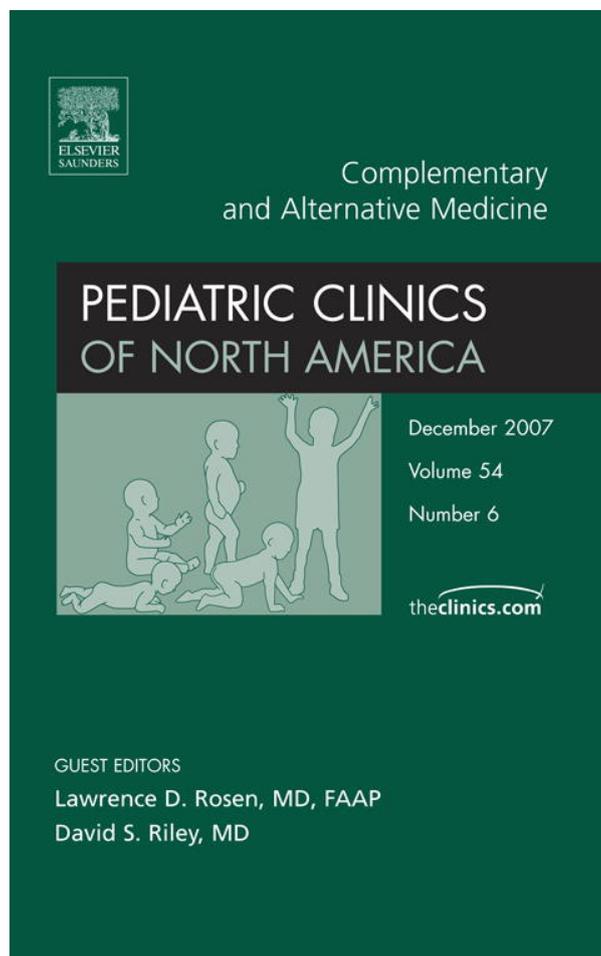


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## Complementary and Alternative Medicine Therapies to Promote Healthy Moods

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Pediatric mood disorders (unipolar depression and bipolar disorder) are serious, common, persistent, and recurrent medical conditions. The US National Institute of Mental Health and the World Health Organization estimate that depression is the leading cause of disability in the United States, and worldwide, it is the second-leading contributor to the global burden of disease for persons 15 to 44 years old [1].

Mood disorders have several nonmodifiable risk factors, including family history, gender, and race. Major depression and suicide are associated with fewer serotonin transporter sites in the prefrontal cortex of the brain. Lower norepinephrine levels are associated with dysphoria and apathy. Central nervous system dopamine levels are also reduced in depression. Before puberty, the prevalence of depression is higher in boys than in girls; after puberty, the rates in girls are about twice those in boys. Native Americans have higher rates of depression, whereas Asians report fewer depressive symptoms than Caucasians.

Mood disorders have a high rate of comorbidity with mental health and medical problems. For example, many children and adolescents suffering from attention-deficit/hyperactivity disorder, anxiety, or substance abuse also suffer from depression, and vice versa. Depressive disorders are also common among patients who have chronic medical conditions, including

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Dr. Kemper is supported in part by the Kohlberg Foundation, by NIH NCCAM K24 AT002207 and NIH NCAM R21 AT001901, and by the Caryl Guth Fund for Holistic and Integrative Medicine. The views expressed in this article are those of the authors and do not necessarily represent the views of the Kohlberg Foundation, the NIH, or Dr. Guth.

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any condition causing chronic pain, obesity, endocrine disorders, inflammatory disorders, cancer, anemia, viral infections, and brain injury. Depression can also be caused by medications, including antihypertensive medications and oral contraceptives. Depression recurs in 70% of those affected. Therefore, even patients who have improved should actively pursue activities to promote positive moods and prevent recurrences.

Mainstream therapies, such as medications, cognitive behavioral therapies, electroconvulsive therapy, and vagal nerve stimulators have been discussed extensively in other reviews [2–5]. Furthermore, given the side effects and stigmatization of standard antidepressant medications, many families turn to complementary therapies. In fact, depression is one of the most common reasons for adolescents and adults to seek complementary therapies [6].

Therefore, the focus of this article is the fundamental lifestyle approaches and complementary therapies that enhance mental health, particularly those that help achieve and maintain healthy moods. The emerging term to describe the use of lifestyle and complementary therapies in combination with traditional, scientific medicine is “integrative medicine.” Integrative medicine is informed by science and is based on four core concepts:

- Patient-centered care (individualized, consistent with patient values and goals)
- Sustainable, healing environment
- Comprehensive approach to therapies
- Health promotion and wellness; promotion of the innate healing potential

### **Health: physical and mental**

Mental health is closely tied to physical health. A successful athlete exhibits strength, flexibility, endurance, coordination, focus, resilience, teamwork, and sport-specific skills. Similarly, a mentally healthy person exhibits confidence, courage, cheerfulness, coping abilities, hardiness, and focused attention. It's not that the fit athlete never stumbles or that he/she always hits a home run, but that, barring a catastrophe, he/she can get up and try again. Similarly, a mentally healthy person occasionally experiences sadness, worry, misery, exhilaration, ecstasy, and the full range of human emotions, recognizing that “into each life, some rain must fall,” but views the rain as a challenge rather than an insurmountable obstacle. Holistic physicians also consider spiritual health as a critical element of overall health. Table 1 shows some of the characteristics of physical, mental, and spiritual health.

Because the mind–body connection is real, promotion of mental health, including healthy moods, relies on very similar strategies to those promoting physical health.

