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TYPE 1 DIABETES MELLITUS

Surgical Specialty:	Other
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Background:

- General Considerations
  - 1.6 million people in the United States have type 1 Diabetes Mellitus (T1D), including 187,000 children and teens.[1]
  - Patients with T1D have little or no endogenous insulin production. Unlike patients with type 2 diabetes, they are completely dependent on exogenous insulin, even while fasting.[1]

- Pathology
  - T1D is caused by pancreatic β-cell destruction, leading to absolute insulin deficiency[2]
  - Insulin functions
    - Facilitate transport of glucose into cells
    - Suppress endogenous glucose production (glycogenolysis, gluconeogenesis)
    - Increase glycogen synthesis and lipogenesis
  - Effects of insulin deficiency[3]
    - Glucose is not transported into cells → hyperglycemia and intracellular energy deficiency
    - Endogenous glucose production increases → hyperglycemia
    - High glucose concentrations in the blood → osmotic diuresis and polyuria → polydipsia in attempt to maintain euvolemia
    - Cells use alternative pathways for energy production → ketogenesis and lipolysis → diabetic ketoacidosis (DKA)

- Patient Considerations
  - Patients with T1D require exogenous insulin, even while fasting. Perioperative fasting and physiologic stressors can significantly impact insulin requirements.[4]
  - Some patients with T1D may require oral antihyperglycemics (e.g., metformin, GLP-1 agonists) in addition to insulin. The perioperative management of these medications is complex and beyond the scope of this summary.
  - HbA1c is measured as an assessment of glycemic control. The target HbA1c for pediatric patients is <7%, however, fewer than 20% of patients achieve this goal. HbA1c values are highest in adolescents.[2]
  - Clear communication between the patient/family, endocrinology, surgical, and anesthetic teams is essential to avoid perioperative hypoglycemia or DKA.

- Associated Comorbidities/Syndromes
  - Patients with T1D are at risk for macrovascular complications, such as heart and cerebrovascular disease, and microvascular complications, such as renal, ophthalmic, and neuropathic disease.
  - Additional comorbidities relevant to anesthesiologists include delayed gastric emptying and limited joint mobility (including the temporomandibular joint, which can make direct laryngoscopy difficult).
  - These comorbidities are more common in long-standing and poorly controlled T1D and are less likely to occur in pediatric or newly diagnosed patients.

- Insulin Therapy
  - Patients with T1D require insulin to regulate endogenous glucose production (basal requirement) and to prevent or correct hyperglycemia from eating (post-prandial or bolus requirement).
  - Subcutaneous insulin regimens

	Multiple Daily Injections (MDI) or Basal-Bolus Regimen	**Continuous Subcutaneous Insulin Infusion (CSII)**
Basal Insulin	Intermediate- or long-acting insulin injected 1-2 times per day	Rapid-acting insulin infused continuously by an insulin pump
Bolus Insulin	Rapid-acting insulin injected multiple times per day	Rapid-acting insulin boluses administered from an insulin pump

    - CSII therapy is used by over 60% of patients with T1D in the US. The most recent ISPAD guidelines recommend an insulin pump as first-line therapy for children with T1D.[2]
    - Note for patients using CSII: because basal insulin needs are met with rapid-acting insulin, the patient will not have any basal insulin coverage if the insulin pump is discontinued.[2,4]
  - Insulin dosing[4]
    - Each patient has a specific insulin dosing regimen, which should be obtained from the patient or their endocrinologist prior to providing anesthesia.

	Insulin-to-carbohydrate (I:C) ratio	**Insulin Sensitivity Factor (ISF) or Correction Factor (CF)**
When to use it	To prevent hyperglycemia after eating	To correct existing hyperglycemia
Description	How much insulin a patient needs per gram of carbohydrate consumed	How much BG will decrease after administering 1 unit of insulin
Example	I:C ratio 1:10 → administer 1 unit of insulin per 10g of carbohydrates	ISF or CF 1:50 → 1 unit of insulin will decrease BG by 50mg/dL

  - Diabetes technology[2]
    - Insulin pumps: Programmable device that delivers continuous insulin infusion and additional boluses subcutaneously.
      - Basal rate may vary by time of day. Bolus doses are calculated based on patient's I:C ratio, ISF, and target blood glucose (BG).
      - The subcutaneous cannula may be plastic or metal.
      - Most models: the insulin is in a wearable pump and connected via catheter to the subcutaneous cannula.

- Omnipod: the insulin is in a pod which is directly attached to the patient (tubeless) and communicates with a separate electronic delivery system.
- Continuous glucose monitors (CGMs): Wearable device that periodically measures glucose in interstitial fluid. Data is transmitted to a dedicated receiver or mobile smart device every 5-15 minutes.
    - CGM readings correlate well with blood glucose (BG) when it is relatively stable, but they may lag >10 minutes when BG is rapidly changing.
    - Physical compression due to patient positioning, hypoperfusion, and hypothermia can cause inaccurate readings.
    - Acetaminophen can cause inaccurate readings with some older CGM models (particularly Dexcom G5).
- Closed-loop systems: Some insulin pump and CGM models work together. The insulin pump contains an algorithm that adjusts insulin delivery based on CGM readings.

