labor. Even the best rural obstetricians cannot be in two places at a time. The operative skills of other family physicians as well as my own will only enhance the urgent obstetrical care we are all able to provide women in rural areas. And I strongly feel that this is what it is all about.

Sigrid R. Johnson, MD, MSc
Family Practice Associates
Madisonville, Tennessee

HEALTH CARE-SEEKING BEHAVIOR

To the Editor:

The article by Drs Norcross, Ramirez, and Palinkas on the influence of women on the health care-seeking behavior of men (*Norcross WA, Ramirez C, Palinkas LA. The influence of women on the health care-seeking behavior of men. J Fam Pract 1996; 43:475-80*) authenticated and confirmed suspicions I have had as a family doctor in practice for more than 20 years.

Years ago I made a joke that I often share with my patients. I asked them what are the two reasons that a male will come in for a physicial examination. The answer is, of course, number 1, his wife, and number 2, his wife.

I have recently changed the answer on some occasions to number 1, his wife, and number 2, his mother.

David R. Grube, MD
Philomath Family Medicine
Philomath, Oregon

DRUG INTERACTIONS PROGRAM

To the Editor:

On reading your review of our drug interactions program (*Fox GN. The Medical Letter Drug Interactions Program for Windows. J Fam Pract 1996; 43:402-3*), I find that you have made serious errors. Two effects are given for the interactions Erthromycins-Seldane and Ketoconazole-Seldane: you only quote excerpts from the second effect in each case. You also failed to read the introductory material, or you would have learned that there is no listing for drugs that do not have documented interactions, such as amoxicillin.

We would appreciate your taking the trouble to read the introduction as well as the complete output for the cited interactions.

Martin A. Rizack, MD, PhD
The Medical Letter
New Rochelle, New York

The preceding letter was referred to Dr Fox, who responds as follows:

The Medical Letter Drug Interactions Program for Windows (DIP-Win) lists 12 drug interactions for penicillin V (including anticoagulants, oral; and contraceptives, oral). Yet, we are asked to infer that amoxicillin and, in fact, amoxicillin-clavulanate (Augmentin), also not listed, have *no* interactions. That penicillin V has greater interaction potential with oral contraceptives and with oral anticoagulants than do amoxicillin and amoxicillin-clavulanate makes little physiologic sense and is incongruent with competitors' interactions listings (eg, *PDR DrugREAX* indicates interaction between amoxicillin and oral contraceptives). To me, the *presumption* that amoxicillin and amoxicillin-clavulanate have *no* drug interactions is actually *less* comforting than considering them penicillin-class drugs. If I purchase software and take the time to look up an interaction, I want affirmation of the presence or absence of interactions.

Dr Rizack is correct that when the user enters "erythromycins" and "Seldane," Seldane" maps to "Antihistamines, H_1-blockers," and several drugs and their interactions are listed. In my zeal for reductive editing, I did sacrifice technical accuracy. In this interaction pair, DIP-Win does specify "Arrhythmias with terfenadine or astemizole...Use antihistamine other than terfenadine or astemizole. ...Possible loratadine toxicity with erythromycin...Clinical significance not established." The main messages stand. In my opinion: (1) A busy clinician who enters "erythromycins" and "Seldane" could more easily, compared with the competition, misread the fine print and err—DIP-Win lacks eye-catching "major severity" warnings. (2) "Class interactions lumping" provides some benefit but as drugs proliferate, intraclass variations are beginning to limit the utility of this approach.

As a practicing clinician, I use these programs; all have limitations. When giving presentations about clinically useful software, I demonstrate both DIP-Win and *DrugREAX*. DIP-Win's strengths are its lower cost and speed. DrugREAX, in its September 1996 incarnation, costs more, is irritatingly slow and extremely buggy, but has a more complete drug list and provides more visual warning of major interactions.

I believe users want to enter specific drugs and obtain specific results rather than presume unlisted drugs lack interactions. I would welcome data that support the counterintuitive contention that amoxicillin and amoxicillin-clavulanate have fewer and less significant drug interactions than penicillin V.

