

## Normal Dosage

The normal dosage varies depending on the condition to be treated. Caution must be exercised in dosing, because non-regulated over-the-counter DHEA supplements may have an actual dose load significantly different than the labeled amount.

### Oral route

Aging: Some evidence of improved well-being was seen with doses of 50 milligrams (mg) once daily in men and women 40 to 70 years of age in a small study (Morales et al, 1994a).

Depression: In one 6-week study, an oral dose of 30 milligrams (mg) once daily for the first two weeks was given, followed by an increase to 30 mg twice daily for 2 additional weeks, then 30 mg three times daily for the 2 final weeks (Wolkowitz et al, 1999).

Erectile dysfunction: Dehydroepiandrosterone 50 milligrams (mg) once daily has been administered for up to 6 months (Reiter et al, 1999).

Hereditary angioedema: Oral doses of 25 to 50 milligrams (mg) have been given either daily, every other day, or every three days (Koo et al, 1983).

Menopausal symptom: Oral doses of 50 milligrams (mg) once daily for up to 6 months have been reported to reduce vasomotor/psychological symptoms in a small study (Stomati et al, 2000b). Lower doses (25 mg daily) have produced beneficial lipid changes in postmenopausal women, including increases in high-density lipoprotein (HDL) cholesterol (Lasco et al, 2001 a).

Systemic lupus erythematosus: A dose of 200 milligrams (mg) daily for up to 6 months has been administered in most studies (van Vollenhoven et al, 1995a; van Vollenhoven et al, 1994a; van Vollenhoven et al, 1999). In one 6-month trial, doses were titrated gradually from 50 mg daily initially to a maximum of 600 mg daily (Barry et al, 1998a).

### Topical application route

Menopausal symptom: Dehydroepiandrosterone 10% topical cream has been applied daily to the thigh area in postmenopausal women for up to one year. The topical dose was based on amounts to achieve dehydroepiandrosterone plasma levels of 20 to 30 nanomols/liter (nmol/L), which correlated to 3 to 5 grams (g) daily (Labrie et al, 1997).

## ADME

Absorption / Bioavailability: Some investigators suggest good oral bioavailability (Yen et al, 1995); however, absolute data are lacking. Bioavailability can be expected to vary among nutritional supplement formulations.

### Distribution

#### A) Distribution Sites:

Protein Binding, dehydroepiandrosterone 10% to 20%; dehydroepiandrosterone sulfate 80% to 90% (Longcope, 1996).

Other distribution sites: Dehydroepiandrosterone penetrates the blood-brain barrier. CSF levels of dehydroepiandrosterone sulfate have ranged from 0.2% to 5% of corresponding plasma levels; higher concentrations of dehydroepiandrosterone

sulfate have been found in brain tissue compared to CSF (Friess et al, 2000; Barrett-Connor et al, 1999).

B) Distribution Kinetics: Distribution Half-Life is 17 minutes (intravenous) (Meno-Tetang et al, 2001). Volume of Distribution of dehydroepiandrosterone, 17 to 38 L (Bird et al, 1978; Longcope, 1996); dehydroepiandrosterone sulfate, about 9 L (Gant et al, 1976). Data are limited; confirmation is required.

## Metabolism

### A) Metabolism Sites and Kinetics

Intestine: Dehydroepiandrosterone is after oral dosing converted (sulfated) to dehydroepiandrosterone sulfate ester in the intestine by sulfotransferases (Arlt et al, 1998; Meno-Tetang et al, 2001; Sulcova et al, 2000).

Liver / Other tissues: extensive (Arlt et al, 1998; Frye et al, 2000; Meno-Tetang et al, 2001) Dehydroepiandrosterone is converted (sulfated) to dehydroepiandrosterone sulfate ester in the intestine (oral doses) and liver and other tissues (oral, transdermal, or parenteral doses) by sulfotransferases (Arlt et al, 1998; Meno-Tetang et al, 2001; Sulcova et al, 2000). There is some interconversion of dehydroepiandrosterone sulfate to dehydroepiandrosterone, although this substantially favors formation of the sulfate ester (Meno-Tetang et al, 2001).

Dehydroepiandrosterone and dehydroepiandrosterone sulfate are converted to androgens and estrogens in peripheral tissues via several enzymes (eg, 3-beta-hydroxysteroid dehydrogenase, 5-alpha reductase, aromatase, 17-beta-hydroxysteroid dehydrogenase) (Arlt et al, 1998; Dean, 2000c; Davidson et al, 2000; Barrett-Connor et al, 1999).

Dehydroepiandrosterone undergoes hepatic 17-alpha- and 17-beta-hydroxylation; dehydroepiandrosterone sulfate undergoes 16-alpha hydroxylation (Frye et al, 2000b; Davidson et al, 2000). Cytochrome P450 (CYP)-3A4 is involved in the hepatic metabolism of both steroids; activity of this isoform is higher in women, which may contribute to the lower dehydroepiandrosterone sulfate levels observed in women (Frye et al, 2000b).

B) Metabolites: Androstenedione (active) (Haning et al, 1991; Morales et al, 1998a); Androsterone sulfate (active) (Bird et al, 1978); Estradiol (active) (Schwarz, 1990; Stomati et al, 2000); Estriol (active) (Schwarz, 1990); Estrone (Arlt et al, 1998; Schwarz, 1990); Dihydrotestosterone (Arlt et al, 1998; Kaufman et al, 1990); 7-Oxo-prasterone (active) (Davidson et al, 2000); Prasterone sulfate (DHEAS) (Davidson et al, 2000; Arlt et al, 1998; Friess et al, 2000; Horowitz, 2000a). Like dehydroepiandrosterone, it remains controversial whether pharmacologic effects are direct or secondary to conversion to androgens, estrogens, other metabolites (eg, 7-oxo-prasterone) (Davidson et al, 2000)), or a combination of these processes; Testosterone (active) (Arlt et al, 1998; Haning et al, 1991).

## Excretion

Kidney: Renal Excretion is 51% to 73% (intravenous dehydroepiandrosterone sulfate) (Zumoff & Bradlow, 1980), based on total excretion (including all metabolites) following intravenous administration of labeled dehydroepiandrosterone sulfate.

Elimination Half-life of the Parent Compound: young women, 8 to 11 hours; elderly men, 5 to 7 hours; elderly women, 7 to 12 hours (Meno-Tetang et al, 2001; Frye et al, 2000b; Arlt et al, 1998). Half-life values have varied somewhat, depending upon gender, age, whether values were for endogenous dehydroepiandrosterone or following exogenous

administration, and possibly dose. The clinical relevance of these differences with respect to exogenous administration is doubtful.

- a) Normal Men – Endogenous: A short half-life of endogenous dehydroepiandrosterone has been reported (about 2 hours (Frye et al, 2000)).
- b) Young Women – Supplementation: In young women receiving exogenous dehydroepiandrosterone, half-life values for dehydroepiandrosterone have been approximately 8 hours after 50 or 100 mg (single doses) and 11 hours after 200 mg daily (multiple doses) (Meno-Tetang et al, 2001; Frye et al, 2000b; Arlt et al, 1998).
- c) Elderly Men – Supplementation doses of 50 or 100 mg (single-dose) and 7 hours after 200 mg (single or multiple doses) (Frye et al, 2000b).
- d) Elderly Women – Supplementation: In elderly women receiving 200-mg doses, the elimination half-life of dehydroepiandrosterone progressively declined, from about 12 hours after the first dose to 9 hours on day 8, and to 7 hours on day 15 (Frye et al, 2000b).

#### Metabolites

young women, 12 to 13 hours; elderly men, 11 to 25 hours; elderly women, about 25 hours (Meno-Tetang et al, 2001; Frye et al, 2000b; Arlt et al, 1998).

a) Half-life values have varied somewhat, depending upon gender, age, and possibly dose. The clinical relevance of these differences is doubtful.

Young Women - Supplementation: In young women receiving exogenous dehydroepiandrosterone, half-life values for dehydroepiandrosterone sulfate have been approximately 13 hours after 50 or 100 mg (single doses) and 12 hours after 200 mg daily (multiple doses) (Meno-Tetang et al, 2001; Frye et al, 2000b; Arlt et al, 1998).

Elderly Men - Supplementation: In elderly men receiving dehydroepiandrosterone supplementation, half-life values for dehydroepiandrosterone sulfate were approximately 11 to 13 hours after doses of 50 or 100 mg (single-dose), and 20 to 25 hours after 200 mg (single or multiple doses) (Frye et al, 2000b).

Elderly Women - Supplementation: In elderly women receiving 200-mg doses, the elimination half-life of dehydroepiandrosterone sulfate was relatively constant after single or multiple dosing (24 to 27 hours) (Frye et al, 2000b).

#### Contraindications

Prior hypersensitivity to prasterone, dehydroepiandrosterone (DHEA) or dehydroepiandrosterone sulfate (DHEAS).

Pregnancy or breastfeeding.

Patients with hypercholesterolemia or ischemic heart disease: prasterone therapy has been associated with HDL lowering, albeit prasterone therapy has also been associated with [a reduced risk of cardiovascular morbidity](#).

Patients with or a history of psychiatric disorders (risk of exacerbation). The risk of mania may be increased during concomitant use with antidepressants (tricyclic or SSRIs) and/or alcohol, or with high prasterone doses, or in patients with a history of mood disorders.

Patients with cancer or at risk of cancer: dehydroepiandrosterone has been associated with growth of some tumor types (e.g., breast cancer, prostate cancer). Patients at risk of breast cancer in women (including postmenopausal women) and prostate cancer; risk may be

higher during dehydroepiandrosterone long-term supplementation. See [Adverse Events / Adverse Reactions](#).

Liver disease or renal impairment (pharmacokinetic data lacking).

### Adverse Events / Adverse Reactions

**Cardiovascular Effects / Cardiovascular finding:** Benign premature atrial contractions and occasional premature ventricular contractions occurred in a 55-year-old man after administration of dehydroepiandrosterone 50 mg daily for 2 weeks. Six months later dehydroepiandrosterone was reinitiated with recurrence of these arrhythmias within 36 hours. On each occasion, dehydroepiandrosterone was discontinued and arrhythmias were controlled by beta-blockers (propranolol, atenolol) (Sahelian & Borken, 1998).

#### Dermatologic Effects / Dermatological findings:

Endocrinologic-related cutaneous manifestations in women have included oily skin, ACNE, facial hirsutism, and enhanced perspiration odor; these have occurred with variable frequency (Morales et al, 1998; Gebre-Medhin et al, 2000; Labrie et al, 1997; Lasco et al, 2001; Davidson et al, 2000a; Barry et al, 1998).

Acneiform dermatitis was seen in about half of women receiving prasterone 200 mg daily for treatment of systemic lupus erythematosus (SLE) (van Vollenhoven et al, 1995; van Vollenhoven et al, 1994).

Mild hirsutism developed in 2 of 10 women with SLE receiving prasterone 200 mg/day with concomitant prednisone. (van Vollenhoven et al, 1994).

**Endocrine/Metabolic Effects / Endocrine finding:** Significant increases in estrogens and particularly androgens, with attendant adverse effects, can occur during dehydroepiandrosterone therapy/supplementation. Acne, oily skin, facial hirsutism, hair loss, mood changes, voice deepening, enhanced perspiration odor, and other signs of masculinization have been reported with variable frequency in women (Morales et al, 1998; Gebre-Medhin et al, 2000; Labrie et al, 1997; Lasco et al, 2001; Davidson et al, 2000a; Barry et al, 1998). Facial acne was observed to clear in one woman with continued supplementation (Morales et al, 1998). None of these effects has been clearly dose-related.

**Metabolic finding:** Although beneficial reductions in total and LDL cholesterol have been observed during dehydroepiandrosterone supplementation in some clinical studies, this has not been confirmed in others. Potentially deleterious reductions in HDL cholesterol, at times significant, have also been reported in various patient groups (men and women) (Morales et al, 1998; Morales et al, 1994; Villareal et al, 2000a; Mortola & Yen, 1990b). The HDL-lowering effect is likely due to increased androgenicity, and is probably dose-related. With use of low doses in postmenopausal women, one study reported increases in HDL cholesterol, as well as beneficial changes in other lipid parameters (Lasco et al, 2001).

**Hepatic Effects / Liver finding:** No significant changes in transaminases or other hepatic function tests were seen during long-term use (eg, 6 months) in some studies (Morales et al, 1998; Villareal et al, 2000a). One case of hepatitis has been reported in a patient with high pretreatment antinuclear antibody (ANA) titers (Buster et al, 1992). Causality is uncertain.

#### Psychiatric Effects: Mania Finding:

Manic reactions during dehydroepiandrosterone therapy (50 to 500 mg daily) have been described in at least three case reports (Dean, 2000b; Pies, 2000). Symptoms

began after 2 weeks to 2 months of supplementation in cases providing these data; psychotic features accompanied one case. Two patients had no history of psychiatric disorders (including the patient with psychotic-like symptoms), whereas the third had a history of bipolar disorder and was also receiving sertraline and abusing alcohol. In all cases, withdrawal of dehydroepiandrosterone and therapy with sodium valproate or divalproex (with haloperidol in the patient with psychotic symptomatology) resulted in improvement of symptoms.

There was no apparent association with patient age (31 to 68 years) in these cases. Risk factors for development of mania/psychosis are considered to be higher doses, combined use with antidepressants (tricyclics or selective serotonin-reuptake inhibitors) or alcohol or benzodiazepines, young patients (20 to 30 years, due to peaking endogenous dehydroepiandrosterone levels), and cytochrome P450 polymorphisms (poor metabolizers) (Dean, 2000b).

**Kidney disease:** No significant changes in renal function tests were observed during long-term use (eg, 6 months) in some studies (Morales et al, 1998; Lasco et al, 2001; Villareal et al, 2000a).

**Oncology:** Prasterone may inhibit or promote breast cancer, and may make hormonally-unresponsive advanced prostate cancer transiently responsive to diethylstilbestrol.

[Jones JA, Nguyen A, Straub M, et al: Use of DHEA in a patient with advanced prostate cancer: a case report and review. \*Urology\* 1997; 50\(5\):784-788](#): Prasterone has been evaluated as a potential treatment for adenocarcinomas, with some initial success. A patient with resistant, advanced prostate cancer (Prostate specific antigen of 2726 ng/mL) with progressive symptomatology (the patient "experienced periods of extreme weakness and breathlessness, requiring emergency room treatment on one occasion," and required blood transfusions every 2-3 weeks) was treated with oral prasterone (up to 700 mg / day). Many symptoms improved on prasterone therapy ("All of his blood cell elements [] increased spontaneously during DHEA therapy, thus eliminating the need for transfusions"), but during prasterone treatment, serum "testosterone had risen to 142 ng/dL and PSA was more than 10,000 ng/mL." Prasterone (700 mg / day) was replaced with diethylstilbestrol diphosphate (50 mg / day), and the previous hormonally-unresponsive cancer subsequently responded transiently to third-line hormonal therapy with diethylstilbestrol. The physician notes, "The dramatic decrease of PSA after discontinuing DHEA is confounded by the initiation of estrogen therapy. The [] question remains: 'would the estrogen therapy alone have had such a dramatic effect had the DHEA not been utilized prior to the reintroduction of hormonal therapy?'"

[Stoll BA: Dietary supplements of dehydroepiandrosterone in relation to breast cancer risk. Eur J Clin Nutr \(1999\) 53\(10\):771-775](#): A review of reports of clinical, epidemiological experimental studies for evidence that prasterone therapy may be a factor in promoting the growth of mammary cancer. RESULTS: Prasterone is reported to inhibit the growth of human mammary cancer cells in vitro and also the growth of chemically-induced mammary cancer in rats. However, growth inhibition occurs only in the presence of high oestrogen concentrations, and growth stimulation occurs in both models in the presence of a low-level oestrogen milieu. Epidemiological studies report a positive correlation between higher serum concentrations of DHEA-S and increased breast cancer risk in the case of postmenopausal, but not premenopausal, women. CONCLUSION: Late promotion of breast cancer in postmenopausal women may be stimulated by prolonged intake of prasterone, and the risk may be increased by the endocrine abnormality associated with pre-existing abdominal obesity. Caution is advised in the use of dietary supplements of prasterone particularly by obese, post-menopausal women.

