Diabetes Mellitus/DKA

Diabetes mellitus is a disorder characterized by inadequate insulin production and/or tissue resistance to insulin, resulting in dysfunction of multiple end-organs including the airway, cardiovascular system, nervous system, and kidneys.

ANESTHETIC CONSIDERATIONS:

- Potential difficult airway (stiff joint syndrome)
- Acute complications of DM
  - Severe dehydration
  - Impaired wound healing
  - Infection
  - Worsening of acute ischemia
  - DKA/HoNKS
  - Hypoglycemia
- Increased perioperative risk due to associated end organ dysfunction (e.g. MI, RF)
- End-organ complications of chronic hyperglycemia
  - Retinopathy
  - Nephropathy – prevent worsening renal insufficiency
  - Neuropathy
  - Peripheral – positioning, document prior to regional anesthesia
  - Autonomic – silent ischemia, arrhythmias, hypotension, hemodynamic instability, gastroparesis/aspiration
    - risk, hypoglycemia unawareness
  - Coronary artery disease – prior ischemia, CHF; perioperative cardiac complications
  - Cerebrovascular disease – prior CVA, risk of perioperative CVA
  - Peripheral vascular disease
  - Soft tissue glycosylation – difficult airway, limited joint mobility, poor wound healing
  - Immunosuppression – infection (strict aseptic techniques)
  - Uteroplacental insufficiency in pregnancy
- Co-existing diseases:
  - autoimmune disease associated with Type I DM
    - Graves' disease, Hashimoto's thyroiditis, Addison's disease, myasthenia gravis
  - Co-existing metabolic syndrome associated with Type II DM
- Perioperative glycemic control – OHAs, insulin

ANESTHETIC GOALS:

- Identify, manage, and prevent perioperative exacerbation of end-organ dysfunction
- Identify cardiac risk factors (maintain high index suspicion for myocardial dysfunction)
- Optimize perioperative glycemic control (hold perioperative OHAs, consider insulin/glucose infusion, avoid extremes of hypo/hyperglycemia)

HISTORY

- Type of DM
- Onset
- Control – blood sugars, hypoglycemia awareness, compliance with meds/diet, hyper/hypoglycemic emergencies
- Complications of chronic hyperglycemia
  - Microvascular – retinopathy, nephropathy, neuropathy (peripheral and autonomic)
  - Macrovascular – cardiac (silent ischemia with autonomic neuropathy; screen for CAD, exercise tolerance), cerebral, peripheral vascular
  - Soft tissue – joint immobility, infection

PHYSICAL

- Airway – standard airway exam, particular attention to neck mobility and mouth opening
- Autonomic neuropathy
  - Orthostatic VS, increased resting HR, decreased HR variability, response to Valsalva, DBP response to sustained exercise, QT interval
    - Orthostatic changes: >20-30mmHg ↓in SPB or >10mmHg in ↓DBP when standing from supine
    - Difference b/w max and min HR with inspiration (N = difference of 15 bpm)

Table 12-12 – Noninvasive Tests for Assessing the Autonomic Nervous System

Clinical Examination	Technique	Normal Value
Parasympathetic		
HR response to a Valsalva maneuver	The seated subject blows into a mouthpiece (while maintaining a pressure of 40 mm Hg) for 15 seconds. The Valsalva ratio is the ratio of the longest R-R interval (which comes shortly after release) to the shortest R-R interval (which occurs during the maneuver)	Ratio of >1.21
HR response to standing	HR is measured as the subject moves from a resting supine position to standing. A normal tachycardic response is maximal around the 15th beat after rising. A relative bradycardia follows that is most marked around the 30th beat after standing. The response to standing is expressed as a 30 : 15 ratio and is the ratio of the longest R-R interval around the 30th beat to the shortest R-R interval around the 15th beat	Ratio of >1.04
HR response to deep breathing	The subject takes six deep breaths in 1 minute. The maximum and minimum heart rates during each cycle are measured, and the mean of the differences (maximum HR − minimum HR) during three successive breathing cycles is taken as the maximum-minimum HR	Mean difference >15 beats/min
Sympathetic		
BP response to standing	The subject moves from resting supine to standing, and standing SBP is subtracted from supine SBP	Difference <10 mm Hg
BP response to sustained handgrip	The subject maintains a handgrip of 30% of the maximum handgrip squeeze for up to 5 minutes. BP is measured every minute, and the initial DBP is subtracted from the DBP just before release	Difference >16 mm Hg

BP, blood pressure; DBP, diastolic blood pressure; HR, heart rate; SBP, systolic blood pressure.