Gary N. Fox, MD
Software Editor

APPETITE SUPPRESSANTS FOR OBESITY

To the Editor:

In her response[1] to comments on her review article,[2] Dr Elks writes: "We fail to treat our patients humanely if we willfully withhold from them agents of low risk that may assist them in improving their health status." I agree, but anorectic agents fail to qualify as such agents.

There simply are no data that long-term use of anorectic agents improves health status. As pointed out by Drs Clemenson and Schmitts in their letters,[3,4] the long-term use of phenteramine and fenfluramine was associated with only 2.9 kg more weight lost than in the control group. The total weight loss in the Weintraub studies[5] after 190 weeks of treatment was 5.9 kg. However, the 95% confidence interval of -8.9 to 20.7 kg lost indicates that a 9-kg weight gain after 3 years of anorectic treatment cannot be reliably excluded. It is difficult to see how this improves one's health status.

Weintaub et al examined lipid status.[6] Their data do not show that anorectic treatment improves lipid status. The table below compares the lipid status of patients who received fenfluramine and phenteramine with those who received placebo during the phase of the trial when a placebo-controlled group was included.

After 190 weeks of treatment, the average total cholesterol went from 199 to 207. The average LDL cholesterol increased from 126 to 133. Again, it is hard to see how this improves one's health status. Weintraub et al do not look at health outcomes other than lipids. Since theirs was not a long-term anorectic vs placebo trial, they would not have examined such outcomes.

Dr Elks gives no data that long-

TABLE

	Baseline Total Cholesterol	Cholesterol After 34 Weeks	Baseline LDL Cholesterol	LDL Cholesterol After 34 Weeks	Baseline HDL Cholesterol	HDL Cholesterol After 34 Weeks
Placebo	197	202	126	128	46	51
Fen-Phen	200	194	128	127	45	50

term anorectic treatment improves long-term diabetic control. I have been unable to find such data. The longest follow-up I could find examining the effects of anorectic agents on diabetes lasted only 3 months. No studies have shown that long-term treatment with anorectic agents reduces mortality—all-cause or from any cause. No studies document sustained improvements in surrogate endpoints such as better control of hypertension, lipids, or diabetes. Since use of anorectic agents has not been demonstrated to improve health status, failure to provide anorectic agents is not a failure to provide humane care.

Brian Budenholzer, MD
Group Heath Northwest
Spokane, Washington

REFERENCES

1. Elks ML. New agents for obesity management [reply to letter to the editor]. J Fam Pract 1996; 43:225.
2. Elks ML. Appetite suppressants as adjuncts in the treatment of obesity. J Fam Pract 1996; 42:287-92.
3. Clemenson ND. New agents for obesity management [letter]. J Fam Pract 1996; 43:224.
4. Schmitt SA. New agents for obesity management [letter]. J Fam Pract 1996; 43:225.
5. Weintaub M, Sundaresan PR, Schuster B, Averbuch M, Stein C, Cox C, Byrne L. Long-term weight control study IV (weeks 156 to 190). Clin Pharmacol Ther 1992; 51:608-14.
6. Weintaub M, Sundaresan PR, Schuster B. Long-term weight control study VII (weeks 0 to 210). Serum lipid changes. Clin Pharmacol Ther 1992; 51:634-41.

The preceding letter was referred to Dr Elks, who responds as follows:

Dr Budenholzer brings up some interesting and important issues in the use of anorectic agents. The papers cited involve universal application of the anorectic agents as opposed to selective use. It has been long recognized that the response to these agents varies considerably from patient to patient, as shown in the board confidence interval for total weight loss. It is true that the aggregate response is modest at best. This can hide the observation that specific patients respond very favorably and such agents can prove to be a valuable adjunct for responding patients in increasing adherence to a recommended treatment program. Thus, I stand by my statement of "may [emphasis mind] assist them in improving their health status." In discussing this option with patients, I let patients know that as few as 25% may experience significant help from the medication, and regaining weight is a common occurrence when the medication is stopped.

Dr Budenholzer is correct in that there are no published data on long-term anorectic treatment in the control of diabetes. I have prepared such papers, but have been unable to publish them because the longitudinal observational nature of my data is not considered worthy of publication.