[Skolnick AA, Scientific verdict still out on DHEA. JAMA 1996; 276\(17\):1365-1367](#):

[Davidson M, Marwah A, Sawchuk RJ, et al: Safety And Pharmacokinetic Study With Escalating Doses Of 3-Acetyl-7-Oxo-Dehydroepiandrosterone In Healthy Male Volunteers, Clin Invest Med 2000; 23\(5\):300-310](#); This paper is listed by DrugDex as providing evidence of an association between prasterone therapy and cancer. That assertion, however, appears incorrect because this paper does not address prasterone nor measure cancer. This paper describes a randomized, double blind, placebo-controlled, escalating dose study to evaluate the safety and pharmacokinetics of a synthetic derivative of prasterone, 3-acetyl-7-oxo-DHEA (3-beta-acetoxyandrost-5-ene-7,17-dione) given orally. Participants (22 healthy males) received placebo (n = 6) or 3-acetyl-7-oxo-DHEA (n = 16) at 50 mg/d for 7 days followed by a 7-day washout; 100 mg/d for 7 days followed by a 7-day washout; and 200 mg/d for 28 days. OUTCOME MEASURES: Safety parameters, evaluated at each dose level, included measurement of total testosterone, free testosterone, dihydrotestosterone, estradiol, cortisol, thyroxin and insulin levels. Analyses for 7-oxo-DHEA-3beta-sulfate (DHEA-S), the only detectable metabolic product of the administered steroid, were conducted on plasma drawn from all subjects at 0.25, 0.5, 1, 2, 4, 6 and 12 hours after the final 100 mg dose of 3beta-acetyl-7-oxo-DHEA. RESULTS: There were no differences in the clinical laboratory values or in reported minor adverse experiences, between treatment and placebo groups. In general, blood hormone concentrations were unaffected by the treatment with 3beta-acetyl-7-oxo-DHEA and remained within the normal range. No changes in vital signs, blood chemistry or urinalysis occurred during treatment with 3beta-acetyl-7-oxo-DHEA compared to placebo. The administered steroid was not detected in the blood but was rapidly converted to 7-oxo-DHEA-S, the concentrations of which were proportional to dose. This steroid sulfate did not accumulate; plasma concentrations 12 hours after the 3beta-acetyl-7-oxo-DHEA dose at 7 and 28 days on the 200 mg/d dose were 15.8 and 16.3 microg/L respectively. The mean time to peak plasma level of 7-oxo-DHEA-S was 2.2 hours; the mean half life was 2.17 hours. The apparent clearance averaged 172 L/h, and the apparent mean volume of distribution was 540 L. CONCLUSION: These results indicate that 3-beta-acetyl-7-oxo-DHEA is safe and well tolerated in normal healthy men at doses up to 200 mg/d for 4 weeks

Urogenital finding: No change in endometrial thickness was observed during 6 months of oral treatment in one study involving early and late postmenopausal women; uterine bleeding was also absent during this period (Stomati et al, 2000a).

## Drug Interactions

### Acetophenazine

- 1) Interaction Effect: reduced effectiveness of phenothiazines
- 2) Summary: Dehydroepiandrosterone (DHEA) levels within the normal range of 100 to 400 microgram/deciliter (mcg/dL) are conducive to optimal treatment of patients with psychosis (Howard, 1992l). In case reports, patients have been resistant to antipsychotics when DHEA levels were elevated (Howard, 1992l). Patients being treated with phenothiazines for psychosis should avoid DHEA supplementation.
- 3) Severity: moderate
- 4) Onset: delayed
- 5) Substantiation: theoretical
- 6) Clinical Management: Avoid concomitant use of dehydroepiandrosterone (DHEA) and phenothiazines. If DHEA is elevated, treatment with dexamethasone 1 mg orally per day may be used to normalize DHEA levels.
- 7) Probable Mechanism: elevated dehydroepiandrosterone (DHEA) blood levels may reduce responsiveness to phenothiazines
- 8) Literature Reports

a) A 24-year-old female diagnosed with schizophrenia was resistant to daily doses of haloperidol 20 milligrams (mg), fluphenazine 40 mg, lithium carbonate 1200 mg, and lithium carbonate 900 mg plus thioridazine 300 mg. The patient appeared Cushingoid with moon face, acne, facial hair, abdominal hair, and a 40 pound weight gain in the previous 8 months. Dehydroepiandrosterone (DHEA) measured as part of an endocrine panel was 725micrograms/deciliter (mcg/dL) (normal: 100 to 400 mcg/dL).

Dexamethasone 1 mg orally at bedtime resulted in substantial improvement within one week. The patient appeared calmer, more alert with improved psychotic symptoms and ability to concentrate. At two weeks, a repeated DHEA level was within normal range (328 mcg/dL). The author concluded that elevated DHEA levels were associated with severe psychosis resistant to conventional anti psychotic therapy (Howard, 1992k).

b) A 13-year-old male decompensated with a subsequent two-year period of emotional problems accompanied by heavy use of LSD, hashish, barbiturates, and alcohol. His mental status included bizarre, disorganized, delusional thinking, auditory and visual hallucinations, paranoia, lack of attention to personal hygiene, agitation, and combativeness. He was diagnosed with chronic paranoid schizophrenia; schizophrenia, chronic undifferentiated type, and schizoaffective disorder, excited type. He was resistant to daily doses of trifluoperazine 40 mg, chlorpromazine 400 mg, and imipramine 100 mg. He was also resistant to combination therapy with chlorpromazine 400 mg with thiothixene 80 mg, thioridazine 1000 mg, perphenazine 48 mg with lithium carbonate 1200 mg, clonazepam 4 mg, and carbamazepine 1200 mg daily. Baseline DHEA level exceeded 900 mcg/dL. A seven-day suppression test with dexamethasone 1 mg orally at bedtime resulted in a normal DHEA level of 200 mcg/dL. By day 5, psychosis improved and the patient was well-oriented, conversational,



and was making good eye contact. Once dexamethasone was discontinued, rapid decompensation and florid psychosis ensued despite "substantial amounts of psychotropic medications." DHEA increased to 536 mcg/dL. The author concluded that elevated DHEA levels were associated with florid psychosis resistant to conventional antipsychotic therapy (Howard, 1992k).

#### Carbamazepine

- 1) Interaction Effect: reduced effectiveness of carbamazepine
- 2) Summary: Dehydroepiandrosterone (DHEA) in a single case report was noted to cause mania in a patient with no previous personal or family history of bipolar disorder (Markowitz et al, 1999c). Elevated DHEA levels have been found in patients with mental disorders; DHEA suppression has led to improvement in psychotic symptoms (Howard, 1992c). Patients taking medication for bipolar disorder or patients with a personal and/or family history of bipolar disorder should not take DHEA until further data is available to characterize this drug-herb interaction.
- 3) Severity: moderate
- 4) Onset: delayed
- 5) Substantiation: theoretical
- 6) Clinical Management: If carbamazepine is being used for manic symptoms, concomitant use of dehydroepiandrosterone (DHEA) may cause a return of symptoms. Patients with a personal or family history of bipolar disorder should be advised to avoid DHEA use.
- 7) Probable Mechanism: proserotonergic activity of dehydroepiandrosterone may predispose patients to manic episodes; dehydroepiandrosterone is a precursor to androgenic steroids, which in high doses may precipitate mania.
- 8) Literature Reports

a) A 68-year-old male with no documented psychiatric history initiated dehydroepiandrosterone (DHEA) 100 milligrams (mg) daily and increased the dose to 200 to 300 mg daily for 6 months. Within 3 months, family members noted the onset of odd behavior with prominent symptoms of agitation, delusional thinking, decreased sleep and appetite, and spending sprees. The patient was not taking any prescribed medication but did ingest alcohol in amounts up to 1 case of beer daily. Another 3 months elapsed, leading to involuntary inpatient admission secondary to rapid, loud, pressured speech with grandiose thoughts. At admission, the patient reported that he had decreased alcohol intake to 2 beers daily due to family concerns about his behavior changes. There was no family history of bipolar disorder. Urinary drug screen was negative. Over the seven-day hospital stay, with the institution of valproic acid 500 mg twice daily, the patient's behavior and sleep patterns improved, and the patient believed DHEA led to his symptoms. There were no ethanol withdrawal symptoms. The patient was discharged with follow-up care from his primary care physician with a diagnosis of substance-induced mood disorder (Markowitz et al, 1999b).

b) A 13-year-old male decompensated with a subsequent two-year period of emotional problems accompanied by heavy use of LSD, hashish, barbiturates, and alcohol. His mental status included bizarre, disorganized, delusional thinking, auditory and visual hallucinations, paranoia, lack of attention to personal hygiene, agitation, and combativeness. He was diagnosed with chronic paranoid schizophrenia; schizophrenia, chronic undifferentiated type, and schizoaffective disorder, excited type. He was resistant to daily doses of trifluoperazine 40 mg, chlorpromazine 400 mg, and imipramine 100 mg.



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#### Chlorpromazine

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#### Citalopram

- 1) Interaction Effect: development of manic symptoms
- 2) Summary: A case has been reported in which concomitant dehydroepiandrosterone (DHEA) and sertraline use was suggested to precipitate a manic episode in a patient with a history of bipolar disorder (Dean, 2000a). DHEA was also noted to cause mania in a patient with no previous personal or family history of bipolar disorder (Markowitz et al, 1999f). Elevated DHEA levels have been found in patients with mental disorders; DHEA suppression has led to improvement in psychotic symptoms (Howard, 1992u). DHEA possesses proserotonergic activity which may predispose patients to manic episodes (Majewska, 1995). DHEA is a precursor to androgenic steroids, which in high doses may precipitate mania (Markowitz et al, 1999f). Patients taking medication for bipolar disorder or patients with a personal and/or family history of bipolar disorder should not take DHEA until further data is available to characterize this drug-herb interaction. Concomitant use of DHEA with selective serotonin reuptake inhibitors (SSRIs) should be avoided due to the potential additive precipitation of mania.
- 3) Severity: moderate
- 4) Onset: delayed
- 5) Substantiation: theoretical
- 6) Clinical Management: Avoid concomitant use of dehydroepiandrosterone (DHEA) and selective serotonin reuptake inhibitors. If patients present with manic symptoms (i.e. agitation, anger, irritability, aggressive behavior), determine if the patient is using DHEA and discontinue DHEA.
- 7) Probable Mechanism: serotonergic activity of dehydroepiandrosterone, possibly increased androgen levels
- 8) Literature Reports

a) A 31-year-old male was admitted following threats to commit suicide and injure family members. He had self-initiated sertraline 100 milligrams (mg) daily for the previous 2 to 3 weeks for depression. Sertraline had been prescribed 3 years prior when he was diagnosed with bipolar disorder, which he discontinued after 2 weeks. He had also taken dehydroepiandrosterone (DHEA) 300 mg to 500 mg daily for the previous 2 months apparently for weight training. Following use of DHEA for a short time, he became more irritable, was not sleeping well, and began threatening a female friend and family members. He also drank alcohol occasionally and reportedly had difficulty controlling his anger when intoxicated. Sertraline was stopped and the patient was treated with valproic acid with the dose titrated to 500 mg twice daily. The combination of DHEA, sertraline, and alcohol was suggested responsible for the developing of the manic episode (Dean, 2000).

#### Clozapine

- 1) Interaction Effect: reduced effectiveness of clozapine

2) Summary: Dehydroepiandrosterone (DHEA) levels within the normal range of 100 to 400 microgram/deciliter (mcg/dL) are conducive to optimal treatment of patients with psychosis (Howard, 1 992h). In case reports, patients have been resistant to antipsychotics when DHEA levels were elevated (Howard, 1 992h). Patients being treated with clozapine should avoid DHEA supplementation.

3) Severity: moderate

4) Onset: delayed

5) Substantiation: theoretical

6) Clinical Management: Avoid concomitant use of dehydroepiandrosterone (DHEA) and clozapine. If DHEA is elevated, treatment with dexamethasone 1 mg orally per day may be used to normalize DHEA levels.

7) Probable Mechanism: elevated dehydroepiandrosterone (DHEA) blood levels may reduce responsiveness to clozapine 8) Literature Reports

a) A 24-year-old female diagnosed with schizophrenia was resistant to daily doses of haloperidol 20 milligrams (mg), fluphenazine 40 mg, lithium carbonate 1200 mg, and lithium carbonate 900 mg plus thioridazine 300 mg. The patient appeared Cushingoid with moon face, acne, facial hair, abdominal hair, and a 40 pound weight gain in the previous 8 months. Dehydroepiandrosterone (DHEA) measured as part of an endocrine panel was 725 micrograms/deciliter (mcg/dL) (normal: 100 to 400 mcg/dL). Dexamethasone 1 mg orally at bedtime resulted in substantial improvement within one week. The patient appeared calmer, more alert with improved psychotic symptoms and ability to concentrate. At two weeks, a repeated DHEA level was within normal range (328 mcg/dL). The author concluded that elevated DHEA levels were associated with severe psychosis resistant to conventional antipsychotic therapy (Howard, 1 992g).

b) A 13-year-old male decompensated with a subsequent two-year period of emotional problems accompanied by heavy use of LSD, hashish, barbiturates, and alcohol. His mental status included bizarre, disorganized, delusional thinking, auditory and visual hallucinations, paranoia, lack of attention to personal hygiene, agitation, and combativeness. He was diagnosed with chronic paranoid schizophrenia; schizophrenia, chronic undifferentiated type, and schizoaffective disorder, excited type. He was resistant to daily doses of trifluoperazine 40 mg, chlorpromazine 400 mg, and imipramine 100 mg. He was also resistant to combination therapy with chlorpromazine 400 mg with thiothixene 80 mg, thioridazine 1000 mg, perphenazine 48 mg with lithium carbonate 1200 mg, clonazepam 4 mg, and carbamazepine 1200 mg daily. Baseline DHEA level exceeded 900 mcg/dL. A seven-day suppression test with dexamethasone 1 mg orally at bedtime resulted in a normal DHEA level of 200 mcg/dL. By day 5, psychosis improved and the patient was well-oriented, conversational, and was making good eye contact. Once dexamethasone was discontinued, rapid decompensation and florid psychosis ensued despite "substantial amounts of psychotropic medications." DHEA increased to 536 mcg/dL. The author concluded that elevated DHEA levels were associated with florid psychosis resistant to conventional antipsychotic therapy (Howard, 1 992g).

#### Conjugated Estrogens

1) Interaction Effect: increased risk of estrogenic adverse effects

2) Summary: Combining dehydroepiandrosterone (DHEA) with estrogen may result in symptoms of estrogen excess. DHEA has increased endogenous estrogen levels in postmenopausal women (Mortola & Yen, 1 990a). Pre- and post-menopausal women

have effective enzymatic systems for the biotransformation of DHEA to C19 and C-18 sex steroids (Mortola & Yen, 1990a), suggesting that increased estrogen levels may occur in all women regardless of menopausal status.

3) Severity: minor

4) Onset: delayed

5) Substantiation: theoretical

6) Clinical Management: Concomitant use of dehydroepiandrosterone (DHEA) and estrogen is not recommended. Monitor for symptoms and adverse effects of estrogen excess in those patients who elect to combine therapies. Such symptoms include (but are not limited to) nausea, headache, intolerance to contact lenses, insomnia, chorea, cholasma, colitis, acute breakthrough or withdrawal bleeding, changes in menstrual flow, leukorrhea, and pancreatitis.

