

Historic and Other Treatments in Psychiatry

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ABSTRACT

Throughout history numerous medications and unique treatments have been tried to diminish the frequency and severity of psychiatric symptoms. Some discovered by serendipity, such as lithium, chlorpromazine, monoamine oxidase inhibitors, and tricyclic antidepressants, have been efficacious and continue to be mainstays of psychiatric treatment. Others, such as insulin coma therapy, chemical convulsive therapies, and continuous sleep therapy, have passed into history. However, due to the fact that Food and Drug Administration-approved drugs have side effects and are efficacious no more than 66% of the time, there has been a need for patients and physicians to attempt to find other agents. This article discusses current orthomolecular agents (amino acids) and herbal agents (Ginkgo biloba, St. John's wort) and assesses their current utility in treating psychiatric illness.

INTRODUCTION: TREATMENTS OF HISTORIC SIGNIFICANCE

Biological therapies for the treatment of mental disorders have been available since the dawn of civilization. Herbs, potions, and other treatments for emotional disturbance date back thousands of years. In the 20th century, many new pharmacologic and other biological therapies have been developed to treat psychiatric disorders. Some treatments,

FOCUS POINTS

- Numerous agents throughout history have been used to treat mental illness.
- Orthomolecular psychiatrists have thought that vitamins and amino acids have helped with respect to mental illness in part as a result of their effects on neurotransmitter systems.
- Herbal medications are agents derived from natural products that can be bought over the counter without Food and Drug Administration regulation.
- Herbal medications include Sam-e, inositol, and St. John's wort, among others.

such as insulin coma therapy, have not survived. It remains to be seen whether newer interventions, described below, will become important tools in modern psychiatric practice or will be quickly dispatched to the vaults of history.

HISTORIC DRUGS

Fenfluramine

Fenfluramine, which in 1997 was available for use in decreasing appetite, was presumed to exert its effects through a serotonergic mechanism; however, it was not a stimulant. In 1987, *d*-fenfluramine, one of its isomers, was introduced in the United States after having been available in Europe for some time and was widely used alone or in combination

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Disclosure: Dr. Peselow is on the speaker's bureaus of Forest and Pfizer. Dr. Malavade is a consultant to and on the speaker's bureau of Eli Lilly. Dr. Lowe reports no affiliation with or financial interest in any organization that may pose a conflict of interest. Dr. Glick is a consultant to Bristol-Myers Squibb, Janssen, Lunbeck, Organon, Pfizer, Shire, Solvay, and Vanda; on the speaker's bureaus of AstraZeneca, Bristol-Myers Squibb/Otsuka, Janssen, Pfizer, and Shire; receives research support from AstraZeneca, Bristol-Myers Squibb/Otsuka, Eli Lilly, GlaxoSmithKline, the National Institute of Mental Health, Shire, and Solvay; and owns stock in Forest as well as Johnson and Johnson.

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with phentermine as “fen-phen” in obesity programs. *d*-Fenfluramine turned out to be associated with changes in the heart valves and with occasionally fatal pulmonary hypertension and was withdrawn from the US market.^{1,2}

CHEMICAL CONVULSIVE THERAPIES

Convulsive therapies for the treatment of serious psychiatric disorders date back hundreds of years, with the Swiss physician Paracelsus reportedly giving camphor by mouth to induce seizures and to treat lunacy in the 16th century. Several European manuscripts from the 1700s describe the benefits of camphor-induced seizures for the treatment of mania and other forms of insanity. These manuscripts were largely forgotten until the work of Ladislav von Meduna in the 1930s. Von Meduna had experimented with intramuscular (IM) camphor monobromide, caffeine, strychnine, brucine, and other compounds in the treatment of schizophrenia.