Table 1  
Physical, mental, and spiritual health characteristics

Physical fitness	Mental health	Spiritual health
Strength	Confidence and courage	Faith
Flexibility	Adaptability	Forgiveness
Endurance	Cheerfulness	Hope
Focus	Focus and attention	Love
Coordination	Harmony	Kindness
Resilience	Hardiness	Charity and generosity
Teamwork	Social network, communication skills, and connection to community	Connection with a higher power

Therapeutic options for achieving healthy moods fall into four major categories:

- Lifestyle
- Biochemical
- Biomechanical
- Bioenergetic

**Lifestyle essentials: the fundamentals for healthy moods**

Successful athletic coaches emphasize the fundamental skills of their sport. When it comes to mental and physical health, the fundamentals are excellent nutrition (including avoiding toxic ingestions and inhalations while optimizing the intake of essential nutrients); exercise balanced with restful sleep; a healthy environment (such as plenty of sunshine; mood-boosting music; minimal environmental and psychosocial toxins; and supportive family, friends, and community); and mind–body therapies and techniques (such as meditation and relaxation) [7]. In a German study, intensive lifestyle therapy was as effective as counseling and medication in improving depressive symptoms [8].

*Nutrition*

Healthy nutrition means taking in optimal amounts of essential nutrients while avoiding or minimizing the intake of toxic substances. Individual genetic variability, previous dietary patterns, medical illnesses, medications, allergies, and environmental exposures may increase the need for specific nutrients in the form of supplements.

Evidence-based guidance includes the following suggestions:

- Promote stable blood sugar by encouraging foods with a low glycemic index, such as proteins and complex carbohydrates [9].
- Encourage patients to eat breakfast, including some protein, to promote stable blood sugar throughout the day [10–12].
- Minimize the use of processed foods.

- Emphasize drinking plenty of pure water and eating fresh fruits and vegetables, legumes, whole grains, fish, and, if dairy and meat are eaten, organic, locally raised products whenever possible.
- Avoid sweetened beverages, processed foods, fatty foods, fried foods, and junk food.

Approximately 6% to 10% of children have allergies or sensitivities to foods, including 1% who cannot tolerate gluten [13]. The most common food sensitivities are to wheat, corn, soy, dairy, eggs, tree nuts, shell fish, and peanuts. Food sensitivities can cause mood problems in addition to rashes, asthma, and rhinorrhea [14,15]. Detection of food sensitivities begins with keeping a careful food diary. In some cases, blood testing, skin testing, endoscopic biopsy (for gluten sensitivity), and elimination diets may be useful in diagnosing food sensitivities. Eliminating the triggering food or foods from the diet can improve mood [14,15] and other symptoms such as chronic headaches, rashes, and gastrointestinal upset. Children with multiple food sensitivities may benefit from nutritional counseling to ensure adequate intakes of essential nutrients [16].

One should avoid toxic ingestions. Some people try to manage their moods by smoking, drinking alcohol, or taking other drugs. Although these may improve mood in the short term, over the longer term, they contribute to many miseries. Rarely, people are sensitive to petrochemicals, artificial flavors, artificial colors, and artificial sweeteners; these food additives are not essential nutrients and can easily be avoided by most people. Choosing organic food is a good way to ensure freedom from chemical residues. Pediatricians can advocate for farm, nutrition, and environmental policies that are health promoting.

One should ensure an adequate intake of the nutrients essential to healthy mood. Nutrients are essential for optimal production of neurotransmitters affecting mood, such as serotonin (made from tryptophan, with B vitamins and zinc as cofactors). The easiest way for most bodies to absorb nutrients is through unprocessed, locally grown, organic foods. Table 2 provides a listing of food sources for nutrients essential for mental health.

### *Exercise and rest*

For many people, vigorous physical exercise is as effective as, or more effective than, antidepressant medications in promoting positive moods. Children who are sedentary report higher levels of depression [12,17,18]. Depressed mood and fatigue are common in individuals deprived of the usual exercise activities (whether from an injury or acute illness), and may be partially mediated by reduced fitness levels [19]. Getting kids away from the television, computer, and electronic games in favor of vigorous activity can improve mood. In a meta-analysis of yoga therapy, five randomized controlled trials (RCTs) in adults suffering from depression all reported positive effects of exercise [20]. No adverse effects were reported, with the

Table 2  
Nutrients essential for mental health and their food sources

Nutrient	Food sources
Essential fatty acids (omega-3 fatty acids such as linolenic acid)	Fish (tuna, salmon, and mackerel) fish oil, flax seeds, flax oil, canola oil, walnut oil, dark green leafy vegetables
Vitamin B <sub>6</sub>	Beans, nuts, legumes Eggs, meats, fish Whole grains and fortified breads and cereals
Vitamin C	(All fruits and vegetables contain some amount of vitamin C.) Green and red peppers, citrus fruits and juices, strawberries, tomatoes, broccoli, turnip greens and other leafy greens, sweet and white potatoes, cantaloupe, papaya, mango, watermelon, Brussels sprouts, cauliflower, cabbage, winter squash, raspberries, blueberries, cranberries, and pineapples
Folate	Beans and legumes Citrus fruits and juices Wheat bran and other whole grains Dark green leafy vegetables Poultry, pork, shellfish Liver
Calcium	Milk, yogurt, buttermilk, cheese Calcium-fortified orange juice Green leafy vegetables (broccoli, collards, kale, mustard greens, turnip greens, and bok choy or Chinese cabbage) Canned salmon and sardines canned with their soft bones Shellfish Almonds, Brazil nuts Dried beans
Vitamin D	Fish, fish oils, oysters Fortified foods such as cow milk, soy milk, and rice milk, and some cereals
Tryptophan	Turkey, chicken, fish Milk, cheese Eggs Soy, tofu Sesame seeds Pumpkin seeds
Zinc	Tree nuts, peanuts, peanut butter Beef, pork, lamb, oysters, dark meat of poultry Peanuts, peanut butter, nuts, and legumes (beans) Fortified cereals

exception of fatigue and breathlessness in participants in one study. The side effects of exercise include over-use injuries, decreased obesity, lower risk of heart disease, improved sleep, less chronic fatigue, improved academic performance, and decreased pain. Clinicians should advise patients suffering from depression to maintain a healthy lifestyle by exercising regularly.

