Published in final edited form as:
Pediatr Clin North Am. 2007 December ; 54(6): 901–x.

CAM Therapies to Promote Healthy Moods

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Keywords

Mental health; pediatric; complementary; St. Johns wort; light; exercise; depression

Introduction

Pediatric mood disorders (unipolar depression and bipolar disorder) are serious, common, persistent and recurrent medical conditions. The US National Institute of Mental Health (NIMH) and World Health Organization (WHO) estimate that in the U.S. depression is the leading cause of disability and worldwide it is the 2nd leading contributor to the global burden of disease for persons 15–44 years old.[1]

Mood disorders have several non-modifiable 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. CNS dopamine levels are also reduced in depression. Prior to puberty, the prevalence of depression is higher in boys than girls; after puberty, the rates in girls are about twice those in boys. Native Americans have higher rates of depression, while Asians report fewer depressive symptoms than Caucasians.

Mood disorders have a high rate of co-morbidity with both mental health and medical problems. For example, many children and adolescents suffering from ADHD, anxiety or substance abuse also suffer from depression and vice versa. Depressive disorders are also common among patients with chronic medical conditions including 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 adolescents and adults seek complementary therapies [6].

Therefore, the focus of this review 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 she always hits a home run, but that barring a catastrophe, 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.

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/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 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 at breakfast 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 6–10% 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 as well as 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(s) from the diet can improve mood[14;15] as well as other symptoms such as chronic headaches, rashes, and GI upset. Children with multiple food sensitivities may benefit from nutritional counseling to ensure adequate intakes of essential nutrients[16].

Avoid toxic ingestions. Some people try to manage their moods by smoking, drinking alcohol or taking other drugs. While 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 might well 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.

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/Rest

For many people, vigorous physical exercise is 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 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 TV, computer, and electronic games in favor of vigorous activity can improve mood. In a meta-analysis of yoga therapy, five randomized controlled trials in adults suffering from depression, all reported positive effects of exercise [20]. No adverse effects were reported with the exception of fatigue and breathlessness in participants in one study. 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 TV 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. Key elements that affect mood in the physical environment (e.g., light, nature), the psychological environment (e.g., TV), the social and cultural environment (racism, sexism, poverty, and social isolation) are touched on here.

Songs, poems and stories as well as folk wisdom support the association between sunshine and happiness and lack of sunshine with 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 winter months. Seasonal affective disorder (SAD) has been well-described. Given 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 a randomized controlled trial published in 2006, bright light was as effective as fluoxetine in improving symptoms of SAD (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 randomized controlled trials 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 most effective. In most trials of light therapy, the patient sits in front of a light box, exposed to 10,000 lux for 30–120 min daily. Trials comparing the effects of light boxes with outdoor activity (e.g., 15 – 60 minutes of sunlight daily) and tanning booths are needed.

Nature

Recently, a new field of inquiry has emerged exploring 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 includes both natural settings alone and also 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 and controlled for the beneficial effect of the natural setting. A significant positive effect was found for 30 adult patients with mild to moderate depression with this approach after two weeks of treatment in this single blind, randomized controlled trial.

Minimizing environmental toxins

Heavy metals (e.g., lead and mercury) are also associated with depressive symptoms[30]. Carbon monoxide poisoning is also associated with depression[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, intelligent, or in possession of more friends, toys or desirable food, clothing, 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 TVs from children's rooms and sharply reducing the time the television is on may contribute to improved mood. Advocacy to eliminate marketing to children (already in place in several European countries) 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 items and kindness items; that is, ways the writer has been kind to others. (book reference: For more information on the appreciation audit, see Dan Baker's book, listed in resources.)

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, 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 profound impact on children's mood.

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 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.

Dialectical Behavior Therapy (DBT)

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

Eye Movement Desensitization and Reprocessing (EMDR)

EMDR significantly improved depression in adult patients of childhood sexual abuse in a RCT of 880 patients[49]. In this study, EMDR was most effective for more recent trauma and significantly outperformed fluoxetine on a variety of measures. Many clinicians treating children are finding EMDR a safe, effective and often faster treatment approach for angry, violent or depressed youth that have suffered abuse.