7) Probable Mechanism: additive estrogenic effect since dehydroepiandrosterone is enzymatically converted into C-19 and C-18 sex steroids

8) Literature Reports

a) Estrone and estradiol levels increased to two-times the basal value following four weeks of dehydroepiandrosterone (DHEA) 400 milligrams (mg) four times daily for 28 days in six postmenopausal

women in a double-blind, placebo-controlled, crossover study. Subjects received DHEA or placebo for 28 days, followed by a 2-

week washout period, then crossed over to the other treatment (DHEA or placebo).

Estrone increased from 58.7 +/- 11.0 to 167.4 +/- 66.6 picomole/liter (pmol/L) and estradiol increased from 36.7 +/- 3.7 to 121.1 +/- 25.7 pmol/L. This corresponds to a maximal percent change of 214 +/- 67 percent and 181 +/- 29 percent for estrone and estradiol, respectively (Mortola & Yen, 1990).

#### Escitalopram

1) Interaction Effect: development of manic symptoms

2) Summary: A case has been reported in which concomitant dehydroepiandrosterone (DHEA) and sertraline use was suggested to precipitate a manic episode in a patient with a history of bipolar disorder (Dean, 2000a). DHEA was also noted to cause mania in a patient with no previous personal or family history of bipolar disorder (Markowitz et al, 1999f). Elevated DHEA levels have been found in patients with mental disorders; DHEA suppression has led to improvement in psychotic symptoms (Howard, 1992u). DHEA possesses proserotonergic activity which may predispose patients to manic episodes (Majewska, 1995). DHEA is a precursor to androgenic steroids, which in high doses may precipitate mania (Markowitz et al, 1999f). Patients taking medication for bipolar disorder or patients with a personal and/or family history of bipolar

disorder should not take DHEA until further data is available to characterize this drug-herb interaction. Concomitant use of DHEA with selective serotonin reuptake inhibitors (SSRIs) should be avoided due to the potential additive precipitation of mania.

3) Severity: moderate

4) Onset: delayed

5) Substantiation: theoretical

6) Clinical Management: Avoid concomitant use of dehydroepiandrosterone (DHEA) and selective serotonin reuptake inhibitors. If patients present with manic

symptoms (i.e. agitation, anger, irritability, aggressive behavior), determine if the patient is using DHEA and discontinue DHEA.

7) Probable Mechanism: serotonergic activity of dehydroepiandrosterone, possibly increased androgen levels

8) Literature Reports

a) A 31-year-old male was admitted following threats to commit suicide and injure family members. He had self-initiated sertraline 100 milligrams (mg) daily for the previous 2 to 3 weeks for depression. Sertraline had been prescribed 3 years prior when he was diagnosed with bipolar disorder, which he discontinued after 2 weeks. He had also taken dehydroepiandrosterone (DHEA) 300 mg to 500 mg daily for the previous 2 months apparently for weight training. Following use of DHEA for a short time, he became more irritable, was not sleeping well, and began threatening a female friend and family members. He also drank alcohol occasionally and reportedly had difficulty controlling his anger when intoxicated. Sertraline was stopped and the patient was treated with valproic acid with the dose titrated to 500 mg twice daily. The combination of DHEA, sertraline, and alcohol was suggested responsible for the developing of the manic episode (Dean, 2000).

#### Esterified Estrogens

1) Interaction Effect: increased risk of estrogenic adverse effects

2) Summary: Combining dehydroepiandrosterone (DHEA) with estrogen may result in symptoms of estrogen excess. DHEA has increased endogenous estrogen levels in postmenopausal women (Mortola & Yen, 1990a). Pre- and post-menopausal women have effective enzymatic systems for the biotransformation of DHEA to C19 and C-18 sex steroids (Mortola & Yen, 1990a), suggesting that increased estrogen levels may occur in all women regardless of menopausal status.

3) Severity: minor

4) Onset: delayed

5) Substantiation: theoretical

6) Clinical Management: Concomitant use of dehydroepiandrosterone (DHEA) and estrogen is not recommended. Monitor for symptoms and adverse effects of estrogen excess in those patients who elect to combine therapies. Such symptoms include (but are not limited to) nausea, headache, intolerance to contact lenses, insomnia, chorea, cholasma, colitis, acute breakthrough or withdrawal bleeding, changes in menstrual flow, leukorrhea, and pancreatitis.

7) Probable Mechanism: additive estrogenic effect since dehydroepiandrosterone is enzymatically converted into C-19 and C-18 sex steroids

8) Literature Reports

a) Estrone and estradiol levels increased to two-times the basal value following four weeks of dehydroepiandrosterone (DHEA) 400 milligrams (mg) four times daily for 28 days in six postmenopausal

women in a double-blind, placebo-controlled, crossover study. Subjects received DHEA or placebo for 28 days, followed by a 2-

week washout period, then crossed over to the other treatment (DHEA or placebo).

Estrone increased from 58.7 +/- 11.0 to 167.4 +/- 66.6 picomole/liter (pmol/L) and estradiol increased from 36.7 +/- 3.7 to 121.1 +/- 25.7 pmol/L. This corresponds to a maximal percent

change of 214 +/- 67 percent and 181 +/- 29 percent for estrone and estradiol, respectively (Mortola & Yen, 1990).

#### Estradiol

- 1) Interaction Effect: increased risk of estrogenic adverse effects
- 2) Summary: Combining dehydroepiandrosterone (DHEA) with estrogen may result in symptoms of estrogen excess. DHEA has increased endogenous estrogen levels in postmenopausal women (Mortola & Yen, 1990a). Pre- and post-menopausal women have effective enzymatic systems for the biotransformation of DHEA to C19 and C-18 sex steroids (Mortola & Yen, 1990a), suggesting that increased estrogen levels may occur in all women regardless of menopausal status.
- 3) Severity: minor
- 4) Onset: delayed
- 5) Substantiation: theoretical
- 6) Clinical Management: Concomitant use of dehydroepiandrosterone (DHEA) and estrogen is not recommended. Monitor for symptoms and adverse effects of estrogen excess in those patients who elect to combine therapies. Such symptoms include (but are not limited to) nausea, headache, intolerance to contact lenses, insomnia, chorea, cholasma, colitis, acute breakthrough or withdrawal bleeding, changes in menstrual flow, leukorrhea, and pancreatitis.
- 7) Probable Mechanism: additive estrogenic effect since dehydroepiandrosterone is enzymatically converted into C-19 and C-18 sex steroids
- 8) Literature Reports

a) Estrone and estradiol levels increased to two-times the basal value following four weeks of dehydroepiandrosterone (DHEA) 400 milligrams (mg) four times daily for 28 days in six postmenopausal women in a double-blind, placebo-controlled, crossover study. Subjects received DHEA or placebo for 28 days, followed by a 2-week washout period, then crossed over to the other treatment (DHEA or placebo). Estrone increased from 58.7 +/- 11.0 to 167.4 +/- 66.6 picomole/liter (pmol/L) and estradiol increased from 36.7 +/- 3.7 to 121.1 +/- 25.7 pmol/L. This corresponds to a maximal percent change of 214 +/- 67 percent and 181 +/- 29 percent for estrone and estradiol, respectively (Mortola & Yen, 1990).

#### Estradiol Cypionate

- 1) Interaction Effect: increased risk of estrogenic adverse effects
- 2) Summary: Combining dehydroepiandrosterone (DHEA) with estrogen may result in symptoms of estrogen excess. DHEA has increased endogenous estrogen levels in postmenopausal women (Mortola & Yen, 1990a). Pre- and post-menopausal women have effective enzymatic systems for the biotransformation of DHEA to C19 and C-18 sex steroids (Mortola & Yen, 1990a), suggesting that increased estrogen levels may occur in all women regardless of menopausal status.
- 3) Severity: minor
- 4) Onset: delayed
- 5) Substantiation: theoretical
- 6) Clinical Management: Concomitant use of dehydroepiandrosterone (DHEA) and estrogen is not recommended. Monitor for symptoms and adverse effects of estrogen excess in those patients who elect to combine therapies. Such symptoms



include (but are not limited to) nausea, headache, intolerance to contact lenses, insomnia, chorea, cholasma, colitis, acute breakthrough or withdrawal bleeding, changes in menstrual flow, leukorrhea, and pancreatitis.

7) Probable Mechanism: additive estrogenic effect since dehydroepiandrosterone is enzymatically converted into C-19 and C-18 sex steroids

8) Literature Reports

a) Estrone and estradiol levels increased to two-times the basal value following four weeks of dehydroepiandrosterone (DHEA) 400 milligrams (mg) four times daily for 28 days in six postmenopausal women in a double-blind, placebo-controlled, crossover study. Subjects received DHEA or placebo for 28 days, followed by a 2-week washout period, then crossed over to the other treatment (DHEA or placebo). Estrone increased from 58.7 +/- 11.0 to 167.4 +/- 66.6 picomole/liter (pmol/L) and estradiol increased from 36.7 +/- 3.7 to 121.1 +/- 25.7 pmol/L. This corresponds to a maximal percent change of 214 +/- 67 percent and 181 +/- 29 percent for estrone and estradiol, respectively (Mortola & Yen, 1990).

#### Estropipate

1) Interaction Effect: increased risk of estrogenic adverse effects

2) Summary: Combining dehydroepiandrosterone (DHEA) with estrogen may result in symptoms of estrogen excess. DHEA has increased endogenous estrogen levels in postmenopausal women (Mortola & Yen, 1990a). Pre- and post-menopausal women have effective enzymatic systems for the biotransformation of DHEA to C-19 and C-18 sex steroids (Mortola & Yen, 1990a), suggesting that increased estrogen levels may occur in all women regardless of menopausal status.

3) Severity: minor

4) Onset: delayed

5) Substantiation: theoretical

6) Clinical Management: Concomitant use of dehydroepiandrosterone (DHEA) and estrogen is not recommended. Monitor for symptoms and adverse effects of estrogen excess in those patients who elect to combine therapies. Such symptoms include (but are not limited to) nausea, headache, intolerance to contact lenses, insomnia, chorea, cholasma, colitis, acute breakthrough or withdrawal bleeding, changes in menstrual flow, leukorrhea, and pancreatitis.

7) Probable Mechanism: additive estrogenic effect since dehydroepiandrosterone is enzymatically converted into C-19 and C-18 sex steroids

8) Literature Reports

a) Estrone and estradiol levels increased to two-times the basal value following four weeks of dehydroepiandrosterone (DHEA) 400 milligrams (mg) four times daily for 28 days in six postmenopausal women in a double-blind, placebo-controlled, crossover study. Subjects received DHEA or placebo for 28 days, followed by a 2-week washout period, then crossed over to the other treatment (DHEA or placebo). Estrone increased from 58.7 +/- 11.0 to 167.4 +/- 66.6 picomole/liter (pmol/L) and estradiol increased from 36.7 +/- 3.7 to 121.1 +/- 25.7 pmol/L. This corresponds to a maximal percent change of 214 +/- 67 percent and 181 +/- 29 percent for estrone and estradiol, respectively (Mortola & Yen, 1990).

## Ethinyl Estradiol

- 1) Interaction Effect: increased risk of estrogenic adverse effects
- 2) Summary: Combining dehydroepiandrosterone (DHEA) with estrogen may result in symptoms of estrogen excess. DHEA has increased endogenous estrogen levels in postmenopausal women (Mortola & Yen, 1990a). Pre- and post-menopausal women have effective enzymatic systems for the biotransformation of DHEA to C-19 and C-18 sex steroids (Mortola & Yen, 1990a), suggesting that increased estrogen levels may occur in all women regardless of menopausal status.
- 3) Severity: minor
- 4) Onset: delayed
- 5) Substantiation: theoretical
- 6) Clinical Management: Concomitant use of dehydroepiandrosterone (DHEA) and estrogen is not recommended. Monitor for symptoms and adverse effects of estrogen excess in those patients who elect to combine therapies. Such symptoms include (but are not limited to) nausea, headache, intolerance to contact lenses, insomnia, chorea, cholasma, colitis, acute breakthrough or withdrawal bleeding, changes in menstrual flow, leukorrhea, and pancreatitis.
- 7) Probable Mechanism: additive estrogenic effect since dehydroepiandrosterone is enzymatically converted into C-19 and C-18 sex steroids
- 8) Literature Reports

a) Estrone and estradiol levels increased to two-times the basal value following four weeks of dehydroepiandrosterone (DHEA) 400 milligrams (mg) four times daily for 28 days in six postmenopausal women in a double-blind, placebo-controlled, crossover study. Subjects received DHEA or placebo for 28 days, followed by a 2-week washout period, then crossed over to the other treatment (DHEA or placebo). Estrone increased from 58.7 +/- 11.0 to 167.4 +/- 66.6 picomole/liter (pmol/L) and estradiol increased from 36.7 +/- 3.7 to 121.1 +/- 25.7 pmol/L. This corresponds to a maximal percent change of 214 +/- 67 percent and 181 +/- 29 percent for estrone and estradiol, respectively (Mortola & Yen, 1990).

## Ethopropazine

- 1) Interaction Effect: reduced effectiveness of phenothiazines
- 2) Summary: Dehydroepiandrosterone (DHEA) levels within the normal range of 100 to 400 microgram/deciliter (mcg/dL) are conducive to optimal treatment of patients with psychosis (Howard, 1992). In case reports, patients have been resistant to antipsychotics when DHEA levels were elevated (Howard, 1992). Patients being treated with phenothiazines for psychosis should avoid DHEA supplementation.
- 3) Severity: moderate
- 4) Onset: delayed
- 5) Substantiation: theoretical
- 6) Clinical Management: Avoid concomitant use of dehydroepiandrosterone (DHEA) and phenothiazines. If DHEA is elevated, treatment with dexamethasone 1 mg orally per day may be used to normalize DHEA levels.
- 7) Probable Mechanism: elevated dehydroepiandrosterone (DHEA) blood levels may reduce responsiveness to phenothiazines
- 8) Literature Reports

a) A 24-year-old female diagnosed with schizophrenia was resistant to daily doses of haloperidol 20 milligrams (mg), fluphenazine 40 mg, lithium carbonate 1200 mg, and lithium carbonate 900 mg plus thioridazine 300 mg. The patient appeared Cushingoid with moon face, acne, facial hair, abdominal hair, and a 40 pound weight gain in the previous 8 months. Dehydroepiandrosterone (DHEA) measured as part of an endocrine panel was 725 micrograms/deciliter (mcg/dL) (normal: 100 to 400 mcg/dL). Dexamethasone 1 mg orally at bedtime resulted in substantial improvement within one week. The patient appeared calmer, more alert with improved psychotic symptoms and ability to concentrate. At two weeks, a repeated DHEA level was within normal range (328 mcg/dL). The author concluded that elevated DHEA levels were associated with severe psychosis resistant to conventional antipsychotic therapy (Howard, 1992k).

b) A 13-year-old male decompensated with a subsequent two-year period of emotional problems accompanied by heavy use of LSD, hashish, barbiturates, and alcohol. His mental status included bizarre, disorganized, delusional thinking, auditory and visual hallucinations, paranoia, lack of attention to personal hygiene, agitation, and combativeness. He was diagnosed with chronic paranoid schizophrenia; schizophrenia, chronic undifferentiated type, and schizoaffective disorder, excited type. He was resistant to daily doses of trifluoperazine 40 mg, chlorpromazine 400 mg, and imipramine 100 mg. He was also resistant to combination therapy with chlorpromazine 400 mg with thiothixene 80 mg, thioridazine 1000 mg, perphenazine 48 mg with lithium carbonate 1200 mg, clonazepam 4 mg, and carbamazepine 1200 mg daily. Baseline DHEA level exceeded 900 mcg/dL. A seven-day suppression test with dexamethasone 1 mg orally at bedtime resulted in a normal DHEA level of 200 mcg/dL. By day 5, psychosis improved and the patient was well-oriented, conversational, and was making good eye contact. Once dexamethasone was discontinued, rapid decompensation and florid psychosis ensued despite "substantial amounts of psychotropic medications." DHEA increased to 536 mcg/dL. The author concluded that elevated DHEA levels were associated with florid psychosis resistant to conventional antipsychotic therapy (Howard, 1992k).

