CATEGORY 1

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Integrative Management of Depressed Mood: Evidence and Treatment Guidelines

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Dr. Lake has indicated he has nothing to disclose.

EDUCATIONAL OBJECTIVES

After reading this article, you will be familiar with:

- Evidence for uses of nonconventional and integrative approaches in the treatment of depression.
- Basic concepts about rational, safe uses of nonconventional and integrative strategies when treating depression.
- Unresolved safety issues pertaining to uses of natural products and other nonconventional treatment approaches.
- Discussion points about the evidence-based use of diverse nonconventional and integrative approaches used to treat depression.

Who will benefit from reading this article?

Psychiatrists, primary care physicians, neurologists, nurse practitioners, psychiatric nurses and other mental health care professionals. Continuing medical education credit is available for most specialties. To determine if this article meets the CE requirements for your specialty, please contact your state licensing board.

More than 30 placebo-controlled trials (Linde et al., 1996; Schrader, 2000; Vorbach et al., 1997, 1994) have confirmed that St. John's wort (SJW) (*Hypericum perforatum*) is as effective as conventional antidepressants (including imipramine [Tofranil], fluoxetine [Prozac], sertraline [Zoloft] and others) for mild or moderate depressed mood. Standardized preparations of SJW 300 mg tid are as effective as conventional antidepressants for moderate depressed mood (Ernst, 1995; Kim et al., 1999; Linde et al., 2005, 1996). There are case reports of severe depression responding to higher doses of SJW (up to 1800 mg/day), but findings from controlled studies are inconsistent (Vorbach et al., 1997). A large multicenter study sponsored by the National Institutes of Health showed that SJW and sertraline were equally ineffective in the treatment of severe depressed mood and that neither treatment was more effective than placebo (Hypericum Depression Trial Study Group, 2002). The validity of these findings has been questioned because of concerns over serious design flaws, including the use of subtherapeutic doses of both SJW and sertraline for the target population, selective recruitment of severely depressed patients who had previously been refractory to most conventional treatments, short duration, and lack of statistical power. In a follow-up study, the majority of nonresponders (n=95) to a standardized SJW preparation responded to conventional antidepressants with significant improvements in depressed mood (Gelenberg et al., 2004). This finding suggested that conventional antidepressants are more effective than SJW in refractory depressed mood and reopened the question of a possibly significant placebo effect for SJW. Cases of possible serotonin syndrome have been reported when SJW is combined with a selective serotonin reuptake inhibitor. Patients who are being treated with warfarin (Coumadin), protease inhibitors, theophylline , monoamine oxidase inhibitors, oral contraceptives and immunosuppressive agents should be cautioned against concurrent use of SJW, which lowers serum levels of those drugs through the induction of cytochrome P450 liver enzymes (Broughton and Denahm, 2000).

Placebo-controlled, double-blind studies and meta-analyses of controlled studies consistently show that S-adenosyl-L-methionine (SAMe) 400 mg/day to 1600 mg/day has comparable or superior antidepressant efficacy compared to conventional antidepressants (Berlanga et al., 1992; Bressa, 1994; Janicak et al., 1988; Kagan et al., 1990). When combined with conventional antidepressants, SAMe accelerates response, improves outcomes and may lower effective antidepressant doses (Alpert et al., 2004; Berlanga et al., 1992). There are case reports of treatment-refractory patients responding to SAMe (De Vanna and Rigamonti, 1992; Rosenbaum et al., 1990). Transient arousal or agitation during titration and rare cases of hypomania have been reported in patients with bipolar disorder (BD) taking SAMe.

Folate alone, in doses from 200 µg to 15 mg, has been shown to result in sustained improvement in depressed mood (Bottiglieri et al., 1990; Crellin et al., 1993). Folate 0.5 mg/day to 1 mg/day augments the effects of conventional antidepressants (Coppen and Bailey, 2000; Papakostas et al., 2004). Folate and vitamin B_{12} are essential cofactors for the synthesis of SAMe (Fava et al., 1997) and should be recommended to patients using SAMe or a conventional antidepressant. Patients with severe depression found to have low serum folate levels are significantly less likely to respond to antidepressants and should be encouraged to take folate (Reynolds et al., 1970). Depressed patients with normal B_{12} serum levels respond better to conventional antidepressants compared to patients who are B_{12} deficient (Hintikka et al., 2003).

Treatments of depressed mood that are not based on a specific pharmacological mechanism of action are gaining widespread acceptance because of cultural values that motivate patients to use them.