Sleep deprivation can lead to poor mood, and insomnia is a common symptom of depression [21]. Many teenagers do not get sufficient sleep. Improving sleep hygiene (using the bed only for sleep, removing the television from the

bedroom, ensuring that the bedroom is dark and cool, taking a hot bath before bed, listening to relaxing music, reading positive or inspiring books, receiving a brief massage from a trusted family member, and writing in a journal before bed) can help improve mood and set the tone for a restful sleep.

### *Environment*

A healthy environment is of critical importance in promoting, maintaining, and restoring healthy mood. An environment that includes poverty, abuse, neglect, or absence of opportunities for work or school can have severe adverse effects on mood that cannot be corrected through medications alone. The key elements that affect mood in the physical environment (eg, light, nature), the psychologic environment (eg, television), the social and cultural environment (racism, sexism, poverty, and social isolation) are touched on here.

Songs, poems, stories, and folk wisdom support the association between sunshine and happiness, and lack of sunshine and sadness (the blues). Bright light suppresses daytime melatonin production and shifts circadian rhythms. Desynchronization of internal rhythms plays an important role in the pathophysiology of depressive disorders. Serotonin levels are lowest during the winter months. Seasonal affective disorder has been well described. Given the modern lifestyles of living indoors and traveling in enclosed vehicles, modern children and adolescents receive far less sunshine than our ancestors. Psychiatrists have noted that depressed patients hospitalized in sunny rooms have shorter lengths of stay than patients in less sunny rooms [22].

Sunlight is an essential component of our natural environment. Daylighting, the practice of enhancing direct daylight exposure for children in classrooms, enhances school performance, reduces illness, and improves attendance [23]. Bright light therapy plays an effective role in the treatment of mood disorders. In an RCT published in 2006, bright light was as effective as fluoxetine in improving symptoms of seasonal affective disorder (67% response rate for both) [24]. Phototherapy has also been as effective as antidepressant medication in treating depression during pregnancy [25]. A 2005 meta-analysis of RCTs of light therapy concluded that bright light treatment for nonseasonal depression is efficacious, with effect sizes equivalent to those in most antidepressant pharmacotherapy trials [26]. Light therapy can also enhance the effectiveness of other treatments [27].

Bright light early in the morning seems to be the most effective. In most trials of light therapy, the patient sits in front of a light box, exposed to 10,000 lux for 30 to 120 minutes daily. Trials comparing the effects of light boxes with outdoor activity (eg, 15–60 minutes of sunlight daily) and tanning booths are needed.

### *Nature*

Recently, a new field of inquiry has emerged that explores the therapeutic effects of nature and the natural environment. Investigators have called this

field biophilia, which emphasizes the connection to our natural environment [28]. This field of study includes both natural settings alone and those combined with contact with animals. One recent study from the *British Medical Journal* [29] explored the value of swimming with dolphins, a variation of animal-assisted therapy, controlled for the beneficial effect of the natural setting. A significant positive effect with this approach was found for 30 adult patients who had mild to moderate depression after 2 weeks of treatment in this single-blind RCT.

### *Minimizing environmental toxins*

Heavy metals (eg, lead and mercury) [30] and carbon monoxide poisoning are also associated with depressive symptoms [31,32]. Checking for toxins and eliminating them may help improve mood. The benefit is well documented with lead and carbon monoxide, but the value for other heavy metals remains a frontier of knowledge at this point.

One of the easiest ways to become depressed is to compare oneself with someone who is more attractive and intelligent, or in possession of more friends, toys, desirable food, or clothing, or has better transportation or housing. Exposure to television and other sources of marketing increases the likelihood that children and adolescents will make these comparisons. Furthermore, the “If it bleeds, it leads” philosophy in the media has resulted in a preponderance of negative, disheartening news on television. Removing televisions from children’s rooms and sharply reducing the time the television is on may contribute to improved mood. The elimination of marketing to children (already in place in several European countries), as a result of advocacy, could also contribute to enhanced mental health. At home, children and families can practice “appreciation audits,” listing the elements in their lives for which they are grateful or keeping a daily journal of appreciation and kindness items (ie, ways the writer has been kind to others). (For more information on the appreciation audit, see Dan Baker’s book, listed in [Appendix 1](#)).

Poverty and lack of opportunity adversely affect mood [33,34]. Racism, sexism, homophobia, and other social injustices also contribute to suffering and decreased access to care [35–39]. Problems within the family and local community, such as child abuse and neglect and child sexual abuse have significant long-term adverse effects on mood [40–42]. Physician advocacy for social justice, equal access to care, and family support services can have a profound impact on children’s moods.

### *Mind–body therapies*

#### *Meditation*

Meditation practice, particularly mindfulness meditation (moment-to-moment nonjudgmental awareness of breathing, physical sensations, emotions, and thoughts), can contribute to enhanced mood, and can change brain activation patterns in ways likely to support ongoing benefits.