## Fluoxetine

1) Interaction Effect: development of manic symptoms

2) Summary: A case has been reported in which concomitant dehydroepiandrosterone (DHEA) and sertraline use was suggested to precipitate a manic episode in a patient with a history of bipolar disorder (Dean, 2000a). DHEA was also noted to cause mania in a patient with no previous personal or family history of bipolar disorder (Markowitz et al, 1999f). Elevated DHEA levels have been found in patients with mental disorders; DHEA suppression has led to improvement in psychotic symptoms (Howard, 1992u). DHEA possesses proserotonergic activity which may predispose patients to manic episodes (Majewska, 1995). DHEA is a precursor to androgenic steroids, which in high doses may precipitate mania (Markowitz et al, 1999f). Patients taking medication for bipolar disorder or patients with a personal and/or family history of bipolar disorder should not take DHEA until further data is available to characterize this drug-herb interaction. Concomitant use of DHEA with selective serotonin reuptake inhibitors (SSRIs) should be avoided due to the potential additive precipitation of mania.

3) Severity: moderate

- 4) Onset: delayed
- 5) Substantiation: theoretical
- 6) Clinical Management: Avoid concomitant use of dehydroepiandrosterone (DHEA) and selective serotonin reuptake inhibitors. If patients present with manic symptoms (i.e. agitation, anger, irritability, aggressive behavior), determine if the patient is using DHEA and discontinue DHEA.
- 7) Probable Mechanism: serotonergic activity of dehydroepiandrosterone, possibly increased androgen levels
- 8) Literature Reports

a) A 31-year-old male was admitted following threats to commit suicide and injure family members. He had self-initiated sertraline 100 milligrams (mg) daily for the previous 2 to 3 weeks for depression. Sertraline had been prescribed 3 years prior when he was diagnosed with bipolar disorder, which he discontinued after 2 weeks. He had also taken dehydroepiandrosterone (DHEA) 300 mg to 500 mg daily for the previous 2 months apparently for weight training. Following use of DHEA for a short time, he became more irritable, was not sleeping well, and began threatening a female friend and family members. He also drank alcohol occasionally and reportedly had difficulty controlling his anger when intoxicated. Sertraline was stopped and the patient was treated with valproic acid with the dose titrated to 500 mg twice daily. The combination of DHEA, sertraline, and alcohol was suggested responsible for the developing of the manic episode (Dean, 2000).

#### Fluphenazine

- 1) Interaction Effect: reduced effectiveness of phenothiazines
- 2) Summary: Dehydroepiandrosterone (DHEA) levels within the normal range of 100 to 400 microgram/deciliter (mcg/dL) are conducive to optimal treatment of patients with psychosis (Howard, 1992). In case reports, patients have been resistant to antipsychotics when DHEA levels were elevated (Howard, 1992). Patients being treated with phenothiazines for psychosis should avoid DHEA supplementation.
- 3) Severity: moderate
- 4) Onset: delayed
- 5) Substantiation: theoretical
- 6) Clinical Management: Avoid concomitant use of dehydroepiandrosterone (DHEA) and phenothiazines. If DHEA is elevated, treatment with dexamethasone 1 mg orally per day may be used to normalize DHEA levels.
- 7) Probable Mechanism: elevated dehydroepiandrosterone (DHEA) blood levels may reduce responsiveness to phenothiazines
- 8) Literature Reports

a) A 24-year-old female diagnosed with schizophrenia was resistant to daily doses of haloperidol 20 milligrams (mg), fluphenazine 40 mg, lithium carbonate 1200 mg, and lithium carbonate 900 mg plus thioridazine 300 mg. The patient appeared Cushingoid with moon face, acne, facial hair, abdominal hair, and a 40 pound weight gain in the previous 8 months. Dehydroepiandrosterone (DHEA) measured as part of an endocrine panel was 725 micrograms/deciliter (mcg/dL) (normal: 100 to 400 mcg/dL). Dexamethasone 1 mg orally at bedtime resulted in substantial improvement within one week. The patient appeared calmer, more alert with improved psychotic symptoms and

ability to concentrate. At two weeks, a repeated DHEA level was within normal range (328 mcg/dL). The author concluded that elevated DHEA levels were associated with severe psychosis resistant to conventional antipsychotic therapy (Howard, 1992k).

b) A 13-year-old male decompensated with a subsequent two-year period of emotional problems accompanied by heavy use of LSD, hashish, barbiturates, and alcohol. His mental status included bizarre, disorganized, delusional thinking, auditory and visual hallucinations, paranoia, lack of attention to personal hygiene, agitation, and combativeness. He was diagnosed with chronic paranoid schizophrenia; schizophrenia, chronic undifferentiated type, and schizoaffective disorder, excited type. He was resistant to daily doses of trifluoperazine 40 mg, chlorpromazine 400 mg, and imipramine 100 mg. He was also resistant to combination therapy with chlorpromazine 400 mg with thiothixene 80 mg, thioridazine 1000 mg, perphenazine 48 mg with lithium carbonate 1200 mg, clonazepam 4 mg, and carbamazepine 1200 mg daily. Baseline DHEA level exceeded 900 mcg/dL. A seven-day suppression test with dexamethasone 1 mg orally at bedtime resulted in a normal DHEA level of 200 mcg/dL. By day 5, psychosis improved and the patient was well-oriented, conversational, and was making good eye contact. Once dexamethasone was discontinued, rapid decompensation and florid psychosis ensued despite "substantial amounts of psychotropic medications." DHEA increased to 536 mcg/dL. The author concluded that elevated DHEA levels were associated with florid psychosis resistant to conventional anti psychotic therapy (Howard, 1992k).

#### Fluvoxamine

1)Interaction Effect: development of manic symptoms

2)Summary: A case has been reported in which concomitant dehydroepiandrosterone (DHEA) and sertraline use was suggested to precipitate a manic episode in a patient with a history of bipolar disorder (Dean, 2000a). DHEA was also noted to cause mania in a patient with no previous personal or family history of bipolar disorder (Markowitz et al, 1999f). Elevated DHEA levels have been found in patients with mental disorders; DHEA suppression has lead to improvement in psychotic symptoms (Howard, 1992u). DHEA possesses proserotonergic activity which may predispose patients to manic episodes (Majewska, 1995). DHEA is a precursor to androgenic steroids, which in high doses may precipitate mania (Markowitz et al, 1999f). Patients taking medication for bipolar disorder or patients with a personal and/or family history of bipolar disorder should not take DHEA until further data is available to characterize this drug-herb interaction. Concomitant use of DHEA with selective serotonin reuptake inhibitors (SSRIs) should be avoided due to the potential additive precipitation of mania.

3)Severity: moderate

4)Onset: delayed

5)Substantiation: theoretical

6)Clinical Management: Avoid concomitant use of dehydroepiandrosterone (DHEA) and selective serotonin reuptake inhibitors. If patients present with manic symptoms (i.e. agitation, anger, irritability, aggressive behavior), determine if the patient is using DHEA and discontinue DHEA.

7)Probable Mechanism: serotonergic activity of dehydroepiandrosterone, possibly increased androgen levels

8)Literature Reports

a) A 31-year-old male was admitted following threats to commit suicide and injure family members. He had self-initiated sertraline 100 milligrams (mg) daily for the previous 2 to 3 weeks for depression. Sertraline had been prescribed 3 years prior when he was diagnosed with bipolar disorder, which he discontinued after 2 weeks. He had also taken dehydroepiandrosterone (DHEA) 300 mg to 500 mg daily for the previous 2 months apparently for weight training. Following use of DHEA for a short time, he became more irritable, was not sleeping well, and began threatening a female friend and family members. He also drank alcohol occasionally and reportedly had difficulty controlling his anger when intoxicated. Sertraline was stopped and the patient was treated with valproic acid with the dose titrated to 500 mg twice daily. The combination of DHEA, sertraline, and alcohol was suggested responsible for the developing of the manic episode (Dean, 2000).

#### Haloperidol

- 1)Interaction Effect: reduced effectiveness of haloperidol
- 2)Summary: Dehydroepiandrosterone (DHEA) levels within the normal range of 100 to 400 microgram/deciliter (mcg/dL) are conducive to optimal treatment of patients with psychosis (Howard, 1992)]. In case reports, patients have been resistant to antipsychotics when DHEA levels were elevated (Howard, 1992)]. Patient being treated with haloperidol should avoid DHEA supplementation.
- 3)Severity: moderate
- 4)Onset: delayed
- 5)Substantiation: theoretical
- 6)Clinical Management: Avoid concomitant use of dehydroepiandrosterone (DHEA) and haloperidol. If DHEA is elevated, treatment with dexamethasone 1 mg orally per day may be used to normalize DHEA levels.
- 7)Probable Mechanism: elevated dehydroepiandrosterone (DHEA) blood levels may reduce responsiveness to haloperidol
- 8)Literature Reports

a) A 24-year-old female diagnosed with schizophrenia was resistant to daily doses of haloperidol 20 milligrams (mg), fluphenazine 40 mg, lithium carbonate 1200 mg, and lithium carbonate 900 mg plus thioridazine 300 mg. The patient appeared Cushingoid with moon face, acne, facial hair, abdominal hair, and a 40 pound weight gain in the previous 8 months. Dehydroepiandrosterone (DHEA) measured as part of an endocrine panel was 725 micrograms/deciliter (mcg/dL) (normal: 100 to 400 mcg/dL).

Dexamethasone 1 mg orally at bedtime resulted in substantial improvement within one week. The patient appeared calmer, more alert with improved psychotic symptoms and ability to concentrate. At two weeks, a repeated DHEA level was within normal range (328 mcg/dL). The author concluded that elevated DHEA levels were associated with severe psychosis resistant to conventional antipsychotic therapy (Howard, 1992i).

b) A 13-year-old male decompensated with a subsequent two-year period of emotional problems accompanied by heavy use of LSD, hashish, barbiturates, and alcohol. His mental status included bizarre, disorganized, delusional thinking, auditory and visual hallucinations, paranoia, lack of attention to personal hygiene, agitation, and combativeness. He was diagnosed with chronic paranoid schizophrenia; schizophrenia, chronic undifferentiated type, and

schizoaffective disorder, excited type. He was resistant to daily doses of trifluoperazine 40 mg, chlorpromazine 400 mg, and imipramine 100 mg. He was also resistant to combination therapy with chlorpromazine 400 mg with thiothixene 80 mg, thioridazine 1000 mg, perphenazine 48 mg with lithium carbonate 1200 mg, clonazepam 4 mg, and carbamazepine 1200 mg daily. Baseline DHEA level exceeded 900 mcg/dL. A seven-day suppression test with dexamethasone 1 mg orally at bedtime resulted in a normal DHEA level of 200 mcg/dL. By day 5, psychosis improved and the patient was well-oriented, conversational, and was making good eye contact. Once dexamethasone was discontinued, rapid decompensation and florid psychosis ensued despite "substantial amounts of psychotropic medications." DHEA increased to 536 mcg/dL. The author concluded that elevated DHEA levels were associated with florid psychosis resistant to conventional antipsychotic therapy (Howard, 1992i).

## Lithium

- 1) Interaction Effect: reduced effectiveness of lithium
- 2) Summary: Dehydroepiandrosterone (DHEA) in a single case report was noted to cause mania in a patient with no previous personal or family history of bipolar disorder (Markowitz et al, 1999a). Elevated DHEA levels have been found in patients with mental disorders; DHEA suppression has led to improvement in psychotic symptoms (Howard, 1992a). Patients taking medication for bipolar disorder or patients with a personal and/or family history of bipolar disorder should not take DHEA until further data is available to characterize this drug-herb interaction.
- 3) Severity: moderate
- 4) Onset: delayed
- 5) Substantiation: theoretical
- 6) Clinical Management: Concomitant use of dehydroepiandrosterone (DHEA) with lithium may cause a return of manic symptoms. Patients with a personal or family history of bipolar disorder should be advised to avoid DHEA use.
- 7) Probable Mechanism: proserotonergic activity of dehydroepiandrosterone may predispose patients to manic episodes; dehydroepiandrosterone is a precursor to androgenic steroids, which in high doses may precipitate mania
- 8) Literature Reports

a) A 68 year-old male with no documented psychiatric history initiated dehydroepiandrosterone (DHEA) 100 milligrams (mg) daily and increased the dose to 200 to 300 mg daily for 6 months. Within 3 months, family members noted the onset of odd behavior with prominent symptoms of agitation, delusional thinking, decreased sleep and appetite, and spending sprees. The patient was not taking any prescribed medication but did ingest alcohol in amounts up to 1 case of beer daily. Another 3 months elapsed, leading to involuntary inpatient admission secondary to rapid, loud, pressured speech with grandiose thoughts. At admission, the patient reported that he had decreased alcohol intake to 2 beers daily due to family concerns about his behavior changes. There was no family history of bipolar disorder. Urinary drug screen was negative. Over the seven-day hospital stay, with the institution of valproic acid 500 mg twice daily, the patient's behavior and sleep patterns improved, and the patient believed DHEA led to his symptoms. There were no ethanol withdrawal symptoms. The patient was discharged with follow-up care



from his primary care physician with a diagnosis of substance-induced mood disorder (Markowitz et al, 1999).

b) A 24-year-old female diagnosed with schizophrenia was resistant to daily doses of haloperidol 20 milligrams (mg), fluphenazine 40 mg, lithium carbonate 1200 mg, and lithium carbonate 900 mg plus thioridazine 300 mg. The patient appeared Cushingoid with moon face, acne, facial hair, abdominal hair, and a 40 pound weight gain in the previous 8 months. Dehydroepiandrosterone (DHEA) measured as part of an endocrine panel was 725 micrograms/deciliter (mcg/dL) (normal: 100 to 400 mcg/dL).

Dexamethasone 1 mg orally at bedtime resulted in substantial improvement within one week. The patient appeared calmer, more alert with improved psychotic symptoms and ability to concentrate. At two weeks, a repeated DHEA level was within normal range (328 mcg/dL). The author concluded that elevated DHEA levels were associated with severe psychosis resistant to conventional antipsychotic therapy (Howard, 1992).

c) A 13-year-old male decompensated with a subsequent two-year period of emotional problems accompanied by heavy use of LSD, hashish, barbiturates, and alcohol. His mental status included bizarre, disorganized, delusional thinking, auditory and visual hallucinations, paranoia, lack of attention to personal hygiene, agitation, and combativeness. He was diagnosed with chronic paranoid schizophrenia; schizophrenia, chronic undifferentiated type, and schizoaffective disorder, excited type. He was resistant to daily doses of trifluoperazine 40 mg, chlorpromazine 400 mg, and imipramine 100 mg. He was also resistant to combination therapy with chlorpromazine 400 mg with thiothixene 80 mg, thioridazine 1000 mg, perphenazine 48 mg with lithium carbonate 1200 mg, clonazepam 4 mg, and carbamazepine 1200 mg daily. Baseline DHEA level exceeded 900 mcg/dL. A seven-day suppression test with dexamethasone 1 mg orally at bedtime resulted in a normal DHEA level of 200 mcg/dL. By day 5, psychosis improved and the patient was well-oriented, conversational, and was making good eye contact. Once dexamethasone was discontinued, rapid decompensation and florid psychosis ensued despite "substantial amounts of psychotropic medications." DHEA increased to 536 mcg/dL. The author concluded that elevated DHEA levels were associated with florid psychosis resistant to conventional anti psychotic therapy (Howard, 1992).

