

Anxiety

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Anxiety disorders are illnesses that cause people to experience exaggerated fright and apprehension in response to external or internal stimuli. These conditions are often related to the biological and psychological makeup of the individual and may be familial in nature. If untreated, these illnesses can significantly reduce productivity and impair a person's ability to function in daily life. Anxiety disorders affect approximately 24 million American adults (Narrow WE et al 2002). Nearly 15 percent of adults will experience an anxiety disorder in their lifetime (Bourden KH et al 1992; Schatzberg AF 1991).

Anxiety can occur independently or in conjunction with other psychiatric or medical conditions, such as depression, phobias, chronic fatigue, cardiac disease, or respiratory compromise. Moreover, chronic anxiety is associated with a higher risk of morbidity and mortality from cerebrovascular and cardiovascular diseases, such as hypertension, cardiac ischemia, and arrhythmias, and it predisposes people to a range of other disorders (Muller JE et al 2005; Weissman MM et al 1990; Coryell W 1986, 1988). People with severe anxiety disorders who experience adverse life events such as divorce or financial disaster may be at increased risk of suicidal behavior (Allgulander C et al 1991).

Typically, anxiety disorders are treated with an array of psychoactive medications that alter or increase levels of neurotransmitters. Unfortunately, these medications also carry sometimes significant side effects, including the risk of dependency. A number of nutrients have been identified that act along pathways similar to those of prescription medications or have a general anti-anxiety effect. In addition, Life Extension has uncovered exciting new research that may alter the way medical science one day looks at anxiety disorders. Elevated homocysteine, which has been implicated in heart disease and depression, may also play a role in anxiety disorders. Also, abnormal hormone levels may exacerbate anxiety disorders. On the basis of the newest research, Life Extension believes that people suffering from anxiety disorders should test for elevated homocysteine and abnormal hormone levels and correct these if necessary.

TYPES OF ANXIETY DISORDERS

Generalized anxiety disorder. Generalized anxiety disorder affects about 4 million adult Americans and is characterized by chronic, excessive worry and tension (Narrow WE et al 2002; Wittchen HU 2002; Wittchen HU et al 1994). Other symptoms may include restlessness, fatigue, difficulty concentrating, irritability, muscle tension, and sleep disturbances. A diagnosis of generalized anxiety disorder is confirmed when an individual experiences excessive worrying about everyday problems and three or more of the above symptoms more days than not for at least six consecutive months (American Psychiatric Association 2000).

Panic disorder. Panic disorder is characterized by repeated episodes of intense fear that appear often without warning and with varying frequency. Panic disorder afflicts about 2.8 million Americans, and its prevalence appears to have been increasing since 1980 (Goodwin RD 2003; Narrow WE et al 2002). Symptoms may include palpitations, accelerated heart rate, sweating, trembling, shortness of breath, feeling of choking, chest pain, nausea or abdominal distress, dizziness, feelings of unreality, fear of losing control or dying, and chills or hot flashes. A panic disorder is diagnosed when a person experiences recurrent, unexpected panic attacks and at least one of the attacks has been followed by one or more of the following: persistent concern about future attacks, worry about the implications of the attack, and a significant change in behavior related to the attacks (American Psychiatric Association 2000).

Obsessive-compulsive disorder. Obsessive-compulsive disorder (OCD) is characterized by recurrent and persistent thoughts and/or impulses and repetitive ritualistic activities and behavior. These rituals provide only temporary relief from anxiety (Jenike MA 2004). OCD affects approximately 4.3 million American adults and 2 to 3 percent of the world's population (Jenike MA 2004; Narrow WE et al 2002). Individuals with OCD may have unwanted thoughts or images or an urgent need to perform certain rituals (e.g., touch, check, or count things repeatedly).

Phobia. Phobias are seemingly inexplicable fears. Social phobias (social anxiety disorders) are characterized by excessive self-consciousness, with an intense fear of humiliation or embarrassment, and feelings of being watched and judged by others while in public situations. These feelings sometimes begin weeks in advance of an event. Social phobias affect about 6.5 million Americans (Narrow WE et al 2002). Physical symptoms of social phobias include blushing, sweating, trembling, nausea, and difficulty speaking. The diagnosis of social phobias is made when people experience a marked and persistent fear of one or more social or performance situations they are exposed to, avoid, or have symptoms of anxiety toward (American Psychiatric Association 2000).

