

Depression

Updated: 05/29/2003

(Reprinted from LE Disease Prevention & Treatment Book)

Almost everyone has, at some point in their lives, experienced "the blues." We all feel sad in the face of significant loss--loss of a job, a loved one, or an adored companion animal. Sometimes reading the morning's news about the latest economic, environmental, or natural disaster is enough to make a person want to crawl back under the covers.

True depression, however, is much more serious than a temporary disappointment or sorrow. People who are depressed can feel a profound and persistent sadness in the absence of an identifiable external cause. Also, the symptoms extend beyond melancholy mood to sleep disruption and loss of appetite and energy. In other words, depression is a "whole body" disease that skews the way we think and behave, often damaging our physical health as well as our emotional state. It is a powerful disease that can leave us debilitated, unable to work, maintain relationships, or deal with other responsibilities. Although external factors play a role, depression and other mood disorders arise primarily from subtle imbalances in brain chemicals called neurotransmitters.

WHO IS AFFECTED?

Depression is an equal-opportunity disease, striking all ages and races, both sexes, and all socioeconomic groups:

- According to the National Institutes of Mental Health, in any given year, major depression afflicts nearly 10 million Americans over the age of 18, or about 5% of the population. When dysthymia (chronic mild depression) is included in the head count, the numbers rise to 18.8 million American adults, or about 9.5% of the population (Narrow 1998).
- Nearly twice as many women as men suffer from major depression each year (Narrow 1998).
- If you have just one episode of major depression, there's a 50/50 chance you'll have more, perhaps as many as one or two a year. Millions of depression cases are never diagnosed or treated.
- Untreated, major depression may last for 6 months to a year, with recurrences becoming more frequent and severe. Without treatment, dysthymic disorder (mild depression) is so persistent that periods of normal mood may last only a few weeks at a time.
- Major depression is the leading cause of disability in the U.S. Depressed mood ranks just behind high

blood pressure as the most common chronic condition doctors see (Wells et al. 1996).

- Depression costs our society an estimated \$44 billion a year, including \$23 billion for lowered productivity and absenteeism at work, and \$12.3 billion for medical and psychiatric care.
- Every year thousands of people commit suicide. In 1997, 30,535 people committed suicide, partly or largely as a result of depression, costing taxpayers billions of dollars.

Depression is one of the most commonly misdiagnosed problems. Many doctors treat the obvious symptoms of depression, such as poor appetite, insomnia, and headaches, but overlook the real problem. Left untreated, depression can become more frequent and severe, leading to physical and emotional suffering, loss of job and relationships, and even to suicide.

WHAT IS DEPRESSION?

Medical textbooks describe depression as a mood disorder, lasting at least 2 weeks, that produces exaggerated, inappropriate feelings of sadness, worthlessness, emptiness, and dejection.

"Exaggerated" and "inappropriate" are two important words to keep in mind. To feel upset because of a job layoff, a broken marriage, a bankruptcy, or the loss of a loved one is a normal response to an unhappy event. Generally, our feelings of sadness are proportional to our loss, and this "reactive depression," as doctors call it, goes away with time.

But endogenous, or major depression often strikes for no apparent reason. It doesn't seem to be caused by outside events, such as the loss of a job. Instead, the black mood grows and grips from within. This crippling darkness can last for weeks, months, or years and may make it impossible for us to carry on our normal lives. The many and varied symptoms of endogenous depression may include:

- Profound, persistent sadness.
- Profound, persistent irritability.
- Unexplained crying.
- Loss of self-esteem.

- Feelings of hopelessness, helplessness, pessimism, worthlessness, guilt, and emptiness.
- Ruminations over the past, particularly the errors you think you've made.
- Changes in sleeping patterns.
- Changes in eating habits.
- Unexplained weight gain or loss. Restlessness.
- Fatigue.
- A "slow down" in physical movements.
- Inability to concentrate.
- Memory difficulties.
- Difficulty making decisions.
- Loss of interest in usually pleasurable activities.
- Loss of interest in sex.
- Social withdrawal.
- Unexplained headaches, stomach upset, or other physical problems that are not helped with standard treatment.
- Thoughts of suicide or death.
- Suicide attempts.

The symptoms may come in any combination. They can build gradually or strike hard and fast. Some of the symptoms, you'll notice, may seem contradictory. Take, for example, appetite. Mildly depressed people may gain weight as they seek comfort in favorite foods, while those more profoundly depressed may lose weight as sadness deadens their appetites. Sleep patterns also may be affected this way. Some depressed people have difficulty falling or staying asleep, while others sleep more than usual, but awaken feeling tired.

Other common mood disorders include:

- Dysthymia: low-grade depression that lasts at least 2 years.
- Mania: periods of elevated, expansive, or irritable mood that last at least one week. During this time, the person becomes very active (including involvement in risky behaviors), restless, grandiose, distractible, and talkative, with racing thoughts.
- Bipolar disorder: recurrent cycles of depression and mania. Also known as manic-depressive illness.
- Seasonal affective disorder: mild to moderate depression with carbohydrate cravings, headaches, low energy, and fatigue occurring regularly in the fall or winter.

- Premenstrual dysphoric disorder: depression, irritability, and anxiety limited to the few days before the onset of menses.

WHAT CAUSES DEPRESSION?

Although we're only beginning to pull back the curtains that hide the inner workings of the human brain, we do know that several neurotransmitters (chemical messengers) including dopamine, norepinephrine, and serotonin, help to regulate our moods and keep us happy. Depressed people tend to have lower levels of norepinephrine, dopamine, and serotonin. If, for any reason, the amounts of these key neurotransmitters drop below critical levels, the result may be an endogenous depression that seems to come from nowhere, lingers forever, saps energy, and ruins lives.

Why do brain levels of mood regulators fall in some people, but not in others? We can't fully answer that question, although we know that genetics plays a major role. Depression, like other mood disorders, tends to run in families. Depression is even more likely to be shared by identical twins: If one is depressed, there's a better than 50% chance that the other will be, too.

Dutch researchers have found more symptoms of depression and lower serotonin levels in men with chronic low cholesterol, as compared with men with normal cholesterol. Cholesterol may affect the metabolism of serotonin, causing the depression (Ainiyet et al. 1996).

A great deal of research has looked into possible environmental or psychological causes of depression. Some investigators believe that people who are pessimistic, often feel overwhelmed by life, or have low self-esteem, are more likely to suffer from depression. It may be that some of us are lucky enough to have large reserves of "happy" neurotransmitters in our brains, but others have just enough to barely keep a smile on their faces.

Although biochemistry is the biggest factor in major depression, we're also affected by what happens to us in our lives. We're all hit by unpleasant events that may cause brain levels of norepinephrine and dopamine to fall temporarily. People with naturally large reserves usually get through the troubling times with minimal difficulties, but those with low chemical levels to begin with are more likely to lapse into depression. Stress has been linked to depression as well; stress increases the production of the immunological signaling chemicals IL-1beta and TNF-alpha and decreases the level of IL-2, IFN-gamma, MHC II, and NK cell activity. Both depression and cancer are linked to this shift in the chemical signals in the body (Maddock et al. 2001; Raison et al. 2001).

Women, moreover, seem to suffer more from depression than men. Some researchers argue that this disparity is caused by gender hormonal differences; others suggest that the difference is due to socialization. Girls in our society are taught to monitor their feelings and to ask for help when they are troubled. Boys, on the other hand, are encouraged to ignore their feelings. It may be that men and women are equally likely to become depressed, but that men are more reluctant to admit that they are down. In any case, it seems clear that biochemistry is the major cause of endogenous depression, with psychology and hormones playing supporting roles.

HOW DOCTORS TREAT DEPRESSION

Several types of medical professionals treat depression, including family doctors, internists, psychiatrists, psychologists, and social workers. The therapies they offer are numerous, but are of three main types: psychotherapy, or "talk therapy;" drugs; and electroconvulsive shock therapy. These treatments may be used alone or in combination.

Types of psychotherapy include behavioral therapy, cognitive therapy, and psychodynamic therapy. These treatments help people learn to restructure the way they behave, think, and relate to others to better improve mental well being.

The central idea of drug treatment is to boost levels of neurotransmitters thought to be low in depression. State of the art treatment has evolved a great deal since the 1950s, when doctors gave depressed patients stimulants such as amphetamines. Though stimulants can boost mood, they also carry serious side effects, including nervousness, increased blood pressure, rapid heartbeat, and irregular heart rhythms. Over time, the drugs have been refined to act more selectively to alleviate depression, but with fewer adverse reactions.

Although not as gruesome as it is in movies, electroconvulsive therapy (ECT) is not a pleasant experience. Electricity shot through the brain can sideline a bout of depression, but it is only a temporary measure. It does not cure the disease and often it destroys parts of the memory.

Which treatment works best? That answer isn't clear. Some research shows that about half of depressed patients will respond to either psychotherapy or drug therapy (Keller et al. 2000). Other research indicates that drug therapy has an advantage over psychotherapy (Thase et al. 2000).

The initial choice depends both upon the individual's preference and the severity and duration of his or her depression. People with mild to moderate depression may find that psychotherapy alone does the trick. For

people with chronic or severe depression, a combination of psychotherapy and medications may be the best option. Electroconvulsive therapy, while effective, is generally reserved for people with chronic depression unresponsive to medication.

COMMONLY USED PRESCRIPTION MEDICATIONS

Today, physicians and psychiatrists have numerous drugs at their disposal. Tricyclic antidepressants (TCAs) include Tofranil (imipramine) and Elavil (amitriptyline). Called tricyclics because of their three-ringed chemical structure, they work by altering the way the brain responds to norepinephrine and serotonin. Hundreds of clinical studies involving tricyclic antidepressants have produced only moderate results. In only about 60% of these tests have the tricyclics proved to be more effective than placebos such as sugar pills.