#### Loxapine Interaction Effect: reduced effectiveness of loxapine

1)Summary: Dehydroepiandrosterone (DHEA) levels within the normal range of 100 to 400 microgram/deciliter (mcg/dL) are conducive to optimal treatment of patients with psychosis (Howard, 1992r). In case reports, patients have been resistant to antipsychotics when DHEA levels were elevated (Howard, 1992r). Patient being treated with loxapine should avoid DHEA supplementation.

2)Severity: moderate

3)Onset: delayed

4)Substantiation: theoretical

5)Clinical Management: Avoid concomitant use of dehydroepiandrosterone (DHEA) and loxapine. If DHEA is elevated, treatment with dexamethasone 1 mg orally per day may be used to normalize DHEA levels.

6)Probable Mechanism: elevated dehydroepiandrosterone (DHEA) blood levels may reduce responsiveness to loxapine

7)Literature Reports

a) A 24-year-old female diagnosed with schizophrenia was resistant to daily doses of haloperidol 20 milligrams (mg), fluphenazine 40 mg, lithium carbonate 1200 mg, and lithium carbonate 900 mg plus thioridazine 300 mg. The patient appeared Cushingoid with moon face, acne, facial hair, abdominal hair, and a 40 pound weight gain in the previous 8 months. Dehydroepiandrosterone (DHEA) measured as part of an endocrine panel was 725 micrograms/deciliter (mcg/dL) (normal: 100 to 400 mcg/dL).

Dexamethasone 1 mg orally at bedtime resulted in substantial improvement within one week. The patient appeared calmer, more alert with improved psychotic symptoms and ability to concentrate. At two weeks, a repeated DHEA level was within normal range (328 mcg/dL). The author concluded that elevated DHEA levels were associated with severe psychosis resistant to conventional antipsychotic therapy (Howard, 1992q). b) A 13-year-old male decompensated with a subsequent two-year period of emotional problems accompanied by heavy use of LSD, hashish, barbiturates, and alcohol. His mental status included bizarre, disorganized, delusional thinking, auditory and visual hallucinations, paranoia, lack of attention to personal hygiene, agitation, and combativeness. He was diagnosed with chronic paranoid schizophrenia; schizophrenia, chronic undifferentiated type, and schizoaffective disorder, excited type. He was resistant to daily doses of trifluoperazine 40 mg, chlorpromazine 400 mg, and imipramine 100 mg. He was also resistant to combination therapy with chlorpromazine 400 mg with thiothixene 80 mg, thioridazine 1000 mg, perphenazine 48 mg with lithium carbonate 1200 mg, clonazepam 4 mg, and carbamazepine 1200 mg daily. Baseline DHEA level exceeded 900 mcg/dL. A seven-day suppression test with dexamethasone 1 mg orally at bedtime resulted in a normal DHEA level of 200 mcg/dL. By day 5, psychosis improved and the patient was well-oriented, conversational, and was making good eye contact. Once dexamethasone was discontinued, rapid decompensation and florid psychosis ensued despite "substantial amounts of psychotropic medications." DHEA increased to 536 mcg/dL. The author concluded that elevated DHEA levels were associated with florid psychosis resistant to conventional antipsychotic therapy (Howard, 1992q).

#### Mesoridazine

- 1)Interaction Effect: reduced effectiveness of phenothiazines
- 2)Summary: Dehydroepiandrosterone (DHEA) levels within the normal range of 100 to 400 microgram/deciliter (mcg/dL) are conducive to optimal treatment of patients with psychosis (Howard, 1992l). In case reports, patients have been resistant to antipsychotics when DHEA levels were elevated (Howard, 1992l). Patients being treated with phenothiazines for psychosis should avoid DHEA supplementation.
- 3)Severity: moderate
- 4)Onset: delayed
- 5)Substantiation: theoretical
- 6)Clinical Management: Avoid concomitant use of dehydroepiandrosterone (DHEA) and phenothiazines. If DHEA is elevated, treatment with dexamethasone 1 mg orally per day may be used to normalize DHEA levels.
- 7)Probable Mechanism: elevated dehydroepiandrosterone (DHEA) blood levels may reduce responsiveness to phenothiazines
- 8)Literature Reports

a) A 24-year-old female diagnosed with schizophrenia was resistant to daily doses of haloperidol 20 milligrams (mg), fluphenazine 40 mg, lithium carbonate 1200 mg, and lithium carbonate 900 mg plus thioridazine 300 mg. The patient appeared Cushingoid with moon face, acne, facial hair, abdominal hair, and a 40 pound weight gain in the previous 8 months. Dehydroepiandrosterone (DHEA) measured as part of an endocrine panel was 725 micrograms/deciliter (mcg/dL) (normal: 100 to 400 mcg/dL). Dexamethasone 1 mg orally at bedtime resulted in substantial improvement within one week. The patient appeared calmer, more alert with improved psychotic symptoms and ability to concentrate. At two weeks, a repeated DHEA level was within normal range (328 mcg/dL). The author concluded that elevated DHEA levels were associated with severe psychosis resistant to conventional antipsychotic therapy (Howard, 1992k).

b) A 13-year-old male decompensated with a subsequent two-year period of emotional problems accompanied by heavy use of LSD, hashish, barbiturates, and alcohol. His mental status included bizarre, disorganized, delusional thinking, auditory and visual hallucinations, paranoia, lack of attention to personal hygiene, agitation, and combativeness. He was diagnosed with chronic paranoid schizophrenia; schizophrenia, chronic undifferentiated type, and schizoaffective disorder, excited type. He was resistant to daily doses of trifluoperazine 40 mg, chlorpromazine 400 mg, and imipramine 100 mg. He was also resistant to combination therapy with chlorpromazine 400 mg with thiothixene 80 mg, thioridazine 1000 mg, perphenazine 48 mg with lithium carbonate 1200 mg, clonazepam 4 mg, and carbamazepine 1200 mg daily. Baseline DHEA level exceeded 900 mcg/dL. A seven-day suppression test with dexamethasone 1 mg orally at bedtime resulted in a normal DHEA level of 200 mcg/dL. By day 5, psychosis improved and the patient was well-oriented, conversational, and was making good eye contact. Once dexamethasone was discontinued, rapid decompensation and florid psychosis ensued despite "substantial amounts of psychotropic medications." DHEA increased to 536 mcg/dL. The author concluded that elevated DHEA levels were associated with florid psychosis resistant to conventional anti psychotic therapy (Howard, 1992k).

#### Methdilazine

- 1) Interaction Effect: reduced effectiveness of phenothiazines
- 2) Summary: Dehydroepiandrosterone (DHEA) levels within the normal range of 100 to 400 microgram/deciliter (mcg/dL) are conducive to optimal treatment of patients with psychosis (Howard, 1992l). In case reports, patients have been resistant to antipsychotics when DHEA levels were elevated (Howard, 1992l). Patients being treated with phenothiazines for psychosis should avoid DHEA supplementation.
- 3) Severity: moderate
- 4) Onset: delayed
- 5) Substantiation: theoretical
- 6) Clinical Management: Avoid concomitant use of dehydroepiandrosterone (DHEA) and phenothiazines. If DHEA is elevated, treatment with dexamethasone 1 mg orally per day may be used to normalize DHEA levels.
- 7) Probable Mechanism: elevated dehydroepiandrosterone (DHEA) blood levels may reduce responsiveness to phenothiazines
- 8) Literature Reports

a) A 24-year-old female diagnosed with schizophrenia was resistant to daily doses of haloperidol 20 milligrams (mg), fluphenazine 40 mg, lithium carbonate 1200 mg, and lithium carbonate 900 mg plus thioridazine 300 mg. The patient appeared Cushingoid with moon face, acne, facial hair, abdominal hair, and a 40 pound weight gain in the previous 8 months. Dehydroepiandrosterone (DHEA) measured as part of an endocrine panel was 725 micrograms/deciliter (mcg/dL) (normal: 100 to 400 mcg/dL).

Dexamethasone 1 mg orally at bedtime resulted in substantial improvement within one week. The patient appeared calmer, more alert with improved psychotic symptoms and ability to concentrate. At two weeks, a repeated DHEA level was within normal range (328 mcg/dL). The author concluded that elevated DHEA levels were associated with severe psychosis resistant to conventional antipsychotic therapy (Howard, 1992k).

b) A 13-year-old male decompensated with a subsequent two-year period of emotional problems accompanied by heavy use of LSD, hashish, barbiturates, and alcohol. His mental status included bizarre, disorganized, delusional thinking, auditory and visual hallucinations, paranoia, lack of attention to personal hygiene, agitation, and combativeness. He was diagnosed with chronic paranoid schizophrenia; schizophrenia, chronic undifferentiated type, and schizoaffective disorder, excited type. He was resistant to daily doses of trifluoperazine 40 mg, chlorpromazine 400 mg, and imipramine 100 mg. He was also resistant to combination therapy with chlorpromazine 400 mg with thiothixene 80 mg, thioridazine 1000 mg, perphenazine 48 mg with lithium carbonate 1200 mg, clonazepam 4 mg, and carbamazepine 1200 mg daily. Baseline DHEA level exceeded 900 mcg/dL. A seven-day suppression test with dexamethasone 1 mg orally at bedtime resulted in a normal DHEA level of 200 mcg/dL. By day 5, psychosis improved and the patient was well-oriented, conversational, and was making good eye contact. Once dexamethasone was discontinued, rapid decompensation and florid psychosis ensued despite "substantial amounts of psychotropic medications." DHEA increased to 536 mcg/dL. The author concluded that elevated DHEA levels were associated with florid psychosis resistant to conventional antipsychotic therapy (Howard, 1992k).

## Molindone

1)Interaction Effect: reduced effectiveness of molindone

2)Summary: Dehydroepiandrosterone (DHEA) levels within the normal range of 100 to 400 microgram/deciliter (mcg/dL) are conducive to optimal treatment of patients with psychosis (Howard, 1992p). In case reports, patients have been resistant to antipsychotics when DHEA levels were elevated (Howard, 1992p). Patient being treated with molindone should avoid DHEA supplementation.

3)Severity: moderate

4)Onset: delayed

5)Substantiation: theoretical

6)Clinical Management: Avoid concomitant use of dehydroepiandrosterone (DHEA) and molindone. If DHEA is elevated, treatment with dexamethasone 1 mg orally per day may be used to normalize DHEA levels.

7)Probable Mechanism: elevated dehydroepiandrosterone (DHEA) blood levels may reduce responsiveness to molindone

8)Literature Reports

a) A 24-year-old female diagnosed with schizophrenia was resistant to daily doses of haloperidol 20 milligrams (mg), fluphenazine 40 mg, lithium carbonate 1200 mg, and lithium carbonate 900 mg plus thioridazine 300 mg. The patient appeared Cushingoid with moon face, acne, facial hair, abdominal hair, and a 40 pound weight gain in the previous 8 months. Dehydroepiandrosterone (DHEA) measured as part of an endocrine panel was 725 micrograms/deciliter (mcg/dL) (normal: 100 to 400 mcg/dL). Dexamethasone 1 mg orally at bedtime resulted in substantial improvement within one week. The patient appeared calmer, more alert with improved psychotic symptoms and ability to concentrate. At two weeks, a repeated DHEA level was within normal range (328 mcg/dL). The author concluded that elevated DHEA levels were associated with severe psychosis resistant to conventional antipsychotic therapy (Howard, 1 992o).

b) A 13-year-old male decompensated with a subsequent two-year period of emotional problems accompanied by heavy use of LSD, hashish, barbiturates, and alcohol. His mental status included bizarre, disorganized, delusional thinking, auditory and visual hallucinations, paranoia, lack of attention to personal hygiene, agitation, and combativeness. He was diagnosed with chronic paranoid schizophrenia; schizophrenia, chronic undifferentiated type, and schizoaffective disorder, excited type. He was resistant to daily doses of trifluoperazine 40 mg, chlorpromazine 400 mg, and imipramine 100 mg. He was also resistant to combination therapy with chlorpromazine 400 mg with thiothixene 80 mg, thioridazine 1000 mg, perphenazine 48 mg with lithium carbonate 1200 mg, clonazepam 4 mg, and carbamazepine 1200 mg daily. Baseline DHEA level exceeded 900 mcg/dL. A seven-day suppression test with dexamethasone 1 mg orally at bedtime resulted in a normal DHEA level of 200 mcg/dL. By day 5, psychosis improved and the patient was well-oriented, conversational, and was making good eye contact. Once dexamethasone was discontinued, rapid decompensation and florid psychosis ensued despite "substantial amounts of psychotropic medications." DHEA increased to 536 mcg/dL. The author concluded that elevated DHEA levels were associated with florid psychosis resistant to conventional antipsychotic therapy (Howard, 1 992o).

## Olanzapine

- 1) Interaction Effect: reduced effectiveness of olanzapine
- 2) Summary: Dehydroepiandrosterone (DHEA) levels within the normal range of 100 to 400 microgram/deciliter (mcg/dL) are conducive for optimal treatment of patients with psychosis (Howard, 1 992t). In case reports, patients have been resistant to antipsychotics when DHEA levels were elevated (Howard, 1 992t). Patients being treated with olanzapine should avoid DHEA supplementation.
- 3) Severity: moderate
- 4) Onset: delayed
- 5) Substantiation: theoretical
- 6) Clinical Management: Avoid concomitant use of dehydroepiandrosterone (DHEA) and olanzapine. If DHEA is elevated, treatment with dexamethasone 1 mg orally per day may be used to normalize DHEA levels.
- 7) Probable Mechanism: elevated dehydroepiandrosterone (DHEA) blood levels may reduce responsiveness to olanzapine
- 8) Literature Reports

a) A 24-year-old female diagnosed with schizophrenia was resistant to daily doses of haloperidol 20 milligrams (mg), fluphenazine 40 mg, lithium carbonate 1200 mg, and lithium carbonate 900 mg plus thioridazine 300 mg. The patient appeared Cushingoid with moon face, acne, facial hair, abdominal hair, and a 40 pound weight gain in the previous 8 months. Dehydroepiandrosterone (DHEA) measured as part of an endocrine panel was 725 micrograms/deciliter (mcg/dL) (normal: 100 to 400 mcg/dL).

Dexamethasone 1 mg orally at bedtime resulted in substantial improvement within one week. The patient appeared calmer, more alert with improved psychotic symptoms and ability to concentrate. At two weeks, a repeated DHEA level was within normal range (328 mcg/dL). The author concluded that elevated DHEA levels were associated with severe psychosis resistant to conventional antipsychotic therapy (Howard, 1992s).

b) A 13-year-old male decompensated with a subsequent two-year period of emotional problems accompanied by heavy use of LSD, hashish, barbiturates, and alcohol. His mental status included bizarre, disorganized, delusional thinking, auditory and visual hallucinations, paranoia, lack of attention to personal hygiene, agitation, and combativeness. He was diagnosed with chronic paranoid schizophrenia; schizophrenia, chronic undifferentiated type, and schizoaffective disorder, excited type. He was resistant to daily doses of trifluoperazine 40 mg, chlorpromazine 400 mg, and imipramine 100 mg. He was also resistant to combination therapy with chlorpromazine 400 mg with thiothixene 80 mg, thioridazine 1000 mg, perphenazine 48 mg with lithium carbonate 1200 mg, clonazepam 4 mg, and carbamazepine 1200 mg daily. Baseline DHEA level exceeded 900 mcg/dL. A seven-day suppression test with dexamethasone 1 mg orally at bedtime resulted in a normal DHEA level of 200 mcg/dL. By day 5, psychosis improved and the patient was well-oriented, conversational, and was making good eye contact. Once dexamethasone was discontinued, rapid decompensation and florid psychosis ensued despite "substantial amounts of psychotropic medications". DHEA increased to 536 mcg/dL. The author concluded that elevated DHEA levels were associated with florid psychosis resistant to conventional antipsychotic therapy (Howard, 1992s).

