- Usual recommended dose is 200–400 mg 2–3 times daily or 1000–1200 mg as a single daily dose. Higher doses have been used in clinical trials with no evidence of increased efficacy.
- Glucosamine 1500 mg is commonly combined with chondroitin in commercial preparations taken either once daily or in three divided doses. The optimal dose of CS, alone or in conjunction with glucosamine, is unclear from current literature.

Assessment Points

System	Drug Effect	Assessment by Hx	PE	Test
MS	Anti-inflammatory, reduction in joint degeneration	Assessment of pain and functionality scores	Joint tenderness and mobility	Radiologic loss of joint space
GI	Nausea or diarrhea (low incidence)	Subjective reporting of GI upset	Abdominal bloating	
CV	Arrhythmia, peripheral edema	Description of arrhythmia	Irregular pulse	ECG
DERM	Hair loss, periorbital swelling			

Key References: Singh JA, Noorbaloochi S, MacDonald R, et al.: Chondroitin for osteoarthritis, *Cochrane Database Syst Rev* 1:CD005614, 2015; Abe A, Kaye AD, Gritsenko K, et al.: Perioperative analgesia and the effects of dietary supplements, *Best Pract Res Clin Anaesthesiol* 28(2):183–189, 2014.

Anticipated Problems/Concerns

- Caution with anticoagulant medications

Chromium

Lee A. Fleisher

Uses

- Body building (ineffective)
- May aid in glycemic control of type II DM and gestational DM
- Hyperlipidemia
- Hypoglycemia (reactive)
- Obesity

Perioperative Risks

- Risks minimal
- Chronic ingestion associated in one case with thrombocytopenia, hepatic dysfunction, renal dysfunction

Worry About

- Nephrotoxicity

Overview

- A trace mineral
- Improves glucose tolerance in type II DM and gestational DM (in some studies)
- Shown to increase insulin sensitivity and decrease serum triglycerides
- Shown to alleviate symptoms of reactive hypoglycemia
- Popular as weight-loss and body-building supplement, but effect not supported in clinical trials

Drug Class/Mechanism of Action/Usual Dose

- Hypothesis: In normal functioning, it increases circulating insulin, resulting in binding of chromium to peripheral insulin-sensitive tissue; increases insulin receptor number; and activates insulin receptor kinase.
- Usual dosage recommended: 50–200 μg/d.
- Available orally or IV
- Taken as supplement of 200–1000 μg/d
- Mixed results in randomized clinical tests

Assessment Points

System	Effect	Test
RENAL	Nephrotoxicity	Cr
ENDO	Insulin sensitivity	Glucose

Key References: Hummel M, Standl E, Schnell O: Chromium in metabolic and cardiovascular disease, *Horm Metab Res* 39(10):743–751, 2007; Suksomboon N, Poolsup N, Yuwanakorn A: Systematic review and meta-analysis of the efficacy and safety of chromium supplementation in diabetes, *J Clin Pharm Ther* 39(3):292–306, 2014.

Perioperative Implications

- No known interaction

Cranberry

Christopher J. Cullom | Alan David Kaye

Uses

- Many cranberry juice consumers are aware of a beneficial link between cranberry juice and the prevention of UTIs.
- High in polyphenol activity.
- Potentially beneficial for prevention of upper GI ulcers, reducing the risks of CV disease, and improving oral hygiene.
- Native Americans and early American sailors used cranberries for treating wounds and blood poisoning, urinary illnesses, diarrhea, DM, and as an antiscorbutic agent.

Perioperative Risks

- Cytochrome P-450 inhibitor based on in vitro evidence, specifically CYP3A4 and CYP2C9.
- Based on in vivo studies, interaction with warfarin, midazolam, fluconazole, or drugs dependent on CYP enzymes appear unlikely, unless cranberry is consumed at large quantities or long durations, yet not excluded completely.
- There is some evidence for alteration in INR with administration of cranberry that warrants consideration.

Worry About

- Theoretical risk of oxalate urinary stone formation (if large volumes consumed daily).
- Consider potential interaction with anticoagulation effects of warfarin or other drugs dependent on CYP enzymes.

Overview/Pharmacology

- Cranberries are a fruit native to New England and belong to *Vaccinium macrocarpon*.
- Most popular form for consumption is the cranberry-juice cocktail, containing about 27% cranberry juice, sweetener, water, and vitamin C.
- Also available as juice concentrate, tablets, or capsules.
- Consist of 90% water and various organic substances such as quinic acid, malic acid, and citric acid as well as glucose and fructose.