Monoamine oxidase inhibitors (MAOIs), such as Nardil (phenelzine) and Parnate (tranylcypromine), act as "shields" to norepinephrine and dopamine, preventing their breakdown by enzymes. MAOIs can have serious side effects if mixed with certain foods (Sullivan et al. 1984; Walker et al. 1984; Mirchandani et al. 1985; Gardner et al. 1996).

Selective serotonin reuptake inhibitors (SSRIs) include Zoloft (sertraline), Paxil (paroxetine), Celexa (citalopram), and Prozac (fluoxetine). These widely prescribed drugs (the SSRIs) enhance or increase serotonin levels by preventing the hormone from being reabsorbed and "taken out of circulation."

The medications have helped many people to regain their sense of equilibrium, but they have potentially serious side effects and must be used with caution. Fortunately, the more serious adverse effects are rare. Common side effects include:

- Tricyclics: headache, dry mouth, constipation, diarrhea, nausea, indigestion, fatigue, weakness, drowsiness, nervousness, anxiety, excessive sweating, tremor, insomnia, weight gain, "sweet tooth."
- MAOIs: dizziness, restlessness, tremors, dry mouth, constipation, difficult urination, blurred vision, "sweet tooth."
- SSRIs: nausea, diarrhea, nervousness, anxiety, drowsiness, insomnia, headache, increased sweating, increased or decreased appetite, and decreased sexual drive (Most of these symptoms wane or disappear with time. Celexa [citalopram], a newer SSRI, seems to be better tolerated.)

In the 1960s, doctors started using lithium to treat bipolar disorder. Potential side effects of lithium--marketed as Carbolith, Euralith, Lithane, and Lithonate--include

dizziness, dry mouth, increased urination, lack of appetite, vomiting, diarrhea, stomach pain, irregular heartbeat, shortness of breath, swelling of hands and feet, slurred speech, headaches and muscle aches, weakness, sleepiness, and confusion. Newer medications, such as the anticonvulsant drug gabapentin (Neurontin), are under investigation as mood stabilizers.

Some medications may contribute to depression. Examples include ibuprofen, Benadryl, Xanax, Valium, Librium, Klonopin, Butisol, Fiorinal, Inderal, Lopressor, Seconal, Halcion, Compazine, Thorazine, Percodan, Darvocet, Percocet, and Dalmane. If you are taking any of these medicines, ask your physician to review with you all of the potential side effects. If you or anyone in your family has or has had problems with depression, make sure your doctor knows about this before he or she writes you a prescription.

Antidepressant medications, while helpful to many people, are not panaceas. Some studies have shown that drugs are of no value in treating about 33% of depression cases. In another 33% of cases, the drugs were only a little more effective than placebos. In addition, they can cause side effects. On the other hand, depression itself is unpleasant and carries the life-threatening risk of suicide (Shea et al. 1992; Emslie et al. 1997; Tanghe et al. 1997).

Caution: If you are already on an antidepressant, do not stop treatment without consulting your physician. Abrupt discontinuation of some of these drugs can lead to unpleasant symptoms such as nausea, vomiting, tremor, fatigue, and headache, not to mention re-emergence of depression. Also know that several of the natural supplements listed below can interact with drug treatment.

NUTRITION AND DEPRESSION

Hippocrates, the great Greek physician and Father of Medicine, said: "From the brain, and from the brain only, arise our pleasures, joys, laughter, and jests, as well as our sorrows, pains, griefs, and tears."

It's startling to learn that there are 15 trillion neurons (nerve cells) in the human brain. There are far more glial cells (neuroglia) that fill the spaces between the neurons, Schwann cells, and miles of blood vessels to nourish the three or so pounds of brain tissue in the average head.

Three pounds isn't much: only 2% of the body weight of a person weighing 150 pounds. Brain cells are hungry cells, demanding nourishment from as much as 30% of circulating blood. We used to think that the brain could somehow protect itself from nutrient deficiencies, but today we know that the brain requires specific nutrients. If the brain doesn't get them, its biochemistry changes,

resulting in fatigue, depression, irritability, and other symptoms.

For example, the brain needs a good supply of B vitamins to act as coenzymes (catalysts) for many functions, including converting nutrients from food to fuel that our bodies can use. Glucose is the brain's primary fuel. If glucose levels fall, we may feel depressed, tired, or unable to think clearly.

B vitamins also are needed to help the brain make neurotransmitters, the "messengers" that enable brain cells to communicate with each other. Vitamin B6 is needed to manufacture serotonin, a neurotransmitter that produces feelings of well-being. Without proper supplies of vitamin B12, the brain could not make acetylcholine, an important neurotransmitter involved in learning and memory. The B vitamin known as folate (folic acid) is needed to make an important group of mood-regulating chemicals called catecholamines, including dopamine, norepinephrine, and epinephrine (Bukreev 1978; Carney et al. 1990; Carney 1995; Fujii et al. 1996; Masuda et al. 1998; Bottiglieri et al. 2000; Zhao et al. 2001).

In many cases, depressed people with blood levels indicating that they lacked key nutrients respond quite well to supplements. Unfortunately, most physicians do not prescribe natural supplements to treat depression (Carney et al. 1990; Carney 1995).

In general, people who are depressed should follow these dietary guidelines:

Avoid Alcohol

It may make us feel giddy at first, but that's only because it's dulling our inhibitions. In the long run, alcohol is a depressant, which is the last thing depressed people need. If you must drink, limit yourself to one drink a day. (One drink means a single serving of a single alcoholic beverage a day, either one ounce of hard liquor, straight or mixed, four ounces of wine, or 12 ounces of beer.)

Quit Caffeine

Caffeine can leave you mentally and physically drained. Avoid the caffeine in coffee, tea, soft drinks, chocolate, and cocoa, as well as the "hidden" caffeine in Excedrin, Midol, Anacin, and many other medicines. (Ask your physician or pharmacist if the medicines you are taking contain caffeine. If they do, talk to your physician about switching to other medications.)

Avoid Sugar

Sugar jolts us with a burst of energy which can make us feel excited, talkative, and ready to take on the world. However, when the body responds by snatching the excess sugar out of circulation, it often takes too much, leaving us tired and depressed. Some depressed patients experience wild, sugar-induced fluctuations in

their moods. Convincing them to stay away from cakes, candy, soda, and refined and processed foods often solves the problem.

NATURAL SUPPLEMENTS TO FIGHT DEPRESSION

Scientific study and clinical experience show that several natural remedies can help alleviate depression.

However, if you are experiencing profound feelings of sadness and hopelessness, please seek professional psychiatric treatment. Unless otherwise noted, follow dosing information on labels, but don't try taking all of these supplements at once. A good rule of thumb is to try one thing at a time to see how it works. Furthermore, three of the supplements listed below--St. John's Wort, SAME (S-adenosylmethionine), and 5-HTP--enhance the serotonin system. Theoretically, a person could raise serotonin levels too high.

SAMe

SAMe is a natural substance that the body can produce from the essential amino acid methionine and adenosine triphosphate (ATP). Found in all our cells, it plays an important role in critical biochemical processes. It serves as a precursor for glutathione, coenzyme A, cysteine, taurine, and other essential compounds, and is needed for the production of serotonin and other neurotransmitters.

Researchers from the University of Alabama at Birmingham found that depressed patients were not making enough SAMe in their brains. After checking red blood cells from patients suffering from depression and schizophrenia, they discovered a decreased amount of methionine adenosyl transferase (MAT), an enzyme necessary for the formation of SAMe. This enzyme was, however, higher in people with mania (Tolbert et al. 1988).

In a study published in the journal *Movement Disorders*, SAMe was administered to 13 depressed patients with Parkinson's disease. All patients had been previously treated with other antidepressant agents and had no significant benefit or had intolerable side effects. SAMe was administered in doses of 800-3600 mg a day for a period of ten weeks; 11 patients completed the study, and ten had at least a 50% improvement on the 17-point Hamilton Depression Scale. One patient did not improve. Two patients prematurely terminated participation in the study because of increased anxiety. One patient experienced mild nausea, and another two patients developed mild diarrhea, which resolved spontaneously. The mean improvement in depression scores from before to after treatment was approximately 64% (Di Rocco et al. 2000).

Although this study was uncontrolled and preliminary, it suggests that SAMe is well tolerated and may be a safe and effective alternative to the antidepressant agents currently used in patients with Parkinson's disease.

Please note that some of these Parkinson's patients received very high doses of SAMe, which could account for the few side effects observed. Previous clinical studies show that doses of 800-1600 mg a day of SAMe produce remarkable antidepressant benefits in otherwise healthy people without significant side effects.

Published scientific studies on SAMe reveal:

- Both oral and injectable forms of SAMe have a fast-acting antidepressant effect (Bottiglieri et al. 1994).
- An analysis of the studies to date concluded that SAMe performed better than placebo treatment, with 17-38% of patients responding and on par with tricyclic antidepressants (Bressa 1994).
- Because it produces quick results, SAMe has been used to hasten the onset of action of the antidepressant imipramine (Norfranil, Impril) (Berlanga et al. 1992).
- A 1993 Italian study found SAMe significantly more effective than placebo in alleviating depression and dysthymia in 80 postmenopausal women (Salmaggi et al. 1993).
- SAMe has also been shown to ease the depression associated with Parkinson's disease (Carrieri et al. 1990).
- Another bonus is that this supplement appears to improve osteoarthritis.

Higher Homocysteine/Lower SAMe

Homocysteine is a by-product of the amino acid, methionine. Normally, homocysteine is converted back to methionine or used to create cysteine and other useful substances in the body. If these conversions are blocked, however, homocysteine accumulates to dangerous levels and can contribute to heart attack, stroke, liver damage, and eye problems.

