

Clinical Case Conference

Use of Alternative Remedies by Psychiatric Patients: Illustrative Vignettes and a Discussion of the Issues

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This clinical conference, in the form of several vignettes, focuses on the increasing importance for clinicians to actively attend to their patients' uses of herbal "alternative" or "complementary" therapies. First, the prevalence of alternative therapy use is remarkably high. According to data from a national follow-up survey (1), in 1997 the probability of visiting an alternative practitioner was 46.3%, up from the initial 1990 survey figure of 33.8%, and the total number of visits to alternative therapy practitioners increased from 427 million in 1990 to 629 million in 1997, representing primarily an increase in the numbers of individuals visiting alternative practitioners, not an increase in the number of visits per person. In 1997 the amount of out-of-pocket money spent for alternative medicine professional services and herbal products was conservatively estimated to be \$27 billion, comparable with the projected 1997 out-of-pocket expenditures for all U.S. physician services; this represents an increase in expenditures of 45.2% between 1990 and 1997. Second, of particular concern to psychiatrists and other mental health professionals, fatigue, headaches, insomnia, depression, and anxiety are among the most common reasons cited for seeking treatment from alternative practitioners (1, 2). These patients of-

ten seek treatment from psychiatrists while still taking, and often still believing in, their alternative remedies. Finally, we are witnessing an explosive marketing push for the development of new "nutraceuticals" or "pharmafoods," i.e., purportedly therapeutic foodstuffs, and the emergence and rapid growth of an industry of food-like herbs marketed as alternative therapies that do not require approval by the U.S. Food and Drug Administration (FDA) (3, 4). This rapidly evolving trend is most clearly seen in herb-laced beverages ranging from brand-named teas to upscale soft drinks, all increasingly available at the local supermarket, as well as at specialty health food emporiums, and we can expect major increases in the rates at which patients seeking psychiatric care will have already been taking herbal alternative remedies that may or may not be active and that may or may not have positive or deleterious interactions with conventional treatments. All of this suggests that clinicians need to

routinely and nonjudgmentally ask patients about their use of herbal alternative and complementary treatments, know enough about the more common ones to assess patients for deleterious effects or interactions, and know where to find legitimate information about other treatments. This clinical conference will first present cases demonstrating use of two of the more commonly used herbal alternative medicine compounds, present a third case dealing with staff-patient interactions concerning the use of herbal remedies, and end with a discussion of perspectives and attitudes that contemporary clinicians may find useful concerning their patients' use of herbal alternative treatments.

CASE 1

Possibly Hazardous Interaction of Valerian Root With Fluoxetine

Mr. W was a 38-year-old Native American who was being treated for alcohol-induced mood disorder with fluoxetine, 20 mg/day, and was referred to the university mental health clinic by his primary care physician for self-inflicted razor blade cuts to the left upper arm. He had a 20-year history of alcohol dependence (one quart per day) and a history of alcoholic hepatitis.

On psychiatric evaluation Mr. W stated that "something happened to my mind," described "a palsy," and said, "It feels like I'm on acid." He stated that he felt he had lost control of his left arm and had become agitated and "obsessed" with this arm, cutting it "to know it was there." He attributed this behavior to a "drug interaction" and on further questioning revealed that approximately 12 hours before cutting his arm he had taken two gel tablets of a friend's valerian root extract for neck spasms. His com-



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plaints resolved over the next 12 hours without sequelae.

Discussion

Valerian root extract is derived from plants in the genus *Valeriana*, a herbaceous perennial native to Europe and Asia (5, 6). *V. officinalis* is the species most commonly used for medicinal purposes (6). The first descriptions of its purported healing properties can be traced to ancient Greece and Rome (7). In the Middle Ages, valerian was used as a sedative and antispasmodic agent (8). Valerian was used to treat "nervous afflictions in women" and anxiety in the tenth century, and it was used to treat "shell shock" in World War I. Currently it is sold in the United States in health food stores (8).

Valerian root preparations are purported to have anxiolytic, sedative, spasmolytic, vasodilatory, and antiarrhythmic effects, as well as antidepressant properties (5–12).

The postulated mechanisms of action of valerian root include γ -aminobutyric acid (GABA) agonist activity due to its affinity for GABA_A receptors (13), inhibition of GABA reuptake (14–16), serotonin 5-HT_A agonism (17), inhibition of monoamine oxidase (MAO) uptake (12, 17), and activity at adenosine receptors (12, 17).

In contrast with its potential beneficial effects, reported valerian-root-related toxicities have raised concerns. MacGregor et al. (18) reported four cases of hepatotoxicity with rapid onset after ingestion of herbal preparations containing both valerian root and skullcap. Overdose with valerian root has also been reported (8, 19). In reported cases (5, 18, 19), ingestion of 12–20 g of valerian root resulted in headache, "excitability," "uneasiness," and cardiac disturbances but no signs of acute hepatitis.

