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

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Xerostomia, acute angle glaucoma (A-ch)	Glaucoma, Hx of administration via face mask, contact with eyes	Eye pain, erythema	
CV	Tachycardia, arrhythmias ($beta_2$, A-ch)	Palpitations	HR	ECG
GI	Nausea, constipation (A-ch)			
RESP	Bronchodilation ($beta_2$, A-ch)	Dose frequency, Hx of exacerbation, Hx of intubation	Screening FET	Spirometry: (FEV_1, FEV_1/FVC)
METAB	Hypokalemia, hypomagnesemia ($beta_2$)	Concurrent use of potassium-wasting medications (thiazide diuretics)		K+
GU	Urinary retention (A-ch)	Increased risk with BPH		
CNS	Anxiety, headache, resting tremor			

Key References: Currie G, Lee DK, Lipworth B: ABC of chronic obstructive pulmonary disease. Pharmacologic management—oral treatment, *Br Med J* 332(7556):1497–1499, 2006; Woods BD, Sladen RN: Perioperative considerations for the patient with asthma and bronchospasm, *Br J Anaesth* 103(Suppl 1):i57–i65, 2009.

Perioperative Implications

Preoperative Concerns

- Elicit Hx of frequent exacerbations, hospitalization, intubation.
- Pretreatment with short-acting $beta_2$ agonist is beneficial.
- Include risk of hypokalemia with concurrent use of potassium-wasting medications (thiazide diuretics).
- Forced expiratory time: Listen over the trachea while the pt exhales forcefully. FET <6 sec indicates airflow limitation.

Induction/Maintenance

- Bronchospasm: Treat with short acting nebulizer or MDI $beta_2$ agonist (albuterol) via ETT
- Increased dosage (8–12 puffs) required due to ETT rainout

Anticipated Problems/Concerns

- Ventilation difficulties in pts with poorly controlled COPD or asthma.
- Bronchoconstriction can lead to severe bronchospasm, air trapping, V/Q mismatch, right heart strain.
- Precipitation of tachyarrhythmias with $beta_2$ agonist or anticholinergic inhalers.
- Systemic effects associated with hypokalemia.
- Rare risk of paradoxical bronchospasm with $beta_2$ agonist.

Insulin

Thomas Schricker | Hiroaki Sato

Uses

- Treatment of pts with insulin-dependent DM, hyperglycemia, DKA, and hyperkalemia

Overview/Pharmacology

- Produced by the beta cells of the pancreatic islets of Langerhans.
- Proteolytic cleavage of the connecting peptide from proinsulin produces the C-peptide and insulin (peptides A and B), which are released into the circulation in equimolar amounts.
- In healthy subjects insulin is secreted at a basal rate of 0.5–0.7 U/h.
- The administration of insulin inhibits its endogenous secretion.
- Insulin's principal target organs are skeletal muscle, adipose tissue, and liver.
- Glycemia is controlled via insulin receptor–mediated effects of insulin on glycogen synthesis, cellular glucose uptake, and gluconeogenesis.
- Stimulates the Na^+K^+-ATPase activity and thus lowers plasma potassium.
- The kidneys are primarily responsible for the clearance of exogenous insulin, while endogenously produced insulin is cleared also by the liver.
- Classified according to onset, peak, and duration of action.
- Can be given IV, IM, and SQ.

Pharmacokinetics of Different Types of Insulin (After SQ Administration)

	Rapid-Acting	Short-Acting	Intermediate-Acting	Long-Acting	Very Long–Acting
	Humalog Novolog Apidra	Regular Humulin R Novolin R	NPH N	Lantus Levemir	Tresiba
Onset	10–30 min	0.5–1 h	1–2 h	1–2 h	1–2 h
Peak (h)	0.5–1.5	2–4	4–12	No peak	No peak
Duration (h)	3–5	5–8	18	<24	>24

- Periop and during critical illness, only short-acting insulin is being used. IM administration results in more rapid time-action profile than SQ injection.
- Effect of IV insulin is also more rapid than that of SQ.
- Maximum effect of IV insulin reached after 20–30 min and can last 1 h.
- Insulin's serum half-life is 7 min.

Dosing

- Wrong insulin dosing ranks among the top five drug administration errors.
- Handwritten abbreviations such as "u" and "iu" are major causes for unintentional administration of 10 or 100 times the prescribed dose.
- Regular human insulin available in two concentrations: 100 U/mL (U-100) and 500 U/mL (U-500).
- When administered IV, only U-100 regular insulin concentration should be used.
- For dosing, insulin should be drawn up with a specific insulin syringe (dilute 100 U in 100 mL normal saline, 1 U = 1mL).
- Effective dose depends on the (often unpredictable) extent of pt's tissue insulin sensitivity and target blood glucose.
- Initial bolus doses to treat hyperglycemia range between 2 and 10 U.
- Continuous insulin infusions typically start at 1–2 U/h (in type 1 diabetic pts, 0.5–1 U/h) and frequently must be titrated to achieve target blood glucose.
- Blood glucose should be measured at least every 30 min.
- Note: Half-life of insulin is prolonged in pts with renal failure.