Table 1 - Types of insulin[4]

Duration of Action	**Name**	**Onset (hr)**	**Peak (hr)**	**Duration (hr)**
Rapid	Lispro (Humalog, Admelog) Aspart (Novolog, Fiasp) Gluisine (Apidra)	<0.25	0.5-1.5	4-6
Short	Regular (Humulin R, Novolin R)	0.5	1.5-2.5	8
Intermediate	NPH (Humulin N, Novolin N)	2-4	4-10	12-18
Long	Detemir (Levemir) Glargine (Lantus, Basaglar)	2-4	none	14-24
	Degludec (Tresiba)	1	none	>42

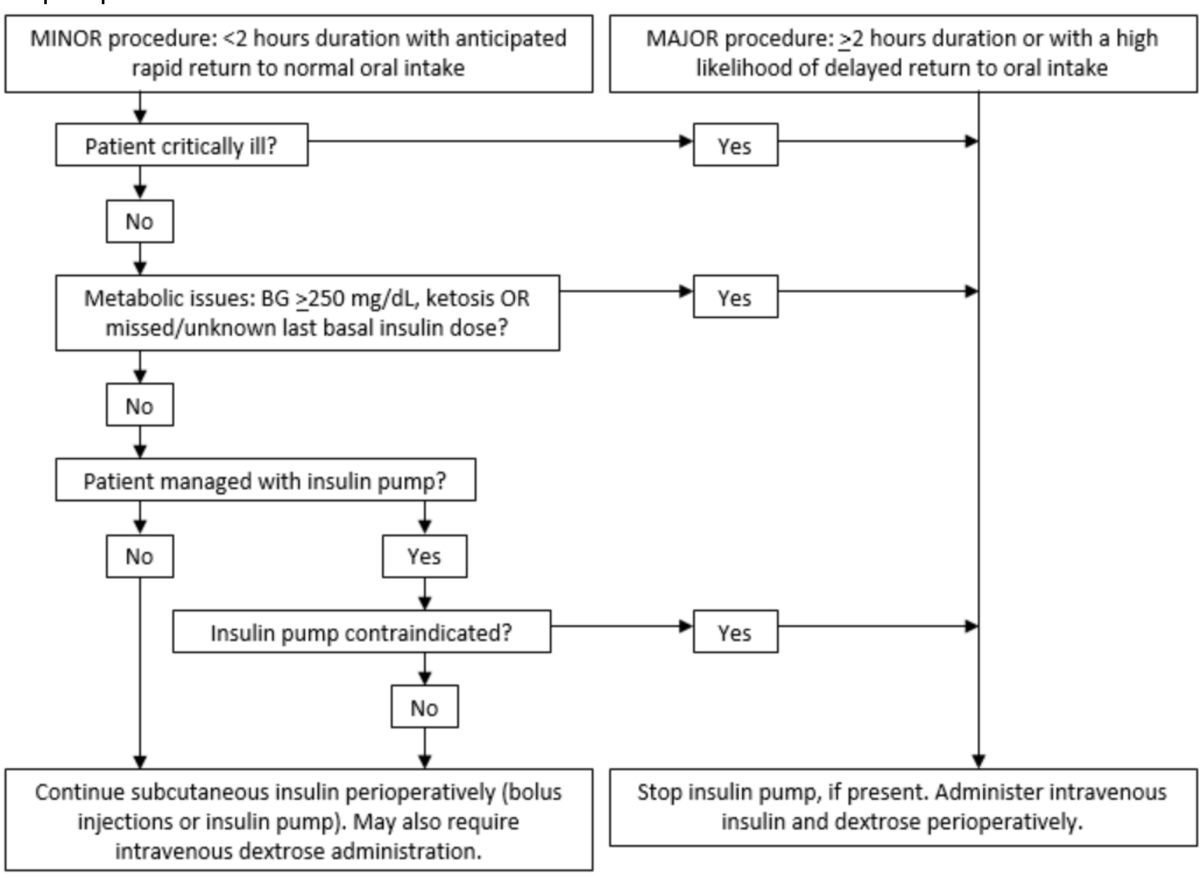
- Mixed formulations that combine short- and long-acting insulin in one medication are not commonly used in pediatrics.
- NPH is the only long-acting (basal) insulin with a peak, which may place the patient at risk for hypoglycemia while fasting. Consult the patient's endocrinologist for perioperative dosing recommendations.