Specifically, meditation training leads to significant increases in left-sided anterior activation, a pattern associated with positive affect [43]. Long-term meditators, compared with age-matched controls, exhibit increased cortical thickness in brain regions associated with attention and sensory processing, including the prefrontal cortex [44]. Side effects of meditation may include improved ability to cope with stress, reduced pain, reduced anxiety, and enhanced immune function.

#### *Dialectic behavior therapy*

Dialectic behavior therapy is a psychosocial therapy based in cognitive behavioral therapy and mindfulness. Originally designed for chronically suicidal patients with borderline personality disorder, dialectic behavior therapy helps people build awareness about their emotional states and about how to gain control over behavior. This technique works well for emotionally labile teens with mood issues and for chronically suicidal teens [45,46]. Recently, one preliminary study [47] found benefits in children with oppositional defiant disorder (who commonly have comorbid mood disorders). A 1-year open trial with bipolar youth also found promising beneficial effects [48].

#### *Eye movement desensitization and reprocessing*

Eye movement desensitization and reprocessing (EMDR) significantly improved depression in adult patients of childhood sexual abuse in an RCT of 880 patients [49]. In this study, EMDR was most effective for more recent trauma and significantly outperformed fluoxetine on various measures. Many clinicians who treat children are finding EMDR a safe, effective, and often faster treatment approach for angry, violent, or depressed youth who have suffered abuse.

#### *Other*

Various evidenced-based approaches that calm the mind may play a role in the care of children with mood disorders. Tai chi and mindfulness techniques have been applied successfully in a Boston public middle school [50] and resulted in the improvement of various measures, including general well-being. Gordon and colleagues [51] applied various mind-body techniques to improve symptoms in a group of war-weary Kosovo students. Music therapy improved mood and depressive scales in a group of grieving children [52]. In an RCT of 69 adult patients hospitalized for stem cell transplantation, music therapy significantly improved mood and anxiety [53]. In a study of 22 children with recurrent abdominal pain (commonly comorbid with depression), guided imagery was a more effective treatment than breathing exercises alone [54]. Reynolds and Coats [55] demonstrated in an RCT that relaxation therapy was as effective as cognitive behavior therapy (a well-researched, evidence-based treatment) for a group of 30 depressed adolescents. Relaxation therapy was also found to be more effective than antidepressant therapy for major depression in one adult trial [56].

### *Social support and spirituality*

Children who attend church regularly have about a 20% lower risk of developing depression than nonattendees. Church may be protective because of inherent spiritual factors and because it provides a sense of social support and cohesiveness and opportunities for connecting with a trusted adult in whom to confide. Numerous studies document benefit from various spiritual paths. The positive factors seem to be faith and community, rather than a specific belief system. Primary care clinicians can also provide important psychosocial support that improves outcomes in depressed adolescents [57].

### **Biochemical therapies**

Because of our individual uniqueness (genomic variability), diet, and environment, some individuals require additional nutrients or benefit from specific biochemical therapies to achieve healthy moods. For example, simple nucleotide polymorphisms represent a significant factor in biochemical individuality. The enzyme delta-5-desaturase converts omega-3 fatty acids such as alpha linolenic acid into eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). If a simple nucleotide polymorphism impairs delta-5-desaturase, a child may require significantly higher levels of alpha linolenic acid, EPA, or DHA in his/her diet to maintain normal cell membrane function and healthy mood.

For this article, the authors focus on vitamins and minerals, herbs, and other dietary supplements. Given the fact that fewer than 1% of American children meet their recommended daily allowance of essential nutrients through diet alone [58], it is likely that many children would benefit from supplementation, in addition to striving to improve their overall diet. Supplementation is especially important for children who eat a restricted diet because of suspected food allergies or sensitivities. Also, any child who restricts calories, whether because he/she performs in such sports as wrestling, gymnastics, and so forth, or because he/she has self-image problems (ie, anorexia), will have enhanced needs. (Stress and conflict also significantly escalate nutrient demands).

### *Essential nutrients (vitamins, minerals, fatty acids, amino acids)*

Here, the authors do not cover all essential nutrients, but focus on a few that are vitally important and often lacking in Americans, some of whom might benefit from nutrient supplementation.

### *Multivitamin–mineral preparations*

Several investigators have concluded that multivitamin–mineral combinations can help improve mood and behavior. In a large British trial in 231 young offenders, violent acts and rule infractions were significantly reduced among those given micronutrient supplementation [59]. Several case

studies and case series support the effectiveness of a proprietary multivitamin–mineral (EMPower) on young people with mood disorders (including depression and bipolar disorders) [60–62]. This product has numerous testimonials, but requires up to 15 capsules daily for a loading dose; it contains significant amounts of calcium, magnesium, and B vitamins. It has not been compared with supplementation with generic versions of these nutrients.

### *Individual vitamins*

#### *B vitamins, including folate*

Vitamin B<sub>6</sub> is essential in metabolizing tryptophan to serotonin. Folate and vitamin B<sub>12</sub> are major determinants of one-carbon metabolism, in which S-adenosylmethionine (SAME, pronounced Sam-ee) is formed. SAME donates methyl groups that are crucial for neurologic function. See later discussion on SAME.

Low levels of pyridoxal phosphate are significantly associated with depressive symptoms [63]. A systematic review suggested that 100 to 200 mg daily supplementation with vitamin B<sub>6</sub> significantly benefits premenstrual depression [64]. The side effects of excessive doses of vitamin B<sub>6</sub> include nausea, vomiting, abdominal pain, anorexia, headache, somnolence, lower B<sub>12</sub> levels, and sensory neuropathy. The last typically occurs with doses of more than 1000 mg daily, but can occur lower with lower doses.