The two most common convulsant therapies used for the treatment of dementia praecox were pentylenetetrazol and hexafluorodiethyl ether. Pentylenetetrazol was reliable and was more soluble than many other compounds and also had a quicker onset of action. These latter two agents were inhaled as vaporizers, and both produced convulsions; they were essentially introduced as substitutes for electroconvulsive therapy (ECT). Von Meduna typically used an initial 5 mL dose of a 10% solution of pentylenetetrazol, followed by additional doses every minute if convulsions were not achieved.^{3,5}

The major drawbacks of these chemical convulsions is that seizures sometimes did not occur and patients would experience significant preictal discomfort, including nausea and anxiety, and, thus, would tend to decline further treatment. In the late 1930s and early 1940s, chemical convulsive therapy was replaced by the considerably more reliable ECT, which has greater safety and ease of administration.⁴

COMA-INDUCING THERAPIES

Insulin coma therapy emerged at approximately the same time in the 1930s as ECT. In 1933, Manfred Sakel observed that dementia praecox patients who went into a coma tended to come out of the coma less symptomatic, exhibiting less severe psychotic symptoms. The treatment involved using incrementally higher doses of IM insulin until the patient became comatose. Comas were initially terminated with glucagon after approximately 15 minutes, but an attempt was made to increase subsequent comas to a maximum of 60 minutes. Patients often required ≥ 60 treatments before results were

observed. Complications, including arrhythmias and laryngeal spasms, were not uncommon, and insulin coma therapy had a fatality rate of at least 1% and, in some samples, considerably higher. The danger of the procedure and a controlled study⁶ in 1962 that suggested that it was no more effective than a similar period of unconsciousness induced by barbiturates hastened the demise of the procedure. The risk of death (caused by irreversibility of the coma) and intellectual impairment led to a general abandonment of this treatment in the US.

However, some patients clearly appeared to respond to insulin coma therapy who did not respond to other available treatments. Insulin coma treatment had its best results in the treatment of the excited paranoid and catatonic patient.⁷

Variations of insulin coma therapy included atropine coma therapy used briefly in the 1950s. Atropine in doses of as low as 15 mg/day IM and as high as 200 mg/day was given to induce comas lasting 6–8 hours. If the patient did not wake up spontaneously, the coma was aborted by IM physostigmine. The patient would take warm and cold showers on awakening. Scopolamine, which has actions similar to atropine, was used in a like manner between 5 mg/day and 100 mg/day and was administered as much as 6 times/week.

As with insulin coma therapy, atropine coma therapy was said to be effective for the treatment of schizophrenia and mania. The most serious complications were hyperthermia (which were treated aggressively with ice packs) and rhabdomyolysis. By the late 1950s, coma therapies had been all but abandoned for safer treatments, including ECT and effective antipsychotics.⁸

CONTINUOUS SLEEP THERAPY

Continuous sleep therapy was introduced by Klaesi in 1920. It continued in use through the 1930s and 1940s. It involved therapies that altered consciousness for extended periods by seizure or coma, as these were thought to be effective in the treatment of psychosis. Even earlier, psychosis was treated by inducing a state of continuous sleep by giving barbiturates, chloral hydrate, or paraldehyde to induce sleep for 20 hours/day. This was repeated for periods ranging from 10 days to 3 weeks. There were brief interruptions from the sleep to allow the patient to eat and to use the bathroom. Complications of barbiturate-induced continuous sleep included allergic reactions, seizures and delirium on withdrawal, and respiratory depression ending in death. Later, the combination of chlorpromazine with benzodiazepines and other hypnotics was used to keep patients asleep for therapeutic purposes. Electrosleep therapy was introduced by Giljarowski in Russia in 1942, whereby a low level of elec-

tric current passed through electrodes applied to the patient's head produced sleep. This was done for 1–2 hours/day for as long as 3 days. Although there are some reports of improvement in anxiety states, obsessive-compulsive disorder (OCD), and schizophrenia, no controlled data are available to support these claims for these treatments. Given the significant morbidity and clear lack of efficacy of this method, it was largely abandoned in the US by the 1960s.⁹