Anesthetic Planning:

- **Pre-Anesthetic Evaluation**
    - Scheduling considerations[4,5]
        - Schedule elective procedures as early as possible (ideally, first case of the day) to minimize fasting time
        - Consider delaying non-emergent procedures if HbA1c >8% (supported in adult literature, however no consensus in pediatrics)
    - Diabetes assessment[4]
        - Consultation with the patient's endocrinologist to create an appropriate perioperative plan is advised
        - Assess glycemic control – HbA1c, typical blood glucose (BG) range, and frequency of complications, such as hypoglycemia, DKA, and hospitalizations
        - Document home insulin regimen – method of administration (MDI vs CSII), type of insulin, dosing schedule, dosing requirements (I:C ratio, ISF)

        - Document use of adjuvant oral medications
    - Detailed fasting and insulin administration instructions should be communicated to the patient and/or family. This is especially important for newly diagnosed patients who may not have experience fasting while taking insulin.[4]
        - Patients should follow standard NPO guidelines. Carbohydrate-containing, clear fluids should be encouraged until 2 hours prior to surgery to prevent fasting hypoglycemia. If the patient becomes hypoglycemic prior to arrival in preop holding, they should manage their hypoglycemia appropriately with glucose gels or tablets. These are not considered an NPO violation in most institutions, though guidelines may vary.
        - Patients should administer basal insulin on their usual schedule. If they are prone to fasting hypoglycemia, the basal insulin dose may be reduced in consultation with their endocrinologist.
        - No short-acting insulin should be administered while fasting.
        - Recommendation for perioperative insulin pump and CGM use have been published[4], but policies may vary by institution. If the insulin pump and/or CGM will be used perioperatively, give instructions regarding appropriate placement, including location (not on an area that will be dependent during surgery) and timing (pump must be placed >12 hours and <60 hours before surgery) to ensure appropriate function.

- **Perioperative Management Plan**
    - Recommendations for perioperative insulin and dextrose management depend on the type of surgery, metabolic status of the patient, and the ability to continue insulin pump and CGM use.[4]



- Contraindications to insulin pump and CGM use: Exact recommendations vary by manufacturer. In general, contraindications include:[2,4]
  - Magnetic resonance imaging (MRI) → must be removed
  - Computed tomography (CT), nuclear medicine scans, cardiac catheterization, AICD/pacemaker implantation, therapeutic radiation oncology → recommend removal
  - X-ray or fluoroscopy → remove from the direct radiation field
  - Electrocautery → position away from the electrocautery site
  - Patient or caregiver unable to explain pump functions or anesthesiologist uncomfortable managing the pump perioperatively → remove pump
- Blood Glucose (BG) Management Plan[2,4]
  - Check glucose at least hourly. Increase to every 30 minutes if changes are made to insulin or dextrose administration. Increase to every 15 minutes if the patient is hypoglycemic.
  - If a CGM is present and not contraindicated, it can be used to follow trends perioperatively. However, confirmation with a blood or serum glucose check is required prior to initiating treatment to ensure accurate measurements. If the CGM is used perioperatively, the anesthesia team must have continuous access to the data display (including any passcodes necessary to use the device).
  - The perioperative BG goal is 90-180 mg/dL.
    - Due to the risk of unrecognized hypoglycemia under anesthesia, higher BG values are tolerated. Correction insulin boluses are typically not administered until the BG reaches 250 mg/dL as long as the patient is otherwise metabolically stable.
    - See complications and pitfalls section for management of hypo/hyperglycemia.

Perioperative Considerations:[2,4]

- **Pre-Operative Holding:**
  - Check BG on arrival and at least hourly throughout the perioperative period.
  - Verify the patient's last oral intake and insulin administration (basal and bolus).
  - If the patient uses an insulin pump and/or CGM, determine if it can be used intraoperatively (see above).
    - Will be used intraoperatively → Verify location and duration of wear. Have patient or family member explain pump functions/alarms to the anesthesia team and verify that basal insulin is currently infusing.
    - Will not be used intraoperatively → Remove completely from the patient and give to the family. IV insulin must be started within 30 minutes of stopping the insulin pump.

- **Intraoperative Recommendations:**
  - Maintain BG 90-180 mg/dL and supply sufficient basal insulin to prevent ketosis.
  - ***Minor surgery AND metabolically stable AND insulin pump can be used*:**
    - Continue subcutaneous insulin intraoperatively.
      - For patients on an MDI regimen: Verify that the most recent long-acting insulin dose was taken appropriately. No additional basal insulin is necessary.
      - For patients using an insulin pump: Continue basal insulin infusion.
    - Administer subcutaneous short-acting insulin to treat BG ≥250 mg/dL.