- Tissue glycosylation
  - Impaired neck mobility (AO joint glycosylation), tight waxy skin
  - Prayer sign (inability to approximate palmar surfaces of interphalangeal joints) – predictor of difficult laryngoscopy

INVESTIGATIONS

Labs

- CBC/D
- Lytes, urea, Cr, blood glucose (BG)
- HbA1C – most accurate assessment of glucose control over previous 2-3mo (↑ing HbA1C → ↑ing complications)
- U/A – glucosuria, proteinuria

Imaging

- EKG – loss of R-R variability, ischemia

Other

- Stress testing/cardiac workup – consider if ≥2 cardiac risk factors and undergoing major surgery

OPTIMIZATION

- Endocrinology consult
- Treat acute hyperglycemia
  - Serum glucose >15 mmol/L preop → delay elective surgery while achieve rapid control with iv insulin
  - Serum glucose > 22 mmol/L preop → postpone elective surgery
  - DKA – cancel elective surgery, delay emergency surgery 4-6h if possible to optimize metabolic status
- Manage insulin and oral hypoglycemic agents perioperatively to avoid hypo/hyperglycemi**a**
  - Tight perioperative blood glucose control beneficial in pregnant diabetics, diabetics undergoing CPB, and those with cerebral ischemia; no evidence of benefit from tight control in other groups, and risk-benefit ratio may be greater
  - Must continue insulin in Type 1 DM

  Preoperative
  - OHAs
    - Hold sulfonylureas, metformin, and α-glucosidase inhibitors 24-48hrs preop
    - May continue thiazolidinediones as they do not predispose to hypoglycemia?
  - Insulin
    - Lispro – take entire hs dose, hold am dose; glargine – take 2/3 of hs dose
    - Administer 2/3 of NPH/regular hs dose and ½ of NPH am dose on day of OR and start D5-1/2 NS at 100cc/hr preop
      or
    - Begin dextrose infusion 2mg/kg/min at time a meal would have been ingested, and begin insulin infusion at 0.5-1.25 U/hr depending on normal insulin dosing and current BG level and monitor BG q1h and adjust infusion according to targets

  Intraoperative
  - When insulin indicated, initiate infusion 2hrs preop
    - Sliding scale sc insulin ineffective for blood glucose >11 mmol/L (require infusion)
    - Monitor BG q1h and adjust infusion according to targets (eg: intraop serum glucose 6.7-10 mmol/L, although no consensus)
      - Patients w/ obesity, liver disease, severe infections, on corticosteroids or undergoing CPB may require higher insulin dosing to maintain target BG
  - Type 1 DM – require insulin
  - Type 2 DM – well controlled: no insulin for minor surgery; insulin for major surgery
    - poorly controlled: require insulin
- Assess and optimize treatment of end-organ dysfunction (CAD, renal disease, etc)
- Aspiration prophylaxis with gastroparesis
  - NPO up to 12hrs
  - Metoclopramide 10mg iv and ranitidine night before and am of surgery; sodium citrate 30min preop

ANESTHETIC OPTIONS

- **Local**
- **Regional**
  - Diabetics have lower local anesthetic requirements
  - Adding epinephrine to local anesthetics ↑s risk for ischemic or edematous nerve injury
  - Higher risk of nerve injury
- **General**

ANESTHETIC SETUP

- **Drugs**
  - Standard emergency drugs
  - Glucose/insulin infusions
  - For patients with CAD, consider β-blockade to blunt stress of induction
- **Equipment**
  - Standard CAS, 5-lead EKG (silent ischemia), temperature probe (susceptible to hypothermia)
  - Consider invasive monitors if CAD and/or significant autonomic dysfunction
  - Consider need for difficult airway cart (stiff c-spine, obesity)
  - Glucometer