Eicosapentaenoic acid (EPA), an omega-3 fatty acid, has been shown to be effective against moderate depressed mood (Peet and Horrobin, 2002) in doses of 1 g/day, 2 g/day or 4 g/day when used alone (Su et al., 2003) or in combination with a conventional antidepressant (Nemets et al., 2002). However, another omega-3 fatty acid, docosahexaenoic acid (DHA), probably does not improve depressed mood (Marangell et al., 2003). Rare cases of hypomania have been reported in depressed patients with BD taking EPA; this population should be followed closely when taking these natural products (Kinrys, 2000; Su et al., 2000).

5-hydroxytryptophan (5-HTP) 300 mg/day is probably as effective as conventional antidepressants

(Please see Integrative Management, *page 92)*

CATEGORY 1

Integrative Management

Continued from page 91

for moderate depressed mood (Birdsall, 1998; Byerley et al., 1987). Like SAMe, 5-HTP augments conventional antidepressants, potentially resulting in a more complete or rapid response (Mendlewicz and Youdim, 1980; van Praag et al., 1974). When combining 5-HTP with an SSRI, it is important to monitor for signs of a serotonin syndrome, though no confirmed reports of this potentially serious adverse effect have been reported in the peer-reviewed medical literature. Some cases of treatment-refractory depression improve when 5-HTP 300 mg/day to 600 mg/day is combined with a conventional antidepressant (Sargent et al., 1998). L-tryptophan 2 g augmented the antidepressant efficacy of fluoxetine 20 mg and improved sleep quality (Levitan et al., 2000). Findings of one study suggested that L-tryptophan 1 g to 2 g combined with bright-light therapy was more effective than either approach alone in seasonal depressed mood (Lam et al., 1997). L-tryptophan can cause sedation and should be dosed at bedtime. Uncommon side effects of L-tryptophan include dry mouth and blurred vision. Serious adverse effects have been reported when L-tryptophan is combined with MAOI antidepressants. No cases of eosinophilia myalgia syndrome have been reported since the early 1990s, and those cases were attributed to a single contaminated batch of one over-the-counter brand of L-tryptophan (Kilbourne et al., 1996). Patients with depression who benefit from L-tryptophan should be tried on 5-HTP, which more readily crosses the blood-brain barrier, is more efficiently converted to serotonin, and has fewer side effects than L-tryptophan.

Acetyl-L-carnitine (ALC) has been investigated in placebo-controlled, double-blind trials in severely depressed patients, elderly depressed patients and depressed demented patients (Bella et al., 1990; Tempesta et al., 1987). In divided doses of 1 g/day to 3 g/day, ALC may be beneficial in elderly depressed or depressed demented patients. In contrast to SAMe, SJW and 5-HTP, no comparison studies have been done on ALC and conventional antidepressants. Acetyl-L-carnitine may ameliorate symptoms of cognitive impairment and should be considered when depression is related to age-related cognitive decline (Bella et al., 1990; Garzya et al., 1990). Inositol 12 g/day to 20 g/day may be beneficial in both unipolar and bipolar depressed mood (Chengappa et al., 2000; Levine et al., 1995). Inositol may have synergistic effects when combined with conventional mood stabilizers (Chengappa et al., 2000). Dihydroepiandosterone (DHEA) 90 mg/day to 450 mg/day has synergistic effects when combined with conventional antidepressants and may be an effective monotherapy for moderate depressed mood (Schmidt et al., 2005). It may be beneficial when depressed mood occurs together with anxiety, psychosis or cognitive impairment (Strous et al., 2003; Wolkowitz et al., 1997). In women with a history of estrogen receptor-positive breast cancer, DHEA should be avoided (Cogan, 2001). Dietary modifications, including restricting caffeine and refined sugar and increasing consumption of whole foods rich in B vitamins and fatty fish, may improve depressed mood or reduce the risk of becoming depressed (Christensen, 1991; Hibbeln, 1998). **Table 1** summarizes doses of nonconventional biological treatments of depressed mood and unresolved safety considerations associated with their use.

