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.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Retinal vascular thrombosis, increased corneal curvature, increased lacrimal secretion, dry-eye syndrome, headaches	Changes or loss of vision, contact lens intolerance, headache	Pale retina with cherry red macula, retinal hemorrhages	Ophthalmologic exam
CV	Fluid retention, Htn, improved lipoprotein profiles: increased HDL, decreased LDL	Swelling and weight gain, Htn	Edema	BP, lipid profile
GI	Pancreatitis	Abdominal pain, bloating, nausea	Epigastric pain	Amylase, lipase, alk phos
HEPAT	Cholestasis, gallstone formation	Abdominal pain, intolerance to fatty food	RUQ pain	RUQ US, LFTs
GU	Abnormal uterine bleeding, changes in cervical secretions, increase in fibroid size, vaginal candidiasis	Vaginal bleeding, vaginal discharge, vaginal itching/burning	Enlarged lobulated uterus, vaginal discharge	Gynecologic exam, gynecologic US, KOH prep test
HEME	Increased coagulation, increased fibrinolysis	DVT, PE, MI, CVA Prolonged bleeding	LE swelling, SOB, CP, neurologic deficits	PT/PTT, D-dimer, duplex US, CT angio fibrinogen, antithrombin III, Protein C
DERM	Melasma, rashes	Skin changes	Hyperpigmentation, acne	Dermatologic exam

Key References: Voican A, Francou B, Novac L, et al.: Pharmacology of hormone replacement therapy in menopause. In Gallelli L, editor: *Pharmacology*, Intech, 2012, pp 313–338. <http://www.intechopen.com/books/pharmacology>. (Accessed 28.06.16); Brighouse D: Hormone replacement therapy and anaesthesia, *Br J Anaesth* 86(5):709–716, 2001.

Perioperative Implications

Preoperative Concerns

- Increased risk for VTE. Pts undergoing procedures associated with moderate to high risk for VTE should stop hormone therapy 4 wk prior to surgery. Rigorous prophylaxis for DVT must be observed in the periop period.
- Risks associated with discontinuation of HRT are withdrawal bleeding, hot flashes, and other menopausal symptoms.

Induction/Maintenance

- Progestin metabolite allopregnanolone may affect the excitability of neurons through direct modulation of the GABA-A receptors, exerting hypnotic/sedative, anxiolytic, and anesthetic effects.
- Alterations in the activity of various cytochrome P450 CYP isozymes may require dose adjustment of hepatically cleared drugs in some pts.
- Activation of fibrinolytic pathways with combined estrogen-progestin replacement therapy may result in periop bleeding.

Postoperative Period

- Increased risk for VTE extends into the postop period. Vigilance for DVT, PE, stroke, and MI is required.

Anticipated Problems/Concerns

- Coagulopathy, especially an increased risk for VTE, remains a top concern for women using HRT.

Inhaled Bronchodilators

Michael Feduska

Uses

- Reversal of airflow limitation via relaxation of airway smooth muscle tissue
- Long-acting formulations used for chronic therapy and short-acting formulations for acute symptom relief.
- Diagnosis of COPD: FEV_1/FVC <0.70 after bronchodilator treatment.

Overview/Pharmacology

- Two classes: $Beta_2$ agonist and anticholinergic.
  - Inhalational administration decreases systemic effects, increases potency, and shortens time to onset.
  - MDI, DPI, or NEB routes.
  - Airway responsiveness is measured by improvement of FEV_1.
  - Combined use of $beta_2$ and anticholinergic is superior to either used as single therapy.
  - Often combined with an inhaled corticosteroid.
- $Beta_2$ agonist:
  - Short-acting (albuterol, levalbuterol, fenoterol, terbutaline): Onset within about 5 min; peak 30 min to 1 h; duration 4 to 6 h; levalbuterol 6 to 8 h
  - Long-acting: Duration 12 h (arformoterol, formoterol, olodaterol, salmeterol), 24 h (indacaterol)
- Anticholinergic:
  - Short-acting (ipratropium bromide, oxitropium): Onset 1 to 3 h; duration 6 to 8 h
  - Long-acting (tiotropium): Duration 24 h

Perioperative Risks

- $Beta_2$ agonist:
  - Sinus tachycardia, cardiac arrhythmias
  - Hypokalemia/hypomagnesemia
  - Paradoxical bronchospasm
- Anticholinergic:
  - Nausea
  - Acute angle glaucoma
  - Urinary retention
  - Tachycardia

Worry About

- Delivery can be compromised by poor technique or coordination.
- $Beta_2$: Concern for additive effect with other drug classes that cause QT prolongation, cardiac arrhythmias, hypokalemia (thiazide diuretics)
- Long-acting $beta_2$ agonist subject to tachyphylaxis, unlike short-acting type
- Beta-blocker: $Beta_1$–selective antihypertensive is ideal
- Anticholinergic additive adverse effects with other anticholinergic medications

Drug Class/Mechanism of Action/Usual Dose

- $Beta_2$ stimulation: G protein–coupled receptor increases cAMP formation, increasing Ca^{2+} influx via L-type Ca^{2+} channel, causing smooth muscle relaxation
- Anticholinergic: Acetylcholine muscarinic receptor (M1, M2, M3) blockade inhibits G-protein signaling, decreases cGMP formation, and prevents bronchoconstriction
  - Short-acting is M2-, M3-selective
  - Long-acting is M1-, M3-selective
- Delivered via MDI, DPI, or nebulizer
- Short-acting salbutamol (albuterol): 2.5 mg/3 mL 0.083%, 5 mg/mL NEB 0.5%, q4-6h prn
- Long-acting arformoterol: 15 µcg/NEB q12h; formoterol: 12 µg/cap DPI q12h; olodaterol: 2.5 µg/MDI q12h; salmeterol: 50 µg/DPI q12h; indacaterol: 75 µg/cap DPI q24h
- Short-acting: Ipratropium 0.5 mg/2.5 mL NEB or 17 µg/spray DPI q6–8h
- Long-acting tiotropium bromide: 18 µg/cap DPI, 1 cap q24h