MANAGEMENT OF ANESTHESIA

- **Induction**
  - RSI (gastroparesis)
    - Awake intubation if suspect difficulty securing airway
  - Exaggerated pressor response to laryngoscopy and hypotension with induction agents (autonomic neuropathy)
    - Caution with propofol and thiopental, consider etomidate to maintain hemodynamic stability, particularly if CAD
- **Maintenance**
  - Careful positioning (peripheral neuropathy)
  - Fluid management and drug doses depend on renal function
  - Routine administration of glucose-containing fluids is *not* recommended

        - Standard glucose dosage is 5-10g/hr (100-200 cc D5W q1h)
    - Monitor blood glucose q1h in high-risk patients (pre/postop chemstrip otherwise sufficient)
        - Glucometers (arterial and capillary blood) may overestimate BG; ABG may underestimate BG (relative to lab values)
        - Target perioperative blood glucose <10 mmol/L, and close to 6.1 mmol/L
    - Blood products containing acid citrate dextrose or adenine can result in significant hyperglycemia
    - Maintain normothermia (autonomic neuropathy predisposes to hypothermia)
- **Emergence**
    - Extubate awake (aspiration risk)

DISPOSITION & MONITORING

- Monitor BG, administer insulin as needed
- If significant autonomic neuropathy consider close continuous cardiac and respiratory monitoring x 24-72h postop
- ↑Risk postoperative MI

COMPLICATIONS

- DKA/HNKKS
- Hypoglycemia
- Myocardial ischemia
- Cerebral ischemia
- Renal insufficiency
- Infection
- Metabolic acidosis (metformin)

OBSTETRICS

- Pregnancy characterized by progressive peripheral insulin resistance in T2-3 (↑counterregulatory hormones – hPL, placental GH, cortisol, progesterone)
- Gestational DM (GDM)
    - Develops in >3% of all pregnancies
    - Risk factors– advanced maternal age, obesity, FmHx Type 2 DM, prior GDM, PCOS, glycosuria, Hx of prior stillbirth, neonatal death, fetal malformation, or macrosomia
    - Postpartum – most GDM patients return to normal glucose tolerance, but ↑risk for T2DM in later life and recurrent GDM in subsequent pregnancy
- Pregestational DM
    - Tight pre-pregnancy glucose control may ↓maternal-fetal complications during pregnancy
    - Insulin requirements in pregnancy
        - Progressive ↑insulin requirements during pregnancy (peripheral insulin resistance)
        - ↓Insulin requirements with onset of labor, ↑ in 2nd stage of labor, ↓markedly during early postpartum period (return to baseline over several weeks)
    - ↑Risk hypoglycemia prior to 20 weeks GA
    - ↑Risk DKA in T2-3 (insulin resistance)
- Effects of DM on mother during pregnancy
    - ↑Risk preeclampsia, progression of retinopathy
- Effects of DM on fetus (↑er risk in PDM compared to GDM)
    - Macrosomia – dystocia, birth trauma, ↑risk c-section
    - Congenital malformations
    - Chronic uteroplacental insufficiency
    - ↑Risk preterm labor/delivery
    - Intrauterine demise
- Effects of DM on neonate
    - ↑Risk respiratory distress syndrome, hypoglycemia, hyperbilirubinemia, glucose intolerance, possible cognitive dysfunction

PATHOPHYSIOLOGY

TYPE I DM

- Epidemiology
    - 5-10% of all cases of DM, typically young (age of onset <40y), non-obese
- Pathophysiology
    - Genetic and environmental factors
    - T cell-mediated autoimmune destruction of pancreatic B cells → absolute insulin deficiency
- Clinical presentation
    - Preclinical DM (duration 9-13 yrs)
    - Clinical DM
        - Hyperglycemia over several days to weeks associated with fatigue, weight loss, polyuria, polydipsia, blurred vision, intravascular volume depletion
        - DKA
    - Additional autoimmune disease in 15%
        - Graves' disease, Hashimoto's thyroiditis, Addison's disease, myasthenia gravis
- Treatment
    - Diet and insulin essential
    - Tight BG control helps prevent onset and progression of microvascular disease