Posttraumatic stress disorder. Posttraumatic stress disorder (PTSD) is precipitated by experiencing or witnessing a traumatic or terrifying life event, such as a serious accident, a violent crime, or a natural disaster. People with PTSD may relive the event in

nightmares or have disturbing recollections of it during waking hours. Ordinary events can trigger flashbacks that may result in a loss of reality, causing the person to believe the event is happening again. Approximately 5.2 million Americans are affected by PTSD, which can occur at any age (Narrow WE et al 2002; Margolin G et al 2000).

Symptoms associated with PTSD include inability to sleep, hypersensitivity to external stimuli, feelings of detachment or numbness, and loss of memory of the time surrounding the traumatic experience. In addition to the presence of these symptoms, doctors considering a diagnosis of PTSD consider whether a patient persistently reexperiences the traumatic event, such as by recollecting it, dreaming about it, experiencing hallucinations or flashbacks, or physically reacting to internal or external cues that symbolize or resemble an aspect of it. For a diagnosis of PTSD, symptoms must be present for more than one month but may occur years after the traumatic event (American Psychiatric Association 2000).

ANXIETY, HOMOCYSTEINE, AND B VITAMINS: AN AREA OF EMERGING RESEARCH

Various studies have conclusively linked decreased folate and elevated homocysteine to depressive disorders. However, little is known about the connection between elevated homocysteine and anxiety disorders. In recent years, a number of research teams around the world have conducted preliminary studies examining the possible role of elevated homocysteine in anxiety. The results have been intriguing.

In one study, for instance, 23 patients with OCD were evaluated for folate and homocysteine levels, and their levels were compared with those of healthy control participants. Researchers found that folate levels were significantly lower in OCD patients than in controls and homocysteine levels were higher. Furthermore, the more severe the OCD, the more severe the folate deficiency (Atmaca M et al 2005). While this study may shed some light on a possible underlying cause of anxiety disorders, the research needs to be duplicated by additional research groups. However, Life Extension recommends that people strive for a homocysteine level of less than 8.00 mmol/L, which has been shown to protect against heart disease. In light of this research, it may be prudent for people with anxiety disorders to also measure and supplement with folic acid and B vitamins to lower homocysteine, especially if they are also depressed.

DIAGNOSIS AND TREATMENT OF ANXIETY DISORDERS

No single laboratory test can diagnose anxiety; instead, medical professionals rely on clinical judgment to make the diagnosis. There are also several screening tests available to help determine the cause, type, and severity of anxiety (Rush AJ Jr et al 2000). Once an anxiety disorder has been diagnosed, treatment will often integrate several approaches, including diet and lifestyle changes, relaxation and massage therapy, psychotherapy (behavioral therapy or cognitive-behavioral therapy), supplementation, and drug intervention.

Cognitive-behavioral therapy involves the modification of thinking patterns that control the thoughts and sensations accompanying anxiety and fear. It helps individuals recognize cognitive distortions, or ways in which they perceive the world that are not accurate. Patients are then shown how these distortions produce reactions such as anxiety and panic, and they are offered special tools to detect when their thinking is distorted and methods to replace distorted thoughts with more accurate ones. Cognitive-behavioral therapy is an effective first-line treatment for anxiety disorders (Otto MW et al 2004). Cognitive-behavioral therapy has been shown to be effective in treating all the anxiety disorders (Rouillon F 2004; Harvey AG et al 2003; Tonks A 2003; Heimberg RG 2002; March JS et al 2001; Goldberg C 1998; Barlow DH 1997; Wakefield M et al 1997).

Behavior therapy uses several techniques, such as diaphragmatic breathing and exposure therapy. Diaphragmatic breathing teaches people how to control the physical signs of anxiety by taking slow, deep breaths, which helps control hyperventilation. Exposure therapy relies on small and progressive exposures to whatever frightens them. The gradual, safe exposures help anxiety sufferers build confidence and control their anxiety.