## Paroxetine

1) Interaction Effect: development of manic symptoms

2) Summary: A case has been reported in which concomitant dehydroepiandrosterone (DHEA) and sertraline use was suggested to precipitate a manic episode in a patient with a history of bipolar disorder (Dean, 2000a). DHEA was also noted to cause mania in a patient with no previous personal or family history of bipolar disorder (Markowitz et al, 1999f). Elevated DHEA levels have been found in patients with mental disorders; DHEA suppression has led to improvement in psychotic symptoms (Howard, 1992u). DHEA possesses proserotonergic activity which may predispose patients to manic episodes (Majewska, 1995). DHEA is a precursor to androgenic steroids, which in high doses may precipitate mania (Markowitz et al, 1999f). Patients taking medication for bipolar disorder or patients with a personal and/or family history of bipolar disorder should not take DHEA until further data is available to characterize this drug-herb interaction. Concomitant use of DHEA with selective serotonin reuptake inhibitors (SSRIs) should be

avoided due to the potential additive precipitation of mania.

3)Severity: moderate

4)Onset: delayed

5)Substantiation: theoretical

6)Clinical Management: Avoid concomitant use of dehydroepiandrosterone (DHEA) and selective serotonin reuptake inhibitors. If patients present with manic symptoms (i.e. agitation, anger, irritability, aggressive behavior), determine if the patient is using DHEA and discontinue DHEA.

7)Probable Mechanism: serotonergic activity of dehydroepiandrosterone, possibly increased androgen levels

8)Literature Reports

a) A 31-year-old male was admitted following threats to commit suicide and injure family members. He had self-initiated sertraline 100 milligrams (mg) daily for the previous 2 to 3 weeks for depression. Sertraline had been prescribed 3 years prior when he was diagnosed with bipolar disorder, which he discontinued after 2 weeks. He had also taken dehydroepiandrosterone (DHEA) 300 mg to 500 mg daily for the previous 2 months apparently for weight training. Following use of DHEA for a short time, he became more irritable, was not sleeping well, and began threatening a female friend and family members. He also drank alcohol occasionally and reportedly had difficulty controlling his anger when intoxicated. Sertraline was stopped and the patient was treated with valproic acid with the dose titrated to 500 mg twice daily. The combination of DHEA, sertraline, and alcohol was suggested responsible for the developing of the manic episode (Dean, 2000).

#### Perazine

1)Interaction Effect: reduced effectiveness of phenothiazines

2)Summary: Dehydroepiandrosterone (DHEA) levels within the normal range of 100 to 400 microgram/deciliter (mcg/dL) are conducive to optimal treatment of patients with psychosis (Howard, 1992). In case reports, patients have been resistant to antipsychotics when DHEA levels were elevated (Howard, 1992). Patients being treated with phenothiazines for psychosis should avoid DHEA supplementation.

3)Severity: moderate

4)Onset: delayed

5)Substantiation: theoretical

6)Clinical Management: Avoid concomitant use of dehydroepiandrosterone (DHEA) and phenothiazines. If DHEA is elevated, treatment with dexamethasone 1 mg orally per day may be used to normalize DHEA levels.

7)Probable Mechanism: elevated dehydroepiandrosterone (DHEA) blood levels may reduce responsiveness to phenothiazines

8) Literature Reports

a)A 24-year-old female diagnosed with schizophrenia was resistant to daily doses of haloperidol 20 milligrams (mg), fluphenazine 40 mg, lithium carbonate 1200 mg, and lithium carbonate 900 mg plus thioridazine 300 mg. The patient appeared Cushingoid with moon face, acne, facial hair, abdominal hair, and a 40 pound weight gain in the previous 8 months. Dehydroepiandrosterone (DHEA) measured as part of an endocrine panel was 725 micrograms/deciliter (mcg/dL) (normal: 100 to 400 mcg/dL). Dexamethasone 1 mg orally at bedtime resulted in substantial improvement



within one week. The patient appeared calmer, more alert with improved psychotic symptoms and ability to concentrate. At two weeks, a repeated DHEA level was within normal range (328 mcg/dL). The author concluded that elevated DHEA levels were associated with severe psychosis resistant to conventional anti psychotic therapy (Howard, 1992k).

b) A 13-year-old male decompensated with a subsequent two-year period of emotional problems accompanied by heavy use of LSD, hashish, barbiturates, and alcohol. His mental status included bizarre, disorganized, delusional thinking, auditory and visual hallucinations, paranoia, lack of attention to personal hygiene, agitation, and combativeness. He was diagnosed with chronic paranoid schizophrenia; schizophrenia, chronic undifferentiated type, and schizoaffective disorder, excited type. He was resistant to daily doses of trifluoperazine 40 mg, chlorpromazine 400 mg, and imipramine 100 mg. He was also resistant to combination therapy with chlorpromazine 400 mg with thiothixene 80 mg, thioridazine 1000 mg, perphenazine 48 mg with lithium carbonate 1200 mg, clonazepam 4 mg, and carbamazepine 1200 mg daily. Baseline DHEA level exceeded 900 mcg/dL. A seven-day suppression test with dexamethasone 1 mg orally at bedtime resulted in a normal DHEA level of 200 mcg/dL. By day 5, psychosis improved and the patient was well-oriented, conversational, and was making good eye contact. Once dexamethasone was discontinued, rapid decompensation and florid psychosis ensued despite "substantial amounts of psychotropic medications." DHEA increased to 536 mcg/dL. The author concluded that elevated DHEA levels were associated with florid psychosis resistant to conventional antipsychotic therapy (Howard, 1992k).

#### Perphenazine

- 1) Interaction Effect: reduced effectiveness of phenothiazines
- 2) Summary: Dehydroepiandrosterone (DHEA) levels within the normal range of 100 to 400 microgram/deciliter (mcg/dL) are conducive to optimal treatment of patients with psychosis (Howard, 1992l). In case reports, patients have been resistant to antipsychotics when DHEA levels were elevated (Howard, 1992l). Patients being treated with phenothiazines for psychosis should avoid DHEA supplementation.
- 3) Severity: moderate
- 4) Onset: delayed
- 5) Substantiation: theoretical
- 6) Clinical Management: Avoid concomitant use of dehydroepiandrosterone (DHEA) and phenothiazines. If DHEA is elevated, treatment with dexamethasone 1 mg orally per day may be used to normalize DHEA levels.
- 7) Probable Mechanism: elevated dehydroepiandrosterone (DHEA) blood levels may reduce responsiveness to phenothiazines
- 8) Literature Reports

a) A 24-year-old female diagnosed with schizophrenia was resistant to daily doses of haloperidol 20 milligrams (mg), fluphenazine 40 mg, lithium carbonate 1200 mg, and lithium carbonate 900 mg plus thioridazine 300 mg. The patient appeared Cushingoid with moon face, acne, facial hair, abdominal hair, and a 40 pound weight gain in the previous 8 months. Dehydroepiandrosterone (DHEA) measured as part of an endocrine panel was 725 micrograms/deciliter (mcg/dL) (normal: 100 to 400 mcg/dL). Dexamethasone 1 mg orally at bedtime resulted in substantial improvement within one

week. The patient appeared calmer, more alert with improved psychotic symptoms and ability to concentrate. At two weeks, a repeated DHEA level was within normal range (328 mcg/dL). The author concluded that elevated DHEA levels were associated with severe psychosis resistant to conventional antipsychotic therapy (Howard, 1992k).

b) A 13-year-old male decompensated with a subsequent two-year period of emotional problems accompanied by heavy use of LSD, hashish, barbiturates, and alcohol. His mental status included bizarre, disorganized, delusional thinking, auditory and visual hallucinations, paranoia, lack of attention to personal hygiene, agitation, and combativeness. He was diagnosed with chronic paranoid schizophrenia; schizophrenia, chronic undifferentiated type, and schizoaffective disorder, excited type. He was resistant to daily doses of trifluoperazine 40 mg, chlorpromazine 400 mg, and imipramine 100 mg. He was also resistant to combination therapy with chlorpromazine 400 mg with thiothixene 80 mg, thioridazine 1000 mg, perphenazine 48 mg with lithium carbonate 1200 mg, clonazepam 4 mg, and carbamazepine 1200 mg daily. Baseline DHEA level exceeded 900 mcg/dL. A seven-day suppression test with dexamethasone 1 mg orally at bedtime resulted in a normal DHEA level of 200 mcg/dL. By day 5, psychosis improved and the patient was well-oriented, conversational, and was making good eye contact. Once dexamethasone was discontinued, rapid decompensation and florid psychosis ensued despite "substantial amounts of psychotropic medications." DHEA increased to 536 mcg/dL. The author concluded that elevated DHEA levels were associated with florid psychosis resistant to conventional anti psychotic therapy (Howard, 1992k).

## Pipotiazine

- 1) Interaction Effect: reduced effectiveness of phenothiazines
- 2) Summary: Dehydroepiandrosterone (DHEA) levels within the normal range of 100 to 400 microgram/deciliter (mcg/dL) are conducive to optimal treatment of patients with psychosis (Howard, 1992l). In case reports, patients have been resistant to antipsychotics when DHEA levels were elevated (Howard, 1992l). Patients being treated with phenothiazines for psychosis should avoid DHEA supplementation.
- 3) Severity: moderate
- 4) Onset: delayed
- 5) Substantiation: theoretical
- 6) Clinical Management: Avoid concomitant use of dehydroepiandrosterone (DHEA) and phenothiazines. If DHEA is elevated, treatment with dexamethasone 1 mg orally per day may be used to normalize DHEA levels.
- 7) Probable Mechanism: elevated dehydroepiandrosterone (DHEA) blood levels may reduce responsiveness to phenothiazines
- 8) Literature Reports

a) A 24-year-old female diagnosed with schizophrenia was resistant to daily doses of haloperidol 20 milligrams (mg), fluphenazine 40 mg, lithium carbonate 1200 mg, and lithium carbonate 900 mg plus thioridazine 300 mg. The patient appeared Cushingoid with moon face, acne, facial hair, abdominal hair, and a 40 pound weight gain in the previous 8 months. Dehydroepiandrosterone (DHEA) measured as part of an endocrine panel was 725 micrograms/deciliter (mcg/dL) (normal: 100 to 400 mcg/dL). Dexamethasone 1 mg orally at bedtime resulted in substantial improvement within one week. The patient appeared calmer, more alert with improved psychotic symptoms and ability to concentrate. At two weeks, a repeated DHEA level was within normal range (328

mcg/dL). The author concluded that elevated DHEA levels were associated with severe psychosis resistant to conventional antipsychotic therapy (Howard, 1992k).

b) A 13-year-old male decompensated with a subsequent two-year period of emotional problems accompanied by heavy use of LSD, hashish, barbiturates, and alcohol. His mental status included bizarre, disorganized, delusional thinking, auditory and visual hallucinations, paranoia, lack of attention to personal hygiene, agitation, and combativeness. He was diagnosed with chronic paranoid schizophrenia; schizophrenia, chronic undifferentiated type, and schizoaffective disorder, excited type. He was resistant to daily doses of trifluoperazine 40 mg, chlorpromazine 400 mg, and imipramine 100 mg. He was also resistant to combination therapy with chlorpromazine 400 mg with thiothixene 80 mg, thioridazine 1000 mg, perphenazine 48 mg with lithium carbonate 1200 mg, clonazepam 4 mg, and carbamazepine 1200 mg daily. Baseline DHEA level exceeded 900 mcg/dL. A seven-day suppression test with dexamethasone 1 mg orally at bedtime resulted in a normal DHEA level of 200 mcg/dL. By day 5, psychosis improved and the patient was well-oriented, conversational, and was making good eye contact. Once dexamethasone was discontinued, rapid decompensation and florid psychosis ensued despite "substantial amounts of psychotropic medications." DHEA increased to 536 mcg/dL. The author concluded that elevated DHEA levels were associated with florid psychosis resistant to conventional antipsychotic therapy (Howard, 1992k).

#### Prochlorperazine

1)Interaction Effect: reduced effectiveness of phenothiazines

2)Summary: Dehydroepiandrosterone (DHEA) levels within the normal range of 100 to 400 microgram/deciliter (mcg/dL) are conducive to optimal treatment of patients with psychosis (Howard, 1992l). In case reports, patients have been resistant to antipsychotics when DHEA levels were elevated (Howard, 1992l). Patients being treated with phenothiazines for psychosis should avoid DHEA supplementation.

3)Severity: moderate

4)Onset: delayed

5)Substantiation: theoretical

6)Clinical Management: Avoid concomitant use of dehydroepiandrosterone (DHEA) and phenothiazines. If DHEA is elevated, treatment with dexamethasone 1 mg orally per day may be used to normalize DHEA levels.

7)Probable Mechanism: elevated dehydroepiandrosterone (DHEA) blood levels may reduce responsiveness to phenothiazines

8)Literature Reports

a) A 24-year-old female diagnosed with schizophrenia was resistant to daily doses of haloperidol 20 milligrams (mg), fluphenazine 40 mg, lithium carbonate 1200 mg, and lithium carbonate 900 mg plus thioridazine 300 mg. The patient appeared Cushingoid with moon face, acne, facial hair, abdominal hair, and a 40 pound weight gain in the previous 8 months. Dehydroepiandrosterone (DHEA) measured as part of an endocrine panel was 725 micrograms/deciliter (mcg/dL) (normal: 100 to 400 mcg/dL).

Dexamethasone 1 mg orally at bedtime resulted in substantial improvement within one week. The patient appeared calmer, more alert with improved psychotic symptoms and ability to concentrate. At two weeks, a repeated DHEA level was within normal range (328 mcg/dL). The author concluded that elevated DHEA levels were

associated with severe psychosis resistant to conventional antipsychotic therapy (Howard, 1992k).

b) A 13-year-old male decompensated with a subsequent two-year period of emotional problems accompanied by heavy use of LSD, hashish, barbiturates, and alcohol. His mental status included bizarre, disorganized, delusional thinking, auditory and visual hallucinations, paranoia, lack of attention to personal hygiene, agitation, and combativeness. He was diagnosed with chronic paranoid schizophrenia; schizophrenia, chronic undifferentiated type, and schizoaffective disorder, excited type. He was resistant to daily doses of trifluoperazine 40 mg, chlorpromazine 400 mg, and imipramine 100 mg. He was also resistant to combination therapy with chlorpromazine 400 mg with thiothixene 80 mg, thioridazine 1000 mg, perphenazine 48 mg with lithium carbonate 1200 mg, clonazepam 4 mg, and carbamazepine 1200 mg daily. Baseline DHEA level exceeded 900 mcg/dL. A seven-day suppression test with dexamethasone 1 mg orally at bedtime resulted in a normal DHEA level of 200 mcg/dL. By day 5, psychosis improved and the patient was well-oriented, conversational, and was making good eye contact. Once dexamethasone was discontinued, rapid decompensation and florid psychosis ensued despite "substantial amounts of psychotropic medications." DHEA increased to 536 mcg/dL. The author concluded that elevated DHEA levels were associated with florid psychosis resistant to conventional antipsychotic therapy (Howard, 1992k).

#### Promazine

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- 3) Severity: moderate
- 4) Onset: delayed
- 5) Substantiation: theoretical
- 6) Clinical Management: Avoid concomitant use of dehydroepiandrosterone (DHEA) and phenothiazines. If DHEA is elevated, treatment with dexamethasone 1 mg orally per day may be used to normalize DHEA levels.
- 7) Probable Mechanism: elevated dehydroepiandrosterone (DHEA) blood levels may reduce responsiveness to phenothiazines
- 8) Literature Reports

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associated with severe psychosis resistant to conventional antipsychotic therapy (Howard, 1992k).