TYPE II DM

- Epidemiology
    - 90-95% of all cases of DM, typical age of onset middle/older, although recent ↑incidence in younger age
- Pathophysiology
    - Genetic and environmental factors
    - Relative β-cell insufficiency and insulin resistance → relative and eventually absolute insulin deficiency

- Initially, peripheral tissue insensitivity to insulin compensated for by pancreatic insulin hypersecretion → normoglycemia maintained; hyperglycemia once pancreas unable to continue producing ↑insulin
- Clinical presentation
  - Preclinical DM (duration 4-7 yrs)
  - Metabolic syndrome
  - Clinical DM – hyperglycemia, HNKS, end-organ damage
- Treatment
  - Diet, exercise, weight reduction
  - Tight BG control – oral hypoglycemics (OHAs) and/or insulin
    - Tight BG control helps prevent onset and progression of microvascular disease

SECONDARY CAUSES OF DIABETES MELLITUS

- Diseases which damage pancreas
  - Pancreatic surgery, chronic pancreatitis, CF, hemochromatosis
- Endocrine conditions that produces hormones which oppose insulin
  - Glucagonoma, pheochromocytoma, acromegaly, glucocorticoids, Cushing disease, pregnancy

DIAGNOSIS

- Normal fasting plasma glucose: 3.9-5.6 mmol/L
- Impaired fasting glucose: 5.6-6.9 mmol/L
- Diagnostic criteria for DM require one of the following:
  - Sx of DM + random plasma glucose ≥11.1 mmol/L
  - Fasting (≥8hrs) plasma glucose ≥7 mmol/L
  - 2-hour plasma glucose >11.1 mmol/L during oral glucose tolerance test
- HbA1C (N range 4-6%)
  - Provides assessment of glucose control over longer term (preceding 2-3mo)
  - Increased risk of microvascular/macrovascular disease complication with HbA1C ≥6.5%

ORAL HYPOGLYCEMIC AGENTS

- 6 classes of OHAs
- Insulin secretagogues (sulfonylureas, meglitinides)
  - ↑Insulin availability – stimulate insulin secretion from β-cells, ↑peripheral tissue sensitivity to insulin
  - S/E – hypoglycemia, inhibit myocardial preconditioning
- Biguanides (metformin)
  - Reduce hepatic gluconeogenesis and peripheral sensitivity to insulin
  - Lower risk of hyperglycemia than with sulfonylureas
  - S/E – lactic acidosis during dehydration
    - Metformin contraindicated in renal insufficiency, CHF, recent MI, hypoxia, EtOH abuse, impaired hepatic function
  - Dosing
    - D/C 24-48hrs preop, hold 48hrs after any procedure using iv contrast; resume only after documenting N renal function
- Thiazolidinediones (rosiglitazone, pioglitazone)
  - Increase peripheral responsiveness to insulin
- α-glucosidase inhibitors (acarbose, miglitol)
  - Delay GI glucose absorption

INSULIN

- Necessary to manage all T1 DM and many T2 DM

Insulins	Onset	Peak	Duration
Short Acting			
Human regular	30 min	2–4 hr	5–8 hr
Lispro (Humalog)	10–15 min	1–2 hr	3–6 hr
Aspart (Novolog)	10–15 min	1–2 hr	3–6 hr
Intermediate			
Human NPH	1–2 hr	6–10 hr	10–20 hr
Lente	1–2 hr	6–10 hr	10–20 hr
Long Acting			
Ultralente	4–6 hr	8–20 hr	24–48 hr
Glargine (Lantus)	1–2 hr	Peakless	~ 24 hr

- Complications of insulin therapy
  - Hypoglycemia (BG < 2.8 mmol/L) most common and dangerous complication
    - Exacerbated by simultaneous EtOH, OHAs, ACEI, MAOIs, non-selective β-blockers, defective counterregulatory hormone responses to hypoglycemia
  - Anaphylaxis