There are several potential mechanisms for the "drug interaction" described by Mr. W. Alcohol has been postulated to act at GABA_A receptors, and disinhibition may have occurred with the combination of alcohol and valerian root, which could explain his behavior. Alternatively, Mr. W's serum levels of valerian root's active ingredients may have been substantially higher than they would have been in a person not taking fluoxetine, either because of fluoxetine's high protein-binding capacity or through fluoxetine's inhibitory effects on hepatic cytochromes. Cytochrome inhibition may have impaired the catabolism of

valerian constituents, especially in light of the patient's history of hepatitis. It is also possible that the delirium-like clinical state reported by our patient resulted from a combination of MAO-like effects of valerian root and the serotonergic effects of fluoxetine. Finally, it is possible that the patient may have had an idiosyncratic reaction to this compound, independent of fluoxetine.

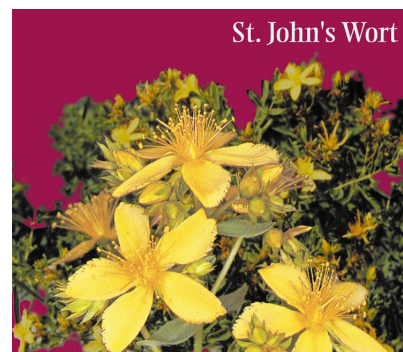
The take-home message of this case is that valerian root is a pharmacologically complex and potentially potent GABA agonist that has several other pharmacological properties. Under certain circumstances, it may interact in significant and potentially deleterious ways with conventional psychopharmacological agents.

CASE 2

Difficulties in Determining the Helpfulness of St. John's Wort in Panic Disorder

Ms. L was a 24-year-old single mother who came to the general psychiatry intake clinic with complaints consistent with a possible diagnosis of panic disorder. By the time she sought treatment at the clinic, she reported having up to four attacks per day, each lasting 2–3 hours on average and consisting of shortness of breath, chest pain, spotty vision, nausea, diarrhea, and a sense of impending doom. For the most part, these symptoms appeared without warning, and over time she began to develop an intense underlying sense of anticipatory apprehension related to the unpredictable and uncontrollable appearance of these spells. Her history included several significant losses that coincided with the onset of her symptoms, including the death of her mother in a motor vehicle accident when she was 18 and the destruction of her house by fire shortly thereafter.

At the age of 18, with the onset of her symptoms, she had been treated with approximately 16 sessions of cognitive behavioral therapy and with lorazepam as needed adjunctively. These treatments had been helpful, but her panic attacks did not entirely subside with treatment. From the age of 22 to 24, just before she came to our university mental health center clinic, she received additional counseling that focused on the loss of her mother. During this period, while Ms. L continued to have panic attacks, she was reluctant to use any pharmaceutical preparations because she was breast-feeding and was concerned



about possible negative effects of medications on her new baby.

On initial assessment by the resident who saw her in the clinic, Ms. L denied the use of any medications but did admit to occasional marijuana and alcohol use. In the course of dialogue about therapy for psychiatric disorders, Ms. L eventually volunteered that she had already investigated a number of different herbal preparations on her own, and this led to a nonjudgmental inquiry about herbal remedies. She acknowledged that she was taking kava, passionflower extract, and wild oat in order to help with her panic symptoms, and she also acknowledged that she had been seeing an herbalist. She initially related that she had not yet tried St. John's wort but was thinking about taking it. In a later session Ms. L related that she had indeed started taking St. John's wort and had experienced a reduction in panic attacks from three or four per day to roughly three or four per week; she attributed the reduction in symptoms to the St. John's wort.

She agreed to another course of cognitive behavioral therapy and was referred for this treatment. Over the next few months she continued to improve, with cognitive behavioral therapy and a continued combination of St. John's wort, passionflower, and wild oat.

Discussion

Although the actual contribution of St. John's wort to the clinical improvement of Ms. L is hard to assess, since she was taking several other herbal preparations and receiving cognitive behavior therapy as well, the case invites a discussion of St. John's wort, an increasingly popular, widely accessible, and commonly used remedy. The use of herbs purported to be St. John's wort has been attributed to ancient physicians, including Hippocrates and Discorides, as well as to medieval practitioners (20). While it fell out of favor

in the nineteenth century with the advent of modern pharmacology, it continued to be used in folk medicine for a range of indications, including depression. In the last 15 years its use has become popular in Europe, where it has been touted as a natural remedy for depression. Approved by the German federal drug regulatory agency, the *Bundesgesundheitsamt*—the German equivalent of the FDA—it is now the leading treatment for depression in Germany; 3 million prescriptions are written for St. John's wort per year, outnumbering fluoxetine prescriptions by 25 to 1. Interest in the use of this herb in the United States continues to grow, in part because of a widely popular book describing its use, *Hypericum and Depression* (20). In addition, a multicenter trial of the herb has been organized in the United States and is being co-conducted by the National Institute of Mental Health and the National Institutes of Health (NIH) Office of Alternative Medicine (21). In this study patients are being enrolled from a variety of settings by internists, general practitioners, gynecologists, and psychiatrists.