A clear association exists between elevated homocysteine and major depression. One study shows that homocysteine, depression, neurotransmitters and folate (folic acid) are connected (Bottiglieri et al. 2000). It also shows that depressed people with the highest elevations in homocysteine (>12 micromoles/liter) have significantly less SAMe--which means they have less capacity to create mood-enhancing neurotransmitters. Low levels of neurotransmitters were, in fact, confirmed in the people with the highest homocysteine and lowest levels of SAMe. In the whole group, higher homocysteine equalled lower SAMe.

Since folate deficiency is one of the main reasons for elevated homocysteine, the researchers also looked at folate levels, both in the blood and in cerebro-spinal fluid. They found that the group with the highest homocysteine levels (>12 micromoles/L) had significantly lower folate in cerebro-spinal fluid, red cells,

and serum. Folate was also lower in red blood cells of the depressed group as a whole. Nearly a third of the depressed inpatients in the study had red cell folate levels below normal (<150 mcg/L). At the same time, half of them had homocysteine levels higher than the levels of two control groups.

Homocysteine, SAMe, and folate all participate in the methylation cycle in which methionine is converted to SAMe, which is used for methylation, producing homocysteine which is then converted back to methionine with enzymes that use folate. One depends on the other. If folate is not available to promote the conversion of homocysteine, homocysteine can build up and block methylation.

Serotonin and other brain chemicals require methylation to be synthesized. When the methylation factor, SAMe, is injected into rats, certain areas of the brain synthesize more serotonin. In turn, serotonin and SAMe are both necessary for the synthesis of melatonin, an important hormone for sleep. It's easy to see how homocysteine (which blocks SAMe) can have far-reaching effects.

The price of SAMe has come down substantially in recent years, making it much more affordable as a treatment option. The suggested dose of SAMe to treat depression ranges from 400-1600 mg a day.

Caution: SAMe is not recommended for people with bipolar disorder or mania. Also, some practitioners recommend gradually increasing the dosage to avoid mild and transient nausea and vomiting occasionally seen at the start of treatment. Joseph Pizzorno, N.D., President Emeritus of Seattle's Bastyr University, author of Total Wellness and coauthor of Encyclopedia of Natural Medicine, recommends 200 mg twice a day for 2 days, 400 mg twice a day on days 3 through 9, then 400 mg three times a day on days 10 through 19, followed by 400 mg four times daily thereafter.

St. John's Wort (*Hypericum perforatum*)

In Germany, where it is covered by health insurance as a prescription drug, some 20 million people take hypericum for depression. A meta-analysis and review of 23 randomized clinical trials involving 1757 people with mild or moderately severe depressive disorders showed that St. John's Wort was 2.67 times superior to a placebo in relieving depressive symptoms and was as effective as standard antidepressant drugs. Side effects occurred in 19.8% of patients on St. John's Wort, compared with 52.8% of those taking standard antidepressant drugs. The conclusion of the researchers was that St. John's Wort is more effective than a placebo for treatment of mild to moderately severe depressive disorders (Linde et al. 1996).

A more recent analysis selected eight of the best-designed studies and found that the response rate (the percentage of volunteers who improved) on St. John's

Wort was 23-55% higher than it was for placebo, but was 6-18% lower than that of tricyclic antidepressants (Gaster et al. 2000).

Most of the studies have examined the benefits of St. John's Wort in people with mild to moderate depression. However, Vorbach et al. (1997) compared 600 mg three times a day, a dosage double the usual prescribed dosage, with 50 mg three times a day of imipramine in patients with severe depression. St. John's Wort proved to be equivalent in efficacy, but with far fewer adverse effects (35.6%, compared to 81.4% for imipramine) (Vorbach et al. 1997). If you have serious depression, please don't interpret this study as an invitation to self-medicate. You owe it to yourself to work with a mental health professional.

One criticism of the St. John's Wort research was that, although the herb had compared favorably to drugs such as imipramine, amitriptyline, and maprotiline, it had yet to be compared to the more commonly prescribed selective serotonin reuptake inhibitors (SSRIs) such as Prozac. Three studies in patients with mild to moderate depression have changed that.

In the first study, Harrer et al. (1999) found 800 mg a day of St. John's Wort extract to be as effective in elderly German patients as Prozac.

In the second study by Schrader (2000), a rather low daily dose of St. John's Wort (500 mg a day) was equivalent to 20 mg a day of fluoxetine (Prozac). Significantly, more of the 240 volunteers responded to St. John's Wort than Prozac (60% versus 40%) and the herb produced significantly fewer side effects (8% of St. John's Wort patients versus 23% of Prozac patients). In a 2000 study, the same low dose (500 mg a day) proved as effective as 75 mg twice a day of imipramine, but with far fewer side effects (Woelk 2000).

A third study by Brenner et al. (2000) judged St. John's Wort extract (600 mg for 1 week, then 900 mg for 6 weeks) as beneficial as sertraline (Zoloft, 50 mg for 1 week, then 75 mg for 6 weeks).

Health practitioners have also found St. John's Wort helpful in treating low mood associated with menopause, premenstrual syndrome, and seasonal affective disorder. Grube et al. (1999) gave menopausal women 300 mg three times daily of St. John's Wort for 12 weeks. Surprisingly, both the psychological and physical symptoms of menopause improved substantially. So did sexual well-being. Kasper (1997) found that St. John's Wort decreased the low mood associated with seasonal affective disorder on par with results the same researcher had found earlier for fluoxetine (Prozac).

The usual dosage for St. John's Wort is 300 mg three times a day of herb standardized to 0.3% hypericin (one

of the active ingredients). Take a 300-mg dose at breakfast, lunch, and dinner or take two of the 300-mg doses in the morning and the third with dinner. Not everyone needs a total of 900 mg a day. Note that two studies found a mere 500 mg of St. John's Wort extract equivalent to imipramine and fluoxetine. Hyla Cass, M.D., assistant clinical professor of psychiatry at UCLA School of Medicine and author of *St. John's Wort: Nature's Blues Buster* (Cass 1998) tailors the daily dose to the individual. Cass says, "While some people need only 300 mg of an extract standardized to contain 0.3% hypericin, most require two to three times that amount."

No research exists on the use of St. John's Wort in children. More importantly, any child suspected of being depressed deserves a psychiatric evaluation.

As with all antidepressants, it takes a while for the effects of hypericum to be felt. Many patients will notice a change in 2-3 weeks, although it may take as long as 4 to 6 weeks. Hypericum's side effects are very mild and are typically limited to slight gastrointestinal irritation.

Caution: Certain light-skinned sheep in Australia have become more sensitive to the sun and may experience serious sunburns after grazing on large amounts of the hypericum leaf. While sunburn does not appear to be a common problem among people taking the recommended doses of hypericum for depression, many practitioners recommend their patients with sun-sensitive skin be sure to wear sunscreen or cover up. The same caution applies to people taking medications such as tetracycline that increase sun sensitivity.

Because of potential adverse herb-drug interactions, St. John's Wort is not recommended in combination with monoamine oxidase (MAO) inhibitors such as Parnate and Nardil or with the SSRIs (serotonin reuptake inhibitors), Prozac, Luvox, Paxil, Zoloft, and Celexa. This is because St. John's Wort may further augment the same neurotransmitters that the drugs increase, leading to dangerously high levels. If you wish to switch from an antidepressant drug to St. John's Wort, talk to your physician about safe ways to do this.

St. John's Wort has been shown to diminish the effectiveness of a growing list of drugs: digoxin, warfarin, phenprocoumon, cyclosporin, amitriptyline, theophylline, oral contraceptives, indinavir, and some anticancer drugs. Primarily, it lowers the blood levels of these drugs. How? Research suggests that active ingredients in the herb crank up the production of a liver enzyme called CYP3A, which breaks down a host of compounds, including many drugs. In other words, St. John's Wort accelerates the liver's breakdown of these drugs (Markowitz et al. 2000; Moore et al. 2000; Vogel 2001).

Because of the growing list of herb-drug interactions, two regulatory groups, the American Herbal Products Association (AHPA) and the Consumer Healthcare

Products Association (CHPA), have made labeling recommendations that alert consumers not to combine St. John's Wort with prescription medication without first asking a health professional (HerbalGram 2000).

St. John's Wort has been reported to aggravate mania, so it should be used with caution by individuals with bipolar disease. As with all antidepressants, St. John's Wort does not work for everyone with depression.

Critics of this herbal supplement point to a study where St. John's Wort was no more effective than placebo in alleviating depression. The fact that it has the potential to adversely interact with a wide variety of prescription drugs limits its use to people who are not taking other prescription medications.

One advantage of St. John's Wort is that it is very inexpensive. It costs far less than prescription drugs or SAME. The most compelling reason to choose SAME over St. John's Wort, however, may be the fact that over the past 5 years, Life Extension members who have been offered the choice of either SAME or St. John's Wort have chosen SAME by a factor of over ninety to one. This real world finding indicates that people are finding a greater effect with SAME than St. John's Wort.

5-Hydroxytryptophan (5-HTP)

To make serotonin, the body first converts the amino acid L-tryptophan to 5-hydroxytryptophan (5-HTP). In people with a personal or family history of depression, a diet devoid of tryptophan can cause moods to crash in a matter of hours (Moreno et al. 2000). Some, but not all studies have shown that supplemental L-tryptophan relieves depression (Moller et al. 1980) and mania (Chouinard et al. 1985). Unfortunately, contaminated tryptophan was linked with a serious disorder called eosinophilia-myalgia syndrome (EMS), causing this supplement to be removed from the U.S. market in 1989.

Does eating more protein help? Although tryptophan is a component of most protein-rich foods, raising brain levels of this amino acid through diet is tricky. In order to cross from the blood into the brain, tryptophan must first bind to a transport molecule, which it shares with five other amino acids. The L-tryptophan concentration in foods is low relative to other amino acids. According to Timothy C. Birdsall, N.D., Director of Naturopathic Medicine, at the Midwestern Regional Medical Center in Zion, Illinois, "as little as one percent of dietary L-tryptophan may be transported into the central nervous system."