Drug therapy is often used in combination with psychotherapy to manage the biochemical and physiological abnormalities that produce anxiety, including alternations in the levels of serotonin, norepinephrine, and cortisol (the stress hormone). The following types of drugs are frequently prescribed to treat anxiety disorders:

- **Benzodiazepines** act in part by modulating and extending the life of gamma-aminobutyric acid (GABA), a brain neurotransmitter (Kent JM et al 2002). Benzodiazepines can relieve anxiety symptoms quickly. However, these drugs can become habit forming, and some people can develop a tolerance to them, which requires increased dosage. When benzodiazepines are reduced or removed, some individuals experience withdrawal symptoms, such as life-threatening seizures, confusion, memory loss, hyperanxiety, and reemergence of the original symptoms (Nemeroff CB 2003). Commonly prescribed benzodiazepines include Valium® (diazepam), Xanax® (alprazolam), Klonopin® (clonazepam), and Ativan® (lorazepam).
- **Nonbenzodiazepines** such as azipirones are anti-anxiety drugs that don't entail the tolerance and dependency issues associated with benzodiazepines. These drugs are partial serotonin receptor agonists. BuSpar® (buspirone) is a member of the azipirone class prescribed to treat general anxiety disorder. Side effects include nausea, headaches, and dizziness.

- **Antidepressant drugs** are effective for treating anxiety, especially when it occurs in conjunction with depression. Types of antidepressant drugs include selective serotonin reuptake inhibitors (SSRIs) and the less commonly used tricyclic antidepressants and monoamine oxidase inhibitors. These drugs may have significant side effects. In 2004 the US Food and Drug Administration announced that the most popular class of antidepressants, SSRIs, must carry a strong black box warning advising patients of the dangers of increased suicide among adolescents using SSRIs. Popular SSRIs include Prozac® (fluoxetine), Zoloft® (sertraline), Luvox® (fluvoxamine), Paxil® (paroxetine), and Celexa® (citalopram).
- **Beta-blockers** such as Inderal® (propranolol) or Tenormin® (atenolol) are used primarily to treat heart conditions but are often prescribed for social phobia to help reduce heart palpitations and other physical symptoms of anxiety. Potential side effects include sexual dysfunction, slow pulse, drowsiness, fatigue, dry mouth, numbness or tingling of fingers or toes, dizziness, diarrhea, nausea, weakness, and cold hands and feet (Bourin M et al 2002).

COMPLEMENTARY NUTRIENTS AND SUPPLEMENTS

In general, people are advised to eat a healthful diet with high quantities of organic fresh fruits and vegetables and plenty of water and to avoid foods that are high in saturated fats and refined carbohydrates. In addition, the following nutrients may support healthy levels of neurotransmitters or relieve anxiety:

Amino acids. Amino acids, particularly neurotransmitter precursors, are essential to normal brain function. The ability of L-tryptophan and L-tyrosine to produce serotonin and norepinephrine varies directly with plasma concentrations of L-tryptophan and L-tyrosine and inversely with plasma concentrations of other large neutral amino acids (Fernstrom J 2000).

Depletion of serotonin and its precursor L-tryptophan increases symptoms of anxiety, particularly panic disorder (Bell C et al 2001). In experimental settings, diets deficient in the amino acids L-tryptophan, L-phenylalanine, and L-tyrosine can rapidly decrease serotonin, causing anxiety symptoms (Leyton M et al 2003).

- **L-tryptophan and 5-hydroxytryptophan.** L-tryptophan can be taken along with a carbohydrate meal to increase amino acid brain levels and subsequent serotonin synthesis. However, high doses should be avoided by individuals with adrenal insufficiency and pregnant women. A study on rats demonstrated that a balanced diet containing natural tryptophan-rich protein can increase the plasma concentration of tryptophan, leading to increased brain serotonin synthesis (Feurte S et al 2001). Another study showed that 5-hydroxytryptophan, which is an intermediate step in the synthesis of serotonin from tryptophan, was able to lower the intensity of panic symptoms in human participants in response to a lab-induced panic challenge (Maron E et al 2004).
- **L-phenylalanine and L-tyrosine.** L-phenylalanine and L-tyrosine taken with a carbohydrate meal can increase synthesis of dopamine and norepinephrine (Sabelli HC et al 1986; Gelenberg AJ et al 1982). There are no reported adverse effects, but high doses should be avoided by pregnant individuals and those taking monoamine oxidase inhibitors.
- **L-lysine.** Dietary L-lysine deficiency increases stress-induced anxiety (Smriga M et al 2002). In one small study, L-lysine supplementation lessened plasma cortisol in response to stress and reduced chronic anxiety (Smriga M et al 2004). L-lysine acts like a partial serotonin receptor antagonist, inhibiting neurotransmitter reuptake in the synapse (Smriga M et al 2003).