HALLUCINOGEN THERAPY

Many cultures have used hallucinogens, including mescaline, psilocybin, and ergots, for thousands of years to gain spiritual and personal insight. These agents had been used experimentally through the early 1950s. Lysergic acid diethylamide (LSD) was synthesized in the 1930s and was marketed to psychiatrists and other practitioners in the late 1940s under the trade name Desylid as a tool for understanding psychosis and for facilitating psychotherapy. The model psychosis produced by LSD was used to see if it could illuminate the understanding of the schizophrenic process. Using LSD reportedly helped patients capture repressed memories and deal with anxiety, and it allowed patients to gain insight through an analysis of the primary process induced by the hallucinogen. Oral doses of 150–250 mg were administered occasionally by psychiatrists throughout the 1950s and early 1960s to facilitate psychotherapy with some patients.^{10,11} In the 1960s, Timothy Leary advocated the widespread use of hallucinogens, but the drugs were outlawed as class I controlled substances in 1965.

Although, overall, these agents are no longer used for therapeutic purposes in this country, LSD has fulfilled part of its early promise as a probe for psychosis. More recent understanding of the pharmacology of LSD and its affinity to serotonin (5-HT)₂ receptors has supported the interest in developing 5-HT–dopamine antagonists (atypical antipsychotics) with the 5-HT₂ receptor-blocking properties. Advocates in the 21st century suggest there may be a role for hallucinogens in psychiatry.¹²

DETOXIFICATION THERAPIES

The notion that some mental disorders may be related to a toxin of some sort is old. Various methods have been used to combat potential toxins suspected to be included in the etiology of psychosis. In 1949, Kielholz¹³ suggested that an endotoxin in the blood caused catatonic schizophrenia. More recent attempts to deal with suspected toxins include the use of blood transfusions in the 1940s and 1950s and

hemodialysis in the 1970s. In 1977, Wegemaker and Cade¹⁴ began to hemodialyze patients with schizophrenia with the hope of removing toxic polypeptides from their blood to alleviate symptoms. A few case reports^{15,16} in the late 1970s suggested that hemodialysis was an effective short-term and maintenance treatment in some schizophrenic patients. Patients were dialyzed daily until improvement was seen and were then maintained with dialysis every 2–8 weeks. Several patients were said to recover with hemodialysis and to relapse when the treatments were stopped. The investigators presumed that a leucine-containing endorphin was the responsible toxin, but they (and other investigators) were unable to replicate their initial findings. To date, it is believed that the previously mentioned treatments are of no appreciable value. Thus, the hemodialysis joined blood transfusions and other detoxification therapies in the annals of psychiatric history.

UNCONVENTIONAL TREATMENTS: WILL THEY BECOME STANDARD IN THE FUTURE OR WILL THEY FADE INTO HISTORY?

Orthomolecular Psychiatry

Some physicians practice holistic medicine with the idea that physical and emotional illness can be caused by deficiencies in naturally occurring substances. It is their belief that these patients can be treated with organic preparations, including vitamins, minerals, amino acids, and, perhaps, herbs and roots. For psychiatric symptoms, practitioners subscribe to the belief that biochemical derangements exist that can be treated with large quantities of agents that compensate for the disorder. Agents used include the B vitamins, lecithin, vitamin C, tryptophan, phenylalanine, and folic acid.

Megavitamin therapy was introduced into psychiatry in 1952 by Osmond and Smythies¹⁷ and Hoffer and colleagues.¹⁸ Their hypothesis was that faulty adrenalin metabolism in schizophrenia caused the production or inadequate removal of highly toxic methylated biogenic amines. These amines were thought to be the basis for symptoms such as hallucinations. Treatment with large doses of vitamins, such as nicotinic acid, which is converted in the body to nicotinamide, is thought to be instrumental in causing demethylation of such biogenic amines, making them nontoxic and thus reducing psychotic symptoms.

In 1968, Pauling coined the term orthomolecular to refer to the connection between the mind and nutrition.¹⁹ Research articles¹⁹ were compiled supporting the notion that

taking many times the recommended minimum daily dose of vitamins is useful in the treatment of schizophrenia and other psychiatric disorders. Pauling²⁰ suggested that large (mega) doses of vitamin C (ascorbic acid) combined with niacin, pyridoxine (vitamin B₆), and folic acid (vitamin B₁₂) were effective in the treatment of mental illness.