Folate is a water-soluble vitamin that donates a methyl group in the one-carbon cycle needed for the production of SAME and the remethylation of homocysteine. Folate deficiency is common and contributes to various psychiatric symptoms, including depression, psychosis, irritability, dementia, and impaired memory.

Considerable research evidence supports the value of folate in maintaining a healthy mood. Folate and B<sub>12</sub> levels are lower in depressed than in nondepressed persons, and replacing deficient folate can lead to remarkable improvements in mood [65–67]. Low folate levels predict treatment resistance to fluoxetine [68]. In one study, folate supplementation was as effective as 150 mg of amitriptyline in treating depressed outpatients [69]. Adding 500 µg of folate to 20 mg of fluoxetine significantly improved the response rate in patients who had major depression [70]. One review concluded that folate supplementation is beneficial in treating depression, whether used as monotherapy or as an augmentation of conventional medications [71]. Primary care clinicians should ensure that children prone to mood disorders have an adequate intake of folate and should consider recommending a multivitamin or a B-vitamin complex containing folate. Given the safety of water-soluble vitamins, a dose of 1 mg per day in symptomatic children is reasonable. It should be given with B<sub>12</sub> to avoid masking a B<sub>12</sub> deficiency.

#### *Vitamin D*

A growing body of research suggests that American youth are vitamin D–deficient, even in older pediatric and adolescent populations that do

not appear to have classic rickets [72–74]. This deficiency may be a particular problem in children taking anticonvulsant medications [75]; those with inflammatory bowel disease [76,77] or arthritis [78,79]; those with chronic renal disease [80]; those living in the inner city [81]; African-Americans [82]; or those who are veiled. Many adolescents have relatively low levels of vitamin D because of an indoor lifestyle and inadequate intake of vitamin D–fortified foods [83]. A recent study found that obese children have significantly depressed vitamin D levels [84], perhaps from inadequate outdoor time. Skin cancer concerns, inactivity, obesity, excessive screen time (eg, too much time watching television, playing electronic games, or working on a computer), and other issues may contribute to sun avoidance and vitamin D deficiency.

Low levels of vitamin D are associated with depressive symptoms, and treatment with vitamin D supplements is associated with improved mood. For example, 25-hydroxyvitamin D<sub>3</sub> and 1,25-dihydroxyvitamin D<sub>3</sub> levels are significantly lower in psychiatric patients than in normal controls [85]. Vitamin D deficiency is associated with anxiety and depression in patients who have fibromyalgia [86]. In an RCT of vitamin D given to 44 Australian patients (none versus 400 IU versus 800 IU vitamin D), vitamin D<sub>3</sub> significantly enhanced mood in a dose-dependent fashion [87].

The recommended daily allowance for vitamin D was set to prevent rickets in young children and may be insufficient to prevent certain health problems in older adults. It may be worthwhile for adolescents to take vitamin D supplements, particularly during winter months, to ensure adequate vitamin D levels and prevent subclinical hypoparathyroidism; supplementation is also worthwhile for patients who have renal disease, inflammatory bowel disease, or juvenile arthritis, and those patients on anticonvulsant drugs that lower vitamin D levels.

### *Minerals*

This section includes brief discussions on the role of calcium, magnesium, chromium, zinc, and iron in promoting and maintaining a healthy mood.

### *Calcium*

Lower levels of calcium and higher levels of parathyroid hormone have been observed in depressed persons. Likewise, depression is commonly noted among patients suffering from hyperparathyroidism [88]. Quality of life and depressive symptoms improve when these patients receive appropriate treatment [89]. Estrogen regulates calcium and parathyroid hormone metabolism [90]; sometimes dysregulation occurs, which is particularly notable in women suffering from premenstrual symptoms. Epidemiologically, normal to high intakes of calcium and vitamin D are associated with a lower risk of depressive mood in patients who have premenstrual syndrome; conversely, lower intakes of calcium and vitamin D are associated with an increased risk of premenstrual syndrome [91]. Small studies suggest that

calcium supplementation may benefit women with premenstrual syndrome-related depression [92,93].

Most adolescent girls do not meet their minimum daily requirement for calcium through diet alone. According to the Continuing Survey of Food Intakes of Individuals (1994-96), the following percentages of Americans do not meet their recommended intake for calcium:

- 44% of boys and 58% of girls aged 6 to 11
- 64% of boys and 87% of girls aged 12 to 19

It is important for clinicians counseling adolescents about mood to address adequate calcium intake (optimally 1200–1500 mg daily) to ensure bone health and promote a healthy mood.

### *Magnesium*

Magnesium is second only to potassium in intracellular concentration. It facilitates the conversion of 5-hydroxytryptophan (5-HTP) into serotonin. Signs of magnesium deficiency include irritability, fatigue, loss of appetite, mental confusion, insomnia, and a predisposition to stress. Historically, magnesium has been used, like lithium, as a treatment for mania or severe agitation [94]. It is not used widely or recommended as a treatment for depression.

Magnesium, like lithium, suppresses hippocampal kindling, regulates N-methyl-D-aspartate receptors, and alters glutamate activity [95,96]. It has been a successful treatment for premenstrual mood changes [97]. Magnesium and verapamil were much more effective than verapamil alone in treating acute mania [98].

Magnesium deficiency is extremely common [99]. Research is currently underway on the value of magnesium supplementation in pediatric bipolar disorder. Ensuring an adequate intake of magnesium is important in maintaining a balanced mood.