        - Use the patient's ISF to calculate the correct dose.
        - To prevent dose stacking, do not administer boluses more often than every 3 hours.
    - Administer dextrose-containing fluids if the patient is hypoglycemic. If the patient is euglycemic, standard perioperative maintenance fluids can be used.
  - ***Major surgery OR metabolically unstable OR insulin pump contraindicated:***
    - Administer intravenous (IV) insulin and dextrose infusions.
        - Infusions should be co-administered through the same IV line.
        - 5% dextrose at the patient's maintenance rate is generally recommended, but 10% dextrose may be required for patients at high risk for hypoglycemia.
    - Suggested IV insulin infusion rates are listed below.[5] Titrate infusion by 0.01-0.03 units/kg/hour to maintain euglycemia. Do NOT bolus IV insulin

IV Insulin Infusion Starting Rates	
Starting BG (mg/dL)	Insulin infusion rate (units/kg/hr)
110-140	0.025
140-220	0.050
220-270	0.075
>270	0.100

    - Pitfalls for IV insulin dosing[2]
        - Published IV insulin dosing regimens are intended for patients in DKA and may drastically overestimate the insulin needs of metabolically stable patients undergoing surgery. Use caution when using these numbers. The patient's home insulin infusion rate may be a better starting value.
        - IV insulin dosing is weight-based (units/kg/hr). Subcutaneous (SC) insulin infusions are NOT weight-based (units/hr). Use caution when converting between SC and IV insulin regimens.
        - The onset and offset time for SC and IV insulins are different. Vigilance is required when converting between routes of administration to avoid iatrogenic hypo- or hyperglycemia.

- **Post-Operative Recommendations:**
  - Continue insulin +/- dextrose administration until patient is tolerating PO intake postoperatively. Once PO intake resumes, transition the patient back to their home insulin regimen. Use the patient's I:C ratio to calculate the correct dose.
  - The half-life of IV insulin is 5 minutes. Subcutaneous insulin should be administered at least 15 minutes before discontinuing the IV insulin infusion.
  - PONV can prevent a return to normal PO intake. Consider administration of two prophylactic antiemetics bearing in mind that dexamethasone can increase blood glucose level. Refractory PONV should raise concern for DKA.

Case Specific Complications/Pitfalls

- **Hyperglycemia/DKA**
  - DKA pathophysiology[3]
    - Insulin deficiency relative to metabolic needs → hyperglycemia and intracellular energy deficiency

            - Hyperglycemia → osmotic diuresis with significant hypovolemia and electrolyte abnormalities due to loss of sodium, potassium, phosphate, and magnesium
            - Energy deficiency → ketogenesis → anion-gap metabolic acidosis
        - Triggers: insufficient insulin administration OR elevated metabolic demands due to physiologic stressors (ie, acute illness, sepsis, trauma)
        - Presentation: volume depletion, tachycardia, tachypnea, nausea/vomiting, abdominal pain, and altered mental status
        - Significance: In children with T1D, incidence is up to 10% per patient per year with up to 0.3% mortality. Patients who develop cerebral edema have up to 25% morbidity and mortality. Cerebral edema often presents with mental status changes, which can be missed under anesthesia.
    - If BG is ≥250 mg/dL, check serum beta hydroxybutyrate (BHB) or urine ketones to evaluate for DKA.
        - If BHB is >1.0 mmol/L or urine ketones are moderate to large → check BMP and VBG (glucose, bicarb and pH), consult the Endocrinology service, and delay surgery if non emergent.[5] Electrolyte, fluid, and dextrose management are critical during DKA and are beyond the scope of this review.[3]
        - If BHB is <1.0 mmol/L or urine ketones are trace/small mmol/L → administer a correction dose of insulin and a bolus of IV 0.9% normal saline.[5] May proceed with surgery. Correction doses of insulin should not be given more often than every 3 hours to prevent dose-stacking.

- **Hypoglycemia**[4]
    - Patients with T1D require insulin to prevent ketosis, even while fasting. Hypoglycemia should be managed by administering glucose, not by stopping basal insulin. If glucose cannot be administered, insulin infusions can be temporarily held (no more than 30 minutes).
    - Hypoglycemia requires treatment when BG <70 mg/dL or the patient is symptomatic (i.e., tremulous, dizzy, lightheaded, fatigued, diaphoretic, tachycardic).
    - Glucose administration
        - >2 hours from surgery start time → Give dextrose-containing clear fluids, glucose gel or tablets orally.
        - <2 hours from surgery start time
            - Obtain IV access. Administer 2 mL/kg of D10%NS, followed by D10%NS infusion at the patient's maintenance rate.
            - If IV access cannot be obtained, administer glucose gels or tabs. These are considered medications in many institutions and are not considered an NPO violation.
        - For severe hypoglycemia (BG <60 mg/dL and/or neurologic impairment) without IV access, give glucagon IM (0.5 mg for patients <20 kg or 1 mg for patients ≥20 kg).
    - Recheck BG every 15 minutes until it is ≥100 mg/dL.

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