Melatonin. Melatonin, a hormone made from serotonin, has neuroprotective and antioxidant properties, detoxifies free radicals, and stimulates antioxidative enzymes (Gupta YK et al 2003). Some research has shown that people with panic disorders have abnormal melatonin patterns (Nathan PJ et al 1998). Taken at night, melatonin can help people obtain refreshing sleep.

Theanine. Theanine is an amino acid found in green tea and produces a calming effect on the brain (Yokogoshi H et al 1998). It easily crosses the blood-brain barrier and produces subtle changes in biochemistry, including increased production of GABA and dopamine, which cause a tranquilizing effect. Research suggests theanine has neuroprotective effects in the brain, particularly in preventing neuronal death in the hippocampus (Kakuda T 2002). In one human study, healthy volunteers were given theanine and a benzodiazepine and subjected to an experimentally induced anticipatory anxiety condition. While neither the prescription drug nor theanine helped with the acute symptoms of anxiety, theanine appeared to outperform the benzodiazepine in the baseline measurement of anxiety (Lu K et al 2004). Theanine is also a caffeine antagonist, offsetting the stimulant properties of caffeine without causing drowsiness (in rats) (Kakuda T et al 2000).

Adapton. Adapton is a naturally occurring substance containing garum armoricum, an extract of garum, a deep sea fish. Adapton consists of unique polypeptides that act as precursors to endorphins and other neurotransmitters that exert a regulatory effect on the nervous system; it also contains an omega-3 fatty acid. There appear to be no major side effects other than minor heartburn, diarrhea, and nervous irritation.

Omega-3 fatty acids. The omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are necessary for proper brain function. In the typical Western diet, people often suffer from an increased ratio of inflammatory omega-6 fatty acids to anti-inflammatory omega-3 fatty acids. It has been established that this imbalance can lead to a number of negative health problems. Fortunately, the imbalance can be addressed easily by supplementing with EPA and DHA, which have been shown to have mood stabilizing effects and possibly other neuropsychiatric effects. In one multipart study that relied on both human student volunteers

and animals, DHA was shown to reduce aggression and anxiety in both stressful and nonstressful settings (Hamazaki T et al 1999). Another human study showed that a mixture of omega-3 and omega-6 fatty acids can reduce test-taking anxiety among students (Yehuda S et al 2005).

Herbs and botanical medicine. Botanical herbs have properties to manage many psychiatric disorders, including anxiety (Cagnacci A et al 2003; Edzard E 2002; Fugh-Berman A et al 1999). Herbal products can vary greatly in their composition, depending on variation in the raw plant material caused by genetic factors, climate, growing season, soil, rainfall, growing methods, and extraction processes. For this reason product preparation, quality, efficacy, and safety can differ widely among manufacturers. The following herbs have antianxiety effects or target key molecular sites associated with neurotransmitters in the central nervous system:

