

Endocrinology

- DKA
- Inpatient Diabetes Guidelines
- Hypothyroidism
- Hyperthyroidism

DKA

Diagnosis

DKA vs HHS:

- DKA sugar ranges from 250 to 500 mg/dL
- HHS typically has sugars > 600 mg/dL
- Serum osmolality > 320 in HHS
- Neurologic symptoms such as stupor and coma are primarily seen in HHS, but can sometimes be seen in severe DKA.
- Little to no ketonuria/ketonemia in HHS
- Anion gap mainly in HHS

There may be focal neurological deficits and/or seizures in HHS.

In DKA, there may be nausea, vomiting, and abdominal pain. The delayed gastric emptying and/or ileus caused by acidosis and electrolyte derangement may be a cause for such symptoms.

Kussmaul respirations are indicative of acidosis since this is a compensatory mechanism. A fruity breath may be from acetone, which is one of the three ketone bodies produced.

Infection or inadequate control of DM are the main causes. Sometimes DKA is the first presentation for DM.

Laboratory and Ancillary Testing

First assess clinical stability of the patient. Ability to protect airway and mental status assessment are important assessments.

A part of the quick assessment is the following STAT orders... (these should already be ordered by ED, but always make sure these are ordered when you accept an admission)

- Basic metabolic panel
- Urine analysis
- Venous blood gases
- Beta Hydroxybutyrate level
- CBC
- CXR (if respiratory symptoms)

- Influenza panel (if in season)
- Blood cultures (if septic)

* remember that in DKA the total water deficits are 6L and for HHS 9L.

Common Laboratory Derrangements

Hypонатremia is often present due to fluid shifting from ICF to ECF. Basically the hyperglycemia causes fluid shifts from ICF to ECF. Be cautious of patients with impaired thirst mechanisms and the summer months where hot weather can cause dehydration.

For every 100 mg/dL increase in serum glucose, expect a 2mEq/L fall in serum sodium.

Hypokalemia or hyperkalemia can be present. Increased osmotic diuresis due to hyperglycemia can cause losses of potassium. Conversely, elevated potassium can be caused by ICF to ECF shifts of potassium due to lack of insulin or significant insulin resistance.

Hypophosphatemia or hyperphosphatemia is present. Dietary causes such as low phosphate intake can be present in uncontrolled DM. Conversely, hyperphosphatemia can be present in metabolic acidosis and hyperglycemia due to ICF to ECF shifts of phosphate.

Lipase and amylase are often elevated and DKA can masquerade as pancreatitis. Clinical judgement is necessary to distinguish the two.

Leukocytosis is present in many DKA or HHS patients. Hypercortisolemia and metabolic potentiators such as excess catecholamines can cause this. Think stress response. Do not forget to think about infectious etiology, WBC > 25K or bandemia with > 10%.

Acute Kidney Injury in the form of increased creatinine or reduced GFR can be present. In this case think dehydration or hypovolemia.

Hyperlipidemia can be present and increased lipolysis can serve as substrates for ketone body generation.

DKA and HHS are treated the same for the most part. It is important to think of the four hallmarks of DKA and HHS treatment which are correction of ...

- Hyperglycemia
- Electrolyte derangement
- Acidosis
- Dehydration

Use the order set in the hospital

1. Fluid Replacement

- a. In the first 2 hours, isotonic (Normal Saline) fluid boluses (1L/hr in average sized person). Be cautious and individualize care on CHF or fluid intolerant patients.
- b. In the 3rd hour, continue fluids using either normal saline or half normal saline. If sodium is below reference range, use NS at 250 to 500 mL/hr. If sodium is normal or above reference range, then half normal.

2. Insulin gtt (regular insulin)

- a. 0.1 units/kg bolus followed by 0.1 units/kg/hr.
- b. If no bolus is used, then 0.14 units/kg/hr.
- c. Nursing will adjust rate based on serial glucose measurements.

Caution - if potassium is < 3.3 , correct the hypokalemia first otherwise you will tank the patient's potassium which is dangerous.

