Assessment Points

System	Effect	Assessment by Hx	PE
HEENT			Dilated, reactive pupils
CV	Retention of sodium and free water	Palpitations Sweating Hyponatremia	Htn/hypotension Tachycardia Autonomic degeneration including: loss of R-R variability on ECG
RESP	No consistent changes	COPD, asthma	Tachypnea, apnea
GI	Abdominal pain, gastritis	IBD, GI ulcer	Abdominal discomfort, guarding
ENDO	Insulin resistance induced hyperglycemia	DM	Sensory deficits from neuropathy
CNS/MS	Euphoria, panic attacks Inhibit calcium absorption Anxiety, mood disorders Hallucinations Sleep disturbances	Cataracts Osteoporosis	Altered mental status Muscle weakness Pathologic fractures Tremors, delirium
DERM		Bruising	Skin changes

Key References: Ericson-Neilsen W, Kaye AD: Steroids: pharmacology, complications, and practice delivery issues, *Ochsner J* 14(2):203–207, 2014; Shaikh S, Verma H, Yadav N, et al.: Applications of steroid in clinical practice: a review, *ISRN Anesthesiol* 2012(7), 2012.

Perioperative Implications

- Special consideration of preop blood glucose and lytes
- Steroid supplementation is necessary in the periop setting if pts have a history of hypoadrenocorticism or suppression of the HPA axis due to a history of steroid intake.
- In presence of adrenal insufficiency, it is important to be hypervigilant to prevent precipitation of adrenal crisis secondary to surgical stress.
  - Preop management should include treatment of hyperkalemia, hyponatremia, and hypovolemia.
  - Stress dose of glucocorticoids (100 mg hydrocortisone phosphate IV) should also be given
  - Avoid medications that are inhibitors of cortisol synthesis. These include ketoconazole, aminoglutethimide, etomidate (selectively inhibits adrenal 11-beta hydroxylase).
- Cushing disease or syndrome:
  - Obese/morbidly obese pts: May present difficult airways; carefully assess Mallampati and TM distance.
  - Pituitary adenoma can result in increased ICP.
  - Use opiates to prevent sympathetic surge associated with intubation.
  - Avoid ketamine to prevent excessive sympathetic effects.
  - Etomidate may be used.

Gold (Auranofin, Aurothioglucose, Aurothiomalate)

Kevin Miller | Jonathan Gavrin

Uses

- Rheumatoid arthritis treatment for patients without sufficient response to initial treatment with NSAIDs, steroids, or other DMARDs.
- May have efficacy in pemphigus vulgaris, psoriatic arthritis, and palindromic rheumatism but lacks trials is and rarely used due to availability of other therapies.
- Availability of other DMARDs, such as biologic TNF inhibitors and methotrexate, has decreased the use of gold.

Perioperative Risks

- IM gold associated with higher dropout rates due to side effects when compared to other DMARDs (up to 19% in one study).
- Cutaneous reactions range from erythema and pruritus (30% of pts) to exfoliative dermatitis.
- Mucous membrane lesions (20% of pts), including stomatitis, pharyngitis, gastritis, and colitis.
- Dermal deposits and chrysiasis (gray-to-blue pigmentation of sun-exposed skin) are possible with large cumulative doses. Effect on transcutaneous Hgb saturation measurement is unknown. Some pts are noted to have corneal deposits.
- Allergic (5% of pts): Anaphylactoid and nitritoid reactions, with transient flushing, nausea, hypotension, dizziness, and diaphoresis (especially seen in pts also taking ACE inhibitors).
- GI (5% of pts): Diarrhea (common in pts taking the oral formulation auranofin), enterocolitis, jaundice and hepatic toxicity (from cholestasis), transaminitis, pancreatitis, and metallic taste.
- Renal: Proteinuria (10–15%, usually resolves with cessation of treatment), renal tubule deposition, acute renal failure, and nephrotic syndrome. Use caution in pts with decreased renal function due to delayed elimination.
- Pulmonary infiltrates and interstitial pulmonary disease are rare and usually resolve with cessation of treatment; difficult to differentiate from underlying RA pulm fibrosis.
- Hematologic: Thrombocytopenia (<5%, usually develops in first 6 mo, immune-mediated attack on bone marrow reverses with cessation of treatment), leukopenia (2%), eosinophilia, bone marrow suppression, rare progression to aplastic anemia. This can be avoided in pts given antimalarials, phenylbutazone, or oxyphenbutazone because of cumulative bone marrow suppression.
- Neurologic: Cranial nerve palsies, encephalitis, Guillain-Barré-like syndrome. Peripheral neuropathy (<1%—painful paresthesias progressing to asymmetric weakness, may be preceded by fever/rash; direct toxic effect vs. hypersensitivity reaction).
- Not usually administered to pregnant pts but limited published data are available.
- Use caution in the elderly (due to underlying renal insufficiency and bone-marrow suppression).

Overview/Pharmacology

- Consider IM (aurothioglucose, aurothiomalate) versus oral (auranofin) use. Monitor closely for side effects; oral administration has less common side effects but higher incidence of immunosuppression and rare side effects.
- Rapidly absorbed; peak serum concentrations after IM injection 2–4 h.
- Highly (~95%) albumin-bound and also binds to macroglobulins.
- Slow elimination, with half-life of single 50-mg dose IM approximately 7 d.
- Can be noted in tissues up to 20 y following the last dose.
- After IM full dose, blood levels return to normal in 40–80 d.
- Elimination: Majority occurs in renal (approximately 75%), with the remainder in feces.