Complementary and Alternative Nonpharmacological Treatments

Treatments of depressed mood that are not based on a specific pharmacological mechanism of action are gaining widespread acceptance because of cultural values that motivate patients to use them and anecdotal evidence supporting their efficacy and safety. In contrast to conventional and nonconventional approaches that target dysfunction in specific neurotransmitter systems associated with depressed mood, many complementary and alternative treatments probably achieve beneficial clinical results by improving feelings of well-being and enhancing mind-body health in general. Somatic, mind-body and energy-information treatments of depressed mood include exercise (Blumenthal et al., 1999), total or partial sleep deprivation, relaxation training (Murphy et al., 1995), yoga, tai chi, and qigong, as well as treatments based on empirically validated forms of energy or information including bright-light exposure and electroencephalograph biofeedback (Brown et al., 2001; Levitt et al., 1991).

Regular exercise at least 30 minutes three times a week may be as effective as conventional antidepressants, SJW and cognitive therapy for moderate depressed mood. Case reports; randomized, controlled trials; and two meta-analyses confirm that regular exercise has beneficial effects on depressed mood (Lawlor and Hopker, 2001; Tkachuk and Martin, 1999). Increased brain levels of mood-elevating endorphins, dopamine, norepinephrine and serotonin following sustained exercise have been proposed as possible antidepressant mechanisms. The antidepressant efficacy of exercise is probably comparable to individual cognitive therapy and group therapy (Tkachuk and Martin, 1999). Exercise and conventional antidepressants may have equiv-

Table 1

Representative Nonconventional Biological Treatments of Depressed Mood

Natural Product	Comments
St. John's wort	• 300 mg tid of 0.3% hypericin extract • Caution against concurrent use with protease inhibitors or anticoagulants
S-adenosyl-L-methionine (SAMe)	• 400 mg bid to 800 mg tid alone or in combination with antidepressants • Best bioavailability if taken before meals • Caution: Monitor for agitation • Caution: Avoid in patients with bipolar disorder
5-hydroxytryptophan (5-HTP)	• 200 mg to 600 mg daily alone or in combination with antidepressants • Caution: Monitor for serotonin syndrome when used in combination with an SSRI • Moderately sedating and better tolerated at bedtime
Omega-3 essential fatty acids	• 1 g/day to 9 g/day EPA fraction most effective • Preliminary findings suggest efficacy alone or in combination with conventional antidepressants • Caution: May prolong bleeding time when taken with aspirin • Caution: Certain brands may cause hypervitaminosis A
Folate	• 800 µg to 5 mg • Improves mood when used alone • Improves response to conventional antidepressants • May enhance antidepressant effect of SAMe
Vitamin B_{12}	• 1 mg/day • Improves mood and enhances energy when used alone • May enhance antidepressant effect of SAMe
Acetyl-L-carnitine (ALC)	• 500 mg/day to 2 g/day in divided doses • Note: Only studies on depressed mood in elderly or elderly demented • Note: Possibly effective in mild dementia (mechanism of action believed to involve correcting cholinergic neurotransmitter deficit in Alzheimer's disease)

EPA=eicosapentaenoic acid

Source: Lake J (2005)

CATEGORY 1

alent efficacy in individuals with moderate depression (Blumenthal et al., 1999). The findings of one study suggested that the therapeutic benefits of regular exercise are comparable to SJW for moderately depressed mood (Ernst et al., 1998). In a 16-week study, 156 patients with depression over age 50 were randomized to aerobic exercise three times a week, medications (sertraline up to 200 mg), or exercise and medications (Blumenthal et al., 1999). All groups had improved significantly by the end of the study, and there were no significant differences in response rates using standardized symptom rating scales assessing mood, self-esteem and negative thoughts. Patients taking an antidepressant only improved faster initially than the other two groups, but patients who exercised only had a lower six-month relapse rate (Babyak et al., 2000). Of patients who exercised only, 60.4% experienced complete remission versus 65.5% of patients taking sertraline and 68.8% of patients who exercised and took a conventional antidepressant (Babyak et al., 2000). Differences in these outcomes were not significant.

Patients with depression who exercise in a brightly lit (2500 lux to 4000 lux) indoor environment experience more significant improvements in mood and greater feelings of vitality compared to individuals with depression who exercise indoors in ordinary room light (400 lux to 600 lux) (Partonen et al., 1998). Women with depression who combined exercise with bright-light exposure while taking a daily vitamin regimen reported significant improvements in mood (Brown et al., 2001). It is difficult to separate beneficial effects of exercise from other lifestyle factors, and it is possible that exercise contributes to overall feelings of wellness while not having specific mood-elevating effects. The optimum duration or frequency of exercise in depressed mood has not yet been determined but probably varies with age and conditioning. A large study is ongoing to determine the amount, type and frequency of exercise that is needed for sustained improvement in depressed mood in the absence of other treatments (Dunn et al., 2002). Medically ill or physically impaired patients should always consult with their physician before starting a strenuous exercise program.

