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

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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.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
METAB	Decreased blood glucose	Use of oral hypoglycemic agents Fasting Alcohol consumption Renal and hepatic impairment	Sweating Tachycardia convulsion tremor Coma	Blood glucose
	Hypokalemia	Mineralocorticoid excess (Cushing syndrome, primary aldosteronism, use of steroids) Diet or parenteral nutrition Use of diuretics	Arrhythmia Weakness Fatigue Polyuria	Serum/urine lytes ECG
	Hypophosphatemia			Serum phosphate
	Protein anabolism	Kwashiorkor Marasmus Cancer cachexia Chronic renal disease	Edema	Serum albumin Whole body nitrogen balance
	Decreased lipolysis			Serum free fatty acids Acid-base balance
CV	Vasodilation Increased skeletal, myocardial, cerebral blood flow Positive inotropic	Use of vasodilators		BP Cardiac output
HEM	Decreased plt aggregation Impact on fibrinolysis	MI Cerebrovascular accident Pulm embolism, DVT Pregnancy Cancer Genetic factors	Chest pain SOB 5 Ps: Pain, paralysis, pulselessness, pallor, paresthesia Neurologic deficit	CT MRI Doppler US BP ECG

Key References: Evans CH, Lee J, Ruhlman MK: Optimal glucose management in the perioperative period, *Surg Clin North Am* 95(2):337–354, 2015; Dhatariya K, Levy N, Kilvert A, et al.: NHS diabetes guideline for the perioperative management of the adult patient with diabetes, *Diabet Med* 29(4):420–433, 2012.

Perioperative Implications

Metabolic Risks

- Hypoglycemia:
  - Glycemia ≤55 mg/dL: Neurologic and adrenergic symptoms including sweating, shaking, anxiety, and tachycardia.
  - Glycemia ≤50 mg/dL: Severe impairment of CNS—for example, headache, fatigue, dizziness, inappropriate behavior (sometimes mistaken for inebriation), confusion, blurred vision, and eventually coma and death.
- Hyperglycemia: Glycemia ≥600 mg/dL: Osmotic diuresis, fever, vision loss, hallucinations, and coma.
- DKA: Typically affects fasting type 1 diabetic pts who stop insulin treatment. Diagnosis is based on increased serum and urinary ketones, signs of dehydration, DVT and pulm embolism, acidosis, and a Kussmaul breathing pattern.
- Hypophosphatemia.
- Hypokalemia.

Preoperative Concerns

- Poor preop glycemic control (HbA_{1c} >8.5%) may warrant referral to diabetes specialist.
- Traditionally, long-acting insulin discontinued 2–3 d before surgery; glucose levels are then stabilized by a combination of intermediate- and short-acting insulin.
- If glycemic control is well managed, may consider continuing long-acting insulin regimen until day of surgery.
- Prandial insulin should be withheld while fasting and blood glucose is measured prior to surgery in all diabetic pts.
- If capillary blood ketones are >300 mol/L or urinary ketones >3+, cancel surgery, follow DKA therapeutic guidelines, and contact a diabetes specialist.
- Symptomatic hyperglycemia >400 mg/dL may also justify delay of surgery.
- In type 1 diabetic pts, rapid-acting analogue insulin may be given SQ assuming that 1 U decreases blood glucose by 54 mg/dL.
- Type 2 diabetic pts may require up to 0.1 U/kg of SQ rapid-acting analogue insulin.
- Blood glucose should be measured 1 h later and, if necessary, IV insulin started.

Intraoperative Concerns

- Surgical trauma reduces tissue insulin sensitivity, resulting in hyperglycemia also in nondiabetic pts.
- Acute insulin resistance is aggravated in the presence of stressors such as cardiopulmonary bypass, use of catecholamines, hypothermia, and after long periods of preop fasting.
- Even moderate hyperglycemia contributes to morbidity and mortality after major surgery.
- Although the ideal level of glycemia with regard to surgical outcomes is unknown, most professional associations recommend a blood glucose level <200 mg/dL.
- From a metabolic perspective, anesthetic techniques seem preferable that allow early return to normal diet, mobilization, and usual pharmacologic diabetes management. Efferent neuraxial blockade has been demonstrated to attenuate the hyperglycemic response to surgery and facilitate recovery.
- Glycemia in anesthetized, unconscious pts must be monitored and hypoglycemia avoided.
- If blood glucose is <72 mg/dL, 100 mL of 20% glucose can be given IV.
- Type 1 diabetic pts receive insulin infusions continuously (at doses equivalent to the daily dose of long-acting insulin prescribed before surgery).

Postoperative Period

- Hyperglycemia can be managed by SQ or IV administration of insulin using so-called sliding scales. However, in the context of surgery and critical illness, traditional insulin sliding-scale protocols are often ineffective (i.e., fail to achieve the quality of glycemic control aimed for).

Latest Developments

- There is evidence to suggest that the quality of preop glycemic control as assessed by HbA_{1c} is associated with clinical outcomes.
- Insulin has been reported to improve memory function in cognitively impaired individuals.
- Therapeutic use of intranasal insulin in pts with Alzheimer disease is under investigation (phase 2 trials).
- Inhaled insulin (Afrezza) was approved by the FDA in 2014.