Drug Class/Mechanism of Action/Usual Dose/Monitoring

- Anti-inflammatory DMARD.
- Free thiol group may contribute to reduction in oxidative stress.
- Gold compounds sequestered in phagocytic cells of reticuloendothelial system (liver, spleen, lymph nodes) and synovial membranes.
- Gold suppresses migration of monocytes and macrophages.
- Suppresses proinflammatory cytokines such as interleukins 1α, 1β and 6, TNF-α, as well as prostaglandin synthesis, C1 inhibition, lysosomal hydrolytic enzymes and elastase inhibition, and B-cell inhibition.
- Slows radiologic progression of RA.
- Initial dose of 10 mg, with 25 mg dose in a wk used to test for hypersensitivity.
- Subsequent doses totaling 50 mg per wk are given until 1 g reached. May not see clinical effect for up to 20 wk.
- Continuing therapy involves 50 mg IM every 2–6 wk.
- Monitor for anemia, leukopenia, and thrombocytopenia with regular blood testing and for proteinuria with urinalysis.
- Auranofin dosage initially should be 6 mg/d in divided doses; may be increased to 9 mg/d in divided doses after 6 mo.

Assessment Points

System	Effect	PE	Test
HEENT/ DERM	Erythema, pruritus, dermatitis, mucous membrane lesions		
MS	Evaluate for manifestations of RA (arthritis, c-spine involvement, TMJ)	ROM, decreased cervical range of motion and oral mouth opening	Lateral neck radiograph, neck CT, MRI
RESP	Inflammation, pulm infiltrates		CXR
GI	Diarrhea, jaundice, hepatitis		LFTs
GU	Proteinuria, nephrotic syndrome, renal failure		Renal function, pregnancy
CNS	Encephalitis, peripheral neuropathy, cranial nerve palsy	CNS exam	

Key References: Bykerk V: Nonimmunosuppressive disease-modifying antirheumatic drugs. In Hochberg MC, Silman AJ, Smolen JS, et al., editors: *Rheumatology,* ed 6, Philadelphia, 2015, Elsevier, pp 434–442; Cohen SA, Stabile MJ, Warfield CA: Pain in the extremities. In Warfield CA, Bajwa ZH, editors: *Principles and practice of pain medicine,* ed 2, New York, 2004, McGraw-Hill, pp 315–342.

Perioperative Implications/Possible Drug Interactions

- No interactions with anesthetic medications have been reported.

Anticipated Problems/Concerns

- Assess pts for musculoskeletal manifestations of RA including C-spine and TMJ involvement; may require additional equipment or planning for endotracheal intubation or may require additional care during positioning. Pts with cutaneous manifestations may have friable tissue, including mucous membranes.
- Review lab evaluation for side effects of treatment causing pulm, hepatic, or renal dysfunction or hematologic disorders.

Hormone Replacement Therapy

Aliya Ahmed | Robyne Irshad Khan

Uses

- Prevention or alleviation of moderate to severe menopausal signs and symptoms such as vasomotor effects, depressive mood changes, vaginal dryness, urogenital atrophy, osteoporosis, cardiovascular disease, and cognitive dysfunction
- Treatment of physiologic and physical manifestations of primary ovarian insufficiency

Perioperative Risks

- Increased risk of VTE due to increased generation of fibrin, reduction in plasma levels of protein S, resistance to activated protein C, and higher levels of C-reactive proteins
- May cause reduction in fibrinogen, decrease in level of plasminogen activator inhibitor-I, leading to enhancement of fibrinolytic potential and prolonged bleeding

Worry About

- Increased risk of VTE including DVT, PE, stroke, and MI with HRT
- Increased risk of fibrinolysis and prolonged bleeding with combination estrogen-progestin

Overview/Pharmacology

- HRT is a generic term for the use of estrogen therapy alone, the combination of estrogen and progesterone, or a chemical analogue called a progestin.
- Conjugated estrogens and synthetic progestins have been most commonly used in HRT.
- Estrogens: A group of 18-carbon steroid compounds that occur naturally in three major forms: estrone, estradiol, and estriol. All steroids contain four condensed rings, designated A to D. The phenolic A-ring is the principal structural feature responsible for selective high-affinity binding to the estrogen receptors. Like most steroid hormones, estrogens can diffuse readily across cell membranes. Once within a cell, they bind and activate estrogen receptors, which, in turn upregulate gene expression. Estrogen receptors are abundant throughout the body and can be found in the female reproductive tract, mammary glands, hypothalamus, endothelial cells, vascular smooth muscle, lung, brain, and bone.
- Progestins: A family of 21-carbon steroids that are synthetic derivatives of the 19-nortestosterone structure. Having effects similar to progesterone, progestins work by binding to an intracellular progesterone receptor. This results in transcriptional activation, causing endometrial proliferation, suppression of uterine contractility, mammary gland development, and thickening of endocervical gland secretions.
- Tibolone: A synthetic compound having mixed estrogenic, progestogenic, and androgenic activities; it is used as an alternative to conventional HRT.
- SERMs: These (e.g., raloxifene) act as estrogen agonist in some tissues while exerting antagonist effects in others.

Drug Class/Usual Dose

- Various formulations are available for oral, parenteral, transdermal, and topical administration. Current recommendation is to use the lowest dosage to control symptoms for the shortest period.
- The typical daily oral dose of conjugated estrogen is 0.625 mg; however, initial treatment should start at 0.3 mg/d, with dose adjustment based on clinical response. For transdermal estrogen, 17-beta estradiol patches of 25, 37.5, 50, 75, and 100 μg/d are available. Subcutaneous implants in doses of 20, 50, and 100 mg—in addition to vaginal gels, rings, and tablets—are also available.
- Progestin is typically given in a cyclic regimen (5–10 mg/d) or continuous regimen (2.5 mg/d). Better choice is a micronized progestin (Prometrium, for example) which does not oppose the effect of estradiol on arterial function. Progestin transdermal and intrauterine preparations are also used.