- *St. John's wort (Hypericum perforatum)*. St. John's wort is an aromatic perennial native to Europe and parts of Asia, North America, and South America. Five of nine controlled studies comparing it with antidepressant drugs found it superior to placebo (Beaubrun G et al 2000). St. John's wort has been shown to increase brain levels of serotonin in animals, operating through pathways slightly different from those of the prescription SSRIs. Other studies have shown that St. John's wort has moderate benefit for people suffering from both depression and anxiety (Muller D et al 2003; Friede M et al 2001). It is contraindicated for use during pregnancy, lactation, and exposure to strong sunlight and should not be taken concurrently with antidepressant medication (Beaubrun G et al 2000). For more important safety information on St. John's wort, please refer to the Safety Appendix.
- *Ginkgo biloba*. Researchers examining Ginkgo biloba have discovered that extracts from this herb exert a mild benzodiazepine effect. In one animal study, rats given Ginkgo biloba in conjunction with Valium® performed better on maze tests, which are commonly used to evaluate anxiety in lab animals, and ginkgo was effective alone when used for seven days (Kuribara H et al 2003).
- *Ashwagandha (Withania somnifera)*. Ashwagandha, or Indian ginseng, has long been used by Ayurvedic practitioners as a rejuvenating tonic. The herb has anti-inflammatory, antitumor, antistress, antioxidant, immunomodulatory, and rejuvenating properties (Mishra LC et al 2000). In one animal study, ashwagandha compared favorably with prescription antidepressants and benzodiazepines in the management of anxiety (Bhattacharya SK et al 2000).
- *Reishi (Ganoderma lucidum)*. Reishi has the unique ability among medicinal mushrooms to calm and support nerve function for people with chronic stress, anxiety, or insomnia (Hobbs C 1995).
- *Kava kava*. Used throughout the South Pacific as a tonic, kava kava has a number of properties that render it effective in treating anxiety. In one survey of common herbs used to treat anxiety disorders, kava kava was shown "beyond reasonable doubt" to have antianxiety effects in humans (Ernst E 2006). The same conclusion was reached by another team of researchers, who compared the efficacy of 108 complementary treatments and found that kava was the most effective for general anxiety (Jorm AF et al 2004). In one review of six placebo-controlled, randomized trials, researchers found that kava was effective in reducing anxiety, especially among women and younger patients. The study's authors also noted that kava has been withdrawn in several overseas markets because of cases of liver failure (Witte S et al 2005). Because of the safety concerns associated with kava, people are urged to use this herb only under the direct care of a physician.
- *Valerian*. This temperate herb has been used for medicinal purposes since the middle Ages. In recent studies, it has been examined for its ability to reduce anxiety. In a double-blind, placebo-controlled study conducted in 2006, valerian extract was combined with lemon balm and measured for its antianxiety effect when 24 study volunteers were subjected to laboratory-controlled stressors. Researchers found that a 600 mg dose of the drug combination reduced anxiety (Kennedy DO et al 2006). Another study compared valerian to placebo and diazepam in the context of anxiety. Both valerian and diazepam were shown to reduce the psychic symptoms of anxiety as measured on the Hamilton anxiety scale (Andreatini R et al 2002).

ANXIETY AND HORMONAL IMBALANCES

By now, it is well known that most steroid hormones (e.g., pregnenolone, estrogen, progesterone, testosterone, and DHEA) are neurologically active. In fact, large quantities of DHEA, as well as estrogen and progesterone receptors, are found in the brain. These hormones have a number of effects within the brain, including regulation of mood. Accordingly, a number of studies have linked abnormalities in hormone levels to various anxiety disorders (Birzniece V et al 2006; Cohen H et al 2006; Strous RD et al 2006). In addition, studies have documented that abnormalities in the hypothalamic-pituitary-adrenal axis, which controls the body's response to stress through the release of cortisol and DHEA, can predispose a person to anxiety and depression (Leonard BE 2005). During times of stress and anxiety, the balance between cortisol and DHEA is altered in favor of cortisol.

In particular, progesterone seems to have a potent antianxiety effect. For instance, in an animal study that compared normal mice to animals that had been bred to have their progesterin receptor knocked out, researchers found that progesterone decreased anxiety behavior through a mechanism of action similar to that of benzodiazepines, by acting on GABA receptors (Frye CA et al 2006). Another study found that a single dose of progesterone given to animals decreased anxiety indicators during stress tests, while the abrupt cessation of progesterone therapy increased measures of anxiety (Saavedra M et al 2006).

It's important to note that all the major sex hormones are related to one another. These hormones are synthesized in a cascade from cholesterol, and alterations in the level of one sex hormone may affect hormones throughout the cascade. Thus, people with

anxiety may benefit from comprehensive hormone testing and, if necessary, a program of bioidentical hormone replacement. Life Extension recommends that you strive to achieve the hormone levels of healthy people in their late 20s.