Management and Monitoring

3. Electrolytes – there is a protocol for electrolyte correction on the hospital order set. Be sure to use this.

- a. Potassium – again replete potassium first if value is < 3.3 . May need to add KCl to replacement fluids above (20 to 40 mEq/hr) if potassium is between 3.3 and 5.5 mEq/L.
- b. Sodium – this will correct with correction of hyperglycemia.
- c. Phosphorus – Correct when < 1 . If there is a cardiac history or potential for arrhythmia, correct if < 3 . Sodium phosphate can be used.

4. Acidosis – No indication for bicarb unless the pH is ≤ 7.35 or if potassium > 6.4 mEq/L.

- a. 100 mEq sodium bicarbonate in 400 mL of water.
- b. Keep in mind that bicarb administration can cause hypokalemia or worsen it.

Monitoring includes....

- Q1h glucose checks
- Q2h metabolic panel
- Q2h VBG

Resolution of DKA and HHS

What we look for...

- Normalization of anion gap (<12)
- Absence of serum beta hydroxybutyrate level.
- Mental lucidity in HHS and plasma osmolality < 315
- Drop in glucose levels to 250 to 200 mg/dL
- Tolerance to PO diet.

CONVERSION TO SUBCUTANEOUS INSULIN

Only initiate subcutaneous insulin if the patient is able to eat and the above criteria regarding resolution of ketoacidosis is met.

HHS

1. **Overlap 2 hours of insulin gtt** when serum glucose reaches 250 to 300 mg/dL

DKA

1. **Overlap 2 hours of insulin gtt** when serum glucose reaches 200 mg/dL
2. In addition two of the following must be met
 - a. Anion gap < 12
 - b. Bicarb ≥ 15
 - c. Venous pH > 7.30

References:

1. Up to Date has the latest and best information
2. SAMC order set for DKA
3. Dr. Michael Moya's DKA Handout

Inpatient Diabetes Guidelines

Definitions

1. **Type 1 DM:** autoimmune. Patients require exogenous insulin to prevent DKA.
2. **Type 2 DM:** insulin resistance and a relative insulin deficiency. Treatment may be with diet, exercise, oral meds, injectable meds, and/or insulin. With severe insulin deficiency, patients also develop DKA.

Physiologic Insulin Regimen

All patients have basal, nutritional, and correctional requirements that must be met with endogenous insulin or with insulin provided to them.

Basal: insulin needed even when the patient is not eating (to control gluconeogenesis).

- Use glargine (q24, typically at bedtime, preferred for type 1), NPH (qHS or qAM+HS), detemir (BID or q24 for larger doses), or a continuous insulin infusion.

Nutritional: insulin to cover carbohydrate intake from food, dextrose in IVF, tube feeds, TPN.

- Use rapid-acting insulin (aspart, lispro, or glulisine) or short-acting insulin (regular).

Correctional: insulin given to bring a high blood glucose level down to target range (130-150 pre-meal and 180-200 before bedtime).

- Use rapid-acting insulin (aspart, lispro, or glulisine) or short-acting insulin (regular).

General Rules

- **Remember that a patient with type 1 DM will *always* need exogenous basal insulin, even if NPO. Failure to do so will lead to DKA.**
- Using correctional ("sliding scale") insulin alone is acceptable for initial titration but should be reevaluated daily.
- Order a carbohydrate controlled meal plan. Each meal contains 60 to 75 grams of carbohydrates.
- Check blood glucose (BG) before meals and at bedtime, +/- at 2am (if suspect hypoglycemia) in a patient who is eating; check BG q 4 or q 6 hours in a patient who is NPO or is receiving continuous tube feeds or TPN.
- Involve the diabetes educator, nurse specialist and dietician.

- Supply glucose meter, lancets, test strips, syringes/pen needles, insulin, glucose tablets, and glucagon kit as discharge prescriptions, if needed. Health insurance dictates which types of supplies will be covered.
- Oral medications: often, oral diabetes medications are held upon admission to the hospital. Hospitalized patients have the potential for renal impairment and tissue hypoxia or need IV contrast, and these are all contraindications to metformin use. Sulfonylureas should generally be held upon admission if you anticipate NPO status due to high risk of hypoglycemia. If patient's status improves and is reliably stable, consider restarting non-insulin medications.
- Nutritional insulin: regular is given within 30 min before meal, rapid-acting within 15 minutes before meal.
- Infection and glucocorticoids increase insulin needs; renal insufficiency decreases insulin needs.
- Total daily dose of insulin needed: type 1 patients require approximately 0.5 units/kg/day; type 2 patients vary in their insulin resistance and may require from 0.5 to 2 units/kg/day.

