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-Völk M, Barrett B, Linde K: Echinacea for preventing and treating the common cold, *J Am Med Assoc* 313(6):618–619, 2015; Charrois TL, Hrudey 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.

Perioperative Risks

- Speculation that EPO may increase risk of temporal lobe epilepsy or reduce the seizure threshold in schizophrenic pts taking epileptogenic drugs (e.g., phenothiazines).
- EPO may cause a decrease in blood clotting.

Worry About

- Obstetrics: Oral EPO administration during pregnancy may have an association with a protracted phase of labor, prolonged rupture of membranes, oxytocin augmentation, vacuum extraction, and arrest of descent. One case report exists of transient petechiae and ecchymosis in a newborn after 6.5 g of oral EPO intake by the mother the week before birth.

Overview/Pharmacology

- EPO is a rich source of the essential fatty acids LA and GLA. These essential fatty acids are involved in prostaglandin biosynthetic pathways.
- DGLA, a metabolite of GLA, is a precursor of both the inflammatory prostaglandin series via arachidonic acid (AA), and the less inflammatory series (PGE_1).
- Actions of PGE_1 include anti-inflammatory, immunoregulatory, and vasodilatory properties; inhibition of plt aggregation and cholesterol biosynthesis; hypotension, and elevation of cyclic AMP.
- GLA has been shown to have a favorable effect on the DGLA:AA ratio. The increase in AA is smaller and less consistent when compared with the increase in DGLA. This is beneficial because DGLA leads to the less inflammatory prostaglandin series PGE_1.
- GLA is not normally obtained from the diet. The body relies on the metabolic conversion of LA to GLA. This conversion is rate limiting in the production of GLA. It has been shown that there is a reduced rate of conversion of LA to GLA in several clinical situations, incl aging, diabetes, CV disorders and high LDL cholesterol concentrations, high alcohol intake, viral infections, cancer, nutritional deficits, atopic eczema, and premenstrual syndrome. Dietary supplementation of GLA, via EPO, bypasses the rate-limiting conversion step and has a beneficial effect on the ratio of inflammatory to less inflammatory prostaglandin synthesis.

Drug Class/Mechanism of Action/Usual Dose

- Dose of EPO is specific for each condition being treated; for example, the EPO dose for atopic eczema is 6–8 g for adults or 2–4 g for children. These doses of EPO are based on standardized products containing 8% GLA. EPO may be swallowed directly, mixed with milk or another liquid, or taken with food. The clinical response is usually seen after 3–4 mo of continuous use.

Drug Effects

System	Effect*
CV	Inhibits increase of serum total cholesterol + VLDL + IDL + LDL cholesterol concentrations in the presence of excess cholesterol in the diet. Serves as an antioxidant in hyperlipemic states. Reduces oxidative stress by inhibiting lipid peroxidation and reinforcing the glutathione-dependent antioxidant defense system.
GI	Has antiulcer and cytoprotective effects on experimentally induced gastric lesions.
HEME	Reduces plt aggregation when subject fed an atherogenic diet.
DERM	May be used for Rx of atopic eczema. Treatment of atopic eczema with EPO is controversial. Clinical studies have been equivocal on whether symptoms of atopic eczema benefit from EPO. May be used for the treatment of limited scleroderma, or CREST syndrome. Clinical studies have been equivocal in relation to fatty acid placebos but have shown qualitative improvement in symptoms of Raynaud phenomenon.
GU	Has been used for PMS and to help reduce frequency of nighttime hot flashes during menopause. Treatment is controversial because clinical studies have not shown a clear benefit of EPO for PMS and menopause. Has been shown to be no better than fatty acid placebo or topical NSAIDs for treatment of mastalgia. Has been used by many midwives to hasten cervical ripening in an effort to shorten labor and ↓ incidence of postdate pregnancies. One retrospective study showed that EPO does not shorten gestation or ↓ length of labor. Moreover, it was found that EPO may be associated with above-mentioned adverse effects on labor.
CNS	Significantly reduced headache in women with PMS. Pts given both EPO and fish oil had fewer symptoms associated with headache, such as depression and fatigue. Animal studies suggest EPO may be useful in the treatment of diabetic neuropathy, although the exact physiologic mechanism remains to be demonstrated.
IMMUNE	In pts with mild RA, EPO has been shown to improve morning stiffness, and there was also improvement in the Ritchie articular index for each pt. Pts with severe RA did not exhibit improvement. Although not scientifically proved, EPO has been taken by asthmatics to gain the anti-inflammatory effects of PGE_1.

*EPO studies are in a preliminary phase; its effects have been proved only in animal models. The effects mentioned here have yet to be proved in humans.

Key References: Stonemetz D: A review of the clinical efficacy of evening primrose, *Holist Nurs Pract* 22(3):171–174, 2008; Evening primrose. *Natural medicines: pharmacist's letter/prescriber's letter natural medicines comprehensive database,* ed 13, Stockton, CA, 2012, Therapeutic Research Faculty, pp 608–611.

Perioperative Implications

Preoperative Concerns

- EPO may cause increased risk of developing temporal lobe epilepsy, specifically in pts taking known epileptogenic drugs such as phenothiazines. Seizures have not been seen in pts not taking phenothiazines.
- Insufficient evidence regarding its use with other drugs, such as antihypertensive agents or pressors, anticoagulants or antiplatelet agents, nonsteroidal anti-inflammatory drugs, as well as herbs and supplements that might affect plt aggregation.

Preinduction/Induction

- No known interactions

Maintenance

- No known interactions

Postoperative Period

- No known interactions

Fish Oil

Alan David Kaye | Rachel J. Kaye | Orlando J. Salinas

Uses

- Active ingredient for brain and retinal health (more than 40% of brain and retina is structural fat and more than 50% of fat in brain and retina is DHA).
- Decreases arrhythmias and deaths related to coronary artery disease.
- Important component for cell signaling.
- Data from the MIDAS trial indicate that 900 mg of DHA (about 3 g of fish oil) per d in pts with minimal cognitive dysfunction restored memory to that of a person 3.5 y younger.
- Data from a trial in non-breastfed infants indicate better IQ by about 16 points in babies who were formula fed with 20 mg of DHA per d compared with those fed formula without DHA.
- While reducing plasma concentrations of triglycerides, also reduces elevated VLDL and chylomicrons and causes slight elevation in HDL; tends to reduce risk of death from CAD as well as the risk of stroke.
- Lowers BP (minimal effect).
- Decreases the risk of arrhythmias and MI.
- Beneficial antithrombogenic from EPA (DHA has no anticlotting effect) and anti-inflammatory effects from DHA or EPA