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#### Promethazine

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- 3) Severity: moderate
- 4) Onset: delayed
- 5) Substantiation: theoretical
- 6) Clinical Management: Avoid concomitant use of dehydroepiandrosterone (DHEA) and phenothiazines. If DHEA is elevated, treatment with dexamethasone 1 mg orally per day may be used to normalize DHEA levels.
- 7) Probable Mechanism: elevated dehydroepiandrosterone (DHEA) blood levels may reduce responsiveness to phenothiazines
- 8) Literature Reports

a) A 24-year-old female diagnosed with schizophrenia was resistant to daily doses of haloperidol 20 milligrams (mg), fluphenazine 40 mg, lithium carbonate 1200 mg, and lithium carbonate 900 mg plus thioridazine 300 mg. The patient appeared Cushingoid with moon face, acne, facial hair, abdominal hair, and a 40 pound weight gain in the previous 8 months. Dehydroepiandrosterone (DHEA) measured as part of an endocrine panel was 725 micrograms/deciliter (mcg/dL) (normal: 100 to 400 mcg/dL). Dexamethasone 1 mg orally at bedtime resulted in substantial improvement within one week. The patient appeared calmer, more alert with improved psychotic symptoms and ability to concentrate. At two weeks, a repeated DHEA level was within normal range (328

mcg/dL). The author concluded that elevated DHEA levels were associated with severe psychosis resistant to conventional antipsychotic therapy (Howard, 1992k).

b) A 13-year-old male decompensated with a subsequent two-year period of emotional problems accompanied by heavy use of LSD, hashish, barbiturates, and alcohol. His mental status included bizarre, disorganized, delusional thinking, auditory and visual hallucinations, paranoia, lack of attention to personal hygiene, agitation, and combativeness. He was diagnosed with chronic paranoid schizophrenia; schizophrenia, chronic undifferentiated type, and schizoaffective disorder, excited type. He was resistant to daily doses of trifluoperazine 40 mg, chlorpromazine 400 mg, and imipramine 100 mg. He was also resistant to combination therapy with chlorpromazine 400 mg with thiothixene 80 mg, thioridazine 1000 mg, perphenazine 48 mg with lithium carbonate 1200 mg, clonazepam 4 mg, and carbamazepine 1200 mg daily. Baseline DHEA level exceeded 900 mcg/dL. A seven-day suppression test with dexamethasone 1 mg orally at bedtime resulted in a normal DHEA level of 200 mcg/dL. By day 5, psychosis improved and the patient was well-oriented, conversational, and was making good eye contact. Once dexamethasone was discontinued, rapid decompensation and florid psychosis ensued despite "substantial amounts of psychotropic medications." DHEA increased to 536 mcg/dL. The author concluded that elevated DHEA levels were associated with florid psychosis resistant to conventional antipsychotic therapy (Howard, 1992k).

#### Propiomazine

1)Interaction Effect: reduced effectiveness of phenothiazines

2)Summary: Dehydroepiandrosterone (DHEA) levels within the normal range of 100 to 400 microgram/deciliter (mcg/dL) are conducive to optimal treatment of patients with psychosis (Howard, 1992l). In case reports, patients have been resistant to antipsychotics when DHEA levels were elevated (Howard, 1992l). Patients being treated with phenothiazines for psychosis should avoid DHEA supplementation.

3)Severity: moderate

4)Onset: delayed

5)Substantiation: theoretical

6)Clinical Management: Avoid concomitant use of dehydroepiandrosterone (DHEA) and phenothiazines. If DHEA is elevated, treatment with dexamethasone 1 mg orally per day may be used to normalize DHEA levels.

7)Probable Mechanism: elevated dehydroepiandrosterone (DHEA) blood levels may reduce responsiveness to phenothiazines

8)Literature Reports

a)A 24-year-old female diagnosed with schizophrenia was resistant to daily doses of haloperidol 20 milligrams (mg), fluphenazine 40 mg, lithium carbonate 1200 mg, and lithium carbonate 900 mg plus thioridazine 300 mg. The patient appeared Cushingoid with moon face, acne, facial hair, abdominal hair, and a 40 pound weight gain in the previous 8 months. Dehydroepiandrosterone (DHEA) measured as part of an endocrine panel was 725 micrograms/deciliter (mcg/dL) (normal: 100 to 400 mcg/dL). Dexamethasone 1 mg orally at bedtime resulted in substantial improvement within one week. The patient appeared calmer, more alert with improved psychotic symptoms and ability to concentrate. At two weeks, a repeated DHEA level was within normal range (328 mcg/dL). The author concluded that elevated DHEA levels were

associated with severe psychosis resistant to conventional antipsychotic therapy (Howard, 1992k).

b) A 13-year-old male decompensated with a subsequent two-year period of emotional problems accompanied by heavy use of LSD, hashish, barbiturates, and alcohol. His mental status included bizarre, disorganized, delusional thinking, auditory and visual hallucinations, paranoia, lack of attention to personal hygiene, agitation, and combativeness. He was diagnosed with chronic paranoid schizophrenia; schizophrenia, chronic undifferentiated type, and schizoaffective disorder, excited type. He was resistant to daily doses of trifluoperazine 40 mg, chlorpromazine 400 mg, and imipramine 100 mg. He was also resistant to combination therapy with chlorpromazine 400 mg with thiothixene 80 mg, thioridazine 1000 mg, perphenazine 48 mg with lithium carbonate 1200 mg, clonazepam 4 mg, and carbamazepine 1200 mg daily. Baseline DHEA level exceeded 900 mcg/dL. A seven-day suppression test with dexamethasone 1 mg orally at bedtime resulted in a normal DHEA level of 200 mcg/dL. By day 5, psychosis improved and the patient was well-oriented, conversational, and was making good eye contact. Once dexamethasone was discontinued, rapid decompensation and florid psychosis ensued despite "substantial amounts of psychotropic medications." DHEA increased to 536 mcg/dL. The author concluded that elevated DHEA levels were associated with florid psychosis resistant to conventional antipsychotic therapy (Howard, 1992k).

#### Quetiapine

- 1) Interaction Effect: reduced effectiveness of quetiapine
- 2) Summary: Dehydroepiandrosterone (DHEA) levels within the normal range of 100 to 400 microgram/deciliter (mcg/dL) are conducive for optimal treatment of patients with psychosis (Howard, 1992f). In case reports, patients have been resistant to antipsychotics when DHEA levels were elevated (Howard, 1992f). Patients being treated with quetiapine should avoid DHEA supplementation.
- 3) Severity: moderate
- 4) Onset: delayed
- 5) Substantiation: theoretical
- 6) Clinical Management: Avoid concomitant use of dehydroepiandrosterone (DHEA) and quetiapine. If DHEA is elevated, treatment with dexamethasone 1 mg orally per day may be used to normalize DHEA levels.
- 7) Probable Mechanism: elevated dehydroepiandrosterone (DHEA) blood levels may reduce responsiveness to quetiapine
- 8) Literature Reports

a) A 24-year-old female diagnosed with schizophrenia was resistant to daily doses of haloperidol 20 milligrams (mg), fluphenazine 40 mg, lithium carbonate 1200 mg, and lithium carbonate 900 mg plus thioridazine 300 mg. The patient appeared Cushingoid with moon face, acne, facial hair, abdominal hair, and a 40 pound weight gain in the previous 8 months. Dehydroepiandrosterone (DHEA) measured as part of an endocrine panel was 725 micrograms/deciliter (mcg/dL) (normal: 100 to 400 mcg/dL). Dexamethasone 1 mg orally at bedtime resulted in substantial improvement within one week. The patient appeared calmer, more alert with improved psychotic symptoms and ability to concentrate. At two weeks, a repeated DHEA level was within normal range (328 mcg/dL). The author concluded that elevated DHEA levels were



associated with severe psychosis resistant to conventional antipsychotic therapy (Howard, 1 992e).

b) A 13-year-old male decompensated with a subsequent two-year period of emotional problems accompanied by heavy use of LSD, hashish, barbiturates, and alcohol. His mental status included bizarre, disorganized, delusional thinking, auditory and visual hallucinations, paranoia, lack of attention to personal hygiene, agitation, and combativeness. He was diagnosed with chronic paranoid schizophrenia; schizophrenia, chronic undifferentiated type, and schizoaffective disorder, excited type. He was resistant to daily doses of trifluoperazine 40 mg, chlorpromazine 400 mg, and imipramine 100 mg. He was also resistant to combination therapy with chlorpromazine 400 mg with thiothixene 80 mg, thioridazine 1000 mg, perphenazine 48 mg with lithium carbonate 1200 mg, clonazepam 4 mg, and carbamazepine 1200 mg daily. Baseline DHEA level exceeded 900 mcg/dL. A seven-day suppression test with dexamethasone 1 mg orally at bedtime resulted in a normal DHEA level of 200 mcg/dL. By day 5, psychosis improved and the patient was well-oriented, conversational, and was making good eye contact. Once dexamethasone was discontinued, rapid decompensation and florid psychosis ensued despite "substantial amounts of psychotropic medications". DHEA increased to 536 mcg/dL. The author concluded that elevated DHEA levels were associated with florid psychosis resistant to conventional antipsychotic therapy (Howard, 1 992e).

#### Risperidone

- 1)Interaction Effect: reduced effectiveness of risperidone
- 2)Summary: Dehydroepiandrosterone (DHEA) levels within the normal range of 100 to 400 microgram/deciliter (mcg/dL) are conducive for optimal treatment of patients with psychosis (Howard, 1 992n). In case reports, patients have been resistant to antipsychotics when DHEA levels were elevated (Howard, 1 992n). Patients being treated with risperidone should avoid DHEA supplementation.
- 3)Severity: moderate
- 4)Onset: delayed
- 5)Substantiation: theoretical
- 6)Clinical Management: Avoid concomitant use of dehydroepiandrosterone (DHEA) and risperidone. If DHEA is elevated, treatment with dexamethasone 1 mg orally per day may be used to normalize DHEA levels.
- 7)Probable Mechanism: elevated dehydroepiandrosterone (DHEA) blood levels may reduce responsiveness to risperidone
- 8)Literature Reports

a)A 24-year-old female diagnosed with schizophrenia was resistant to daily doses of haloperidol 20 milligrams (mg), fluphenazine 40 mg, lithium carbonate 1200 mg, and lithium carbonate 900 mg plus thioridazine 300 mg. The patient appeared Cushingoid with moon face, acne, facial hair, abdominal hair, and a 40 pound weight gain in the previous 8 months. Dehydroepiandrosterone (DHEA) measured as part of an endocrine panel was 725 micrograms/deciliter (mcg/dL) (normal: 100 to 400 mcg/dL). Dexamethasone 1 mg orally at bedtime resulted in substantial improvement within one week. The patient appeared calmer, more alert with improved psychotic symptoms and ability to concentrate. At two weeks, a repeated DHEA level was within normal range (328 mcg/dL). The author concluded that elevated DHEA levels were

associated with severe psychosis resistant to conventional antipsychotic therapy (Howard, 1992m).

b) A 13-year-old male decompensated with a subsequent two-year period of emotional problems accompanied by heavy use of LSD, hashish, barbiturates, and alcohol. His mental status included bizarre, disorganized, delusional thinking, auditory and visual hallucinations, paranoia, lack of attention to personal hygiene, agitation, and combativeness. He was diagnosed with chronic paranoid schizophrenia; schizophrenia, chronic undifferentiated type, and schizoaffective disorder, excited type. He was resistant to daily doses of trifluoperazine 40 mg, chlorpromazine 400 mg, and imipramine 100 mg. He was also resistant to combination therapy with chlorpromazine 400 mg with thiothixene 80 mg, thioridazine 1000 mg, perphenazine 48 mg with lithium carbonate 1200 mg, clonazepam 4 mg, and carbamazepine 1200 mg daily. Baseline DHEA level exceeded 900 mcg/dL. A seven-day suppression test with dexamethasone 1 mg orally at bedtime resulted in a normal DHEA level of 200 mcg/dL. By day 5, psychosis improved and the patient was well-oriented, conversational, and was making good eye contact. Once dexamethasone was discontinued, rapid decompensation and florid psychosis ensued despite "substantial amounts of psychotropic medications". DHEA increased to 536 mcg/dL. The author concluded that elevated DHEA levels were associated with florid psychosis resistant to conventional antipsychotic therapy (Howard, 1992m).

#### Sertraline

- 1) Interaction Effect: development of manic symptoms
- 2) Summary: A case has been reported in which concomitant dehydroepiandrosterone (DHEA) and sertraline use was suggested to precipitate a manic episode in a patient with a history of bipolar disorder (Dean, 2000a). DHEA was also noted to cause mania in a patient with no previous personal or family history of bipolar disorder (Markowitz et al, 1999f). Elevated DHEA levels have been found in patients with mental disorders; DHEA suppression has led to improvement in psychotic symptoms (Howard, 1992u). DHEA possesses proserotonergic activity which may predispose patients to manic episodes (Majewska, 1995). DHEA is a precursor to androgenic steroids, which in high doses may precipitate mania (Markowitz et al, 1999f). Patients taking medication for bipolar disorder or patients with a personal and/or family history of bipolar disorder should not take DHEA until further data is available to characterize this drug-herb interaction. Concomitant use of DHEA with selective serotonin reuptake inhibitors (SSRIs) should be avoided due to the potential additive precipitation of mania.
- 3) Severity: moderate
- 4) Onset: delayed
- 5) Substantiation: theoretical
- 6) Clinical Management: Avoid concomitant use of dehydroepiandrosterone (DHEA) and selective serotonin reuptake inhibitors. If patients present with manic symptoms (i.e. agitation, anger, irritability, aggressive behavior), determine if the patient is using DHEA and discontinue DHEA.
- 7) Probable Mechanism: serotonergic activity of dehydroepiandrosterone, possibly increased androgen levels
- 8) Literature Reports

a) A 31-year-old male was admitted following threats to commit suicide and injure family members. He had self-initiated sertraline 100 milligrams (mg) daily for the previous 2 to 3 weeks for depression. Sertraline had been prescribed 3 years prior when he was diagnosed with bipolar disorder, which he discontinued after 2 weeks. He had also taken dehydroepiandrosterone (DHEA) 300 mg to 500 mg daily for the previous 2 months apparently for weight training. Following use of DHEA for a short time, he became more irritable, was not sleeping well, and began threatening a female friend and family members. He also drank alcohol occasionally and reportedly had difficulty controlling his anger when intoxicated. Sertraline was stopped and the patient was treated with valproic acid with the dose titrated to 500 mg twice daily. The combination of DHEA, sertraline, and alcohol was suggested responsible for the developing of the manic episode (Dean, 2000).