Although some severe vitamin deficiencies may result in syndromes with a psychiatric component (eg, niacin deficiency resulting in pellagra), empirical data and an American Psychiatric Association task force have failed to find evidence supporting the notion that schizophrenia and other disorders respond to vitamin therapies. However, that is not to say that vitamins and amino acids are of no importance in preserving mental health. Evidence indicates that severe vitamin deficiencies can result in psychiatric symptoms and that amino acid supplements may be pharmacologically useful in the treatment of some disorders. These are briefly reviewed in the following sections.

Thiamine, Vitamin B₁₂, and Folate

In industrialized societies, severe vitamin deficiencies are rarely encountered, except in certain populations. Those who are elderly, alcohol dependent, or chronically ill or who have certain types of gastrointestinal surgery are at greatest risk. Among the forms of vitamin deficiency most commonly encountered in the emergency room is acute thiamine depletion from alcohol dependence. Thiamine deficiency is seen in patients who have beriberi. Although the chronic forms of thiamine deficiency that lead to beriberi are rarely seen in the Western world, the fulminant depletion of already low stores of thiamine results in Wernicke's encephalopathy and Korsakoff's syndrome. Wernicke's encephalopathy²¹ classically presents with the triad of ataxia, ophthalmoplegia, and mental confusion, but confusion and a staggering gait are perhaps most common. Although Wernicke's encephalopathy is an acute process, Korsakoff's syndrome²² may be the permanent residue of this encephalopathy. Patients with Korsakoff's syndrome exhibit a well-circumscribed retrograde and anterograde amnesia that results from destruction of the mammillary bodies, and psychotic symptoms are also reported. Wernicke's encephalopathy is a medical emergency that responds to acute treatment with 50 mg of thiamine intravenously followed by 250-mg IM injections daily until a normal diet is attained. The treatment of uncomplicated acute thiamine deficiencies usually involves 100 mg given orally 1–3 times per day. Thiamine deficiency is also seen in peripheral neuritis associated with pellagra, and should be considered in alcoholic patients with altered sensorium. Dietary sources of thiamine include legumes, pork, beef,

whole grains, fresh vegetables, and yeast. Complete dietary abstinence can lead to a disease state in 3 weeks.²³

Vitamin B₁₂ deficiency or pernicious anemia is often seen in elderly adults, patients with gastric surgery, and malnourished depressed patients.²⁴ Vitamin B₁₂ is used in the treatment of pernicious anemia; vitamin B₁₂ deficiency; or increased vitamin B₁₂ requirements due to pregnancy, hemorrhage, malignancy, thyrotoxicosis, or liver or kidney disease.²⁵ In addition, anti-convulsants may decrease the absorption of vitamin B₁₂. The most typical psychiatric presentations include apathy, malaise, depressed mood, confusion, and memory deficits. Vitamin B₁₂ concentrations of 150 mg/mL of serum are sometimes associated with these symptoms. Vitamin B₁₂ deficiency is a more common cause of reversible dementia and is typically assessed in dementia evaluations. The treatment of pernicious anemia usually involves daily IM injections of 1,000 mg of vitamin B₁₂ for approximately 1 week, followed by maintenance doses of 1,000 mg every 1–2 months.²⁶

Folic acid is used in the treatment of megaloblastic and macrocytic anemias due to folate deficiency.²⁷ Folate deficiency has been associated with depression and dementia. Other psychiatric symptoms occasionally associated with folic acid deficiency include paranoia, psychosis, agitation, and confusion.^{28–30} The relationship of folate to depression has been debated over the years. Folate deficiency may be the consequence of anorexia in depressed patients and may also contribute to depression by interfering with the synthesis of norepinephrine and 5-HT. Folate deficiency has been associated with anticonvulsant use (particularly phenytoin, primidone, and phenobarbital) and the sex steroids, including oral contraceptives and estrogen replacement. Perhaps the most common cause of folate deficiency is the malnourishment associated with alcoholism. Many folate deficiencies respond to folate 1 mg/day orally; however, some more severe forms may require dosages of 5 mg as much as three times a day. Dietary supplements of folic acid are often necessary to prevent neural tube defects in pregnant women, particularly those taking anticonvulsants.³¹