The pharmacology of St. John's wort is complex. Among the many compounds it contains, those most likely to be responsible for antidepressant-like effects are hypericin and pseudohypericin. Other important compounds contained in St. John's wort are flavonoids, such as quercetin, as well as tannin, volatile oil, hypericin, and rutin (22–24). The mechanisms of antidepressant actions by St. John's wort have not been fully elucidated. Several possible activities for the herb have been suggested, among them MAO_A inhibition, inhibition of serotonin receptor expression, serotonin reuptake inhibition, and reduction of cytokine expression (interleukin-6). It has also been shown that hypericin binds to *N*-methyl-D-aspartic acid (NMDA), GABA_A, and GABA_B receptors and that it inhibits synaptosomal GABA uptake (25, 26). The components of the herb that inhibit MAO have not definitely been established but may be flavonoids (since they are similar in structure to the known MAO_A inhibitors toloxatone and brofaromine) or xanthones. However, the concentrations of these compounds in St. John's wort are thought to be well below those needed for clinically significant MAO inhibition (25, 26).

Although St. John's wort has been classified as an MAO inhibitor by the *Bundesgesundheitsamt*, as described in

The Complete German Commission E Monographs (27), some evidence suggests it may be a relatively stronger serotonin reuptake inhibitor than MAO inhibitor. In a study using rat synaptosomes (28), hypericum extract was found to inhibit serotonin uptake in a dose-dependent fashion, and a 50% inhibition of serotonin reuptake was achieved at 6.2 µg/ml of hypericum extract. (To provide perspective, these data suggest that the potency of St. John's wort as a serotonin reuptake inhibitor is on the order of 10,000 times less than that of clomipramine.)

St. John's wort has been used widely throughout Europe with reports of only minor side effects. Studies to date have generally shown that there is a lower incidence of adverse events with St. John's wort than with standard antidepressants. Gastrointestinal effects, including nausea, gastrointestinal pain, loss of appetite, and diarrhea, occurred at a rate of 0.55% in a German study of 3,250 patients taking 300 mg t.i.d. (29). Dermatologic effects, including exanthema and pruritis, occurred in 17 (0.52%) of 3,250 patients (29). With higher doses or long-term use, St. John's wort may cause sunburn-like reactions and inflammation of the mucosa, and it is recommended that treatment be discontinued if these side effects occur. No human fatalities have been linked to its use (27).

Because of St. John's wort's pharmacology, reactions with tyramine-containing foods, meperidine, or sympathomimetics might be significant. Likewise, a serotonin syndrome could be a concern. However, no reports of adverse drug interactions have as yet been noted in the literature to our knowledge.

Although clinical studies regarding the efficacy of St. John's wort are currently under way in the United States, most original studies have been German. In the vast majority of studies the patients examined had mild to moderate depression. Linde et al. (30) reviewed all trials they could locate through MEDLINE and other databases. Their criteria for reviewing the trials were as follows: randomized or quasi-randomized clinical trials using standardized classifications of depression, comparison of St. John's wort with either placebo or conventional antidepressants, and the use of either symptom measurement or depression rating scales for outcome. They found 23 trials in all that met these criteria. Twenty trials were double-blind, one was single-blind, and two were open.

The largest study had 135 patients, the smallest 30. The dose of extract varied from 300 to 1000 mg per day (corresponding to 0.4 to 2.7 mg of hypericin per day). The duration of studies varied from 2 to 12 weeks.

Fifteen studies compared hypericum with placebo (1,008 patients total). Of 13 trials that compared hypericum to placebo and provided treatment response data, the pooled results showed that 55.1% of the subjects in the hypericum group responded versus 22.3% in the placebo group. In the nine trials using the Hamilton Depression Rating Scale, the pooled results revealed that subjects receiving hypericum obtained a mean score 4.4 points better than that for subjects receiving placebo.

Eight studies (with 749 patients) compared hypericum with other antidepressants or sedatives. These included maprotiline, diazepam, imipramine, bromazepam, amitriptyline, and desipramine. Among trials comparing hypericum alone with another antidepressant, the pooled response rates were 63.9% for hypericum and 58.5% for standard antidepressants. Hypericum in combination with other herbal preparations (such as valerian root) was also compared to standard antidepressants. The pooled response rates were 67.7% for the herbs and 50.0% for standard antidepressants.