Partial sleep deprivation improves moderate depressed mood (Leibenluft et al., 1993). One night of total sleep deprivation followed by sleep phase advance often improves severe depressed mood (Riemann et al., 1999). Partial sleep deprivation combined with maintenance lithium (Eskalith, Lithobid) therapy and morning bright-light exposure may be more effective than either approach alone in bipolar depression (Colombo et al., 2000).

Mindfulness training is probably as effective as cognitive therapy in moderate depressed mood (Murphy et al., 1995). Of the various mind-body disciplines used to obtain relief from psychiatric symptoms, more studies have been done on yoga than any other discipline (Shannahoff-Khalsa, 2004). It has been suggested that the mechanism of action of yogic breathing might be similar to vagal nerve stimulation (VNS) in that both approaches involve modulation of the balance of parasympathetic and sympathetic autonomic tone (Brown et al., 2001). The consistent practice of yoga has been shown to improve overall quality of life, including indicators of moderately depressed mood (Janakiramaiah et al., 2000). Regular yoga practice, including specialized breathing techniques and postures, may be as effective as conventional antidepressants in severe depressed mood (Janakiramaiah et al., 2000). Yogic breathing achieves desirable changes through a variety of specific breathing exercises that differentially affect the brain stem and limbic system while VNS relies on a weak electrical current to achieve desirable changes in brain autonomic activity that mediate improved mood or reduced anxiety. Like yogic breathing techniques, the regular practice of various yoga postures (asanas) probably results in beneficial changes in the autonomic nervous system, resulting in improved cardiorespiratory performance and increased feelings of psychological well-being (Harinath et al., 2004). Many styles of yoga are probably beneficial in depressed mood. A particular style of yogic breathing called Sudarshan Kriya yoga has been extensively evaluated as a potential treatment of depressed mood and other mental or emotional symptoms (Shannahoff-Khalsa et al., 1999). In a group of hospitalized patients with severe depression, improvements associated with Sudarshan Kriya breathing practice were comparable to responses from conventional antidepressants and only slightly less robust than patients receiving electroconvulsive therapy (Janakiramaiah et al., 2000). Emerging evidence suggests that the regular practice of yoga forms that do not include specialized breathing exercises also improve depressed mood, including Hatha yoga, Omkar meditation and Iyengar yoga. Regular practitioners of Hatha yoga and Omkar meditation also had significant increases in melatonin secretion, possibly related to increased serotonin, an established benefit of meditation (Walton et al., 1995). In a small randomized, case-control study, mildly depressed practitioners of Iyengar yoga reported significant improvements in mood following semiweekly yoga practice for five weeks (Woolery et al., 2004).

Many complementary and alternative treatments probably achieve beneficial clinical results by improving feelings of well-being and enhancing mind-body health in general.

The absence of double-blinding is a significant limitation of studies on yoga or any mind-body practice, as enrolled patients are necessarily aware of engaging in specific movements or breathing exercises of a particular mind-body practice. Many patients with depression have difficulty becoming motivated to start a mind-body practice and should be gently encouraged to take classes at the start of their practice and slowly transition to a daily self-directed program if they find it beneficial to their mood and general state of well-being.

Regular qigong or tai chi practice results in generally improved emotional well-being, including improved mood (Schwartzman, 1998; Tang et al., 1990; Wang, 1997). Brief psychotic episodes have been reported during qigong in histrionic or psychotic patients and individuals diagnosed with personality disorders (Lake, 2001). In fact, the *DSM-IV* describes psychotic symptoms that can occur as a consequence of erroneous qigong as a culture-bound syndrome (qigong psychotic reaction). Combining mindfulness training or guided imagery with conventional antidepressants may be more effective than either conventional antidepressants or cognitive-behavioral therapy alone (Bernal i Cercos et al., 1995; Mason and Hargreaves, 2001; Rees, 1995).