Amino Acids

Amino acids provide the substrate for neurotransmitters and have been used as adjunctive agents in the treatment of depression and sleep. L-Tryptophan was used for many years in the US and elsewhere to treat insomnia and to augment standard antidepressants. L-Tryptophan, the precursor to 5-HT, must be obtained from the diet.

It was believed that, after oral administration of L-tryptophan, free and protein-bound L-tryptophan increase rapidly, and

the free fraction is transported into the central nervous system (CNS). It is hypothesized that CNS levels of tryptophan may stimulate 5-HT synthesis and may reverse the depressive episode. Mendels and colleagues³² did not confirm these findings.

L-Tryptophan had been used for many years combined with antidepressants or lithium to decrease response time and had been reported as a reasonable adjunct in converting partial antidepressant responders to full responders.³³

Combination treatments of monoamine oxidase inhibitors plus tryptophan have suggested antidepressant efficacy. L-Tryptophan was also noted to be effective when added to clomipramine but did not seem to be effective when added to tricyclic antidepressants (TCAs).

Patients who respond to serotonergic antidepressants may rapidly relapse into depression on a diet that is deficient in L-tryptophan. Interestingly, patients who respond to more noradrenergic antidepressants appear less vulnerable to relapse with an L-tryptophan-free diet.

The immediate precursor of 5-HT, 5-hydroxytryptophan, has been shown efficacious in two studies^{34,35} as an augmentor to chlorimipramine. Numerous small studies³⁶ have suggested that, although tryptophan or 5-hydroxytryptophan did have some effect on augmenting antidepressants, it had little antidepressant effect of its own.³⁷

L-Tryptophan was also used as an over-the-counter (OTC) treatment of insomnia in the US. Numerous studies³⁸ suggested that L-tryptophan in doses of 1–6 g before bedtime decreased sleep latency. L-Tryptophan has been unavailable in the US since 1989 because of its association with the eosinophilia-myalgia syndrome, which may have been secondary to an impurity resulting from the processing of the compound. Before this finding, it was believed that, with the exception of rare nausea or the exacerbation of psoriasis, L-tryptophan was well tolerated.

Another amino acid that has been examined as an augmentor to antidepressants is phenylalanine. Phenylalanine is converted to tyrosine as a catecholamine precursor. Phenylalanine has been added to selegiline successfully in the treatment of some patients with refractory major depressive disorder (MDD). However, Mann and colleagues³⁹ noted minimal improvement in depressive symptoms with phenylalanine alone. Tyrosine has been investigated as an augmentor to TCAs and may also have some mild antidepressant activity itself.

Conclusions Regarding Orthomolecular Agents

The above agents are frequently used and promoted for overall mental and physical health. How useful they will prove remains to be seen.

HERBAL AGENTS

Natural medications are medications that are derived from natural products, and are not approved by the US Food and Drug Administration for their proposed indication. In the US, the public spends approximately \$4 billion on supplements with little or no data on what to expect.⁴⁰ Consumers often believe that because a remedy is “natural” it is, therefore, safe. Moreover, since these remedies are most often purchased OTC, there is no clear mechanism for reports of toxicity to reach those who use them.⁴⁰

Herbal agents used in mood disorders include omega-3 fatty acids, St. John’s Wort, S-Adenosylmethionine (SAME) and inositol.

Omega-3 Fatty Acids

Omega-3 fatty acids are polyunsaturated lipids which are cardioprotective.⁴¹ The most promising data, however, are in the treatment of both bipolar disorder and unipolar depression; positive studies⁴²⁻⁴⁵ have been reported in each of these domains. Psychotropically active doses are generally thought to be in the range of 1–2 g/day, with dose-related gastrointestinal distress being the major side effect. There is also a theoretical risk of increased bleeding, so concomitant use with high-dose nonsteroidal anti-inflammatory drugs or anticoagulants is not recommended.