## Testosterone

- 1) Interaction Effect: increased risk of adverse androgenic and hepatic effects
- 2) Summary: Patients electing to take both dehydroepiandrosterone (DHEA) and testosterone are at increased risk for androgenic side effects. Data are conflicting on the extent that DHEA increases the testosterone-epitestosterone (T/E) ratio (Bowers, 1999a; Bosy et al, 1998a). The effect appears to be dose-dependent, and at doses commonly used by body-builders (e.g. 1000 milligrams), androgenic effects are likely. Concomitant use is not advised.
- 3) Severity: moderate
- 4) Onset: rapid
- 5) Substantiation: theoretical
- 6) Clinical Management: Avoid concomitant use of dehydroepiandrosterone (DHEA) and testosterone. DHEA may increase testosterone levels, increasing the incidence of adverse androgenic adverse effects such as oligospermia (in men), gynecomastia, prostatic hypertrophy (especially in elderly males), and virilization in women (deepening voice, hirsutism, acne, clitoromegaly, and menstrual irregularities). Libido may increase or decrease. Adverse hepatic effects may also occur (peliosis hepatitis, hepatic neoplasms).
- 7) Probable Mechanism: additive androgenic effect, since dehydroepiandrosterone sulfate appears to act as a pro-hormone for testosterone
- 8) Literature Reports

a) Dehydroepiandrosterone (DHEA) increased the testosterone/epitestosterone (T/E) ratio in an uncontrolled study of 4 human volunteers. Two over the counter DHEA preparations were used in this study. Nature's Pride "DHEA 50 mg+" (product A) contained DHEA 50 milligrams (mg), suma 25 mg, Korean ginseng 25 mg, muira pauma 25 mg, shitake mushroom concentration 15 mg, and green tea extract 5 mg. The second product, YourLife DHEA (product B), contained DHEA 25 mg as the only active ingredient listed on the label. Neither product contained testosterone as detected by gas chromatography-mass spectrometry (GC-MS) analyses. All subjects (except subject 4) took the product once daily for 4 days at breakfast. Subject 1 (age 47) took both preparations at 3 dosage levels at different times over a 6 month period: product A 50 mg/day, product A 100 mg/day, and product B 150 mg/day for 4 days. Subjects 2 (age 61) and 3 (age 28) took product B 50 mg/day and 100 mg/day, respectively. Subject 4 (age 27) took product A 100 mg/day for 2 days. A 24-hour urine was collected on day 3 and spot urine samples were taken in the morning and evening of day 4. Subject 1 at DHEA doses of 50 mg/day,

100 mg/day, and 150 mg/day had T/E ratios of 8.1, 11.4, and 14.4, respectively, compared to a pre-dose ratio of 2.4. Pre-dose T/E ratios for subjects 2 and 3 were 1.3 and 1.7, respectively, and T/E ratios were 1.6 and 3.9, respectively after DHEA. Subject 4 had a pre-dose T/E ratio of 0.8 and a T/E ratio of 1.1 following DHEA. Ratios exceeding 6:1 are used by several organizations including the United States Military and the International Olympic Committee (IOC) as an indication that additional tests are warranted to rule out use of exogenous physiological steroids. Manipulation of the steroid endocrine system to improve athletic performance has led some DHEA supplement providers on the internet to recommend up to 1000 mg/day (Bowers, 1999).

b) Differences in baseline mean T/E ratios and dehydroepiandrosterone (DHEA) treatment mean ratios were not significant in 7 healthy subjects. Mean baseline T/E ratio was 0.67 (range: 0.1 to 1.2). DHEA 50 mg was taken each morning for 30 days with urinary samples collected before and two to three hours after ingestion with no voiding before collection. Individual variation was prevalent. The greatest individual variation from baseline to treatment mean T/E ratio was 1.20 to 2.11. The greatest difference from baseline mean to peak treatment mean T/E ratio was 1.2 to 3.7. A single dose of DHEA 250 mg resulted in a 40% increase in the T/E ratio relative to the pre-dose value (peak T/E ratio equal to 1.2). DHEA at this dose had a minimal effect on urine T/E ratios and would not be expected to result in a positive screen for testosterone abuse as the T/E ratio must exceed 6:1 (Bosy et al, 1998).

c) Two female volunteers demonstrated three to four fold increases in plasma testosterone levels following dehydroepiandrosterone (DHEA) 100 mg administration. In subject 1, the pre-DHEA testosterone level was 0.07 mcg/100 mL compared to a maximum level of 0.28 mcg/100 mL ninety minutes after DHEA administration. In subject 2, the pre-DHEA testosterone level was 0.08 mcg/100 mL compared to a maximum level of 0.28 mcg/100 mL sixty minutes after DHEA administration. This demonstrates that in vivo conversion of DHEA to testosterone occurs in women as well as men (Mahesh & Greenblatt, 1962).

## Thioridazine

- 1) Interaction Effect: reduced effectiveness of phenothiazines
- 2) Summary: Dehydroepiandrosterone (DHEA) levels within the normal range of 100 to 400 microgram/deciliter (mcg/dL) are conducive to optimal treatment of patients with psychosis (Howard, 1992). In case reports, patients have been resistant to antipsychotics when DHEA levels were elevated (Howard, 1992). Patients being treated with phenothiazines for psychosis should avoid DHEA supplementation.
- 3) Severity: moderate
- 4) Onset: delayed
- 5) Substantiation: theoretical
- 5) Clinical Management: Avoid concomitant use of dehydroepiandrosterone (DHEA) and phenothiazines. If DHEA is elevated, treatment with dexamethasone 1 mg orally per day may be used to normalize DHEA levels.
- 6) Probable Mechanism: elevated dehydroepiandrosterone (DHEA) blood levels may reduce responsiveness to phenothiazines
- 7) Literature Reports
  - a) A 24-year-old female diagnosed with schizophrenia was resistant to daily doses of haloperidol 20 milligrams (mg), fluphenazine 40 mg, lithium carbonate 1200 mg, and lithium carbonate 900 mg plus thioridazine 300 mg. The patient appeared Cushingoid

with moon face, acne, facial hair, abdominal hair, and a 40 pound weight gain in the previous 8 months. Dehydroepiandrosterone (DHEA) measured as part of an endocrine panel was 725 micrograms/deciliter (mcg/dL) (normal: 100 to 400 mcg/dL). Dexamethasone 1 mg orally at bedtime resulted in substantial improvement within one week. The patient appeared calmer, more alert with improved psychotic symptoms and ability to concentrate. At two weeks, a repeated DHEA level was within normal range (328 mcg/dL). The author concluded that elevated DHEA levels were associated with severe psychosis resistant to conventional antipsychotic therapy (Howard, 1992k).

b) A 13-year-old male decompensated with a subsequent two-year period of emotional problems accompanied by heavy use of LSD, hashish, barbiturates, and alcohol. His mental status included bizarre, disorganized, delusional thinking, auditory and visual hallucinations, paranoia, lack of attention to personal hygiene, agitation, and combativeness. He was diagnosed with chronic paranoid schizophrenia; schizophrenia, chronic undifferentiated type, and schizoaffective disorder, excited type. He was resistant to daily doses of trifluoperazine 40 mg, chlorpromazine 400 mg, and imipramine 100 mg. He was also resistant to combination therapy with chlorpromazine 400 mg with thiothixene 80 mg, thioridazine 1000 mg, perphenazine 48 mg with lithium carbonate 1200 mg, clonazepam 4 mg, and carbamazepine 1200 mg daily. Baseline DHEA level exceeded 900 mcg/dL. A seven-day suppression test with dexamethasone 1 mg orally at bedtime resulted in a normal DHEA level of 200 mcg/dL. By day 5, psychosis improved and the patient was well-oriented, conversational, and was making good eye contact. Once dexamethasone was discontinued, rapid decompensation and florid psychosis ensued despite "substantial amounts of psychotropic medications." DHEA increased to 536 mcg/dL. The author concluded that elevated DHEA levels were associated with florid psychosis resistant to conventional antipsychotic therapy (Howard, 1992k).

#### Triazolam

- 1) Interaction Effect: increased central nervous system depression
- 2) Summary: Dehydroepiandrosterone (DHEA) inhibited metabolism of triazolam in humans through inhibition of CYP3A isoenzymes (Frye et al, 2000a). As a result of increased triazolam levels, patients may be at increased risk for adverse effects of triazolam.
- 3) Severity: moderate
- 4) Onset: rapid
- 5) Substantiation: probable
- 6) Clinical Management: In patients taking dehydroepiandrosterone (DHEA) and triazolam concomitantly, monitor closely for signs of triazolam toxicity such as excessive sedation, hypotension, tachycardia, ataxia, slurred speech, and respiratory depression.
- 7) Probable Mechanism: inhibition of liver cytochrome P450 3A by DHEA metabolite, DHEA-S with resultant increase in triazolam levels
- 8) Literature Reports

a) Dehydroepiandrosterone (DHEA) metabolite dehydroepiandrosterone sulfate (DHEA-S) inhibited metabolism of triazolam in human liver microsomes and in 13 elderly subjects (ages 65-79 years). Placebo was given to subjects for 7 days, followed by DHEA 200 milligrams (mg) daily for 14 days. Triazolam 0.25 mg was administered on days 1 and 22.

Triazolam clearance/bioavailability (CL/F) was reduced from 27.8 +/- 3.5 to 23.3 +/- 3.6 (p equal to 0.0067) (Frye et al, 2000).

#### Trifluoperazine

- 1) Interaction Effect: reduced effectiveness of phenothiazines
- 2) Summary: Dehydroepiandrosterone (DHEA) levels within the normal range of 100 to 400 microgram/deciliter (mcg/dL) are conducive to optimal treatment of patients with psychosis (Howard, 1992l). In case reports, patients have been resistant to antipsychotics when DHEA levels were elevated (Howard, 1992l). Patients being treated with phenothiazines for psychosis should avoid DHEA supplementation.
- 3) Severity: moderate
- 4) Onset: delayed
- 5) Substantiation: theoretical
- 6) Clinical Management: Avoid concomitant use of dehydroepiandrosterone (DHEA) and phenothiazines. If DHEA is elevated, treatment with dexamethasone 1 mg orally per day may be used to normalize DHEA levels.
- 7) Probable Mechanism: elevated dehydroepiandrosterone (DHEA) blood levels may reduce responsiveness to phenothiazines
- 8) Literature Reports

a) A 24-year-old female diagnosed with schizophrenia was resistant to daily doses of haloperidol 20 milligrams (mg), fluphenazine 40 mg, lithium carbonate 1200 mg, and lithium carbonate 900 mg plus thioridazine 300 mg. The patient appeared Cushingoid with moon face, acne, facial hair, abdominal hair, and a 40 pound weight gain in the previous 8 months. Dehydroepiandrosterone (DHEA) measured as part of an endocrine panel was 725 micrograms/deciliter (mcg/dL) (normal: 100 to 400 mcg/dL).

Dexamethasone 1 mg orally at bedtime resulted in substantial improvement within one week. The patient appeared calmer, more alert with improved psychotic symptoms and ability to concentrate. At two weeks, a repeated DHEA level was within normal range (328 mcg/dL). The author concluded that elevated DHEA levels were associated with severe psychosis resistant to conventional antipsychotic therapy (Howard, 1992k).

b) A 13-year-old male decompensated with a subsequent two-year period of emotional problems accompanied by heavy use of LSD, hashish, barbiturates, and alcohol. His mental status included bizarre, disorganized, delusional thinking, auditory and visual hallucinations, paranoia, lack of attention to personal hygiene, agitation, and combativeness. He was diagnosed with chronic paranoid schizophrenia; schizophrenia, chronic undifferentiated type, and schizoaffective disorder, excited type. He was resistant to daily doses of trifluoperazine 40 mg, chlorpromazine 400 mg, and imipramine 100 mg. He was also resistant to combination therapy with chlorpromazine 400 mg with thiothixene 80 mg, thioridazine 1000 mg, perphenazine 48 mg with lithium carbonate 1200 mg, clonazepam 4 mg, and carbamazepine 1200 mg daily. Baseline DHEA level exceeded 900 mcg/dL. A seven-day suppression test with dexamethasone 1 mg orally at bedtime resulted in a normal DHEA level of 200 mcg/dL. By day 5, psychosis improved and the patient was well-oriented, conversational, and was making good eye contact. Once dexamethasone was discontinued, rapid decompensation and florid psychosis ensued despite "substantial amounts of psychotropic medications." DHEA increased to 536 mcg/dL. The author concluded that elevated DHEA levels were associated with florid psychosis resistant to conventional antipsychotic therapy (Howard, 1992k).

#### Trifluoperazine

- 1) Interaction Effect: reduced effectiveness of phenothiazines
- 2) Summary: Dehydroepiandrosterone (DHEA) levels within the normal range of 100 to 400 microgram/deciliter (mcg/dL) are conducive to optimal treatment of patients with psychosis (Howard, 1992l). In case reports, patients have been resistant to antipsychotics when DHEA levels were elevated (Howard, 1992l). Patients being treated with phenothiazines for psychosis should avoid DHEA supplementation.
- 3) Severity: moderate
- 4) Onset: delayed
- 5) Substantiation: theoretical
- 6) Clinical Management: Avoid concomitant use of dehydroepiandrosterone (DHEA) and phenothiazines. If DHEA is elevated, treatment with dexamethasone 1 mg orally per day may be used to normalize DHEA levels.
- 7) Probable Mechanism: elevated dehydroepiandrosterone (DHEA) blood levels may reduce responsiveness to phenothiazines
- 8) Literature Reports

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b) A 13-year-old male decompensated with a subsequent two-year period of emotional problems accompanied by heavy use of LSD, hashish, barbiturates, and alcohol. His mental status included bizarre, disorganized, delusional thinking, auditory and visual hallucinations, paranoia, lack of attention to personal hygiene, agitation, and combativeness. He was diagnosed with chronic paranoid schizophrenia; schizophrenia, chronic undifferentiated type, and schizoaffective disorder, excited type. He was resistant to daily doses of trifluoperazine 40 mg, chlorpromazine 400 mg, and imipramine 100 mg. He was also resistant to combination therapy with chlorpromazine 400 mg with thiothixene 80 mg, thioridazine 1000 mg, perphenazine 48 mg with lithium carbonate 1200 mg, clonazepam 4 mg, and carbamazepine 1200 mg daily. Baseline DHEA level exceeded 900 mcg/dL. A seven-day suppression test with dexamethasone 1 mg orally at bedtime resulted in a normal DHEA level of 200 mcg/dL. By day 5, psychosis improved and the patient was well-oriented, conversational, and was making good eye contact. Once dexamethasone was discontinued, rapid decompensation and florid psychosis ensued despite substantial amounts of psychotropic medications." DHEA increased to 536 mcg/dL. The author concluded that elevated DHEA levels were associated with florid psychosis resistant to conventional antipsychotic therapy (Howard, 1992k).

#### Valproic Acid

- 1) Interaction Effect: reduced effectiveness of valproic acid

2) Summary: Dehydroepiandrosterone (DHEA) in a single case report was noted to cause mania in a patient with no previous personal or family history of bipolar disorder (Markowitz et al, 1999e). Elevated DHEA levels have been found in patients with mental disorders; DHEA suppression has led to improvement in psychotic symptoms (Howard, 1992d). Patients taking medication for bipolar disorder or patients with a personal and/or family history of bipolar disorder should not take DHEA until further data is available to characterize this drug-herb interaction.

3) Severity: moderate

4) Onset: delayed

5) Substantiation: theoretical

6) Clinical Management: If valproic acid is being used for manic symptoms, concomitant use of dehydroepiandrosterone (DHEA) may cause a return of symptoms. Patients with a personal or family history of bipolar disorder should be advised to avoid DHEA use.

7) Probable Mechanism: proserotonergic activity of dehydroepiandrosterone may predispose patients to manic episodes; dehydroepiandrosterone is a precursor to androgenic steroids, which in high doses may precipitate mania

8) Literature Reports

a) A 68-year-old male with no documented psychiatric history initiated dehydroepiandrosterone (DHEA) 100 milligrams (mg) daily and increased the dose to 200 to 300 mg daily for 6 months. Within 3 months, family members noted the onset of odd behavior with prominent symptoms of agitation, delusional thinking, decreased sleep and appetite, and spending sprees. The patient was not taking any prescribed medication but did ingest alcohol in amounts up to 1 case of beer daily. Another 3 months elapsed, leading to involuntary inpatient admission secondary to rapid, loud, pressured speech with grandiose thoughts. At admission, the patient reported that he had decreased alcohol intake to 2 beers daily due to family concerns about his behavior changes. There was no family history of bipolar disorder. Urinary drug screen was negative. Over the seven-day hospital stay, with the institution of valproic acid 500 mg twice daily, the patient's behavior and sleep patterns improved, and the patient believed DHEA led to his symptoms. There were no ethanol withdrawal symptoms. The patient was discharged with follow-up care from his primary care physician with a diagnosis of substance-induced mood disorder (Markowitz et al, 1999d).