

- events (Rancho-Bernardo study); later found to be untrue in a larger Rancho-Bernardo study.
- Banned by athletic agencies such as the NCAA, the NFL, and the Olympics.
- Marketed as a dietary supplement because it can be manufactured from natural sources, such as soy and wild yam. However, many of these products, depending on source and metabolism, are not converted into DHEA in humans and are not recommended or preferable.
- No data indicate benefits greater than long-term risk.
- Endogenous production in liver, adrenal gland, testes, and brain in minute quantities.
- Hepatic metabolism, urinary excretion with a 12-h half-life.
- Steroid hormone produced by adrenals, interconverted to testosterone, estrone, estradiol, androsterone.

- Considered a prohormone, so effects similar to those of anabolic steroids.
- May increase protein synthesis in skeletal muscles. However, increase of serum testosterone or enhancement of strength during resistance training is controversial. A placebo-controlled, randomized clinical trial reported in the *New England Journal of Medicine* in 2006 found that supplementation in the elderly had no significant beneficial effects on body composition, physical performance, insulin sensitivity, or quality of life.
- Decreasing serum cortisol levels may cause early activation of the anterior cingulate cortex (ACC) secondary to neuronal recruitment of the steroid sensitive ACC that may be involved in pre-hippocampal memory processing, thereby improving memory.

- DHEA levels decrease with CHF, oxidative stress, aging, and cancer.
- May have apoptotic effects in some cancer lines but is also shown to stimulate hormone-producing tumors.

Usual Dose

- 30–90 mg/d for depression, memory improvement, or cognition (two studies)
- 50–100 mg daily for 3–24 mo for possible improvements in well-being, cognitive function, body compositions
- 20-50 mg PO daily for adrenal insufficiency
- Vaginal: 10% cream; apply topically daily

Assessment Points

System	Effect	Hx Assessment	PE	Test
HEENT	Hirsutism			
CV	Anabolic steroids associated with sudden cardiac arrest, Htn; DHEA rarely causes arrhythmias	Determine chronic and acute dose and duration of self-administration; palpitations	HR	Preop ECG for chronic or excessive use, may show ventricular hypertrophy
GI	Anabolic steroids assoc with hepatitis, cholestatic jaundice			
HEME	Inhibits plt aggregation in vivo Antiglucocorticoid actions		Ecchymoses	Bleeding time, preop glucose for diabetics
DERM	Increased acneiform dermatitis			
GU	Hypogonadism with anabolic steroids, prostate tumor growth	Prostate exam		PSA
CNS	Anabolic steroids may cause aggressiveness; DHEA binds to NMDA, sigma, GABA receptors	Increased pituitary tumor growth		ACTH

Key References: Nair KS, Rizza RA, O'Brien P, et al.: DHEA in elderly women and DHEA or testosterone in elderly men, *N Engl J Med* 355(16):1647–1659, 2006; Labrie F, Archer D, Bouchard C, et al.: Intravaginal dehydroepiandrosterone (Prasterone), a physiological and highly efficient treatment of vaginal atrophy, *Menopause* 16(5):907–922, 2009.

Perioperative Implications

Preoperative Concerns

- Insulin resistance; check preop glucose.
- Synergism with corticosteroids.

Induction/Maintenance

- Unknown effects of inhibition of steroid synthesis if combined with etomidate or immunosuppressives for transplantation.

Postoperative Concerns

- Unknown effects on stress response

Anticipated Problems/Concerns

- Unpredictable CV effects

Echinacea (American Coneflower, Purple Coneflower, *E. Angustifolia*,

E. Purpurea, *E. Pallida*)

Kirk Lalwani

Uses

- Purported immunostimulation and prevention and treatment of respiratory tract infections.
- Adjuvant in the treatment of other bacterial, viral, or fungal infections of the urinary and respiratory tract.
- Anti-inflammatory when used topically for conditions such as eczema, psoriasis, and herpes simplex.
- Promotes wound healing when used topically (i.e., in leg ulcers and burns).
- Adjuvant for cancer therapy and in the treatment of chronic fatigue syndrome.

Perioperative Risks

- No known drug interactions or toxicities
- No known sedative, CV, or coagulation effects relevant to anesthesia

Worry About

- Immunostimulation may counteract the effect of steroids and immunosuppressant drugs in transplant recipients and pts with autoimmune disease.

Overview

- Most common side effects are GI symptoms, allergic reactions, and rashes.
- Allergic reactions are more common in atopic individuals and individuals with a Hx of sensitivity to the Asteraceae-Compositae family of plants (e.g., ragweed, chrysanthemums, marigolds, daisies) and can be serious.
- Echinacea may exacerbate autoimmune diseases such as MS, SLE, rheumatoid arthritis, AIDS, tuberculosis, and pemphigus vulgaris.
- Echinacea may inhibit cytochrome P450 (CYP 1A2, 3A4) enzymes, altering levels of drugs metabolized by these enzymes.
- Tachyphylaxis may occur with prolonged, uninterrupted use.

Drug Class/Mechanism of Action/Usual Dose

- Increases phagocytosis and lymphocyte activity, possibly by release of TNE, IL-1, and interferon.

- Anti-inflammatory activity by inhibition of cyclooxygenase and 5-lipoxygenase.
- Promotes wound healing by protecting type 3 collagen from free radical damage and inhibiting bacterial hyaluronidase.
- Concentration of active ingredients varies widely according to species and preparation used.
 - 1–3 mL of the fluid extract or cold-pressed juice of plant (or root) 3 times daily.
 - 1 g of powdered root 3 times daily (capsules, tablets)
- Echinacea appears to modestly inhibit cytochrome P450 1A2 (CYP1A2), and to induce hepatic cytochrome P450 3A4 (CYP3A4), but inhibit intestinal CYP3A4 (opposing effects).