LIFESTYLE CHANGES

People with anxiety disorders can take a number of lifestyle steps to reduce their symptoms. These range from general lifestyle changes, such as getting enough sleep and exercise, to more specific recommendations, such as avoiding caffeine. Studies have shown that stimulants such as caffeine can generate anxiety in people with diagnosed anxiety disorders (Bruce M et al 1992). Caffeine is contained in coffee, certain teas, chocolate, and the herb guarana. Individuals prone to anxiety disorders should avoid caffeine and other stimulants (e.g., ephedra, or ma-huang) unless they are ordered by a physician.

Self-awareness and conscious breath control may be used to reduce instances of breath-holding or hyperventilation that may trigger attacks. Breath control may be achieved through self-awareness exercises, meditation, and stress reduction activities. Meditation is a tool to relax the body, mind, and spirit and has demonstrated both short- and long-term effectiveness in reducing generalized anxiety disorder and panic disorder symptoms (McCarty R et al 1998; Shapiro SL et al 1998; Miller JJ et al 1995; Kabat-Zinn J et al 1992; Kabat-Zinn J 1990, 1994; Gaylord C et al 1989).

Relaxation from listening to music, visual imagery, muscle relaxation, biofeedback, yoga, tai chi, and even social support sessions can all decrease symptoms of anxiety (Malathi A et al 1999; Field T et al 1997; Jin P 1992). Massage therapy may also help relax the body, promote circulation, and release tension (Field T et al 1996). Massage techniques using aromatherapy demonstrate mild, transient anxiety-reducing effects in some studies (Cook B et al 2000).

Individuals with a predisposition to anxiety disorders must be sure to get adequate sleep and exercise and avoid depressants such as alcohol or stimulants such as caffeine. Studies suggest that consequences of not getting enough sleep are anxiety and irritability, along with a host of other unpleasant follow-ons (Bourdet C et al 1994). Daily physical activity, particularly cardiovascular exercise such as walking, running, swimming, or biking, is beneficial for establishing a normal and healthy sleep pattern (Salmon P 2001). Sleep buffers people against physical symptoms and reduces anxiety associated with minor stress (Carmack CL et al 1999; Katula JA et al 1999).

LIFE EXTENSION FOUNDATION RECOMMENDATIONS

People suffering from anxiety disorders are encouraged to eat well, exercise as often as possible, make sure they get good sleep, and experiment with various therapies, such as massage, acupuncture, and psychotherapy. In addition, the following herbs and nutrients may exert antianxiety effects:

- **L-tryptophan**—500 to 1000 milligrams (mg) daily
- **D,L-phenylalanine**—500 to 1000 mg in the morning, not to be taken with protein foods
- **L-tyrosine**—500 to 1000 mg in the morning, not to be taken with protein foods
- **Melatonin**—300 micrograms (mcg) to 3 mg in the evening, one half hour prior to bedtime
- **EPA/DHA**—1000 mg daily EPA and 1400 mg daily DHA
- **Adapton**—4 capsules in the morning on an empty stomach for 15 days; then 2 capsules in the morning. For panic attacks, 10 mg propranolol or 25 mg atenolol in combination with Adapton may be highly effective.
- **Theanine**—100 mg daily to produce a calming effect or 400 mg (4 capsules) throughout the day for a mood-enhancing effect
- **Ginkgo biloba**—120 mg daily
- **St. John's wort**—300 to 900 mg daily
- **Kava kava**—10 drops liquid extract in water, three times daily
- **Valerian**—40 mg daily
- **B vitamin complex**—If homocysteine is above 8.0 mmol/L, it can be lowered with a B-vitamin complex containing 800 mcg folic acid, 1000 mg vitamin B12, and 75 mg vitamin B6.
- **DHEA**—15 to 75 mg daily, followed by blood testing in three to six weeks to be sure optimal blood levels are maintained

In addition, comprehensive hormone testing should be considered, followed by a program of bioidentical hormone replacement therapy if levels of steroid hormones are low or abnormal. Progesterone creams are available that can be applied directly to the skin, while estrogen and testosterone can be prescribed by a physician. For more specific information on bioidentical hormone therapy, please see the chapters "Male Hormone Modulation" or "Female Hormone Modulation."