Other

A variety of 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 successfully applied in a Boston Public Middle School[50]. This resulted in the improvement of a variety of measures including general well being. Gordon[51] applied a variety of mind body techniques to improve symptoms in a group of war torn Kosovo students. Music therapy improved mood and depressive scales in a group of grieving children[52]. In a 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 co-morbid with depression), guided imagery was a more effective treatment than breathing exercises alone[54]. Reynolds[55] demonstrated in a 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 anti-depressant therapy for major depression in one adult trial[56].

Social Support & Spirituality

Children who attend church regularly have about 20% lower risk of developing depression than non-attendees. Church may be protective because of inherent spiritual factors as well as improving a sense of social support and cohesiveness and providing opportunities for connecting with a trusted adult in whom to confide. Numerous studies document benefit from a variety of 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 (SNPs) represent a significant factor in biochemical individuality. The enzyme delta-5-desaturase (D5D) converts omega three fatty acids such as alpha linolenic acid (ALA) into eicosapentanoic acid (EPA) and docosahexanoic acid (DHA). If a SNP impairs D5D, a child may require significantly higher levels of ALA, EPA or DHA in their diet to maintain normal cell membrane function and healthy mood.

For this chapter we will consider 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. This is especially important for children who eat a restricted diet due to suspected food allergies or sensitivities. Also, any child that restricts calories, whether from a performance basis (wrestling, gymnastics, etc) or self-image basis (i.e. anorexia), will have enhanced needs (stress and conflict also significantly escalate nutrient demands).

Essential nutrients (Vitamins, Minerals, Fatty Acids, Amino Acids)

Here we will not cover all essential nutrients, but focus on a few that are vitally important and often lacking in the American diet or for which some individuals benefit from 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, there was a significant reduction in violent acts and in rule infractions among those given on micronutrient

supplementation [59]. Several case studies and case series support the effectiveness of a proprietary multivitamin/mineral (EMPower®) on young people with mood (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 B6 is essential in metabolizing tryptophan to serotonin. Folate and vitamin B12 are major determinants of one-carbon metabolism, in which S-adenosylmethionine (SAM-E) is formed. SAM-E donates methyl groups that are crucial for neurological function. See more on SAM-E below.

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 B6* significantly benefits premenstrual depression[64]. The side effects of excessive doses of vitamin B6 include: nausea, vomiting, abdominal pain, anorexia, headache, somnolence, lower B12 levels, and sensory neuropathy. The latter typically occurs with doses over 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 s-adenosylmethionine and the remethylation of homocysteine. Folate deficiency is common and contributes to a variety of psychiatric symptoms: depression, psychosis, irritability, dementia and impaired memory.

Considerable research evidence supports the value of folate maintaining a healthy mood. Folate and B12 levels are lower in depressed than non-depressed 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 micrograms of folate to 20 mg of fluoxetine significantly improved the response rate in patients with major depression[70]. One review concluded that folate supplementation is beneficial in treating depression whether used as monotherapy or in augmenting conventional medications [71]. Primary care clinicians should ensure that children prone to mood disorders have an adequate intake of folate and consider recommending a multivitamin or a B-vitamin complex containing folate. Given the safety of water soluble vitamins, a dose a dose of 1 mg per day in symptomatic children is reasonable. It should be given with B-12 to avoid masking a B-12 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 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]; and those living in the inner city, [81] African-Americans[82] or those who are veiled. Many adolescents have relatively low levels of vitamin D due to 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 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 D3 and 1,25-dihydroxvitamin D3 levels are significantly lower in psychiatric patients than in normal controls [85]. Vitamin D deficiency is associated with anxiety and depression in patients with

fibromyalgia[86]. In a randomized controlled trial of vitamin D given to 44 Australian patients (none, 400 IU versus 800 IU vitamin D) vitamin D3 significantly enhanced mood in a dose-dependent fashion [87].

The RDA 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 with renal, inflammatory bowel or juvenile arthritis and those patients on anti-convulsant drugs that lower vitamin D levels.