Regular bright-light exposure (10,000 lux for 30 to 40 minutes/day) improves depressed mood and may have more rapid onset than conventional antidepressants (Golden et al., 2005; Levitt et al., 1991). Benefits of bright-light exposure are greater when depressive mood changes follow a seasonal pattern. Bright artificial light and natural light are probably equally effective. Bright-light exposure is a safe and effective treatment of depression in pregnant women (Oren et al., 2002). Regular exposure to dim red or blue light may be as effective as bright-light exposure in seasonal depression (Wileman et al., 2001). Dim green light two hours before exposure to natural light may accelerate response to conventional antidepressants (Benedetti et al., 2003). Evening bright-light exposure may cause insomnia, and rare cases of hypomania have been reported in patients with BD (Bauer et al., 1994). Transient mild adverse effects of bright-light exposure include jitteriness, headaches and nausea. Regular daily exposure to high-density negative ions is probably an effective treatment of seasonal depressed mood (Terman and Terman, 1995). Antidepressant effects of exposure to high-density negative ions and bright light may be equivalent (Terman et al., 1998).

Attentive listening to music probably improves moderately depressed mood (Drohan, 1999). Case reports suggest that listening to binaural sounds in the beta frequency range (16 Hz to 24 Hz) may improve depressed mood (Lane et al., 1998; Milligan and Waldkoetter, 2000). Listening to music or patterned sounds may produce positive or negative emotional effects depending on culture and individual preferences (Smith and Noon, 1998). In one study, listening to tranquil music improved mood in depressed outpatients, who also experienced beneficial changes in heart rate and blood pressure (Lai, 1999). In another study, patients with cancer who participated in weekly sessions of combined music and guided imagery reported greater improvements in depressed mood and overall quality of life compared to patients in a wait-list group (Burns, 2001). Patients with cancer who received music therapy while undergoing autologous stem cell transplantation reported significantly greater improvements in both anxiety and depressed mood compared to patients who did not receive music therapy (Cassileth et al., 2003). Combined EEG-heart rate variability biofeedback training may improve some cases of depressed mood (McCraty et al., 2001).

Chinese medical treatments of depressed mood, including standard acupuncture, electro-acupuncture

(Please see Integrative Management, *page 94)*

CATEGORY 1

Integrative Management

Continued from page 93

and computer-controlled electro-acupuncture, show promising results, however, the mechanism of action remains unclear. Detailed reviews of the evidence for Chinese medical treatments of mental and emotional symptoms are available in two textbooks (Allen et al., 1998; Flaws and Lake, 2001). The findings of a large prospective, controlled study showed equivalent antidepressant efficacy of a specific electro-acupuncture protocol and amitriptyline (Luo et al., 1998). Findings from a sham-controlled study suggested that conventional acupuncture is effective in some cases of severe depressed mood (Allen et al., 1998). Electro-acupuncture alone may be as effective as electro-acupuncture combined with amitriptyline or other conventional antidepressants (Luo et al., 1998). Computer-controlled electro-acupuncture using high frequency currents may be more effective than standard acupuncture or electro-acupuncture (Luo et al., 1995). Rare cases of HIV, hepatitis B and C, pneumothorax, and cardiac tamponade have been reported in patients treated with acupuncture (Ernst and White, 1997).

Spiritual and religious beliefs, spiritual healing approaches, and "energy medicine" are widely used to treat depressed mood in North America and Europe (Druss and Rosenheck, 2000; Kessler et al., 2001). However, limited numbers of controlled trials, small study sizes and inherent study design problems continue to obscure understandings of putative underlying mechanisms or efficacy of these approaches. Spirituality and religious beliefs are associated with reduced risk of depressed mood (Kendler et al., 2003). Regular support groups with spiritual-religious themes reduce the severity of depressed mood and increase emotional well-being (Sageman, 2004). Regular healing touch or therapeutic touch treatments may reduce the severity of depressed mood and bereavement (Robinson, 1996). **Table 2** summarizes the evidence for uses of nonpharmacological treatments of depressed mood.

Integrative Mental Health Care—Basic Considerations

Integrative medicine strives to find a balance between the "rigor" of empirical research and the "relevance" of personal information through the use of both quantitative and qualitative information during treatment planning. Treatment planning takes into account conventional and nonconventional approaches that have been tried previously and the strength of evidence for treatments that have not been tried in the context of patient preferences and realistic constraints on cost and availability. The optimum treatment plan is the ideal combination of treatments addressing the identified causes of a symptom pattern. The choice of conventional versus nonconventional approaches depends on many factors, including symptom severity, previous successful treatment strategies, concerns over adverse effects or interactions, patient preferences, and the availability of qualified conventional or alternative medical practitioners. There will sometimes be a discrepancy between the "optimum" integrative treatment plan and a realistic plan that takes these factors into account. The practitioner should encourage the patient to initially use treatments for which there is compelling evidence for the principal symptom(s) being addressed. For