Although several reports in the published literature show that 5-HTP may be as effective as some antidepressants, the Life Extension Foundation does not endorse its use in the U.S based on certain findings.

The process by which 5-HTP is converted into serotonin is called decarboxylation. If decarboxylation occurs before 5-HTP is absorbed by the brain, blood levels of serotonin will elevate significantly, but very little serotonin will enter the brain.

When Europeans take 5-HTP, they are often prescribed the decarboxylase inhibitor carbidopa that prevents 5-HTP from being converted into serotonin until it reaches the brain. Americans do not take carbidopa with 5-HTP and the result is possible serotonin overload in the blood, with virtually no serotonin reaching the brain.

Americans taking 5-HTP are more vulnerable to blood serotonin overload because, unlike most Europeans who are vitamin deficient, Americans who use 5-HTP usually take vitamin B6 as well. Vitamin B6 rapidly converts 5-HTP into serotonin before it reaches the brain. Even when combined with carbidopa, high levels of vitamin B6 will break through the carbidopa barrier and ensure that 5-HTP converts into serotonin in the blood before it can reach the brain. Excess serum serotonin is especially dangerous in those with underlying coronary artery disease as serotonin in the blood can induce arterial constriction.

Omega-3 Fatty Acids

According to Michael A. Schmidt, Ph.D., author of *Smart Fats* (1997), our culture consumes too much saturated fat (found in animal fats) and omega-6 fatty acids (found in the corn and soybean oils used in so many processed foods), and too little of the omega-3 fatty acids (found in fish oils and some plants such as flax seed). This sort of imbalance has been associated with increased levels of depression (Hibbeln et al. 1995).

Omega-3 fatty acids control various enzyme systems, cell membrane fluidity, inflammatory processes, and several aspects of neurotransmitter function. Depressed people seem to have low levels of omega-3 fatty acids in their diet and in their cell membranes (Edwards et al. 1998). One study in the *Archives of General Psychiatry* found that 9.6 grams a day of omega-3 fatty acids for 4 months benefited people with bipolar disorder (alternating episodes of depression and mania) significantly more than a placebo (olive oil) (Stoll et al. 1999).

Michael A. Schmidt recommends eating cold-water fish 2-3 times a week. Fish contains docosapentaenoic acid (DHA), which is particularly critical to brain function. Eggs, depending upon what the chickens eat, contain varying amounts of DHA. Although the conversion is not terribly efficient, the body can also create eicosapentaenoic acid (EPA) and DHA from the alpha-linolenic acid (ALA) found in green leafy vegetables, flaxseed, chia seeds, rapeseed, pumpkin seeds, Brazil nuts, and walnuts.

When using supplements, Schmidt recommends a daily dose of between 400-1000 mg of DHA and 400-1000 mg of EPA.

Caution: Because of fish oil's mild blood-thinning effect, high-dose omega-3 supplements should only be combined with anticoagulant drugs under the supervision of a physician. Fish, however, is fine to eat.

Ginkgo (Ginkgo biloba)

An extract from the leaf of the ginkgo tree increases blood circulation to the head and other parts of the body. It also acts as an antioxidant and stabilizes cell membranes and scavenges free radicals, particularly in the brain. Although better known for improving mental function in normal people and those with Alzheimer's and other types of depression, ginkgo may be of value in older people with depression. In one study, elderly depressed people with mild depression who had failed to improve on antidepressant drugs did respond when a Ginkgo biloba extract was added (Schubert et al. 1993). Because ginkgo improves circulation, it has been proposed for reversing the sexual dysfunction associated with some antidepressant drugs.

A study conducted in 1999 failed to find that a ginkgo extract alleviated the depression of seasonal affective disorder (Lingaerde et al. 1999).

In rats, Ginkgo biloba extract increases the number of serotonin binding sites in old, but not young rats. This suggests the herb might counteract some of the reduction of serotonin binding sites associated with human aging (Huguet et al. 1994). The recommended dosage is 120 mg a day of a Ginkgo biloba extract standardized to 24-28% ginkgo flavonglycosides.

Caution: Because ginkgo has a mild blood-thinning effect, it could theoretically cause bleeding problems if combined with blood-thinning drugs such as warfarin, heparin, aspirin, or pentoxifylline.

Ginseng

There are two main types of ginseng; the stronger Asian variety (Panax ginseng) and the milder American ginseng (Panax quinquefolius). Eleuthero or Siberian ginseng (Eleutherococcus senticosus), is a relative of ginseng that, though mild, has similar properties. All three plants are adaptogens, substances that help the body adapt to stress. Eleuthero ginseng, however, has not demonstrated antidepressant activity, according to the medical literature.

In the Orient, ginseng has long been prized as an overall tonic and rejuvenator. Practitioners of Traditional Chinese Medicine generally do not recommend daily use of Asian ginseng in people under 40, unless they are in a stressful occupation or environment or are debilitated. Indeed, the only research examining the potential benefit

of ginseng in depression has focused on older women. Specifically, two studies have found that Asian ginseng (*Panax ginseng*) reduces depression and generally improves well-being in menopausal women (Tode et al. 1999; Wiklund et al. 1999).

Caution: *Panax ginseng*, but not *eleuthero*, has mild estrogenic effects. Rarely, it may cause menstrual abnormalities and breast tenderness in women. Asian ginseng can be stimulating. At high doses, side effects such as elevated blood pressure, increased heart rate, and insomnia have been reported. Such stimulation may be augmented when ginseng is combined with caffeine. Avoid Asian ginseng if you are pregnant or have heart irregularities, high blood pressure, or a family history of high blood pressure. (American ginseng and Siberian ginseng don't carry these cautions.) If you have diabetes, do not take Asian or American ginseng on a regular basis unless you are under the care of a physician. Because true ginseng can lower blood sugar levels, insulin dosages need to be adjusted. This herb may also interact with MAO inhibitors and blood-thinners such as warfarin.

Adrafinil

This is a European antidepressant drug that is being successfully used by Europeans and Americans who import it for personal use. The dose is usually 2 tablets twice a day.

Phenylalanine and Tyrosine

Phenylalanine and tyrosine are both amino acids. Our bodies can convert phenylalanine to tyrosine and phenylethylamine (PEA). Tyrosine is the precursor to several neurotransmitters, including norepinephrine and dopamine. PEA is found in high concentrations in chocolate, occurs naturally in the brain, and seems to elevate mood. Low urinary levels have been found in depressed patients. Both amino acids have been shown to increase urinary and brain levels of PEA.

Most neurobiologists believe that insufficient activity of serotonin and norepinephrine is central to the onset of depression. In the 1970s and 1980s, many people were treated with neurotransmitter precursors to alleviate depression. Meyers (2000) did a literature search of the early studies (1970s and 1980s) on neurotransmitter precursor loading, focusing mainly on 5-HTP and tryptophan, the serotonin precursors, and phenylalanine and tyrosine, the dopamine and norepinephrine precursors. He concluded that although it was difficult to draw definitive conclusions from the literature, precursor loading may be of therapeutic value for patients with mild to moderate depression (Meyers 2000).

Insufficient activity of the neurotransmitters serotonin and norepinephrine is a central element of the model of depression most widely held by neurobiologists today. In the late 1970s and 1980s, numerous studies were performed in which depressed patients were treated with

the serotonin precursors L-tryptophan and 5-hydroxytryptophan (5-HTP), and the dopamine and norepinephrine precursors tyrosine and L-phenylalanine. The nature of the studies makes it difficult to draw firm conclusions regarding the efficacy of neurotransmitter precursors for treating depression. While there is evidence that precursor loading may be of therapeutic value, particularly for the serotonin precursors 5-HTP and tryptophan, more studies of suitable design and size might lead to more conclusive results. However, the evidence suggests neurotransmitter precursors can be helpful in patients with mild or moderate depression.

Deprenyl (selegiline) is a drug approved for use in Parkinson's disease that irreversibly inhibits monoamine oxidase type B (MAO-B). Monoamine oxidase is an enzyme that inactivates the monoamine neurotransmitters norepinephrine, serotonin and dopamine.

The action of Deprenyl and L-phenylalanine was studied in 155 unipolar depressed people. Both oral and intravenous administration of the combination showed beneficial effects in 90% of outpatients and 80.5% of inpatients. The researchers concluded that the antidepressive action was based on the accumulation of L-phenylalanine in the brain (Birkmayer et al. 1984).

Phenylalanine comes in two chemical forms: L-phenylalanine and its mirror image D-phenylalanine. When using a 50/50 mix of both forms, called DL-phenylalanine, the typical dosage is 500-1000 mg a day. For tyrosine, the typical recommended dosage is between 500-1500 mg a day.

Caution: Although tyrosine appears to be generally safe, high dosages have been reported to cause nausea, diarrhea, vomiting, or nervousness.

For phenylalanine, dosages over 1500 mg a day can cause anxiety, headache, and mildly elevated blood pressure. People with phenylketonuria (a rare, congenital disease wherein this amino acid cannot be metabolized) should not take it. This amino acid may also increase the side effects of antipsychotic medications.

Safety and appropriate dosing of supplementary phenylalanine and tyrosine has not been established for children, pregnant or nursing women, or people with severe liver or kidney disease, nor has long-term safety been evaluated. Cancer patients should not take extra phenylalanine and tyrosine because these amino acids can contribute to cancer cell proliferation.

DMAE (Dimethylaminoethanol)

DMAE is a naturally occurring nutrient, found in sardines and other foods, that may help relieve depression and/or fatigue. A brain stimulant, DMAE passes through the

blood-brain barrier into the brain, where it helps increase the levels of acetylcholine (a neurotransmitter that plays an important role in both mood and energy levels).

DMAE has been shown to elevate mood; improve memory and learning; and increase intelligence and is even more effective when taken with vitamin B5 (pantothenate). DMAE has also been used with great success in the treatment of attention deficit disorder (ADD) in children and adults.