Assessment Points

System	Effect	Test
IMMUNE	Immunostimulation, anti-inflammatory activity	Phagocytic activation, IL-1 and TNF activity
HEPAT	P450 CYP1A2 inhibition	Caffeine clearance test

Key References: Karsch-Völkl M, Barrett B, Linde K: Echinacea for preventing and treating the common cold, *J Am Med Assoc* 313(6):618–619, 2015; Charrois TL, Hrudej J, Vohra S, et al.: Echinacea, *Pediatr Rev* 27(10):385–387, 2006.

Perioperative Implications

- Possible antagonism of antirejection drugs used following bone marrow or organ transplantation.
- Possibly related to two case reports of liver failure, one in a child and one in an adult.

Ephedra (Ma-Huang)

Bracken J. De Witt

Uses

- Ephedra is a plant that contains a variety of ephedrine alkaloids, including ephedrine and pseudoephedrine.
- Dietary supplements containing ephedra were marketed in USA as agents that may aid in wt reduction and energy enhancement. Ephedra may be used in the manufacture of methamphetamine.
- In 2004, USA banned the sale of ephedra-containing supplements with a subsequent marked decrease in reported poisonings.
- Although banned in USA, sale of ephedra-containing supplements continues via internet resources.
- Some supplements have been marketed as “ephedrine-free” or as legal ephedra products, in which ephedra is replaced with other herbal stimulants such as bitter orange.

- Ephedra-containing substances are also known as ma-huang, Mormon tea, squaw tea, and herbal ecstasy.

Perioperative Risks

- Risks associated with an increase in the sympathetic nervous system activity and dysrhythmias and Htn

Worry About

- Lethal cardiac arrhythmias, Htn, myocarditis, MI, angina, increased thermogenesis
- Hemorrhagic and/or ischemic stroke, subarachnoid hemorrhage, cerebral vasculitis, seizures
- Bronchial dilation, acute hepatitis
- Preterm labor

Overview/Pharmacology

- Mechanism of action is via increases in sympathetic stimulation.
- Ephedrine is an indirect-acting sympathomimetic that exerts its effects mainly by stimulating release of norepinephrine.
- Other ephedrine alkaloids in ephedra have direct-acting effects on both α - and β -adrenoceptors.
- Ephedra is often packaged with guarana-derived caffeine, which may synergistically augment adrenergic stimulation.

Drug Class/Mechanism of Action/Usual Dose

- Works via stimulation of the sympathetic nervous system.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Arrhythmias, Htn, myocarditis, MI, angina thermogenesis	Chest pain	BP Increased temperature	BP/HR, ECG, cardiac enzymes Temperature probe
GU	Acute hepatitis			LFTs
CNS	Stroke, subarachnoid hemorrhage, vasculitis, seizure	Decreased mental status Headache	Neuro exam	CT, vascular biopsy, EEG
RESP	Bronchial dilation			PFTs

Key References: Ang-Lee MK, Moss J, Yuan CS: Herbal medicines and perioperative care, *J Am Med Assoc* 286(2):208–216, 2001; Wang CZ, Yuan CS, Moss J: Anesthetic implications of complementary and alternative medications. In Miller RD, editor: *Miller's anesthesia*, ed 8, Philadelphia, 2015, Elsevier, pp 1226–1239.

Perioperative Implications**Preoperative Period**

- Ephedra may produce adverse pt reactions with medications such as MAO inhibitors, digoxin, cold medications containing ephedrine, diuretics, and antihypertensives.
- Assess preop BP, HR, and ECG.
- Consider as a potential cause of preterm labor.

Preinduction/Induction Period

- Control hemodynamics before induction.
- Observe ECG for arrhythmias.

Maintenance Period

- Response to ephedrine may be hampered secondary to tachyphylaxis; therefore, control hypotension

with direct-acting adrenergic agonists, like phenylephrine.

- Ephedra may interact with volatile anesthetics (e.g., enflurane) to promote dysrhythmias.

Postoperative Period

- Assess postop BP, HR, and ECG for CV changes.

Evening Primrose

John A. Helmstetter | Alan David Kaye

Uses

- Evening primrose oil (EPO) is obtained from the seed of the plant species *Oenothera biennis*.
- EPO is also known as fever plant, huile d'onagre, king's cureall, night willow-herb, scabish, suncups, and sundrops.
- EPO may be used as a food supplement for the essential fatty acids, linoleic acid (LA), and γ -linolenic acid (GLA).

- Infusion of the whole plant has been used for asthma, GI disorders, whooping cough, and as a sedative pain killer.
- Other evidence indicates that orally administered primrose oil does not relieve symptoms of premenstrual syndrome and does not have any effect in shortening the length of pregnancy and labor.
- EPO had been licensed in Britain for treatment of atopic eczema and cyclic and noncyclic mastalgia.

Cochrane meta-analysis found that evening primrose oil capsules were ineffective for eczema.

- Other potential uses for EPO include PMS, psoriasis, MS, hypercholesterolemia, rheumatoid arthritis, Raynaud phenomenon, Sjögren's syndrome, postviral fatigue syndrome, asthma, and diabetic neuropathy. Without solid evidence it is effective, but with recurrent anecdotal evidence of beneficial outcomes.