Table 2

Representative Somatic, Mind-Body and Energy-Information Treatments of Depressed Mood

Treatment	Comments
Exercise	• Regular exercise may be as effective as conventional antidepressants, St. John's wort and cognitive-behavioral therapy for moderate depressed mood • Caution: Medically ill patients should consult their physician before starting a rigorous exercise program
Sleep deprivation	• Partial sleep deprivation effective in moderate depressed mood • One night of total sleep deprivation improves severe depressed mood • Partial sleep deprivation combined with lithium therapy and morning bright-light exposure may be more effective than either approach alone in bipolar depression
Mindfulness training	• Regular mindfulness training is probably as effective as cognitive therapy in moderate depressed mood • Combining mindfulness training or guided imagery with conventional antidepressants may be more effective than either conventional antidepressants or cognitive-behavioral therapy alone
Yoga, qigong and tai chi	• Regular yoga practice may be as effective as conventional antidepressants in severe depressed mood • The consistent practice of yoga, qigong or tai chi improves overall quality of life and is beneficial in moderately depressed mood • Caution: Brief psychotic episodes reported during qigong in histrionic, psychotic or borderline patients
Light	• Regular bright-light exposure (10,000 lux for 30 to 40 minutes/day) improves depressed mood and may have more rapid onset than conventional antidepressants • Bright artificial light and natural light are probably equally effective • Bright-light exposure is a safe and effective treatment of depression in pregnant women • Regular exposure to dim red or blue light may be as effective as bright-light exposure in seasonal depression • Dim green light two hours before exposure to natural light may accelerate response to conventional antidepressants • Caution: Evening bright-light exposure may cause insomnia, and rare cases of hypomania have been reported in patients with bipolar disorder
High-density negative ions	• Regular daily exposure to high-density negative ions is probably an effective treatment of seasonal depressed mood • Regular exposure to high-density negative ions and bright light may have equivalent antidepressant efficacy
Music and sound	• Attentive listening to music probably improves moderately depressed mood • Combining music with guided imagery is more beneficial than either approach alone • Listening to binaural sounds in the beta frequency range (16 Hz to 24 Hz) may improve depressed mood • Note: Listening to music or patterned sounds may produce positive or negative emotional effects depending on culture and individual preferences
Biofeedback	• Combined EEG-heart rate variability biofeedback training may be beneficial in some cases of depressed mood
Acupuncture	• Equivalent antidepressant efficacy of a specific electro-acupuncture protocol and amitriptyline • Conventional acupuncture may be effective in some cases of severe depressed mood • Electro-acupuncture alone may be as effective as electro-acupuncture combined with amitriptyline or other conventional antidepressants • Computer-controlled electro-acupuncture using high frequency currents may be more effective than standard acupuncture or electro-acupuncture • Caution: Rare cases of HIV, hepatitis B and C, pneumothorax, and cardiac tamponade have been reported in patients treated with acupuncture
Spirituality and religion	• Spirituality and religious beliefs are associated with reduced risk of depressed mood • Regular support groups with spiritual-religious themes reduce the severity of depressed mood and increase emotional well-being
Healing touch/ therapeutic touch	• Regular healing touch or therapeutic touch treatments may reduce the severity of depressed mood and bereavement

Source: Lake J (2005)

example, aerobic exercise and improved sleep hygiene should be recommended if a patient with moderate depression is reluctant to take supplements or is not interested in trying a mind-body practice. It is important that at the outset the practitioner and patient agree on criteria for assessing beneficial changes and a time frame in which improvement can be reasonably expected.

In managing any complaint, the integrative management of mental health problems always begins with a thorough history, including documentation of the severity and course of symptoms; identification of comorbid psychiatric or medical problems; and a review of biological, psychological and cultural factors associated with the patient's complaint. Different strategies are appropriate when managing moderate versus severe mental and emotional symptoms. When severely symptomatic patients are initially seen by a conventionally trained physician, it is only appropriate to refer them to an alternative medical practitioner after it has been established that patients are not suicidal, homicidal or grossly psychotic, and informed consent has been obtained for referral to a qualified local practitioner of the recommended modality.