Depression often manifests itself as fatigue. By directly increasing energy levels and through its ability to alleviate depression, DMAE attacks fatigue on two levels. In summary, this nutrient:

- Increases physical energy
- Decreases daytime fatigue and allows for more natural sleep at night
- Is a safe antidepressant that elevates the mood
- Increases the ability to learn (it can raise IQ while you are taking it)
- Helps reduce "brain debris" called lipofuscin, thereby improving brain function
- Increases longevity as measured in laboratory animals

KH3

KH3 is a European drug that inhibits the enzyme monoamine oxidase (MAO). Inhibiting this enzyme has helped many people to overcome depression, but many standard MAO-inhibitors can have several side effects. KH3 works without producing negative side effects. It is mild and inexpensive.

L-Carnitine

L-Carnitine is an amino acid that has been reported to safely alleviate depression in some people in doses of 1000 mg twice a day. Acetyl-L-carnitine is a form of carnitine that has shown superior absorption effects to regular L-carnitine.

NADH (Nicotinamideadenine Dinucleotide)

NADH enhances brain cell energy and has alleviated depression in studies of people who took 5-10 mg a day. NADH is a coenzyme molecule formed from vitamin B3, found in all living cells and essential for their development.

Thyroxine

High-dose thyroxine, a thyroid hormone usually used for the treatment of hypothyroidism, has been found to alleviate depression in patients with treatment-resistant chronic depression when the thyroxine is taken in concurrence with their normal medication. The effective dosage seems to be 150-300 mcg a day, built up from

an initial dosage of 50 mcg a day. However, it is not clear whether thyroxine cures depression in people with normal thyroid function or whether hypothyroidism is underdiagnosed and the patients responded to the normalization of their thyroid levels (Hickie et al. 1996). Chronic use of high doses of thyroxine is not recommended. Correcting an underlying thyroid hormone deficiency, however, is extremely important. (Refer to the Thyroid Hormone Replacement protocol for specifics.)

Natural Hormone Replacement

Only 20-30% of postmenopausal women in the United States take conventional HRT (using estrogen alone or in combination) even though proper hormone modulation can prevent degenerative disease and improve physical and emotional functioning. Why? The reason is that many women are concerned about the life-threatening effects of synthetic hormones. There are, however, natural hormone therapies available to both men and women who may be suffering the consequences of a deficiency in certain hormones. Scientific studies continue to show that depression is often one of the consequences of hormonal deficiency.

DHEA

Dehydroepiandrosterone (DHEA) is produced by the adrenal glands and gonads. It serves as a parent compound for estrogen and testosterone. It is important for brain function. The brain contains six and a half times more DHEA than any other organ. From puberty, DHEA levels rise steadily, peaking at about the age of 25. By age 70 or 80, there is only about 10% of that peak amount left. Thus, it may be helpful for many people to take supplemental DHEA. Preliminary research suggests that it is helpful in treating adrenal insufficiency and in improving well-being in menopausal women and elderly men (Yen et al. 1995; Morales et al. 1998; Hunt et al. 2000).

Researchers have different theories about how DHEA alleviates depression. Both DHEA and DHEA sulfate (DHEA-S) can cross the blood-brain barrier and interact with the brain directly. DHEA can affect serotonin, GABA receptors, and other brain factors. A 1999 study indicates it might modulate the serotonin signaling pathway (Inagaki et al. 1999). In addition, DHEA is the precursor for estrogen and testosterone which have been reported to enhance mood.

DHEA also has anti-stress effects that may be part of its antidepressant action. Research shows that cortisol, the stress hormone, is elevated in major depression. DHEA counteracts cortisol. Calmness appears to be associated with higher levels of DHEA. People who practice transcendental meditation have higher levels of DHEA than those who do not. People who took part in a stress reduction program were able to increase their DHEA by

100%. At the same time, they reduced their stress hormone by 23%.

Preliminary research suggests that DHEA supplementation in people with adrenal insufficiency and in postmenopausal women and older men improves, among other things, psychological well-being (Hoeger et al. 1999; Hunt et al. 2000; Rigaud et al. 2001). A 1997 study conducted at the University of California at San Francisco School of Medicine found that elderly patients with depression and low DHEA levels respond well to DHEA supplementation, with dosing ranging between 30-90 mg a day (Wolkowitz et al. 1997).

In the first double-blind, placebo-controlled study on DHEA's potential as an antidepressant, 11 patients with major depression were given up to 90 mg a day of DHEA for 6 weeks, and 11 were given a placebo. One week before the study actually started, all patients were given a placebo to weed out people who would respond to a sugar pill. People getting the DHEA received 30 mg a day for the first 2 weeks; 60 milligrams the second 2 weeks; and 90 milligrams the last 2 weeks. The idea of the graduated dose was to bring patients up to the DHEA levels they had when they were 20-30 years old (DHEA declines with age). Although the amount of DHEA was not adjusted individually, the graduated dose approximates what it takes to reach a "youthful" level in most people, according to Dr. Owen Wolkowitz, principle investigator of the study (Wolkowitz et al. 1999).

Some of the participants were taking antidepressants. For these people, the antidepressants were either working partially or not at all. Only people who had been on the same antidepressant for at least 6 weeks without changing were allowed in the study, and no changes could be made in anyone's medication during the study.

After 6 weeks, psychological tests indicated that about half the participants responded to DHEA therapy, with an overall enhancement of mood scores by 30.5%. This is close to the response rate of antidepressant drugs (Wolkowitz et al. 1999).

A study by Bloch et al. (1999) at the National Institute of Mental Health found that 90 mg a day of DHEA for 3 weeks significantly lessened depression among 15 dysthymic patients who were 45 years old and older. A battery of psychological tests was administered, including the Hamilton Depression Rating Scale, the Beck Depression Inventory, a visual analogue scale, and the Cornell Dysthymia Scale. (In addition, a day's worth of cognitive function tests were given, but DHEA did not show a significant effect on cognition in this study. However, the researchers note a trend toward better cognition that could have played out if the study had lasted longer.) Seven symptoms in particular got much better: lack of pleasure; low energy; low motivation; emotional numbness; sadness; inability to cope; and excessive worry. DHEA worked for most people within

10 days. If the supplement was stopped, symptoms came back. Overall, the response rate was 60% which is better than what antidepressants usually do for dysthymia (Bloch et al. 1999).

The researchers subsequently gave patients 450 mg of DHEA a day for 3 more weeks, but found that it was not necessary to go to such a high dose in order to improve mood.

Caution: DHEA supplementation is contraindicated in men and women with hormone-related cancers. Consult the DHEA Replacement Therapy protocol for more information. A blood test can determine if DHEA levels are low. If you need supplementation, periodic blood monitoring can determine whether your DHEA levels have risen to the youthful normal range.

Progesterone

Women experience a gradual loss of the critical sex hormone progesterone throughout adult life. This decline becomes significant as women get closer to menopause. Symptoms of a progesterone deficit include premenstrual discomfort, night sweats, and hot flashes, along with feelings of depression. During and after menopause, natural progesterone synthesis often grinds to a halt, setting the stage for a host of menopausal miseries and degenerative diseases. In addition to making people feel better, progesterone may help to prevent the mental decline that occurs with aging. Progesterone has been shown to increase neuronal energy production and to protect brain cells.

Dr. John Lee (one of the world's foremost experts on progesterone therapy) has found studies showing that 20 times more progesterone is concentrated in brain cells than blood serum levels. He postulates that progesterone may help prevent mental decline in the elderly and that recovery after brain trauma is better if progesterone levels are higher.

Dr. Lee also has pointed out that progesterone has been shown to increase brain cell energy production while suppressing hyperexcitotoxicity. Excitotoxicity occurs when too much (or too little) of neurotransmitters such as glutamate is released from brain cells. This type of toxicity is now considered a cause of brain aging and degenerative neurological disease.

The issue of synthetic versus natural hormones is as important with progesterone as it is with estrogen. Just as the pharmaceutical industry created their dangerous estrogen drug Premarin, they produced a pseudoprogesterone named Provera. As with Premarin, the warning label on Provera is full of dangers including the possibility of birth defects, breast cancer, blood clots, fluid retention, acne, rashes, weight gain, and depression. Such drugs as Provera are classified as "progestins," not as progesterones. The side effects of Premarin and Provera may be the main reason women

stop taking their replacement hormones and are the reason that HRT has such a questionable and spotty reputation.

An alternative to progestins is using natural progesterone products. Products like Life Extension's Pro-Fem use progesterone synthesized from soybeans. Not only are such soy-derived natural progesterones far safer than synthetic drugs, they are as easily utilized as the real progesterone manufactured within the human body. The preferable forms of natural progesterone are creams that are rubbed into appropriate areas of soft tissue such as the chest, breast, underarms, face, abdomen, buttocks, or inner thighs. This route of administration bypasses the liver and allows hormone delivery to the place where it is needed the most. For example, progesterone cream applied to the breasts slows cell proliferation and eases breast pain. As for safety, according to Northrup (1994), "there is virtually no danger of overdose."

In a study conducted at the Mayo Clinic, 176 women using hormone replacement therapy were changed from synthetic progesterone to natural progesterone. Of the total, 147 were menopausal. The remainder of the women were premenopausal with amenorrhea. Women reported significant improvement in eight of nine domains tested in the study, including sleep disturbance; anxiety; depression; somatic symptoms; menstrual problems; cognitive difficulties; sexual functioning; and vasomotor symptoms. The majority of respondents (80%) reported excellent satisfaction with the natural progesterone; 65% thought it was better than any other previous regimen they followed; and more than 70% believed that the current regimen would reduce future health risks (Fitzpatrick et al. 2000). (Consult the Female Hormone Modulation Therapy protocol for additional information on natural hormone replacement.)