In all, side effects were reported by 19.8% of the subjects taking hypericum or hypericum combinations versus 52.8% of those taking standard medications. The dropout rates were 4.0% for hypericum and 7.7% for standard medications.

The take-home message is that St. John's wort is also pharmacologically complex and potentially potent. Although considerable research has already been conducted in Germany, and the results of the meta-analysis by Linde et al. (30) are promising, there are many problems with the quality of many of the published series and studies on St. John's wort (31). Clinical trials now under way in the United States will help clarify its utility.

CASE 3: PATIENT-STAFF INTERACTIONS INVOLVING ALTERNATIVE THERAPIES

Ms. B, a 24-year-old woman with chronic anorexia nervosa, sought admission to the university mental health center after the naturopath, general internist, and psychologist who were treating her in the community became

increasingly alarmed at her weight loss and felt that her condition was too medically precarious for them to continue to take responsibility for her as an outpatient.

On admission to our general psychiatry adult inpatient unit Ms. B, who was 5 feet 4 inches tall, weighed 80 lb. Her maximum adult weight was reported to be 100 lb. The anorexia nervosa began in earnest when she was 11. She had never had a menstrual period. In the western state where she grew up, she had been hospitalized psychiatrically and medically on several occasions for treatment of her anorexia nervosa and malnutrition, and intermittently she had been in outpatient psychiatric treatment that included, off and on, individual and family psychotherapy and treatment with a variety of antidepressant medications, most notably several selective serotonin reuptake inhibitors, none of which appeared to have prevented the development of a chronic, debilitating illness. She moved to our area a year before the current admission to train as an artist. During this year, her weight fell about 15 lb.

Her clinical picture was that of anorexia nervosa, restrictor subtype, with features of obsessive-compulsive disorder. She became anxious and tearful about any alteration in her careful schedule of eating. Her exercise consisted of walking about an hour per day. She denied a history of binge eating, purging, or use of illicit drugs, diet pills, or other substances that might alter her mood or weight. She was extremely ritualistic, about both her patterns of eating and the content of her meals. Her food choices, as well as amounts, were severely limited. She acknowledged being underweight and said that she thought she should weigh about 100 lb. (A minimum healthy weight for this small-boned woman, i.e., the weight at which someone of her height and frame might start to menstruate and ovulate spontaneously, would probably fall in the range of 110–115 lb.)

The psychiatric staff's initial assessment and treatment plan focused on nutritional rehabilitation. The plan was to provide the patient with a structured, advancing meal program, with increasing numbers of calories from tray food supplemented if necessary by liquid food supplement if Ms. B was unable to meet the calorie intake requirements through regular meals. The initial treatment plan did not include standing orders for any psychiatric

medications. When she entered the inpatient service Ms. B brought along a large shopping bag filled with a variety of natural remedies she had been taking, and she asked that she be permitted to continue to take them during her hospital stay. She believed that they helped, and she felt extremely threatened by the possibility of being refused permission to use them. Such refusal on the part of the ward staff would constitute yet an additional assault on her carefully crafted eating rituals and therapeutic belief systems. The ward staff agreed to review the various items in her shopping bag and permit her to continue to take the substances about which they had no concern. The bag contained the following items: protein powder for shakes, St. John's wort, kava, passionflower extract, spirulina, and biopyrrin. The ward staff reviewed the contents of each item.

Staff opinion was divided regarding how to proceed. Some argued that since these were "medications," the patient should not be permitted to take any of them while she was on the unit. The issue of the importance of staff "taking control" was raised in this regard. Others argued that the natural remedies were relatively benign products and that Ms. B should be given free access to all of them to help reduce her anxiety and increase her compliance. The compromise arrived at by the staff and Ms. B was to make taking herbs contingent on her cooperating with the nursing program. She was permitted to take her protein shakes (their caloric values were incorporated into her food plan), and as long as she continued to take her meals as prescribed, she would be permitted to use the products, under nurses' administration, that were considered to be benign and to pose low risks. If conventional medications proved to be needed, it was clearly understood that since the herbal products were complex substances that have not been adequately studied for interactions with prescription medications (32), the staff would withhold any herbal product that might have potentially deleterious interactions with them. The staff was particularly concerned about the potential interactions of St. John's wort and kava. The latter, touted as an anxiolytic, was described in a case report as having adverse interactions with alprazolam (33). Decisions regarding the other remedies were based on the staff's summary assessment of the potential risks (reasonably low) and benefits (on the whole, "couldn't hurt")

and constituted part of a respectful, negotiated treatment plan (34). Ms. B remained on the unit for 4 weeks. Although she gained about 8 lb during the hospitalization, her chronic anorexia nervosa ultimately proved to be just as resistant to treatment in our facility as it previously was in several different eating disorders treatment centers around the country. Since discharge from the hospital, she has been followed as an outpatient and has made little further progress in gaining additional weight. She maintains good relationships with our staff, whom she has consistently perceived as helpful.