Many nonconventional treatment modalities of depressed mood have been validated by consistent positive results from controlled, double-blind studies, and, in some cases, systematic reviews or meta-analyses. As discussed in this article, combining conventional antidepressants with certain nonconventional treatments accelerates the rate of treatment response or improves outcomes overall. Examples of empirically validated nonconventional biological treatments of depressed mood include SJW, SAMe, 5-HTP, folic acid, EPA, and, to a lesser extent, ALC and DHEA. Advantages of augmenting a synthetic antidepressant with one of these natural products include equivalent response rates at reduced antidepressant doses, improved tolerance and compliance, and faster response rates. Patients with depression taking SAMe or EPA should be monitored for signs of hypomania. When combining 5-HTP with an SSRI, the clinician should monitor for signs of a serotonin syndrome. Although fewer studies have been done on ALC than other natural products used to treat depressed mood and no studies have compared ALC with synthetic antidepressants, results to date are promising.

Research on many nonconventional treatments is at an earlier stage. Nonconventional treatments of depressed mood for which there is provisional evidence include EEG biofeedback, specific acupuncture protocols and some mind-body techniques. Preliminary findings suggest that conventional acupuncture and electro-acupuncture are beneficial in some cases of depressed mood, though the mechanism of action underlying putative beneficial effects is unclear.

The following two sections incorporate the basic concepts discussed above into specific integrative treatment approaches for moderate and severe depressed mood.

Integrative Management of Moderate Depressed Mood

A patient complaining of depressed mood should be considered as a candidate for nonconventional or integrative treatment strategies only after underlying medical causes have been excluded by a psychiatrist or primary care physician. Issues of efficacy and safety should be discussed during the initial consultation. In order to ensure good care, all patients for whom nonconventional treatments constitute a reasonable option should be referred to a qualified practitioner after informed consent for the referral is obtained and documented. It is reasonable and ethical to refer a patient with moderate depression to a Chinese medical practitioner (Flaws and Lake, 2001). However a patient with severe depression should not be referred to a Chinese medical practitioner in view of limited research findings that fail to substantiate the benefits of acupuncture for severe depressed mood.

The question of combining many approaches in an integrative treatment plan, versus successive single treatments, should be addressed in the initial consultation. If patients elect to try only one or a few approaches, they should be encouraged to explore therapies for which there is compelling evidence of both efficacy and safety. Other conventional or nonconventional therapies can be tried subsequently if mood symptoms do not improve following an agreed-upon period of time. It is important at the outset that the clinician and patient agree on subjective criteria for monitoring changes in mood, and a time frame in which improvement is reasonably expected in response to the selected integrative treatment plan. Combining self-directed approaches including improved nutrition, lifestyle changes, supplements and mind-body practices may improve moderate depressed mood as effectively as conventional medications, while avoiding issues of adverse medication effects and poor compliance.

If patients with moderate depression elect to start an antidepressant after considering reasonable conventional and nonconventional treatment options, they should be referred to a psychiatrist or primary care physician to review the risks and benefits of different medications. In cases where moderate depressed mood worsens or is unimproved following one month of consistent self-directed lifestyle changes and appropriate mind-body treatments (if any), patients should be encouraged to consider biological treatment choices, including conventional antidepressants and natural products that are known to be effective in depressed mood. If medicinal herbals or other natural products are being considered, patients should be referred to a qualified naturopathic physician or skilled herbalist with an established reputation for treating mental health problems.

To minimize the risk of an unfavorable outcome or noncompliance, it is important to obtain a thorough history of treatment responses and side-effect issues associated with previous conventional and nonconventional biological treatments. This information will help the psychiatrist or primary care physician formulate an effective integrative treatment plan. This integrative strategy may permit a reduction in the dose of the conventional antidepressant with a commensurate reduction in the risk of adverse effects and improved compliance.

Integrative Management of Severe Depressed Mood

In contrast to moderate depressed mood, it is always prudent to include a conventional antidepressant when developing an integrative treatment plan addressing severe depressed mood. Patients should be encouraged to consistently follow self-directed changes in nutrition, exercise and stress management; certain supplements; and possibly also a mind-body practice that is congruent with their beliefs. The initial consultation should always include a thorough medical history and any appropriate laboratory tests (e.g., thyroid studies, electrolytes and complete blood count) to rule out contributing medical problems. A thorough history will generally establish or exclude a history of mood swings, psychotic symptoms or an evolving neurologic disorder. Appropriate referrals to medical specialists should be made if laboratory studies are found to be abnormal. Patients with severe depression should always be asked about suicidal thoughts and plans and referred immediately to the nearest emergency department with appropriate precautions if there is a reasonable risk of suicide.

Many nonconventional treatment modalities of depressed mood have been validated by consistent positive results from controlled double-blind studies.