Hypoglycemia Protocol

- BG <70 mg/dL: if patient is alert and taking PO, give 20 grams of oral fast-acting carbohydrate either as glucose tablets or 6 oz. fruit juice. If the patient cannot take PO, give 25 mL D50 IV push.
- Check BG every 15 minutes and repeat above treatment until BG is ≥ 100 mg/dL.

Insulin Regimens

- The guidelines below may assist with initial determination and subsequent adjustment of insulin doses.
- Reevaluate insulin doses on a daily basis.

Correctional insulin (rapid or short acting): select between sensitive, average, or resistant based on BMI.

- Sensitive: BMI <20, or <50 units/day.
- Average: BMI 25-30, or 50-90 units/day.
- Resistant: BMI >30, or >90 units/day.

Nutritional insulin (rapid or short acting): continue with home nutritional doses, or can start based on meal consumption and titrate up as necessary. Remember to adjust and increase nutritional dosing as you observe daily insulin requirements. Example:

- Not eating: 0 units pre-meal dose.
- Eating <50% of meals: 1 unit pre-meal dose.
- Eating 50-75% of meals: 2 units pre-meal dose.
- Eating >75% of meals: 3 units pre-meal dose.

Insulin regimen for a patient controlled only with diet at home, but needing insulin in hospital:

- Day 1: order correctional insulin based on BMI (sensitive = BMI<25, average = BMI 25-30, resistant = BMI>30)
- Day 2: if BG pre-meals are >150 mg/dL, add nutritional insulin based on meal consumption (see above). Also, if AM fasting BG is >150 mg/dL, add bedtime basal insulin dosed 0.1 unit/kg.
- Day 3: adjust insulin doses based on BG pattern. Increase or decrease basal insulin based on AM fasting BG, and adjust nutritional insulin based on pre-meal BG levels. Approximately half the daily dose should be given as basal insulin, and the other half as divided doses with meals.

Insulin regimen for a patient on oral agent(s) at home:

- Day 1: start nutritional insulin based on meal consumption (see “Nutritional insulin” above). Also, order correctional insulin based on BMI (see “Correctional insulin” above).
- Day 2: if AM fasting BG is >150 mg/dL, add bedtime basal insulin dosed 0.1 unit/kg.
- Day 3: adjust insulin doses based on BG pattern. Increase or decrease basal insulin based on AM fasting BG, and adjust nutritional insulin based on pre-meal + bedtime BGs.

Insulin regimen for a patient on insulin at home:

- Assess home BG control, appetite, renal function, and risk for hypoglycemia.
- Basal insulin: continue home regimen if patient has been well-controlled at home, but consider giving only 80% of home dose to reduce the risk of in-hospital hypoglycemia. Or, start bedtime glargine or NPH dosed 0.2 units/kg.
- Nutritional insulin: order based on appetite, or consider pre-meal dosing of 0.2 units/kg divided by 3 for the dose at each meal.
- Correctional insulin: order based on total insulin dose or BMI.

Insulin regimen when a patient is made NPO for a procedure: a patient will always require his or her basal insulin, even while NPO, and should not become hypoglycemic if that basal is dosed appropriately. For safety purposes, however:

- The night before, give the usual dose of bedtime NPH, or decrease the usual dose of bedtime glargine by 25%.
- The morning of the procedure decrease the usual dose of morning NPH by 50%, or decrease the usual dose of morning glargine by 25%.
- Stop nutritional insulin (while patient is not eating), but continue the usual correctional insulin.

Insulin regimen for an ICU or surgical patient who is NPO: consider insulin infusion therapy. See your hospital-specific standardized protocol.