GENERAL DISCUSSION

The Patient's Perspective

Why do such large numbers of Americans use alternative therapies? The results of one community-based survey (2) suggest that individuals use such therapies because these alternative approaches are congruent with their own values, beliefs, and philosophical orientations toward health care and a holistic philosophy of life in which the health of "body, mind, and spirit" are linked. That survey also indicated that the large majority of respondents using alternative therapies also used conventional therapy, with only 4.4% of the respondents reporting that they relied primarily on alternative therapies. Contrary to expectations, dissatisfaction with conventional care did not predict the use of alternative therapies. Among respondents who were highly satisfied with their conventional care, 39% still used alternative therapy, whereas 40% of those who reported high dissatisfaction with conventional care (9% of respondents) used alternative medicine. For some, alternative therapies are culturally familiar folk remedies (35). Recognizing the popular interest in alternative therapies, and responding to political tides, this year Congress included \$50 million for research on alternative medicine and instructed NIH to upgrade the Office of Alternative Medicine to a full-fledged center, now renamed the National Center for Complementary and Alternative Medicine (21).

From the broader perspective of "self-care," a majority of individuals use one or another form of alternative therapy, "nutraceutical," and/or over-the-counter agent as folk remedies and to modify mood and energy. The most common include compounds and elixirs—such as strong coffees, teas, colas,

chocolates, beers, wines, whiskeys, and chicken soups—and herbs—such as tobacco and marijuana. In more refined forms, alternative herbal therapies include various plant-based substances, including cocaine and heroin. Their most effective pharmacological delivery systems include ingesting, smoking, inhaling, and injecting. These alternative treatments have effective marketing, merchandising, and distribution systems. Distribution sites range from supermarkets to liquor stores, crack houses, and drug dealers who make house calls and home deliveries. (Patients have only half-jokingly suggested that conventional care systems could greatly improve customer satisfaction by delivering immediate relief by using the always-on-call ordering and delivery systems perfected by local drug and pizza dealers.) Alternative therapies will always be used if they are thought to be safe, helpful, reasonably priced, endorsed by a significant subpopulation—and are effectively marketed. Just as for conventional treatments, an individual's decision concerning the use of alternative therapies is likely to be guided by one's health belief system, in which decisions are based on the perceived seriousness of the problems and the perceived benefits versus perceived "costs" of the available treatments (36).

The Clinician's Perspective

From the evidence-based perspectives of conventional medicine, alternative/complementary treatments are usually interventions that have not been subjected to rigorous controlled studies and whose utility is unclear. Clinicians often have limited knowledge of these treatments, and on the basis of their own judgment and knowledge they usually think about various alternative and complementary treatments as falling into one or more of the following broad types: 1) dangerous and toxic; 2) perhaps OK on its own but risks worrisome drug interactions with conventional medications; 3) wastes time and money and interferes with patients' seeking conventional care in a timely manner; 4) couldn't hurt! and may help people feel better and at worst serves as a placebo; 5) may actually be effective; and 6) seems to work as well as and to be less costly and less toxic than most of what conventional medicine has to offer for the problem.

To make informed decisions about various alternative treatments, to decide which of the just-listed prototypes

best characterize the various alternative treatments used, and to best help patients who are using or thinking about using them, clinicians need to be open-minded, educated about alternative treatments, clinically cautious, and humble. They need to use well-established rules for clinical decision making based first and foremost on evidence-based medicine, as well as on good clinical logic, available clinical consensus, and common sense for alternative treatments where controlled clinical trials are not yet available.

We do not advocate recommending unproven alternative therapies. However, every clinician should be open to exploring and discussing their patients' uses of and questions about alternative treatments, using the following guidelines, modified in part from those of Eisenberg (37).

Guidelines

1. *Routinely question patients about alternative therapies.* Given the high prevalence of the use of herbs and other alternative therapies, clinicians should routinely question patients about their use of these therapies and alternative practitioners. To help patients be open and honest in their answers, the questions must be asked in a supportive, understanding, and non-judgmental manner. The information can alert the clinician to potentially deleterious herb-medication interactions.

2. *Discuss safety and efficacy.* Clinicians should be prepared to review issues involving the safety and efficacy of commonly used alternative treatments. They should be prepared to discuss with patients how "natural" substances are not inherently safe (e.g., snake venoms and poison ivy oils) (37).

3. *Discuss merits of alternative treatments.* When a patient reveals the types of alternative treatments and practitioners he or she is using, the clinician should ask about the specific problems for which the patient sought help, the reasons the patient sought help from the alternative rather than conventional health care system for those problems, and the patient's assessments of the effectiveness, costs, and other features of the alternative treatments. Clinicians should be very open-minded, respectful, and noncompetitive when patients praise their alternative providers, as they will often do. Depending on the clinician's own attitudes and beliefs about these alternative treatments, and the extent to which the clinician becomes defensive

in reaction to the patient's choosing alternative approaches, the clinician and patient may be able to have a helpful dialogue about these matters.