Assuming that primary medical causes of severe depressed mood have been excluded, weekly follow-up appointments should be scheduled after the patient has started the recommended treatment plan. When underlying medical problems and comorbid psychiatric symptoms have been ruled out, the use of certain nonconventional treatments can reasonably be considered in combination with a conventional antidepressant. If patients request a nonconventional treatment or a referral to a nonconventional medical practitioner, they should be encouraged to consider only approaches that have demonstrated efficacy against severe depressed mood. It is important for the psychiatrist who is managing the patient's care to obtain informed consent before referring to or exchanging information with other conventional or nonconventional practitioners and to clearly document reasons for the referral in the patient's chart. The integrative treatment plan should be reviewed on a continuous basis and modified as needed until an effective and cost-effective strategy is identified and the patient maintains good compliance with treatment recommendations.

In cases where severe depressed mood has failed to respond to the recommended treatment after a period of time when it is reasonable to expect improvement, or when symptoms worsen, it is appropriate to carefully review and clarify both the

(Please see Integrative Management, *page 96)*

CATEGORY 1

Integrative Management

Continued from page 95

medical and psychiatric differential diagnoses. This process may result in referrals to a neurologist or other medical specialists to rule out a confounding or possibly undiagnosed medical disorder that may be interfering with treatment response, including hypothyroidism, other endocrinological disorders, degenerative neurological disorders or cancer. As in the management of moderate depressed mood, it is important to invite the patient with severe depression to participate in all treatment decisions in order to improve the therapist-patient alliance, enhance patient autonomy and increase compliance with recommendations.

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Category 1 Posttest

CME LLC encourages you to take this posttest for your professional enrichment. The correct answers are listed below on the left.

Circle correct choice(s):

1. When compared to conventional antidepressants, SAMe is
   i. only marginally effective and of limited usefulness due to unresolved safety issues.
   ii. a commonly prescribed antidepressant in many European countries.
   iii. more effective but not widely used because it induces mania in a large percentage of depressed patients.
   iv. probably equally effective and associated with few relatively mild side effects.
   a. i, ii and iii
   b. ii and iv
   c. i and iii
   d. iv only

2. Advantages of integrative strategies include:
   a. Augmentation of conventional antidepressants
   b. Accelerated response rates
   c. Lower doses of conventional drugs and reduced incidence of adverse effects
   d. All of the above

3. St. John's wort should be avoided in patients who are taking all but which of the following conventional medications concurrently?
   a. Protease inhibitors
   b. Warfarin
   c. MAOIs
   d. Ibuprofen

4. Which of the following statements about SAMe in the treatment of depression is untrue?
   a. SAMe is effective against depression in doses from 800 mg/day to 1600 mg/day in divided doses.
   b. Some cases of depression that are refractory to conventional antidepressants have reportedly responded to SAMe.
   c. Combining SAMe with most conventional antidepressants is unsafe, may cause a hypertensive crisis and should be strictly avoided.
   d. The antidepressant efficacy of SAMe is augmented when it is taken in combination with folate.

5. All but which of the following statements is true of ALC?
   a. ALC augments conventional antidepressants but is not beneficial against depressed mood when used alone.
   b. To date, no studies have directly compared ALC with conventional antidepressants.
   c. Because of its cognitive enhancing effects, ALC is a reasonable choice in depressed patients with dementia.
   d. Typical doses of ALC for depressed individuals with dementia range from 1 g/day to 3 g/day in divided doses.

6. When recommending exercise to a patient with depression, all but which of the following state ments is correct?
   a. Regular exercise is probably as effective as cognitive therapy, conventional antidepressants and St. John's Wort for individuals with moderate depression.
   b. The antidepressant mechanism of exercise is probably related to decreased levels of dopamine and endorphins.
   c. Antidepressant benefits require longer to take place compared to conventional treatments.
   d. The same duration and intensity of exercise under bright light is probably more effective than exercise alone.

Answers: 1. b; 2. d; 3. d; 4. c; 5. a; 6. b.

Activity Evaluation

The article met the stated objectives.	❒ Agree	❒ Disagree
The author presented the material in a coherent, understandable manner.	❒ Agree	❒ Disagree
I found this article to be fair, balanced and objective.	❒ Agree	❒ Disagree
This material will assist me in applying practical new skills and/or knowledge to enhance patient care.	❒ Agree	❒ Disagree

What was the single most important idea you gained from this article?

_____

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_____

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