        - Protamine-derived insulin made from fish sperm; can cause immunologic sensitization when protamine reversal of heparin administered after CPB
        - Protamine reaction includes pulmonary vasoconstriction, noncardiogenic pulmonary edema, and severe hypotension

COMPLICATIONS OF DM

1. Diabetic ketoacidosis

- A metabolic emergency characterized by hyperglycemia, ketoacidosis, and dehydration 2° to an absolute or relative insulin deficiency
- Precipitants
    - Infection, ischemia (MI, CVA), pancreatitis, trauma, hypovolemia (eg: ↓intake, diuretics) in 30-40%
    - Insulin omission in 15-20%
    - New onset DM in 15-20%
    - Other – bowel obstruction, burns, renal failure, endocrinopathy
- Signs/Sx result of abnormal carbohydrate and fat metabolism
    - Polyuria, polydipsia, weight loss, N/V, abdominal pain, confusion, coma
    - Fruity breath, tachypnea
    - Severe dehydration, hypovolemia
    - Cerebral edema → ↑ICP
- dDx
    - Sepsis, acute surgical abdomen
    - Other causes metabolic acidosis (MUDPILES)
- Pathophysiology
    - High glucose levels exceed threshold for renal tubular absorption → osmotic diuresis → hypovolemia → dehydration → hypotension/shock
        - Vomiting, hyperventilation and anorexia also contribute
    - Insulin deficiency and excess counterregulatory hormones → mobilization and oxidation of fatty acids → ketone production → ketoacidosis (β-hydroxybutyrate, acetoacetate, acetone; wide anion-gap)
    - Significant deficits of Na, K, Mg, PO4 (NB: lab values may appear N or elevated)
- Investigations
    - ABG (glucose, pH, PaCO2, K, Na, HCO3), lytes, osmolarity, ketones, urea/Cr
    - Urinalysis (incl ketones)
    - Attempt to determine etiology – WBC, pancultures, troponin, toxicology screen
    - ECG, CXR (ARDS)
- Management
    - Cancel elective surgery, transfer to ICU for resuscitation, consult Endocrinology
    - Delay emergency surgery 2-4hrs if possible for stabilization
        - Correct life-threatening fluid and electrolyte disturbances
        - Do not continue to delay surgery in attempt to completely eliminate ketoacidosis if underlying surgical condition will lead to further metabolic deterioration
        - Intraop monitoring – blood glucose, pH, lytes and fluid balance q1h
    - Repeat glucose, lytes, ABG, anion gap q1-2h until normalized
    - Foley to monitor U/O
    - Invasive hemodynamic monitors if CAD, CHF, or renal failure
    - Intubation if obtunded or respiratory distress – hyperventilation may be needed to counteract severe metabolic acidosis
    - Fluid rehydration (crystalloid)
        - Target SBP >100, HR < 100, U/O 0.5-1 cc/hr
        - 0.9% NS bolus 1-2L initially then 0.25-1L/hr; may require up to 7L fluid
    - Insulin
        - Loading dose 0.1 U/kg then infusion at 0.1 U/kg/hr until acidosis resolves
            - Add dextrose to fluid once blood glucose 14 mmol/L (typically D5W at 100 cc/hr)
    - Electrolyte supplementation
        - Replace K once K <5 mmol/L and U/O >0.5 mL/kg/hr
        - Replace Mg and PO4 as needed
    - Acid-base balance
        - Acidemia normally corrects on its own w/ fluid resuscitation and insulin
        - Administer bicarbonate for pH < 7.1, HCO3 <10mEq/L, or severe hyperkalemia
    - Address and treat underlying cause of DKA (antibiotics, PCI, laparotomy, dialysis, etc)
- Complications
    - Cerebral edema, hypernatremia
    - Mortality 5-10% overall