4. *Provide information.* When patients ask about the value of alternative treatments for a specific problem, physicians should be open about the limitations of their own knowledge about these alternative treatments. Where controlled studies regarding effectiveness exist, clinicians should share such information with patients. Where such information is unavailable, clinicians should indicate that to their knowledge there are no evidence-based studies to support the specific effectiveness of the alternative interventions for the stated problems. They should review what they know, and what they do not know, about safety issues, including the potential risks of the alternative treatments and deleterious effects of interactions with drugs. Given the potential for unintended drug-drug interactions, Eisenberg advocated that patients who take prescription medications, especially medications known to be toxic to the liver or kidneys, be cautioned about, if not dissuaded from, simultaneously using herbs, supplements, and other substances with poorly understood pharmacologies. Clinicians should also review potential "indirect toxicities" of alternative therapies, including those that may delay the use of proven treatments and those that are likely to be disappointing for the specific complaint (37). Also, clinicians should then carefully review with patients any available effective conventional treatments for the patients' complaints.

5. *Learn about alternative therapies.* At the same time, clinicians should be ready and willing to learn more about the substances being sold as alternative therapies. The Medical Economics Company, publisher of the *Physicians' Desk Reference (PDR)*, has recently published an 800-page *Physicians' Desk Reference for Herbal Medicines* (38), containing a comprehensive list of natural remedies and including information on indications, pharmacological effects, proper doses, precautions, adverse reactions, symptoms of overdose, recommended emergency treatments, contraindications, and interactions with prescription medications, other herbal remedies, and foods. Since herbal remedies are not investigated and approved by the FDA, this information is explicitly not considered FDA-approved prescribing information. However, the book does

contain extensive literature citations and includes the findings of Europe's principal source of information about herbal medicine, the report of the German Commission E (27). Critical reviews concerning herbal remedies in psychiatric practice (31) and complementary therapies for depression (39) have recently been published. The interest of psychiatry in alternative medicine is increasing, as evidenced by a symposium at the American Psychiatric Association's 1998 annual meeting, which included presentations regarding the dangers of potential interactions between herbal remedies and drugs and the potential risks and benefits of St. John's wort, kava, and ayahuasca ("Herbal Medicine: Ancient Roots to Modern Use," Michael W. Smith and Charles S. Grob, co-chairpersons).

6. *Determine characteristics of proposed alternative treatments and practitioners.* Eisenberg stated that if patients are already going to or contemplating going to alternative providers, the following are some helpful questions the clinician may ask the patient or the patient may wish to ask potential alternative providers.

a. Is the provider credentialed and licensed?

b. Is the provider's experience in treating the patient based on personal clinical experiences with other patients with similar problems? (And, if so, may the patient speak with one of the other patients treated by that provider?)

c. Of what exactly does the therapy consist?

d. How many weeks are likely to pass before the patient and provider decide that the therapy is or is not working?

e. How much will each session cost with or without medications, and what is the anticipated total cost for the specified time period?

f. Are the services covered by third-party payments?

g. What are the potential side effects?

h. With the patient's permission, is the provider willing to communicate diagnostic findings, therapeutic plans, and follow-up information to the patient's conventional providers? Are there any limitations to these communications? Eisenberg suggested that follow-up visits or telephone calls with the patient should be scheduled to explicitly review the alternative provider's responses to these questions, any treatments suggested by the alternative provider, and, if treatment is in-

stituted, a follow-up to consider responses to the treatment (37).

i. All of these interactions should be carefully documented in the medical record. Studdert et al. (40) reminded physicians that, although infrequent, liability for referral to alternative practitioners is possible in certain situations and should be taken seriously. Medicolegal concerns and cautions should be kept in mind and appropriate consultations sought as indicated by the treatment situation.

Other Types of Treatments

We will end with some brief remarks about alternative/complementary treatments that do not involve herbs or other ingested substances. Most concern "high-touch" hands-on treatments, such as massage or skeletal manipulations, and various talking treatments. Various hands-on treatments and conventional and unconventional talking treatments may yield symptom relief and in some instances come close to conventional psychotherapies in their manner and style of delivery. In their study of the use of alternative and complementary treatments in the United States, Eisenberg et al. (1) found that relaxation techniques, guided imagery, spiritual healing, and hypnosis were among those most commonly used. These often provide the "high-talk" and "high-touch" experiences that many patients find lacking in the conventional practice of medicine (41). Even in the conventional practice of psychiatry, "high talk" appears to be less common than it once was. If patients do not receive these therapies conventionally, they increasingly will seek them from alternative practitioners. It is ironic that increasing numbers of patients seek a bedside manner from alternative therapists because there are fewer and fewer ways to obtain these experiences in conventional treatment settings. These trends are most likely related to differences in out-of-pocket costs to patients between alternative therapists and psychiatrists and to the limited access to psychotherapeutic care by psychiatrists that is permitted by contemporary medical insurance coverage.