### *Chromium*

Chromium, a dietary trace mineral, has a crucial role in glucose and fat metabolism and neurotransmitter synthesis. Chromium improves insulin sensitivity and increases free brain levels of serotonin, norepinephrine, and melatonin. In an RCT of bipolar II patients and patients who had atypical depression, chromium had a significant benefit [100]. Five patients responded to chromium supplementation after failing conventional depression treatment [101]. An RCT of chromium picolinate (600 µg daily) in patients whose depression was characterized by carbohydrate craving showed significant improvement in craving and depressive symptoms [102].

Chromium is well tolerated but can have a stimulating effect. The recommended daily allowance for chromium is 120 µg. The daily dietary intake of chromium for a typical American adult is only 25 to 50 µg per day. The dose range in studies of its effects on mood is typically 200 to 600 µg per day.

Dietary sources rich in chromium include breads, cereals, spices, fresh vegetables, meats, fish, and brewer's yeast.

### *Zinc*

Zinc is an essential mineral that is found in almost every cell. It stimulates the activity of approximately 100 enzymes. Low serum zinc levels have been linked to major depression. Zinc, an antagonist of the glutamate/N-methyl-D-aspartate receptor, exhibits antidepressant-like activity in rodent models of depression. Like antidepressants, zinc induces brain-derived neurotrophic factor gene expression and increases the level of the synaptic pool of zinc in the hippocampus [103]. Furthermore, zinc treatment has been shown to have an antidepressant effect [104].

The American recommended dietary allowance for zinc ranges from 5 mg daily for younger children to 11 mg daily for teenagers. Vegetarians may need as much as 50% more zinc than nonvegetarians because of the lower absorption of zinc from plant foods, so it is important for vegetarians to include good sources of zinc in their diet. Breastfeeding depletes zinc, and some experts suggest that because breast milk contains relatively low levels of zinc, breastfed infants should receive zinc supplementation after 7 months of age.

Low zinc status has been observed in 30% to 50% of alcoholics. Alcohol decreases the absorption of zinc and increases the loss of zinc in urine. In addition, many alcoholics do not eat an acceptable variety or amount of food, so their dietary intake of zinc may be inadequate. If an adolescent has a drinking problem in addition to a mood problem, it is especially important to ensure adequate mineral supplementation.

Zinc toxicity occurs with intakes of 150 to 450 mg of zinc per day and appears as low copper status, altered iron function, reduced immune function, and reduced levels of high-density lipoproteins.

### *Iron*

Iron deficiency anemia is often accompanied by depression. Long-term iron deficiency in infancy and early childhood is associated with mood and learning problems, even years after the deficiency is corrected [105]. It is important to ensure that adolescents be checked for iron sufficiency, particularly female adolescents who may not be meeting their needs for iron to replace menstrual losses [106]. Primary care clinicians should ensure that their patients consume adequate amounts of iron through either diet or supplementation.

### *Fatty acids*

#### *Linolenic, eicosapentaenoic, and docosahexaenoic acids*

The human brain is 60% fat, and the essential fatty acids contribute a substantial portion of that weight. Essential fatty acids are crucial to normal fetal and neonatal maturation of the brain. Three common essential fatty acids (EPA, DHA, and arachidonic acid), are crucial building blocks

of neuronal membranes. Fatty acids also form the precursors of prostaglandins and leukotrienes. Fatty fish such as salmon, mackerel, and herring are excellent sources of EPA and DHA.

Fish consumption and levels of omega-3 fatty acids have a strong epidemiologic correlation with protection from depression and suicide [107–111]. Furthermore, clinical trials suggest that supplemental essential fatty acids (EPA and DHA) can improve mood and decrease hostility and violence, even in patients hospitalized for severe depression or suicidality [112–115]. The doses in these studies range from 1 g per day to 10 g per day.

The benefit of omega-3 supplementation for bipolar disorder is less clear [116]. Stoll and colleagues' [117] double-blind study augmenting treated bipolar patients with fish oil (9.6 g per day) or placebo found significant reductions in relapse and all other outcome measures with fish oil. However, another trial with 120 bipolar patients found no significant treatment effect [118]. A 2007 study of pediatric bipolar disorder [119] found a modest, but statistically significant, improvement in an open-label trial of 20 children, 6 to 17 years of age. The intervention was 1290 to 4300 mg of an EPA–DHA combination.

In children, the developmental requirements and absence of serious toxicity suggest that daily supplementation with 1 to 3 g of fish oil (EPA–DHA) can support healthy mood. Product testing has revealed no significant contamination with mercury, dioxins, or other contaminants in molecularly distilled fish oil products. More potent and palatable forms of molecularly distilled fish oils make these dietary recommendations easier to swallow. Small children can take one of the liquid forms often easily hidden in food. Recently, a prescription brand of fish oil entered the scene, further increasing treatment options.

### *Amino acids*

#### *L-tryptophan*

5-HTP is the immediate precursor of serotonin in its metabolism from dietary L-tryptophan (L-trp). Unlike tryptophan, which faces competitive inhibition in its absorption, 5-HTP does not, and it appears to be a better choice for increasing central nervous system levels of serotonin.

Tryptophan depletion leads to depressive symptoms in rats and humans. Various smaller (open and controlled) studies [120–125] have found 5-HTP useful in depression. A Cochrane meta-analysis of trials involving 64 patients suggested 5-HTP and L-trp are better than placebo in treating depression [126]. The doses given in most trials start at 50 mg three times a day. The typical dosing is 50 mg, slowly increasing to 150 mg, two or three times daily on an empty stomach, based on size. A large single dose of 200 to 400 mg can be used by slowly increasing the dose. The maximum recommended dose is 1200 mg daily.