2. Hyperglycemia hyperosmolar syndrome (HONKS)

- Complication of decompensated Type 2 DM characterized by severe hyperglycemia, hyperosmolarity, dehydration
- Precipitants and clinical presentation similar to DKA
- Compared to DKA
    - No ketone production (sufficient insulin present to prevent lipolysis/fatty acid oxidation/ketosis but not enough insulin to prevent hyperglycemia)
    - More severe hyperglycemia, hyperosmolarity and dehydration; less severe acidosis and electrolyte disturbances
    - No ketosis
- Treatment
    - Fluid resuscitation (up to 10L often required)
        - Risk of cerebral edema if overly rapid correction of hyperosmolarity
    - Insulin – regular insulin 0.1 U/kg iv then infusion of 0.1 U/kg/hr
    - Electrolyte replacement

- Complications
  - Cerebral edema, mesenteric artery thrombosis, DIC, end-organ ischemia
  - Mortality 10-15%

3. Microvascular complications (retinopathy, nephropathy, neuropathy)

- Strict glycemic control ↓s risk of microangiopathic complications and delays their onset and progression
- Retinopathy
- Nephropathy
  - HTN, hyperglycemia, hypercholesterolemia, microalbuminuria accelerate ↓GFR
  - ESRF in 30-40% of T1 DM, 5-10% of T2 DM
- Peripheral neuropathy
  - Polyneuropathy – diffuse symmetrical distal sensorimotor polyneuropathy most common
  - Mononeuropathies
  - Sensory deficits more significant than motor and appear in toes or feet, progressing proximally (stocking-glove distribution)
  - Mechanical trauma with loss of cutaneous sensitivity → foot ulcers, infections, Charcot joints, amputation
- Autonomic neuropathy
  - Clinical presentation
    - Cardiac
      - Resting tachycardia, blunted HR response to exercise, atropine and B-blockers, loss of HR variability with deep breathing
      - Orthostatic hypotension (>30 mmHg change in SBP with standing), syncope
      - Limited exercise tolerance
      - Arrhythmias, systolic and diastolic dysfunction, silent ischemia
    - Respiratory
      - Impaired ventilatory responses to hypoxia and hypercarbia
    - GI
      - Impaired gastric secretion and motility → gastroparesis (aspiration risk)
      - Diarrhea (nocturnal), constipation
    - GU
      - Erectile or bladder dysfunction
    - Metabolic
      - Temperature dysregulation; susceptible to hypothermia

4. Macrovascular complications (CAD, stroke, HT, PVD)

- Glycemic control does *not* affect risk of macrovascular complications or their progression
- Accelerated atherosclerosis

5. Soft tissue complications

- Tissue glycosylation
- Limited joint mobility (including atlantooccipital, TMJ → difficult airway) and hands
  - Prayer sign as predictor of difficult intubation
- Infection
- Edema

6. Acute hyperglycemia (BG > 11 mmol/L)

- Dehydration → thrombogenesis, hemodynamic instability
- Decreased vascular reactivity
- Impaired wound healing
- Immunosuppression → ↑infection, especially skin and soft tissue
- Worsening of ischemic CNS injury

7. Hypoglycemia

- Definition
  - Adults: serum glucose < 2.8 mmol/L
  - Children: serum glucose < 2.2 mmol/L
- Risk factors
  - Administration of insulin or sulfonylureas without supplemental glucose
  - Renal insufficiency (prolonged effect of insulin and OHAs)
- Clinical presentation
  - Irritability, seizures, bradycardia, hypotension, respiratory failure
  - Hypoglycemia awareness
    - Low glucose levels stimulate catecholamine release resulting in early adrenergic Sx
      - Anxiety, diaphoresis, tremors, palpitations
      - Masked by autonomic neuropathy, anesthetics, sedatives, analgesics, β-blockers, sympatholytics
    - Hypoglycemia eventually impairs CNS function → late neuroglycopenic Sx (confusion, ataxia, coma)
- Management
  - Juice 8oz
  - 25g D50W (50% dextrose) which increases glucose by 5.6 mmol/L
  - Glucagon 1 mg im

REFERENCES

- Anesthesia and Coexisting Disease p.365-378
- Miller p.1022-1023, 1069-1076, 1716-1721
- Barash p.1295-1300
- Chestnut p.913-922