Insulin regimen for a patient starting continuous tube feeds:

- Consider insulin infusion therapy. See your hospital-specific standardized protocol.

- Estimate the tube feed formula's 24-hour carbohydrate load (discuss with nutritionist).
- Estimate the total daily dose (TDD) of insulin, starting with 1 unit insulin for every 10 grams of carb.
- Basal need: divide the estimated TDD by 2 for the nightly glargine or total bid NPH dose.
- Nutritional insulin: divide the estimated TDD by 10 for the total nutritional dose, to be given q 4 hours (rapid acting insulin) or q 6 (regular insulin) hours.
- Correctional insulin: order based on total insulin dose or BMI.

Insulin regimen for a patient receiving TPN:

- Standard TPN often contains 25% glucose, which, if 100 ml/hour, yields 25 g glucose/hour; discuss with nutritionist to determine exact glucose load.
- Basal and nutritional insulin: adding insulin to the TPN can be a safe strategy, as the unexpected discontinuation of TPN will also mean the discontinuation of the insulin. Start with 0.1 unit per gram glucose.
- If the patient has previously required basal insulin, convert this dose to regular insulin and add to TPN (dose reduce to 80% for safety purposes).
- Correctional insulin: order based on BMI.

Insulin regimen to transition from an insulin infusion to subcutaneous insulin:

- Calculate the patient's TDD of insulin, based on the most recent insulin infusion rate. For safety purposes, take 80% of that dose.
- Basal need: divide 80% of the TDD by half for basal insulin dose.
- Nutritional insulin: if the patient is eating, divide 80% of the TDD by half, and then split over three meals. If the patient is receiving tube feeds, divide 80% of the TDD by 10 for the nutritional dose, to be given q 4 hours (rapid acting) or 6 hours (regular).
- If the patient is not receiving nutrition, do not order nutritional insulin.
- Correctional insulin: order based on total insulin dose or BMI.
- Give the first basal insulin SQ injection 1-2 hours before the infusion is discontinued. If the transition is being made in the morning, consider using a one-time AM NPH injection or $\frac{1}{2}$ of daily glargine dose to bridge until bedtime glargine or NPH begins.

Insulin regimen for a patient receiving steroids:

- Glucocorticoids will dramatically increase postprandial BG levels. Often, BG levels are very high during the day while steroids are active, then lower overnight.
- Anticipate post-prandial hyperglycemia by increasing the nutritional insulin doses.
- With glucocorticoids, give only 25% of TDD as basal insulin and 75% as pre-meal insulin.

Insulin Adjustments

- There are no validated formulas for making these adjustments, but the following are generally accepted rules of thumb.
- Basal insulin: adjusted based on fasting glucose (FBG) levels. For example:
- If FBG <140, no change.

- If FBG 141-160, increase basal dose by 2-3 units.
- If FBG 161-180, increase basal dose by 4-5 units.
- If FBG 181-200, increase basal dose by 6-7 units.
- If FBG >200, increase basal dose by 8 units.
- With this approach, the basal insulin can be titrated up to the patient's actual requirement relatively quickly.
- Nutritional insulin: the adequacy of the nutritional insulin dose is based on the glucose level prior to the next meal. For example, the glucose level just before lunch will indicate whether the insulin given at breakfast was appropriate. A simple approach is as follows:
 - If there was no significant change in the glucose level from before breakfast to before lunch, then the total dose of insulin the patient received at breakfast (nutritional plus correctional) should be used as the nutritional dose for breakfast the next day.
 - If there was a significant increase in the glucose level from before breakfast to before lunch, then the total dose of insulin the patient received at breakfast (nutritional plus correctional) should be increased and should become the nutritional dose for breakfast the next day.
 - If the glucose level before breakfast was high, and the glucose level at lunch was at goal, then no change in the nutritional dose will be required for the next day.
 - Finally, no matter what the glucose level was at breakfast, if the glucose level after breakfast or before lunch was low, then the breakfast nutritional dose should be decreased for the next day.