Minerals

This chapter will include brief discussions of 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 (PTH) 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 PTH metabolism [90]; sometimes there is dysregulation which is particularly notable in women suffering from premenstrual symptoms. Epidemiologically, normal to high intakes of calcium and vitamin D are associated with lower risks depressive mood in patients with premenstrual syndrome; conversely, lower intakes of calcium and vitamin D are associated with increased risk of PMS [91]. Small studies suggest that calcium supplementation may benefit women with PMS-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% boys and 58% girls ages 6–11
- 64% boys and 87% girls ages 12–19

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 widely used or recommended as a treatment for depression.

Magnesium, like lithium, suppresses hippocampal kindling, regulates NMDA receptors, and alters glutamate activity[95, 96]. It has been a successful treatment for the premenstrual mood changes [97]. Magnesium and verapamil were much more effective than verapramil 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 a randomized controlled trial of patients with atypical depression and bipolar II patients, chromium had a significant benefit [100]. Five patients responded to chromium supplementation after failing conventional depression treatment [101]. A randomized controlled trial of chromium picolinate (600 micrograms 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 RDA for chromium is 120 micrograms. The daily dietary intake of chromium for a typical American adult is only 25 - 50 micrograms per day. The dose range in studies of its effects on mood is typically 200–600 micrograms 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 (NMDA) receptor, exhibits antidepressant-like activity in rodent models of depression. Similarly to antidepressants, zinc induces brain derived neurotrophic factor (BDNF) gene expression and increases level of synaptic pool of zinc in the hippocampus [103]. Furthermore, zinc treatment has been shown to have an antidepressant effect[104].

The US Recommended Dietary Allowance for zinc ranges from 5 milligrams daily for younger children to 11 milligrams daily for teenagers. Vegetarians may need as much as 50% more zinc than non-vegetarians because of the lower absorption of zinc from plant foods, so it is very important for vegetarians to include good sources of zinc in their diet. Breastfeeding depletes zinc, and some experts suggest that because breastmilk contains relatively low levels of zinc, that breastfeeding infants after 7 months of age receive zinc supplementation.

Low zinc status has been observed in 30% to 50% of alcoholics. Alcohol decreases the absorption of zinc and increases 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, particularly females who may not be meeting their needs for iron to replace menstrual losses, be checked for iron sufficiency [106]. Primary care clinicians should ensure that their patients consume adequate amounts of iron either through diet or supplementation.

Fatty acids

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

There is strong epidemiologic correlation between fish consumption, levels of omega three fatty acids and protection from depression and suicide [107–111]. Furthermore, clinical trials suggest that supplemental EFAs (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 gram per day to 10 grams per day.

The benefit of omega three supplementation for bipolar disorder is less clear [116]. Stoll's (1999) double blind study augmenting treated bipolar patients with fish oil (9.6 grams/day) or placebo found significant reductions in relapse and all other outcome measures with fish oil [117]. 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 6–17 years of age. The intervention was 1290–4300mg of EPA/DHA combination.

In children the developmental requirements and absence of serious toxicity suggest that daily supplementation with 1–3 grams 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-Hydroxytryptophan (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 appears to be a better choice for increasing CNS levels of serotonin.

Tryptophan depletion leads to depressive symptoms in rats and humans. A variety of 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 TID. The typical dosing is 50mg slowly increasing to 150mg two or three times daily on an empty stomach based on size. A large single dose of 200–400mg 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, drowsiness (which may make it useful at bedtime); they may cause serotonergic syndrome if used in combination with SSRI medications; they may also be associated with decreased carbohydrate intake and weight loss [127]. Eosinophilia-myalgia syndrome (EMS) was reported in numerous people taking L-trp, which led to its removal from the American market; however, investigations revealed that the problem was related to contaminated lot from one manufacturer, and L-trp 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 (SAM-E)—S-adenosyl-L-methionine (SAMe, pronounced Sam - ee) 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 anti-depressant potency.

Over 25 controlled trials have evaluated the effectiveness of SAM-E for patients with mood disorders. A 2002 review by the Agency for Healthcare Quality and Research (AHRQ) concluded that compared to 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 similar potency 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 – 1600 mg of SAM-E daily. Benefits typically appear within two weeks of starting the medication. Although product variability is a major problem in many dietary supplements, a review of SAM-E products by ConsumerLabs revealed that only 1/11 products tested failed their rigorous standards.