Future Trials

How effective are alternative treatments? In the future we can anticipate an increase in the extent to which alternative remedies and treatments are subject to rigorous scrutiny as funding

to test effectiveness pours into this area. As Fontanarosa and Lundberg stated in a recent editorial in *JAMA* (42), "There is no alternative medicine. There is only scientifically proven, evidence-based medicine supported by solid data or unproven medicine, for which scientific evidence is lacking." A recent "methodological manifesto" regarding alternative medicine (43) suggested that established methods are quite satisfactory for addressing the majority of study questions related to alternative medicine. We are likely to see an increasing number of evidence-based studies in this area. Many of the earlier studies suffered from methodological problems that limit the extent to which their results can be fully accepted. Certainly, case reports are not sufficient. In the future, greater adoption by investigators and journal editors of the Consolidated Standards of Reporting Trials guidelines (44) for psychopharmacological studies, including those involving herbal remedies, will increase the extent to which practitioners and patients can accept published results as reliable and valid.

REFERENCES

1. Eisenberg DM, David RB, Ettner SL, Appel S, Wilkey S, Van Rompay M, Kessler RC: Trends in alternative medicine use in the United States, 1990-1997: results of a follow-up national survey. *JAMA* 1998; 280: 1569-1575
2. Astin JA: Why patients use alternative medicine: results of a national study. *JAMA* 1998; 279:1548-1553
3. Cattani D: Pharmafoods in the pantry. *Futurist* 1998; 32:2
4. Nutraceuticals: new opportunities for alternative/complementary practitioners. *Alternative Health Practitioner* 1998; 4:247
5. Tyler V: *Herbs of Choice: The Therapeutic Use of Phytomedicinals*. Binghamton, NY, Pharmaceutical Products Press, 1994, p 209
6. Bisset NG (ed): *Herbal Drugs and Phytopharmaceuticals: A Handbook for Practice on a Scientific Basis*. Boca Raton, Fla, CRC Press, 1994
7. Petkov V: Plants and hypotensive, antiatheromatous and coronarodilating action. *Am J Chin Med* 1979; 7:197-236
8. Willey LB, Mady SP, Cabaugh DJ, Wax PM: Valerian overdose: a case report. *Vet Hum Toxicol* 1995; 37:364-365
9. Leathwood PD, Chauffard F, Heck E, Munoz-Box R: Aqueous extract of valerian root (*Valeriana officinalis* L) improves sleep quality in man. *Pharmacol Biochem Behav* 1982; 17:65-71
10. Leathwood PD, Chauffard F: Quantifying the effects of mild sedatives. *J Psychiatr Res* 1982-1983; 17:115-122
11. Hazelhoff B, Malingre TM, Meijer DK: Antispasmodic effects of valeriana compounds: an in-vivo and in-vitro study on the guinea-pig ileum. *Arch Int Pharmacodyn Ther* 1982; 257:274-287
12. Sakamoto T, Mitana Y, Nakajima K: Psychotropic effects of Japanese valerian root