Side effects of 5-HTP and L-trp include nausea and drowsiness (which may make it useful at bedtime); they may cause serotonergic syndrome if

used in combination with selective serotonin reuptake inhibitor (SSRI) medications; they may also be associated with decreased carbohydrate intake and weight loss [127]. Eosinophilia-myalgia syndrome was reported in numerous people taking L-tryptophan, which led to its removal from the American market; however, investigations revealed that the problem was related to a contaminated lot from one manufacturer, and L-tryptophan is again available. During the time it was off the market, many people turned to 5-HTP supplements instead to ensure safety. Experts now recommend using products that are tested and free of a “Peak X” contaminant.

### *S-Adenosylmethionine*

SAMe is a methyl donor in more than 35 reactions in the brain and body. It plays a crucial role in the production of monoamine neurotransmitters, nucleotides, and neuronal membrane phospholipids. SAMe has been found to be the most potent chemical trigger for the induction of mania in bipolar patients, a reflection of its antidepressant potency.

More than 25 controlled trials have evaluated the effectiveness of SAMe for patients with mood disorders. A 2002 review by the Agency for Health care Quality and Research (AHRQ) concluded that, compared with placebo, 3 weeks of treatment with SAMe was associated with a significant improvement in depression [128]. Several studies published since the AHRQ 2002 report confirm its effectiveness in improving mood, and suggest it has a potency similar to tricyclic antidepressants [129–132]. It may also be helpful in patients for whom antidepressant medications have been ineffective [133]. Furthermore, it can also be a useful adjunctive treatment, along with conventional antidepressant medications [133].

Typical doses are 800 to 1600 mg of SAMe daily. Benefits typically appear within 2 weeks of starting the medication. Although product variability is a major problem in many dietary supplements, a review of SAMe products by ConsumerLabs revealed that only 1 out of 11 tested products failed their rigorous standards.

SAMe has fewer side effects than conventional antidepressant medications and works more quickly. Side effects include triggering mania and increasing the risk of serotonergic syndrome in patients taking SSRI medications. It should not be used by patients who have bipolar disorder. Furthermore, it is expensive (50 cents to \$1 per 200 mg tablet) and is not usually covered by insurance.

### *Herbs for mood*

#### *St. John's wort*

The herb most commonly used as a complementary or alternative remedy for depression is St. John's wort. Studies on its effectiveness have had mixed results, with most of the positive studies coming from European trials using standard extracts [134]. See Table 3 for a listing of the compounds used in the studies with positive results and the American imports containing these

Table 3  
St. John's wort products used in studies reporting positive effects

Products with positive results in clinical studies	Brand name (manufacturer)
LI 160 and LI 160S	Quanterra Emotional Balance (Warner-Lambert); Kira (Lichtwer Pharma US/Germany)
WS 5570 and WS 5572	Neuroplant (Schwabe Pharmaceuticals) Perika (Schwabe Pharmaceuticals, imported by Nature's Way Products, Inc)
Ze 117	Remotiv (Bayer Vital GmbH and Zeller AG)

*Courtesy of Paula Gardiner, MD, Boston, MA.*

compounds. For example, in a German RCT, St. John's wort was as effective as sertraline in improving depressive symptoms [135]. A similar German study showed its comparability to citalopram [136]. Two open-label trials in adolescents showed improvement within 2 weeks in 25 out of 33, and 9 out of 11 patients in separate studies [137,138]; patients who improved in these studies generally showed improvement within 2 weeks of starting therapy. It is reasonable to stop treatment or change to a higher dose or a different product if no benefit has been noted within 3 weeks.

St. John's wort is generally safer than most antidepressant medications. A meta-analysis of 16 post-marketing surveillance studies including 34,804 patients recorded an incidence of adverse events between 0% and 6%; of the four large-scale surveillance studies with a total of 14,245 patients, the rate of adverse events ranged from 0.1% to 2.4% and a drop-out rate due to adverse events of 0.1% to 0.9% [139]. This finding is at least ten-fold lower than that recorded with synthetic antidepressants. The adverse events associated with St. John's wort were mild and transient in nearly all cases.

St. John's wort can, however, have direct adverse effects and serious interactions with commonly used medications. The most common direct effects are phototoxicity and stomach upset. The most serious adverse effects are drug interactions in which St. John's wort reduces the serum levels of other medications including contraceptives, digoxin, immunosuppressants, theophylline, clarithromycin, erythromycin, cyclosporine, tacrolimus, protease inhibitors, and certain chemotherapeutic agents. It should not be used in conjunction with SSRIs because such use may increase the risk of serotonergic syndrome.

St. John's wort preparations have substantial variability in quality. Patients who wish to use it may use a product tested in a large RCT or refer to product testing conducted by ConsumerLabs (see [Appendix 1](#)).

### *Other dietary supplements*

#### *Inositol*

Inositol, an isomer of glucose, works as an intracellular messenger that relays the neurotransmitter message to the cell nucleus. One review found

that inositol was useful in panic disorder, obsessive-compulsive disorder, and depression [140]. In a large comparative study of treatments for bipolar depression, the recovery rate was 23.8% for lamotrigine, 4.6% for risperdone, and 17.4% for inositol [141]. It has been suggested that inositol can trigger mania episodes in patients who have bipolar disorder [142]. Inositol can be mildly sedating and has also been used as a sleep aid. Inositol had far fewer side effects in all comparison studies. As a sweet-tasting powder that can be mixed into any liquid, inositol offers a well-tolerated intervention for children with mood disorders. The typical starting dose is 1 to 2 g two or three times daily, increasing up to 12 to 18 g per day in divided doses.