Pregnenolone

Pregnenolone is another hormone produced by the ovaries and by the adrenal glands in men and women. It can be very useful for treating depression. Some studies have shown that depressed people have less than normal amounts of pregnenolone in their spinal fluid. Pregnenolone likely works by preventing the brain from being overwhelmed by GABA (gamma-aminobutyric acid) and other hormones that slow its activity.

Although pregnenolone may help relieve depression, it may earn its greatest accolades through its beneficial effect upon the mind, especially the memory. Studies have shown that giving this hormone to older men and women improves their performance on tests of memory and concentration. Research, moreover, indicates that pregnenolone:

- Improves the ability to remember and retrieve information

- Increases the ability to handle stress
- Has a beneficial effect on the myelin sheath membranes, which protect the brain and nervous system
- Helps to keep the nervous system on an even keel

Testosterone

As men enter their 40s, hormonal changes occur that often produce a noticeable effect on physical, sexual, and cognitive energy levels, as well as a loss of feeling of well being. Until recently, these changes were attributed to "growing old," and men were expected to accept the fact that their body was entering into a long degenerative process that would some day result in death.

Data gathered over the last few years indicates that many of the diseases that men begin experiencing over age 40, including depression, abdominal weight gain, prostate, and heart disease, are directly related to hormone imbalances that are correctable with currently available drug and nutrient therapies. Unfortunately, conventional doctors typically prescribe antidepressant, cholesterol-lowering, and other drugs to correct symptoms of a possible hormone imbalance. If doctors checked their male patient's blood levels of estrogen, progesterone, testosterone, prolactin, thyroid, and DHEA (instead of prescribing drugs to treat symptoms), they might be surprised to learn that many problems could be eliminated by adjusting hormone levels to fit the profile of a healthy 21 year old.

A consistent finding in the scientific literature is that testosterone replacement therapy produces an increased feeling of well-being. Published studies show that low testosterone correlates with symptoms of depression and other psychological disorders (Moger 1980; Barrett-Connor et al. 1999; Schweiger et al. 1999; Seidman et al. 1999; Rabkin et al. 1999).

A common side effect of prescription antidepressant drugs is the suppression of libido. Those with depression either accept this drug-induced reduction in quality of life or get off the antidepressant drugs so they can at least have a somewhat normal sex life. If more psychiatrists tested their patients' blood for free testosterone and prescribed natural testosterone therapies to those with low free testosterone, the need for libido-suppressing antidepressant drugs could be reduced or eliminated. As previously described, testosterone replacement often enhances libido, the opposite effect of most prescription antidepressants.

One study showed that patients with major depression experienced improvement that was equal to that achieved with standard antidepressant drugs (Rabkin et al. 1999).

Androderm is one of several natural testosterone-replacement therapies that can be prescribed by doctors. A 12-month clinical trial using this FDA-approved drug resulted in a statistically significant reduction in the depression score (6.9 before versus 3.9 after). Also noted were highly significant decreases in fatigue: from 79% before the patch to only 10% after 12 months (Androderm Testosterone Transdermal System). According to Jonathan Wright, M.D., co-author of *Maximize Your Vitality & Potency*, the following effects have been reported in response to low testosterone levels:

- Loss of ability to concentrate
- Moodiness and emotionality
- Touchiness and irritability
- Great timidity
- Feeling weak
- Inner unrest
- Memory failure
- Reduced intellectual agility
- Passive attitudes
- General tiredness
- Reduced interest in surroundings
- Hypochondria

The above feelings can all be clinical symptoms of depression. Testosterone replacement therapy has been shown to alleviate these conditions. Testosterone thus has exciting therapeutic potential in the treatment of depression in men.

Testosterone, however, is one of the most misunderstood and mistakenly maligned hormones. Body builders tarnished the reputation of testosterone by injecting large amounts of it into their youthful bodies. Testosterone abuse can produce detrimental effects, but this has nothing to do with the benefits a man over age 40 can enjoy by properly restoring his testosterone to a youthful level.

Some early studies showed testosterone replacement therapy to be ineffective in treating the symptoms of aging because the testosterone showed only a temporary benefit, with the positive effects wearing off within a few weeks. These studies failed to identify that exogenously administered testosterone readily converts to estrogen in the body. The higher estrogen level negates the benefits of the exogenously administered testosterone. The solution to the estrogen-overload problem is to block the conversion of testosterone to estrogen in the body so that aging men can restore their strength, stamina, cognitive function, heart function, sexuality, and their outlook on life, i.e., alleviate

symptoms of depression (Baker et al. 1976; Berkovitz et al. 1985). Several natural supplements described in the Male Hormone Modulation Therapy protocol will help remove excess estrogen from the blood or inhibit its formation from testosterone.

Testosterone is much more than a sex hormone. There are testosterone receptor sites in cells throughout the body, most notably in the brain and heart. Youthful protein synthesis for maintaining muscle mass and bone formation requires testosterone. Testosterone improves oxygen uptake throughout the body, helps control blood sugar, regulate cholesterol, and maintain immune surveillance. The body requires testosterone to maintain cardiac output and neurological function. Of critical concern to psychiatrists are studies showing that men experiencing depression have lower levels of testosterone than age-matched controls. For some men, elevating free testosterone levels could prove to be an effective antidepressant therapy. (Men who have depression can refer to the Male Hormone Modulation Therapy protocol). This describes safe ways of boosting free testosterone levels in a way that can alleviate or eliminate certain types of depression. Women should refer to the Female Hormone Replacement Therapy and the DHEA Replacement Therapy protocols for more information on what they can do to adjust their hormone status to improve their mood and alleviate depression.

Vitamins and Minerals to Fight Depression

A host of vitamins and minerals help maintain normal brain function. A deficiency of any one of them can lead to depression and other mental disorders. The following are some you may want to consider.

Folic Acid

Folic acid is a member of the B family of vitamins. Low levels have been linked to depression and bipolar disorder in a number of studies. Insufficient folic acid is one of the most common nutritional deficiencies, and one third of depressed adults are low in this vitamin (Alpert et al. 1997). Other nervous system disorders associated with folic acid deficiency include dementia, schizophrenia-like syndromes, insomnia, irritability, forgetfulness, organic psychosis, peripheral neuropathy, myelopathy, and restless legs syndrome (Young et al. 1989).

Many studies have examined folic acid's ability to fight depression, including one in which 36 patients with either endogenous depression or schizophrenia had low levels of folic acid: 13 of them were given standard treatment plus folic acid, while the remaining 26, acting as the control group, received only the standard treatment. Results were that 92% of the folic acid group made a full recovery, compared with only 70% of the control group. Folic acid was especially helpful to those with endogenous depression. Those who received the vitamin spent only 23.3 days in the hospital, while those

in the control group averaged 32.9 days (Young et al. 1989, 1993; Carney 1995; Kelly 1998).

Studies have also linked low folic acids levels with poor response to antidepressants. So does folic acid supplementation enhance antidepressant efficacy? According to a British study, the answer is yes (Coppen et al. 2000). Researchers took 127 depressed patients and gave half of them 20 mg of fluoxetine (Prozac) plus 500 micrograms of folic acid or fluoxetine plus a placebo. In women, the addition of folic acid significantly improved the antidepressant action of fluoxetine and reduced the side effects related to this medicine. Why did men not reap similar benefits? They seem to require higher doses. The 500-mcg dose significantly increased blood levels of this vitamin, more so in women than in men. In women, but not men, the vitamin supplement reduced levels of homocysteine, an amino acid damaging to arterial linings and nerves (Coppen et al. 2000).

The effectiveness of supplementation may be due to the fact that people with folic acid deficiency have decreased synthesis of serotonin and dopamine. It has been reported that people with folic acid deficiencies do not respond to Prozac as well as people who have sufficient levels. Folic acid deficiency alone can cause severe depression, as can vitamin B12 deficiency.

Note: The usual methods of measuring these two vitamins in people is not very accurate. Additionally, because they work together, it is sometimes hard to tell which vitamin is deficient.)

The RDA for folic acid is 400 mcg a day. If you are depressed, you may want to take 800 mcg a day. You also may want to eat green leafy vegetables (especially spinach and kale), whole wheat bread, wheat germ, bananas, and other foods containing this member of the B family of vitamins.

Caution: Folic acid supplementation can mask a vitamin B12 deficiency resulting in nerve damage. For this reason, it's best to take a balanced B-vitamin complex that includes at least 300 mcg of vitamin B12. Some drugs (e.g., methotrexate) work by blocking the activation of folic acid. If you are taking such medication, do not supplement with folic acid without consulting your physician.

Vitamin B12

Vitamin B12 (also called cobalamin) is needed by the body only in very small quantities. A major deficiency causes a serious disease called pernicious anemia. Lesser deficiencies, which are common among the elderly, can produce depression, confusion, and other symptoms. B12 may help to fight depression by inhibiting monoamine oxidase (MAO), an enzyme that metabolizes some of the neurotransmitters that help to elevate mood. In that sense, B12 works like the monoamine oxidase inhibitors (MAOI), drugs prescribed

for depression. Because the vitamin is not as strong as these drugs, it lacks their side effects.

Although B12 deficiency is not as common as folic acid deficiency, it can contribute to depression, particularly in the elderly. We know that perhaps 20% of senior citizens have difficulty absorbing B12 from their intestines which means that they can have a deficiency even if there is plenty of the vitamin in their food. The resultant B12 deficiency may be one reason depression is more common among the elderly. Fortunately, the treatment is simple, inexpensive, and safe.

You will find this vitamin in beef liver, chicken liver, clams, oysters, and sardines, with smaller amounts in eggs, many fish, and cheeses. Vegetarians who eat no foods coming from animals should scrutinize their diets and consider taking supplements to make sure they are getting enough of this vitamin. For the treatment of depression, 500 mcg of sublingual B12 (methylcobalamin) twice a day is recommended.