PRODUCT AVAILABILITY

All the nutrients and supplements discussed in this section are available through the Life Extension Foundation Buyers Club, Inc. For ordering information, call anytime toll-free 1-800-544-4440, or visit us online at www.LifeExtension.com.

ANXIETY SAFETY CAVEATS

An aggressive program of dietary supplementation should not be launched without the supervision of a qualified physician. Several of the nutrients suggested in this protocol may have adverse effects. These include:

Choline

- Do not take choline if you have primary genetic trimethylaminuria.
- Choline can cause fishy body odor, excessive perspiration, hypotension (low blood pressure), depression, and gastrointestinal symptoms such as nausea and diarrhea.

D,L-Phenylalanine

- Do not take D,L-phenylalanine if you have phenylketonuria.
- Do not take D,L-phenylalanine if you are taking nonselective monoamine oxidase inhibitors (MAOIs).
- Do not take D,L-phenylalanine if you have schizophrenia. D,L-phenylalanine can exacerbate tardive dyskinesia (involuntary facial movements) in people who have schizophrenia.
- Consult your doctor before taking D,L-phenylalanine if you have high blood pressure. D,L-phenylalanine can exacerbate high blood pressure. D,L-phenylalanine can also cause high blood pressure.

DHEA

- Do not take DHEA if you could be pregnant, are breastfeeding, or could have prostate, breast, uterine, or ovarian cancer.
- DHEA can cause androgenic effects in woman such as acne, deepening of the voice, facial hair growth and hair loss.

EPA/DHA

- Consult your doctor before taking EPA/DHA if you take warfarin (Coumadin). Taking EPA/DHA with warfarin may increase the risk of bleeding.
- Discontinue using EPA/DHA 2 weeks before any surgical procedure.

Folic Acid

- Consult your doctor before taking folic acid if you have a vitamin B12 deficiency.
- Daily doses of more than 1 milligram of folic acid can precipitate or exacerbate the neurological damage caused by a vitamin B12 deficiency.

Ginkgo Biloba

- Individuals with a known risk factor for intracranial hemorrhage, systematic arterial hypertension, diabetes, or seizures should avoid ginkgo.
- Do not use prior to or after surgery.
- Avoid concomitant use of ginkgo with NSAIDs, blood thinners, diuretics, or SSRI's.
- Gastrointestinal symptoms (nausea and diarrhea) may occur.
- Allergic skin reactions may occur.
- Elevations in blood pressure may occur.

Kava Kava

- Do not take kava if you are taking levodopa-based medication, alcohol, barbiturates, or other mood-altering drugs.
- Do not take kava if you have a depressive disorder. Kava may deepen a depressed mood.
- Do not take kava with the tranquilizer Xanax. Taking kava with Xanax can cause coma.
- Do not take kava for more than 3 months without consulting a physician.
- Do not take high doses of kava. High dose, long-term use of kava can cause a scaly rash, unwanted weight loss and hepatitis.

- Kava can cause an allergic reaction, a slight yellowing of the skin, gastrointestinal complaints, impaired or abnormal movement, loss of balance, pupil dilation, and difficulty focusing.

L-Tryptophan

- Do not take L-tryptophan if you have carcinoid tumors.
- Do not take L-tryptophan while taking monoamine oxidase inhibitors (MAOIs) (type A) or within 2 weeks of discontinuing MAOIs.
- Do not take L-tryptophan with any antidepressant medications, including selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants or MAOIs.
- Do not take L-tryptophan with serotonin 5-HT receptor agonists, including naratriptan, sumatriptan and zolmitriptan.
- Do not take L-tryptophan if you have ischemic heart disease (e.g., a history of myocardial infarction, angina pectoris or documented silent ischemia), coronary artery spasm (e.g., Prinzmetal angina), uncontrolled hypertension or any other significant cardiovascular disease.
- L-tryptophan can trigger excess serotonin formation in tissues other than the target organ and cause significant adverse reactions.?
- L-tryptophan can cause nausea, diarrhea, loss of appetite, vomiting, difficulty breathing, pupil dilation, abnormally sensitive reflexes, loss of muscle coordination, blurry vision and cardiac dysrhythmia.