St. John’s Wort

St. John’s Wort (*Hypericum perforatum L.*) is one of the biggest-selling natural medications on the market. There have been 27 studies⁴⁶ looking at St. John’s Wort versus placebo. In MDD there is thought to be minimal benefit; in non-MDD or milder depression there is thought to be possible benefit. St. John’s Wort versus standard antidepressants (TCAs and selective serotonin reuptake inhibitors yield similar efficacy.⁴⁷ Suggested doses range from 900–1,800 mg/day depending on the preparation, and adverse effects include dry mouth, dizziness, constipation, and phototoxicity. Care should be taken in patients with bipolar disorder due to the possibility of a switch to mania. St. John’s Wort may reduce the therapeutic activity of numerous common medications, including warfarin, cyclosporine, oral contraceptives, theophylline, digoxin, and indinavir.

S-Adenosylmethionine

SAME is an essential methyl group transfers. It is the principal methyl donor in the one-carbon cycle with SAME levels depending on levels of the vitamins folate and B₁₂. SAME

is involved in the methylation of neurotransmitters.

SAMe has been shown to elevate mood in depressed patients in doses of between 300–1,600 mg/day. Studies^{48,49} support antidepressant efficacy of SAMe when compared with placebo and TCAs. Potential adverse effects are relatively minor and include anxiety, agitation, insomnia, dry mouth, bowel changes, and anorexia. Sweating, dizziness, palpitations, and headaches have also been reported.

Inositol

Inositol is a natural isomer of glucose that is present in common foods. Inositol has been found in various small studies⁵⁰⁻⁵³ to be effective in the treatment of depression, panic disorder, OCD, and possibly bipolar depression. Effective doses are thought to be in the range of 12–18 g/day. Adverse effects are generally mild and include gastrointestinal upset, headache, dizziness, sedation, and insomnia.

HERBAL AGENTS USED FOR ANXIETY DISORDERS: MELATONIN, VALERIAN, AND KAVA

Melatonin

Melatonin is a hormone derived from 5-HT and manufactured in the pineal gland. It is actually commercially available, as supplies are derived synthetically or from hog pineal glands. It is useful for individuals who travel across several time zones, as it can help rest one's biological clock by reorganizing one's circadian rhythm.

Melatonin is a popular OTC hormone used by many Americans on a regular basis for insomnia, and anecdotal reports⁵⁴ suggest that melatonin can reduce the insomnia associated with jet lag. The hormone is released naturally by the pineal gland early in the sleep cycle and appears to contribute to natural sleep cycles. A number of small, brief studies⁵⁵ melatonin can act as a hypnotic in doses of 0.2 mg and 5.0 mg at night, although other placebo-controlled studies⁵⁵ have disagreed on the efficacy of melatonin versus placebo in doses ranging from 0.5 mg to 10.0 mg/day. Some uncontrolled reports⁵⁵ suggest that melatonin has mild antidepressant effects. However, because of its reciprocal relationship to β -adrenergic receptor activity, it may worsen depression in some patients.

High doses may cause daytime somnolence and confusion. The drug can interact with the hypothalamic-pituitary-

adrenal axis and thymus and can cause immunosuppression; thus, it must be used cautiously with steroids. The long-term effects of melatonin use are unknown and the efficacy of melatonin has been inconclusive at this time given the widespread use of the drug. Indeed, a recent study by Spitzer and colleagues⁵⁶ showed no significant differences between melatonin and placebo (dose range from 0.5–5.0 mg) in the treatment of jet lag.

Valerian

Valerian (*Valeriana officinalis*) is a flowering plant extract that has been used to promote sleep and to reduce anxiety for over 2,000 years. Valerian was thought to be better than placebo in six of seven double-blind studies⁵⁷ of insomnia (though Valerian has an odor which may have compromised the blind). The onset of action is slow, taking 2–3 weeks to have an effect. Sedative effects are dose-related with usual dosages in the range of 450–600 mg approximately 2 hours before bedtime. In anxiety disorders, there have only been open studies.⁵⁸ Adverse effects, including blurry vision, gastrointestinal symptoms, headache, and a mild hangover seem to be uncommon.