Vitamin B6

Vitamin B6 (also known as pyridoxine) is needed for conversion of the amino acid tryptophan to serotonin. While serious deficiencies of B6 are not common, minor deficiencies are and they can cause depression, convulsions, and other problems. Alcoholics are more likely to be lacking this vitamin as are those who have heart disease, liver disease, diarrhea, or other illnesses or injuries. Women who are pregnant, lactating, or taking oral contraceptives may also be at risk for B6 deficiency.

Levels of this vitamin are often low in people with depression, particularly women taking oral contraceptives, because the synthetic hormones antagonize B6. For this reason, B6 supplements may be particularly helpful for women who develop depression as a result of taking oral contraceptives.

Vitamin B6 has also been shown to ease the emotional difficulties associated with premenstrual syndrome and as part of the treatment for depression in postmenopausal women. Furthermore, a study by Bell et al. (1992) (Department of Psychiatry at the Harvard Medical School) found that when 14 elderly patients with depression took 10 mg each of vitamins B1, B2, and B6, this B combination augmented the efficacy of tricyclic antidepressant treatment. Start out with 50 mg of supplemental B6 in divided doses or take it as part of a good B-complex supplement. Eat plenty of food rich in this vitamin such as brewer's yeast, sunflower seeds, soybeans, walnuts, lentils, lima beans, hazelnuts, brown rice, avocados, and many other foods.

Vitamin B1

Vitamin B1 (also known as thiamin) was the first of the B family of vitamins to be discovered. A severe lack of this vitamin leads to beriberi which causes confusion, high blood pressure, problems with the heart, and other

symptoms. A more subtle deficiency leads to depression and fatigue, as well as constipation and numbness or a "pins-and-needles" sensation in the legs. Taking B1 supplements, or in some cases simply eating lots of foods rich in this vitamin, has resolved side effects of antidepressant medication, such as dry mouth, insomnia, and stomach upset--inexpensively and with no side effects. Begin with 100 mg a day of vitamin B1 or look for a B-complex that contains at least 100 mg of this vitamin. Eat plenty of foods containing B1, including kale, spinach, turnip greens, green peas, lettuce, cabbage, and many other vegetables.

Vitamin B3

Vitamin B3 (also known as niacin or niacinamide) helps to "beat the blues." The body needs B3 to convert the amino acid tryptophan into serotonin, a neurotransmitter that plays an important role in keeping us happy. Not enough B3 means not enough serotonin, with resultant depression and anxiety. Prozac and the other SSRIs work by increasing brain levels of this neurotransmitter.

The vitamin B3 story began in the early part of the 20th century, when an old disease called pellagra made a resurgence in the southern United States. Pellagra causes the "4Ds:" diarrhea, dermatitis, dementia, and death. The rapid rise in the number of pellagra cases was caused by refined corn meal.

You see, many Southerners lived on the "3M Diet," which consisted of meat (mostly fatback), molasses, and meal (cornmeal), but improvements in food refining and railroad transportation led to many Southerners dropping "whole" corn meal in favor of the refined version. Unfortunately, the outer husk of the corn is discarded in the refining process, along with vitamin B3.

Without sufficient B3, the body cannot convert tryptophan into serotonin, leading to deterioration in mood. The treatment is raising B3 intake. When the U.S. government ordered that certain vitamins be added back into refined flour and other foods, the pellagra problem receded.

In 1950, physician Abram Hoffer followed up on the B3/pellagra connection by treating schizophrenia patients with a nutritional program featuring B3. Many of the patients improved immediately and were still doing fine when rechecked 15 years later. These were not pellagra patients. Instead, they were suffering from "vitamin dependency," a condition in which they need larger amounts of a vitamin or vitamins than do the rest of us. No studies have investigated the benefits of this B-vitamin in treating depression.

Caution: Because high-dose niacin can be toxic to the liver, it is not a good idea to take this vitamin alone unless a physician monitors your liver function. Niacin can also impair glucose tolerance which means diabetics also need a physician's supervision when supplementing

with this vitamin. A more minor annoyance is the skin flushing that can occur, particularly with the initial dose.

The safest plan (and one that does not require a physician's blessing) is to take a balanced B-complex that contains 50 mg of niacin and also eat niacin-rich foods such as torula or brewer's yeast, brown rice, whole wheat, seeds, nuts, peanuts, and other legumes.

Vitamin B2

Vitamin B2 (also known as riboflavin) has been linked to mood. In 1973, researchers discovered that if normal, healthy men were given diets nearly devoid of this vitamin, they would soon score higher ratings on tests designed to detect depression. Take 50 mg of B2 or a B-complex tablet each day. Because it is also a good idea to eat foods containing this vitamin, add asparagus, broccoli, spinach, almonds, wheat germ, millet, and whole wheat bread to your diet.

Choline

Choline is a member of the B family of vitamins that is converted by the body into the neurotransmitter acetylcholine which plays an important role in learning and memory. Choline is more effective when taken with vitamin B5 which helps convert choline to the neurotransmitter acetylcholine. Some depressed people get worse when they take choline, however. You may find that 2000 mg a day, taken in divided doses, is a good starting point. Also eat plenty of choline-containing foods, including eggs, brewer's yeast, soybeans, green peas, and peanuts.

Inositol

An unofficial member of the B vitamin family, inositol is present in all tissues with highest levels in the brain and heart. It functions closely with choline and is also a component of cell membranes. Proper action of several neurotransmitters, including serotonin and acetylcholine, requires inositol.

In 1995, Levine conducted two preliminary studies that found inositol benefited people with depression (Levine et al. 1995a, 1995b). In 1997, he investigated the effects of inositol supplementation in patients with various neuropsychiatric problems, including depression. For 4 weeks, 28 depressed patients took 12 grams a day of inositol. At the end of the study, people experienced significant improvement compared to placebo treatment. No side effects or changes in laboratory tests were noted (Levine 1997).

To match the large amount of inositol used in this study, it is more convenient to take powdered inositol dissolved into liquids than capsules. Scott Shannon, M.D., President of the American Holistic Medical Association and an integrative psychiatrist practicing in Fort Collins, Colorado, finds that as little as 1000 mg twice daily is often effective.

Vitamin D

Vitamin D is considered both a vitamin and a hormone because our bodies, given exposure of the skin to sunlight, can produce it. During the winter, there is less sunlight and we also tend to spend less time outdoors. At this time of year, we are most vulnerable to becoming low in vitamin D. Winter is also the time when vulnerable people develop seasonal affective disorder or "winter blues." One treatment for this disorder involves the use of "light boxes" to artificially increase exposure to light. One theory is that this works by stimulating, via the eye's retina, the brain's pineal gland. It may also promote vitamin D production.

A study by Lansdowne et al. (1998) supports the vitamin D theory. During the Australian winter, researchers gave 44 healthy students either 400 IU, 800 IU, or no vitamin D3 for 5 days. Both dosages of vitamin D3 significantly enhanced mood. Because vitamin D is a fat-soluble vitamin, it can accumulate in tissues and become toxic. Vitamin D3 can safely be taken in daily doses up to 1400 IU.

Vitamin C

Vitamin C (also known as ascorbic acid) acts as an antioxidant and helps to maintain the immune system, manufacture collagen, guard against cancer and heart disease, reduce the risk of cataracts, and otherwise encourages health. Deficiency of vitamin C can lead to depression and mental confusion, among other problems. In fact, depression is the first clinical symptom detected when humans are deliberately deprived of vitamin C for purposes of study.

One study found that vitamin C intake was lower among depressed women who attempted suicide than among those who did not. And when researchers compared the amount of vitamin C in the blood of 885 psychiatric patients and 110 healthy controls, the psychiatric patients were found to have significantly lower levels. No studies, however, have examined the effects of supplementation (Schorah et al. 1983).

If you wish to supplement your diet with vitamin C, a 1000-mg capsule is a good place to start. This vitamin also is found in red chili peppers, guavas, parsley, green and sweet red peppers, broccoli, strawberries, oranges, mangoes, cantaloupe, and many other foods.

Potassium

Potassium is a mineral that helps to keep the heart beating regularly and has also been linked to depression. Mood upsets, fatigue, and weakness, all symptoms of depression, have been associated with low levels of the mineral. These problems can occur if there is not enough of the mineral inside the cells, even if there is enough potassium in the body fluids (outside the cells). Lower levels of potassium in the brain have been found in suicide victims. Replenishing potassium stores helps to reverse the fatigue and muscle weakness that

may be associated with depression--or may be present on its own.

Unless potassium levels are dangerously low, it is probably best to get more of the mineral by increasing your intake of foods high in potassium, such as bananas, nonfat milk, oranges, and fresh peas. Enjoying four to five servings of fresh vegetables and fruit a day is usually enough to ensure that you are getting enough of this mineral.

Caution: Although many depressed people benefit from natural treatments, none of the above therapies may be effective in patients who have serious clinical depression or manic depression. Such patients may require FDA-approved antidepressant drugs and/or lithium. Anyone who has clinical depression of any type should be under the care of a physician.

Mood-Boosting Lifestyles

Exercise

Depressed people tend to be less physically active than their happier counterparts. Part of the problem is that to the depressed person everything seems futile, hopeless, and requiring too much energy. Hard as this sounds, if you feel sad and can make yourself get off the couch and move, chances are you will feel better.

Several studies have shown that both aerobic exercise and strength training significantly reduce depressive symptoms. Unfortunately, habitual physical activity has not been shown to prevent the onset of depression (Paluska et al. 2000). In one of the most impressive testaments to the healing power of exercise, researchers from Duke University Medical Center divided 156 depressed men and women into three treatment groups: aerobic exercise (using a treadmill or stationary bicycle for 30 minutes, 3 times a week); antidepressant treatment with Zoloft (sertraline); or combined exercise and medication. Initially, people who took Zoloft improved faster, but after 16 weeks of treatment, all three groups experienced similar benefits. In other words, exercise was ultimately as effective as antidepressant therapy (Blumenthal et al. 1999).