- extracts. *Chem Pharm Bull (Tokyo)* 1992; 40:758-761
13. Santos MS, Ferreira F, Cunha AP, Carvalho AP, Ribeiro CF, Macedo T: Synaptosomal GABA release as influenced by valerian root extract—involvement of the GABA carrier. *Arch Int Pharmacodyn Ther* 1994; 327: 220-231
 14. Santos MS, Ferreira F, Cunha AP, Carvalho AP, Macedo T: An aqueous extract of valerian influences the transport of GABA in synaptosomes (letter). *Planta Med* 1994; 60:278-279
 15. Santos MS, Ferreira F, Faro C, Pires E, Carvalho AP, Cunha AP, Macedo T: The amount of GABA present in aqueous extracts of valerian is sufficient to account for [^3H]GABA release in synaptosomes (letter). *Planta Med* 1994; 60:475-476
 16. Riedel E, Hänsel H, Ehrke G: Inhibition of γ -aminobutyric acid catabolism by valerianic acid derivatives. *Planta Med* 1992; 46:219-220
 17. Oshima Y, Matsuoka S, Ohizumi Y: Antidepressant principles of *Valeriana fauriei* roots. *Chem Pharm Bull (Tokyo)* 1995; 43: 169-170
 18. McGregor FB, Abernethy VE, Dahabra S, Cobden I, Hayes PC: Hepatotoxicity of herbal remedies. *BMJ* 1989; 229:1156-1157
 19. Chan TY, Tang CH, Critchley JA: Poisoning due to an over-the-counter hypnotic, Sleep-Qik (hyoscyne, cyproheptadine, valerian). *Postgrad Med J* 1995; 71:227-228
 20. Bloomfield HH, Nordfors M, McWilliams P: *Hypericum and Depression*. Los Angeles, Prelude Press, 1996
 21. Couzin J: Beefed-up NIH center probes unconventional therapies. *Science* 1998; 282: 2175-2176
 22. Baureithel KH, Buter KB, Engesser A, Burkard W, Schaffner W: Inhibition of benzodiazepine binding in vitro by amentoflavone, a constituent of various species of *Hypericum*. *Pharm Acta Helv* 1997; 72: 153-157
 23. Nahrstedt A, Butterweck V: Biologically active and other chemical constituents of the herb of *Hypericum perforatum* L. *Pharmacopsychiatry* 1997; 30:129-134
 24. Kartnig T, Gobel I, Heydel B: Production of hypericin, pseudohypericin and flavonoids in cell cultures of various *hypericum* species and their chemotypes. *Planta Med* 1996; 62:51-53
 25. Cott JM: In vitro receptor binding and enzyme inhibition by *Hypericum perforatum* extract. *Pharmacopsychiatry* 1997; 30: 108-112
 26. Cott JM: NCDEU update: natural product formulations available in Europe for psychotropic indication. *Psychopharmacol Bull* 1995; 31:745-751
 27. Blumenthal M, Busse WR, Goldberg A, Gruenwald J, Hall T, Riggins CW, Rister R (eds): *The Complete German Commission E Monographs—Therapeutic Guide to Herbal Medicines*. Austin, Tex, American Botanical Council, 1998
 28. Perovic S, Muller WE: Pharmacological profile of hypericum extract: effect on serotonin uptake by postsynaptic receptors. *Arzneimittelforschung* 1995; 45:1145-1148
 29. Woelk H, Bukard G, Grunwald J: Benefits and risks of the hypericum extract LI 160: drug monitoring study with 3,250 patients. *J Geriatr Psychiatry Neurol* 1994; 7(suppl 1):S34-S38
 30. Linde K, Ramirez G, Mulrow CD, Pauls A, Weidenhammer W, Melchart D: St John's wort for depression—an overview and meta-analysis of randomised clinical trials. *BMJ* 1996; 313:253-258
 31. Salzman C: St John's wort. *Harv Rev Psychiatry* 1998; 5:333-335
 32. Wong AHC, Smith M, Boon HS: Herbal remedies in psychiatric practice. *Arch Gen Psychiatry* 1998; 55:1033-1044
 33. Almeida JC, Grimsley EW: Coma from the health food store: interaction between kava and alprazolam. *Ann Intern Med* 1996; 125:940-941
 34. Lazare A, Eisenthal S: Clinician/patient relations, I: attending to the patient's perspective, in *Outpatient Psychiatry: Diagnosis and Treatment* (2nd ed). Edited by Lazare A. Baltimore, Williams & Wilkins, 1989, pp 125-136
 35. Pachter LM: Culture and clinical care: folk illness beliefs and behaviors and their implications for health care delivery. *JAMA* 1994; 271:690-694
 36. Becker MH, Haefner DP, Kasl SV, Kirscht JP, Maiman LA, Rosenstock IM: Selected psychosocial models and correlates with individual health-related behaviors. *Med Care* 1979; 15(May suppl):27-46
 37. Eisenberg DM: Advising patients who seek alternative medical therapies. *Ann Intern Med* 1997; 127:61-69
 38. Gruenwald J (ed): *Physicians' Desk Reference for Herbal Medicines*. Oradell, NJ, Medical Economics, 1998
 39. Ernst E, Rand JI, Stevinson C: Complementary therapies for depression. *Arch Gen Psychiatry* 1998; 55:1026-1032
 40. Studdert DM, Eisenberg DM, Miller FH, Curto DA, Kaptchuk TJ, Brennan TA: Medical malpractice implications of alternative medicine. *JAMA* 1998; 280:1610-1615
 41. Toffler A: *The Third Wave*. New York, William Morrow, 1980
 42. Fontanarosa PB, Lundberg GD: Alternative medicine meets science. *JAMA* 1998; 280: 1618-1619
 43. Levin JS, Glass TA, Kushi LH, Schuck JR, Steele L, Jonas WB: Quantitative methods in research on complementary and alternative medicine: a methodological manifesto, NIH Office of Alternative Medicine. *Med Care* 1997; 35:1079-1094
 44. Begg C, Cho M, Eastwood S, Horton R, Moher D, Olkin I, Pitkin R, Rennie D, Schulz KF, Simel D, Stroup DF: Improving the quality of reporting randomized controlled trials: the CONSORT statement. *JAMA* 1996; 276:637-639