SAM-E 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 with bipolar disorder. Furthermore, it is expensive (50 cents to $1 per 200 mg tablet) and not usually covered by insurance.

Herbs for Mood

St Johns wort—The herb most commonly used as a complementary or alternative remedy for depression is St. Johns 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 US imports containing these compounds. For example, in a German randomized controlled trial, St. Johns 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 two weeks in 25/33 and 9/11 patients in separate studies [137, 138]; patients who improved in these studies generally showed improvement within two weeks of starting therapy. It is reasonable to stop treatment or change to a higher dose or different product if no benefit has been noted within three weeks.

St. Johns 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 (AEs) between 0% and 6%; of the four large-scale surveillance studies with a total of 14,245 patients the rate of AEs ranged from 0.1% to 2.4% and a drop-out rate due to AEs of 0.1–0.9% [139]. This is at least ten-fold lower than that recorded with synthetic antidepressants. The adverse events associated with St. Johns wort were mild and transient in nearly all cases.

However, St. Johns wort can 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. Johns 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.

There is substantial variability the quality of SJW preparations. Patients who wish to use it may use a product tested in a large randomized, controlled trial or refer to product testing conducted by Consumerlabs (see Table 4).

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]. There has been some suggestion that inositol can induce bipolar conversion into mania [142]. Inositol can be mildly sedating and has been also 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 for mood disorders. The typical starting dose is 1–2 grams two or three times daily increasing up to 12–18 grams per day in divided doses.

Biomechanical therapies: *Massage*—Massage is widely used 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 (PFC) activity in those with right dominance [143]. The left prefrontal cortex has been associated with positive mood, while dominance of the right PFC is associated with depressed mood [144]. Furthermore, massage decreases cortisol levels and increases levels of serotonin and dopamine in patients with 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 a variety of 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 five days a week. In order to achieve this frequency cost-effectively, parents are generally trained to provide massage for pediatric 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 with low platelet counts. Careful discussion and respect for individual patients is extremely important for patients with a history of physical or sexual abuse.

Bioenergetic Therapies: *Acupuncture*—Acupuncture involves the stimulation (using pressure, heat, needles, magnets) of specific points on the body with the intention of promoting healing. Randomized controlled trials suggest that acupuncture has significant benefits for depressed adults and may be comparable in effectiveness to prescription antidepressant medications [151]. For example, in a randomized controlled trial 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 authors concluded that "the effect of electroacupuncture may not be

significantly different from antidepressant medication," with weighted mean difference in comparison trials of −0.43(95% CI −5.61 to 4.76) [153].

Acupuncture rarely causes bleeding, bruising, infection; it causes sleepiness in about 5% of patients. In general, it has fewer side effects than medications. Serious side effects are extremely 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 constantly growing. It is helpful to have a list of resources to address common questions and concerns as well as emerging knowledge about the safety and effectiveness of therapies and approaches to promote healthy moods. See Table 4.

Summary

Depression is the 2nd 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. A variety of resources are available to clinicians to help patients and families promote mental health.

Acknowledgements

Dr. Kemper is supported in part by the Kohlberg Foundation, NIH NCCAM K24 AT002207 and by NIH NCAM R21 AT001901 as well as by the Caryl Guth Fund for Holistic and Integrative Medicine. The views expressed in this chapter 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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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/Attention	Love
Coordination	Harmony	Kindness
Resilience	Hardiness	Charity/generosity
Teamwork	Social Network/communication skills/connected to community	Connection with a higher power

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 oil) fish oil, flax seeds, flax oil, canola oil, walnut oil, dark green leafy vegetables.
Vitamin B6	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, and 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 Tree Nuts, Peanuts, Peanut butter
Zinc	Beef, pork, and lamb; oysters; dark meat of poultry. Peanuts, peanut butter, nuts and legumes (beans) Fortified cereals

Table 3

St. Johns 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)

Table courtesy of Dr. Paula Gardiner

Table 4

Resources on Integrative Approaches to Pediatric Mood Disorders

Internet Resources	
Resource	**URL**
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/
ConsumerLabs – compares dietary supplement brands	www.consumerlabs.com

Books

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