Six months after the trial ended, the researchers checked in with these volunteers and found that the benefits of exercise endured. People from the exercise-only group had significantly lower relapse rates than either those in the Zoloft-only or Zoloft-plus-exercise groups (Babyak et al. 2000). Why taking a pill undermined long-term benefits is not clear. Perhaps the people who exercised felt a greater sense of control and satisfaction. A study of a small group of obese women found that a 6-month program of exercise and relaxation training, although it did not significantly shed pounds, significantly improved depression (Hayward et al. 2000). Among breast cancer survivors, women who regularly

exercise have significantly less depression and anxiety than those who do not (Segar et al. 1998).

Does exercise have to be aerobic to boost mood? No. Martinsen et al. (1998) compared aerobic to nonaerobic exercise and found that both treatments significantly improved depression, with no significant difference between the two.

Yoga and Meditation

Several studies have shown that various types of yoga and meditation can reduce symptoms of anxiety and stress. In many people, stress triggers depression and anxiety accompanies low mood. It makes sense that yoga and meditation might lift depression. A study randomly assigned 45 hospital inpatients with newly diagnosed depression to one of the treatment groups. One group took six sessions a week of Sudarshan Kriya Yoga (SKY) for 4 weeks. This type of yoga alternates three cycles of rhythmic hyperventilation with normal breathing, then finishes with a quarter hour tranquil period. The second group received electroconvulsive therapy (ECT) three times a week for the 4 weeks. The third group received 150 mg of imipramine a day for 4 weeks. All three treatments significantly lowered measurements of depression, with greatest benefits for those receiving ECT. The authors concluded, "although inferior to ECT, Sudarshan Kriya Yoga can be a potential alternative to drugs in melancholia as a first line treatment" (Janakiramaiah et al. 2000).

In another study, researchers assigned a group of 87 college students to take one of three classes: swimming, yoga, or a lecture (which served as the control treatment). Compared to sitting in a lecture, yoga and swimming reduced both depression and also feelings of anger, tension, fatigue, and confusion. This study not only reinforces the psychologic benefit of yoga, but also shows again that exercise need not be aerobic to enhance mood (Berger et al. 1992).

In addition to reducing anxiety, meditation seems to buoy mood. In a study involving patients enrolled in a "happiness enhancement program," half of the people also learned to meditate. This group improved significantly more than the group who did not meditate (Smith et al. 1995).

Relaxation

One study compared the relative effectiveness of cognitive behavioral therapy (examining and repatterning one's thoughts and actions), relaxation training, and a tricyclic antidepressant. Both non-drug treatments were superior to the tricyclic antidepressant medication. Cognitive behavioral therapy was slightly, but not significantly better than relaxation training (Murphy et al. 1995).

Receiving a massage is a wonderful way to unwind. Among its other virtues, massage therapy diminishes depression and stress (Field 1998).

Acupuncture

Traditional Chinese Medicine seeks to restore the body's balance, chiefly through the use of acupuncture and herbs. One study found that acupuncture significantly improved symptoms in patients with depression or anxiety (Eich et al. 2000). Another study found that patients who received acupuncture plus an antidepressant improved more than those who received only the drug (Roschke et al. 2000).

Summary

Although depression is a serious illness, it is sometimes possible to treat the underlying cause without taking synthetic drugs. Several natural remedies have brought relief to many people who have depression:

SAME, a natural substance derived from the amino acid methionine, works faster than the tricyclic antidepressants, but with far fewer side effects. Dosages typically range from 400-1600 mg daily. Some practitioners recommend gradually increasing the dosage to avoid mild and transient nausea occasionally seen at the start of treatment. Joseph Pizzorno, N.D. (author of *Total Wellness* and coauthor of *Encyclopedia of Natural Medicine*) recommends 200 mg twice a day for 2 days, then 400 mg twice a day on days 3 through 9, then 400 mg three times a day on days 10 through 19, then 400 mg four times daily thereafter.

The usual dosage for St. John's Wort is 300 mg of the herb, three times a day, standardized to 0.3% hypericin, one of the active ingredients. Take either a 300-mg dose at breakfast, lunch, and dinner or take two of the 300-mg doses in the morning and the third with dinner. Not everyone needs a total of 900 mg a day; two studies found a mere 500 mg of St. John's Wort extract equivalent to imipramine and fluoxetine.

Caution: Do not combine with antidepressant medication. Because St. John's Wort can speed the liver's breakdown of drugs, talk to your physician before combining this herb with any prescription medications. If you are taking SAME, you do not need to take St. John's Wort.

Omega-3 fatty acids seem to influence neurotransmitter function. Depressed people tend to have low levels of omega-3 fatty acids in their diet and in their cell membranes. You can take between 400-1000 mg of DHA and 400-1000 mg of EPA. Mega EPA provides 800 mg of EPA and 600 mg of DHA in two softgels.

Ginkgo biloba improves circulation to the brain and stabilizes and protects nerve cells. Studies show it

improves cognition and may also help relieve depression in older people. The recommended dosage is 120 mg daily of a standardized extract.

DHEA is a natural hormone that enhances brain functioning and promotes well-being. Dosages typically range from 15-75 mg. (Refer to the DHEA Replacement Therapy protocol for safety information.)

Natural progesterone applied subdermally is recommended over synthetic formulas that present increased risk of side effects. Natural progesterone should be considered as part of a natural hormone replacement regimen in menopausal women. Pro Fem is a natural progesterone made from soy and applied to the soft tissue areas of the body. It may be used by both men and women under different dosing regimens. Follow directions on label for initial treatment and maintenance. Pro Fem is also recommended in the treatment of osteoporosis.

Pregnenolone is another natural hormone that is often found in below-normal amounts in people with depression. Pregnenolone can be taken in doses of 50-200 mg daily. If more than 50 mg of pregnenolone is taken, it should be in divided doses.

DMAE (found in sardines and other foods) has been shown to elevate mood and is even more effective when taken with vitamin B5 (pantothenate). Recommended dosage is 300-900 mg daily depending upon stimulation tolerance.

L-Carnitine is an amino acid that can alleviate depression in some people in doses of 1000 mg twice a day. Acetyl-L-carnitine is better absorbed.

NADH (nicotinamide-adenine dinucleotide) enhances brain cell energy and has alleviated depression in studies of people who took 5-10 mg daily.

Phenylalanine and tyrosine are two amino acids that the body uses to make neurotransmitters. Phenylalanine comes in two chemical forms, L-phenylalanine and its mirror image D-phenylalanine. When using a 50/50 mix of both forms, called DL-phenylalanine, the typical dosage is 500-1000 mg daily. For tyrosine, the typical recommended dosage is between 500-1500 mg daily. Do not take these amino acids if you have cancer or suffer uncontrolled hypertension.

Folic acid (a B vitamin) deficiency is common in many people with depression; 400 mcg a day is the RDA; however, people who are depressed may want to take 800 mcg a day.

Vitamin B12 (cobalamin) helps fight depression by inhibiting monoamine oxidase (MAO), an enzyme that "attacks" and destroys certain neurotransmitters that

help to elevate mood; 500 mcg sublingually, twice a day is recommended.

Vitamin B6 (pyridoxine) is also needed for conversion of tryptophan to serotonin. A deficiency of B6 is often found in pregnant or lactating women, in women taking oral contraceptives, and in alcoholics. Doses of 100-300 mg a day are recommended.

Vitamin B1 (thiamin) deficiency can lead to depression and fatigue; 100 mg daily is recommended. You can also find this amount in most B-complex formulas.

Vitamin B3 (niacin) converts tryptophan into serotonin, an important neurotransmitter that helps us stay happy. The safest bet (and one that does not require a physician's blessing) is to take a balanced B-complex that contains 50 mg of niacin and eat niacin-rich foods such as torula or brewer's yeast, brown rice, whole wheat, seeds, nuts, peanuts and other legumes.

Vitamin B2 (riboflavin) deficiency can lead to depression; 50 mg daily is recommended or a balanced B-complex that contains this amount.

Choline plays an important role in learning and memory; 2000 mg daily in divided doses is recommended.

Inositol is a B vitamin relative shown to improve depression and anxiety. Although studies have used 12,000 mg daily, some psychiatrists find that 1,000 mg twice daily is often effective.

Vitamin D supplementation was shown to improve seasonal affective disorder or "winter blues." It can be taken as 400 IU daily. Because it is a fat-soluble vitamin and can accumulate in tissues, do not exceed 1400 IU daily.

Vitamin C (ascorbic acid) deficiency has been found in depressed people. A 1000-mg supplement is a good place to start. Also eat plenty of vitamin C-rich fruits and vegetables.

Potassium is a mineral that has been linked to depression. Unless levels are dangerously low in the body, potassium should be replenished by natural foods such as bananas, nonfat milk, oranges, and fresh peas.

Testosterone levels may decrease in men over 40. Low levels of testosterone may lead to depression. (Consult the Male Hormone Modulation Therapy protocol for indications and dosing recommendations. Women should consult the DHEA Replacement Therapy and Female Hormone Replacement Therapy protocols for more information on hormone levels and depression.)

Alcohol, caffeine, and sugar, known to cause abrupt changes in energy and mood, should be avoided.

Exercise, yoga, meditation, and relaxing activities such as massage can buoy mood. Consider incorporating them into your lifestyle.

Note: Many of the vitamins and minerals recommended in this protocol can be obtained in the Life Extension Mix multi-nutrient formula.

For more information

Contact the National Depressive and Manic Depressive Association (800) 826-3632.

Product availability

SAME, St. John's Wort extract, DHEA, ginkgo, Life Extension Mix (containing essential vitamins and minerals), NADH, progesterone, pregnenolone, Cognitex (containing choline), acetyl-L-carnitine, B vitamins, methylcobalamin lozenges, DMAE, Mega EPA, DL-phenylalanine, L-tyrosine, and other products are available by calling (800) 529-1163. Natural testosterone is a prescription drug.

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