My therapeutic approach with patients involves discussing available options (pros and cons) and helping the patients to make the choices that are appropriate to them (and discontinuing agents that fail to be effective in a given patient). I agree that it would be wrong to uniformly use such agents in all obese individuals with diabetes. I also feel that these agents are very helpful for certain patients and that it is humane to use such agents responsibly in well-selected responding patients.

M. L. Elks, MD, PhD
Texas Tech University
Health Sciences Center
Lubbock, Texas

HAIR LOSS ASSOCIATED WITH NEFAZODONE

To the Editor:

Nefazodone is a new antidepressant that antagonizes 5-HT_2 receptors and also inhibits both serotonin and norepinephrine reuptake.[1] We report a case of hair loss associated with nefazodone. A MEDLINE search did not reveal any prior reports of hair loss associated with nefazodone.

A 40-year-old woman with a 2-month history of DSM-IV major depression was started on nefazodone 100 mg twice a day by her family physician. Because the patient did not respond, the dosage was increased 2 months later to 200 mg twice daily and a psychiatric consultation was sought.

At the time of the psychiatric examination, her symptoms included difficulties in concentration, insomnia, and loss of interest in pleasurable activities. She had a tearful affect, but no suicidal ideation. There was no prior history of psychiatric treatment. Her medical history was significant for hypertension and asthma. Her medications included losartan 50 mg for hypertension (started 9/95), nefazodone 200 mg twice daily (started 3/96), triamcinolone inhaler two puffs three times daily (started 11/95), and ipratropium inhaler two puffs three times daily (started 1/96). Laboratory tests, including a general health panel and thyroid functions studies, were within normal limits.

As the dosage of nefazodone had been recently increased (2 days prior to the psychiatric visit), no further dosage changes were made. During a follow-up visit 2 weeks later, the patient reported hair loss, which she described as "clumps" of hair coming out after combing and "ringing" the bathtub after bathing. Detailed questioning revealed that the hair loss began after initiation of nefazodone and accelerated after dosage increase. Her depressive symptoms remained unimproved. Nefazodone was discontinued and she was started on paroxetine 20 mg daily. Two weeks after starting paroxetine, the patient reported a 50% reduction in hair loss

and also noted improvement in depressive symptoms. After taking paroxetine for 2 months, the patient is much improved and has returned to work.

Our case patient had no prior history of hair loss associated with the start of any of her other medications. In this instance, the hair loss appears to be temporally associated with an increase in dosage of nefazodone from 100 mg/d to 200 mg/d. No other medication dosages were altered.

A literature review revealed that hair loss has been reported with all selective serotonin reuptake inhibitors[2-5] and tricyclic antidepressants,[4] occurring more frequently in women than men. As the hair loss may vary from mild to severe, it may be important for physicians to inquire about its occurrence.

Sanjay Gupta, MD
William R. Gilroy, Jr, RPh
Olean General Hospital West
Olean, New York

REFERENCES

1. Eison ES, Eison MS, Torrene JR, Wright RN, Yocca FD. Nefazodone: preclinical pharmacology of a new antidepressant. Psychopharmacol Bull 1990; 26:311-5.
2. Jenike MA. Severe hair loss associated with fluoxetine. Am J Psychiatry 1991; 148:392.
3. Gupta S, Major LF. Hair loss associated with fluoxetine. Br J Psychiatry 1991; 159:737-8.
4. Wheatley D. Hair loss with antidepressants. Hum Psychopharmacol 1993; 8:439-41.
5. Bourgeois JA. Two cases of hair loss after sertraline use. J Clin Psychopharmacol 1996; 16:91-2.

CORRECTION

An error was published in a recent article in the Journal (*Young RA, Buchanan RJ, Kinch RAH. Use of the protein/creatinine ratio of a single voided urine specimen in the evaluation of suspected pregnancy-induced hypertension. J Fam Pract 1996; 42:385-9*).

In the abstract, in the last sentence of the Results section it reads ". . . a ratio less than .15 efficiently ruled out significant PIH." "Significant PIH" should have read *significant proteinuria.* This distinction is important because one can have pregnancy-induced hypertension without having proteinuria. PIH is properly diagnosed with measurement of the blood pressure. The protein/creatinine ratio may be useful for assessing the amount of proteinuria only. Dr Young brought this error to our attention and provided the text of the correction.