Drug Class/Mechanism of Action/Usual Dose

- Increases concentration of hippuric acid and increases acidification of urine.
- Inhibits bacterial adherence to mucosal surface by at least two kinds of inhibitors: fructose and proanthocyanidins.
- Fructose and proanthocyanidins in cranberries inhibit type I–fimbriated *Escherichia coli* adhesion.
- Cranberry products have been shown to reduce the incidence of UTIs in women at 12 mo.

Assessment Points

System	Drug Effect	Assessment by Hx	PE	Test
HEENT	Reduces dental plaque, periodontal and gum disease	Toothache	Dental exam	
CV	Improves ability of LDL to resist oxidative stress (antioxidation)			ECHO of arteries
GU	Prevents UTI, stone formation	Frequency and urgency and painful urination	Cloudy urine, low back pain	UA culture
HEME	Potential warfarin interaction	H/o anticoagulant use	Petechiae, bleeding	CBC, PT, PTT, INR

Key References: Guay DRP: Cranberry and urinary tract infections, *Drugs* 69(7):775–807, 2009; Lilja JJ, Backman JT, Neuvonen PJ: Effects of daily ingestion of cranberry juice on the pharmacokinetics of warfarin, tizanidine, and midazolam, *Clin Pharmacol Ther* 81(6):833–839, 2007.

Perioperative Implications

Preoperative Concerns

- Hx of recurrent UTI, possible urolithiasis, need for antibiotics.

Induction/Maintenance

- Routine monitoring.
- Consider antibiotic coverage if a UTI is present.
- Drugs administered depend on cytochrome P-450.

Postoperative Concerns

- Immediate resumption not necessary.

Anticipated Problems/Concerns

- Assess for UTI, antibiotic use, urolithiasis, anticoagulation status, or drug interactions for medications dependent on CYP enzymes.

Creatine

R. Blaine Easley | Lee A. Fleisher

Uses

- Medical: Historically used to lower cholesterol and treat rare conditions of heart failure due to creatine deficiencies; it has proposed benefits to decrease myalgias and myositis with statins.
- Fitness: Increased usage of creatine over past decade to increase muscle mass and enhance physical performance. Initially used by professional athletes, it is now used as a nutritional supplement in almost all areas of exercise fitness (in both casual and competitive athletes).
- Incidence: Unknown incidence in the population.

Perioperative Risks

- Unknown. Theoretical problems in pts with impaired renal function; potential for drug interactions, though no definitive studies

Worry About

- Hypovolemia and/or dehydration if nutrition inadequate.

Overview/Pharmacology

- Commercially available as creatine citrate, creatine monohydrate, and creatine phosphate.
- Creatine exists intracellularly in skeletal muscle, cardiac muscle, brain, and testes as creatine phosphate, otherwise called phosphocreatine. Phosphocreatine contains a high-energy phosphate bond, used for short, intense muscle activity via the phosphagen energy system.
- Studies in animal and human subjects have demonstrated increase of cellular phosphocreatine levels in skeletal muscle following creatine ingestion. Few studies demonstrate an increase in muscle strength or endurance.
- Recent randomized trials have shown neither increased strength nor increased stamina.
- Increase in muscle mass is thought to be related to increase in intracellular H_2O content brought about by influx of phosphocreatine into myocyte.
- Creatine is eliminated from the body by renal excretion as creatinine, the anhydrous form of creatine.
- Creatine is usually ingested after being dissolved in fluid.
- Use creatine to increase muscle mass and performance. Special concern should be paid to athletes desiring weight loss (i.e., wrestlers, gymnasts, body builders, football players) in examining renal function.

Drug Class/Usual Dose

- Creatine is classified as a nutritional or dietary supplement; therefore, it is unregulated by the FDA.
- Typical usage: Initially 20–25 g ingested daily for 5–7 d, followed by 5–10 g daily for 10–12 wk. However, some individuals take higher dosages continually.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
CV	Hypovolemia/hypotension	Exposure	BP, HR	Lytes

Key Reference: Shao A, Hathcock JN: Risk assessment for creatine monohydrate. *Regul Toxicol Pharmacol* 45(3):242–251, 2006.

Possible Drug Interactions

Preoperative Concerns

- Because of the associated risk of hypovolemia/dehydration in pts using creatine, there are theoretical problems when used with the following classes of medications: diuretics, H_2 antagonists (e.g., cimetidine), NSAIDs, probenecid, and trimethoprim, or when taken near the time of exercise.

Induction/Maintenance

- No known interactions. May need bolus of intravascular fluids and careful attention to BP at time of induction.

Adjuvants/Regional Anesthesia/Reversal

- No known interactions. Consider pro/cons of NSAID usage intraop, especially if no assessment of renal function.