Kava

In treating anxiety, kava has been effective in seven double blind studies.¹ A meta analysis of three of these studies⁵⁹ has shown that kava is superior to placebo on the Hamilton Rating Scale for Anxiety. The suggested dose is 60–120 mg/day. Major side effects include gastrointestinal upset, headaches, and dizziness. Toxic reactions, including ataxia, hair loss, respiratory problems, yellowing of the skin, and vision problems, have been seen at high doses or with prolonged use. There have also been more than 70 published reports⁶⁰ of severe hepatotoxicity worldwide. Overall, worldwide there have been 11 cases of liver transplants and four deaths associated with Kava.⁶⁰ Kava has been banned in the European Union and Canada and has an FDA advisory in the US.

HERBAL AGENTS USED FOR COGNITIVE DISORDERS AND DEMENTIA

Ginkgo biloba has been used in Chinese medicine for thousands of years. This natural medication comes from the seed of the Ginkgo tree and has generally been used for the treatment of impaired cognition and affective symptoms in dementing illnesses; however, there may be a role in the management of antidepressant-induced sexual dysfunction.

The suggested dose of ginkgo biloba is 120–240 mg/day with a minimum 8-week course of treatment. However, it may take up to 1 year to appreciate the full benefit. Since ginkgo has been shown to inhibit platelet-activating factor and has been associated with increased bleeding risk (though results are mixed), it should probably be avoided in those at high risk of bleeding.⁶¹ Other noted side effects include headache, gastrointestinal distress, headache, seizures in epileptics, and dizziness. With regard to dementia, the data is inconsistent and the cholinesterase inhibitors and memantine are preferred.⁶²

Dehydroepiandrosterone

Dehydroepiandrosterone (DHEA), a precursor hormone for estrogens and androgens, is available OTC. It is an abundantly produced adrenal steroid that has been evaluated as a treatment for psychiatric disorders since the 1950s.

Recent years have seen an interest in DHEA for improving cognition, depression, sex drive, and general well-being in elderly adults. Some reports^{63,64} suggest that DHEA in doses of 50–100 mg/day increases the sense of physical and social well-being in women 40–70 years of age. Reports also exist⁶⁵ of androgenic effects, including irreversible hirsutism, hair loss, voice deepening, and other undesirable sequelae. In addition, DHEA has at least a theoretical potential of enhancing tumor growth in people with latent, hormone-sensitive malignancies, such as prostate, cervical, and breast cancers. Despite its significant popularity, there is a dearth of controlled data on the safety or efficacy of DHEA.

DHEA has become popular as an OTC drug that can enhance quality of life. Because of the fact that it is reputed to diminish fat, to increase muscle mass, to increase libido, to increase sense of well-being, and to decrease depression, as well as to prevent various diseases (heart disease, cancer, diabetes, Parkinson's disease, and Alzheimer's disease), it is highly used. A recent double-blind depression study⁶⁶ showed some efficacy in the treatment of depression.

CONCLUSION: HERBAL MEDICATION

One out of every three people in the US will use at least one form of alternative medication. It is important to note that the FDA has no established definition for an herbal supplement. Although traditionally used as drugs, herbal products are generally unable to pass the stringent requirements imposed by the FDA for new molecular entities, such as new medications.

The Dietary Supplement Health and Education Act of 1994 prohibits the FDA from the regulation of dietary supplements as food additives.

An estimated 70% of patients do not inform their doctors about the use of alternative therapies, causing 15 million Americans to be at risk for potential drug-dietary supplement interaction. Many of these therapies may prove to be a valuable addition to the armamentarium of treatments available to psychiatrists in the future.

Overall, the jury is still out. Whether these agents will prove to be safe and effective and used appropriately for psychiatric indications or whether they will pass into history remains to be seen. **PP**

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