### **Biomechanical therapies: massage**

Massage is used widely to improve mood. In fact, therapeutic massage struggles to overcome an historical connection with the “entertainment” industry. Despite its marketing problems, massage has many medical uses. Therapeutic massage contributes to increased blood flow and lymphatic drainage; muscle relaxation; stress reduction; and social support. Physiologically, massage balances right and left prefrontal cortex activity in those with right dominance [143]. The left prefrontal cortex has been associated with positive mood, whereas dominance of the right prefrontal cortex is associated with depressed mood [144]. Furthermore, massage decreases cortisol levels and increases levels of serotonin and dopamine in patients who have depression [145]. In depressed women, massage, compared with progressive relaxation, led to higher dopamine and serotonin levels and lower levels of cortisol and norepinephrine [146]. Massage significantly reduced aggression in 17 adolescent psychiatric inpatients [147]. A simple 30-minute back rub daily reduced anxiety and improved cooperation in 52 pediatric psychiatric inpatients [148].

Considerable research has been published on the pervasive and persistent negative effects of maternal depression on childhood mental health [149]. The infants of depressed mothers who received massage scored higher on various measures in the Brazelton scale than mothers who only received light touch [150], thus reducing the ensuing emotional risk to the unborn child.

In the studies showing positive effects, massage has generally been provided 5 days a week. To achieve this frequency cost effectively, parents are generally trained to provide massage for children and adolescents. Massage is generally safe if care is taken to avoid wounds, burns, intravenous lines, pumps or other subcutaneous devices, and vigorous strokes in patients who have low platelet counts. Careful discussion and respect for individual patients is important for patients who have a history of physical or sexual abuse.

### **Bioenergetic therapies: acupuncture**

Acupuncture involves the stimulation (using pressure, heat, needles, and magnets) of specific points on the body, with the intention of promoting

healing. RCTs suggest that acupuncture has significant benefits for depressed adults and may be comparable in effectiveness to prescription antidepressant medications [151]. For example, in an RCT of true acupuncture, sham acupuncture, and massage provided to 61 pregnant women with major depressive disorder, response rates were statistically significantly higher for acupuncture (69%) than for massage (32%), with an intermediate sham acupuncture response rate (47%) [152]. In a meta-analysis published in 2005, the investigators concluded that “the effect of electroacupuncture may not be significantly different from antidepressant medication,” with a weighted mean difference in comparison trials of  $-0.43$  (95% CI  $-5.61$  to  $4.76$ ) [153].

Acupuncture rarely causes bleeding, bruising, or infection; it causes sleepiness in about 5% of patients. In general, it has fewer side effects than medications. Serious side effects are rare. Pediatric patients will accept it, but it's not usually their first choice of therapies. Those who receive it generally report that it is helpful and, unlike their expectations, pleasant [154].

## Resources

Research in this area is growing constantly. It is helpful to have a list of resources to address common questions and concerns and to keep abreast of emerging knowledge about the safety and effectiveness of therapies and approaches to promote healthy moods. See [Appendix 1](#).

## Summary

Depression is the second-leading cause of illness and disability among young people worldwide. A healthy lifestyle and healthy environment are the cornerstones for promoting positive moods. In addition, several complementary therapies, including nutritional supplements, herbs, mind–body therapies, massage, and acupuncture can be helpful. Various resources are available to clinicians to help patients and families promote mental health.

## Appendix 1. Resources on integrative approaches to pediatric mood disorders

### *Internet resources*

American Academy of Pediatrics Provisional Section for Complementary, Holistic and Integrative Medicine (<http://www.aap.org/sections/chim/>)

American Academy of Pediatrics, Committee on Environmental Health (<http://www.aap.org/visit/cmte16.htm>)

National Institutes of Health, Institute on Mental Health (information on depression in children and adolescents) (<http://www.nimh.nih.gov/healthinformation/depchildmenu.cfm>)

National Library of Medicine, Medline Plus (information on many medications, nutrients, and dietary supplements) (<http://www.nlm.nih.gov/medlineplus/>)

Natural Medicines Comprehensive Database (<http://www.naturaldatabase.com/>)

Natural Standard (<http://www.naturalstandard.com/>)

World Health Organization (information on depression) ([http://www.who.int/mental\\_health/management/depression/definition/en/](http://www.who.int/mental_health/management/depression/definition/en/))

ConsumerLabs (comparison of dietary supplement brands) ([www.consumerlabs.com](http://www.consumerlabs.com))

### *Books*

Baker D. What happy people know: how the new science of happiness can change your life for the better. New York: St. Martin's Press; 2003.

Baumel S. Dealing with depression naturally. Los Angeles (CA): Keats Publishing; 2000.

Emmons H. The chemistry of joy. New York: A Fireside Book (Simon and Schuster); 2006.

Hallowell EM. The childhood roots of adult happiness: five steps to help kids create and sustain lifelong joy. New York: Ballantine Books; 2002.

Lake J. Textbook of integrative mental health. New York: Thieme Medical Publishers; 2007.

Lake JH; Spiegel D. Complementary and alternative treatments in mental health care. Washington, DC: American Psychiatric Publishing; 2007.

Larson JM. Depression-free naturally. New York: Ballantine Books (Random House); 1999.

Shannon S, ed. Handbook of complementary and alternative therapies in mental health. San Diego (CA): Academic Press (Elsevier); 2001.

Shannon S. Please don't label my child. New York: Rodale Press; 2007.

Werbach MR. Nutritional influences on mental illness: a sourcebook of clinical research. Tarzana (CA): Third Line Press, Inc; 1999.

Williams M, Teasdale J, Segal Z, et al. The mindful way through depression: freeing yourself from chronic unhappiness. New York: Guilford Press; 2007.

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