L-Tyrosine

- Do not take L-tyrosine if you have inborn errors of metabolism alkaptonuria and tyrosinemia type I and type II.
- Do not take L-tyrosine if you are taking non-selective monoamine oxidase (MAO) inhibitors.
- Do not take L-tyrosine if you have hypertension.
- Do not take L-tyrosine if you have melanoma

Melatonin

- Do not take melatonin if you are depressed.
- Do not take high doses of melatonin if you are trying to conceive. High doses of melatonin have been shown to inhibit ovulation.
- Melatonin can cause morning grogginess, a feeling of having a hangover or a “heavy head,” or gastrointestinal symptoms such as nausea and diarrhea.

Niacin (Nicotinic Acid)

- Do not take high doses of nicotinic acid (1.5 to 5 grams daily or more) if you have liver dysfunction, an unexplained elevation in your serum aminotransferase (transaminase) level, active peptic ulcer disease, arterial bleeding, or if you consume large amounts of alcohol.
- Consult your doctor before taking high doses of nicotinic acid if you have a history of jaundice, peptic ulcer disease, gastritis, disease of the liver or bile ducts, gout, kidney dysfunction, or cardiovascular disease (especially acute myocardial infarction or unstable angina).
- Consult your doctor before taking high doses of nicotinic acid if you have diabetes. High doses of nicotinic acid can negatively affect glucose tolerance. Monitor your serum glucose level frequently if you take nicotinic acid and have diabetes.
- Have your doctor monitor your serum aminotransferase level if you take high-doses of nicotinic acid.
- Nicotinic acid may cause flushing, principally of the face, neck, and chest. This flushing is thought to be prostaglandin-prostacyclin mediated. Histamine may also play a role in the flushing.
- Nicotinic acid can cause dizziness, palpitations, rapid heartbeat, shortness of breath, sweating, chills, insomnia, nausea, vomiting, abdominal pain, and muscle pain.
- High doses of nicotinic acid can cause blurred vision, macular edema, toxic amblyopia, and cystic maculopathy.

PABA (Para-aminobenzoic Acid)

- Do not take PABA if you are taking sulfonamides or have a kidney disease.
- PABA can cause anorexia, nausea, vomiting, fever, and rash.

Saint John's Wort

- St. John's wort can increase sensitivity to sunlight. To avoid sunburn while taking St. John's wort, minimize your exposure to

the sun.

- St. John's wort can cause bloating and constipation.

Trimethylglycine (Betaine)

- Do not take trimethylglycine (betaine) if you have gastritis, gastroesophageal reflux disease (GERD), or peptic ulcer disease.

Valerian

- Do not operate machinery or drive for several hours after taking valerian. Valerian can cause a sedative effect.
- Do not take valerian with other sedatives, including barbiturates such as Nembutal and benzodiazepine medications such as Ativan, Halcion, Librium, Valium, and Xanax.
- Do not take valerian with alcohol.
- Valerian can cause gastrointestinal symptoms, allergic reaction, headache, restlessness, sleeplessness, pupil dilation, and heart problems.

Vitamin B1 (Thiamin)

- Consult your doctor before taking vitamin B1 for a thiamin deficiency, lactic acidosis secondary to thiamin deficiency, Wernicke-Korsakoff syndrome, Wernicke's encephalopathy, or Korsakoff's psychosis.

Vitamin B2 (riboflavin)

- High doses of vitamin B2 (riboflavin) may interfere with the Abbott TDx drugs-of-abuse assay.
- Riboflavin absorption is increased in hypothyroidism and decreased in hyperthyroidism.
- If you are taking nucleoside reverse-transcriptase inhibitors, even a mild riboflavin deficiency can increase your risk of lactic acidosis.

Vitamin B6

- Individuals who are being treated with levodopa without taking carbidopa at the same time should avoid doses of 5 milligrams or greater daily of vitamin B6.

Vitamin B12 (cyanocobalamin)

- Do not take cyanocobalamin if you have Leber's optic atrophy.

For more information see the Safety Appendix

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