Reference: Hospitalist Handbook

Hypothyroidism

Definition

Primary Hypothyroidism: High TSH and Low T4

Secondary (central) Hypothyroidism: Low T4 and TSH that is low

Subclinical Hypothyroidism: High TSG with normal T4

Myxedema coma: severe hypothyroidism causing multi-organ dysfunction. A medical emergency with a high mortality rate

Presentation

Early: Usually asymptomatic, but may have fatigue, weight gain, cold intolerance, menorrhagia or amenorrhea, constipation, dry skin, thin hair, delayed DTR, diastolic HTN and hyperlipidemia

Late: Slow speech, brawny edema, hoarseness, loss of outer third of eyebrows, puffy face/eyelids, thickened tongue, myxedema, bradycardia, hypotension, and hypothermia

Myxedema coma: Endocrine emergency. Can present with AMS, hypothermia, hypoventilation, hyponatremia, hypoxia, hypercapnia, hypotension, convulsion, confusion, lethargy and coma.

Management

Levothyroxine: Full replacement is approx 1.6mcg/kg/day. Patient not requiring full replacement can be started on lower dose

Monitoring and dose adjustment based on TSH every 4-8 weeks until stable dose achieved

Pregnancy: Goal TSH varies by trimester, consultation with endocrinology is indicated

Elderly with CAD or high risk CAD, long standing untreated hypothyroidism: Start levothyroxine 25mcg/day

Subclinical hypothyroidism: Treatment generally not necessary unless TSH is >10, anti TPO positive, presence of a goiter, pregnancy or other compelling complication. Typically lower doses of levothyroxine are needed. Start with 15-50mcg. Follow up in 4-8 weeks of treatment initiation.

Thyroid Cancer: Patient who had total thyroidectomy for thyroid cancer need higher doses of thyroid hormone to suppress TSH

Myxedema coma:

- Immediate endocrine consult to help guide therapy,
- draw cortisol level first and administer steroid (hydrocortisone 50-100mg q6-8h) until adrenal insufficiency can be ruled out. Thyroid hormone therapy can increase cortisol clearance, precipitating adrenal insufficiency.
- Thyroid replacement: 200-400mcg IV load followed by 50-100mcg IV daily. Consider lower IV load doses in elderly patients or patient with cardiac conditions

<https://pubmed.ncbi.nlm.nih.gov/23246686/>

Hospitalist handbook

Hyperthyroidism

Symptoms and signs

- Signs of hypermetabolic state: restlessness, tachycardia, diaphoresis, hyper-defecation, weight loss, palpitation
- Apathetic hyperthyroidism: elderly patients often don't have classic symptoms, but may present with lethargy, weight loss, SOB and afib
- Thyroid Storm: Fever, delirium, stupor, coma, tachycardia, arrhythmias, CHF, vomiting/diarrhea, hepatic failure

Work up

- TSH suppressed (except in pituitary disease), T4 and/or T3 increased
- ESR can be increased in subacute thyroiditis
- Anti TPO Ab often positive in silent thyroiditis
- Radioactive iodine uptake can be useful to differentiate between causes (contraindicated in pregnant patients): diffuse high uptake in graves', focal high uptake with toxic nodule, very low uptake in subacute thyroiditis.
- Burch-Wartofsky Point Scale (BWPS) is a scoring system to help identify thyroid storm

Management

Medical Therapy

Symptom Management: Propranolol to control symptoms and tachycardia (blocks adrenergic effects and peripheral conversion of T4 to T3). Beta blockade can be stopped once anti-thyroid treatment takes effect.

Inhibition of hormone synthesis: Methimazole or PTU. Methimazole is generally preferred due to better side effect profile (PTU preferred in pregnancy). Obtain baseline CBC and LFT's

Definitive therapy: Radioactive iodine ablation

Thyroid storm

- Consult endocrinology
- Supportive therapy with IVF, Oxygen and acetaminophen, likely ICU
- Avoid ASA as it can displace T4 from TBG
- Immediately start PTU 200-300mg PO q4-6hr

- Follow with saturated solution of potassium iodide to inhibit conversion of T4 to T3
- Consider propranolol 60-80mg PO q4-6hr to control tachycardia (caution in Heart Failure)
- Consider hydrocortisone 50-100mg IV q6-8hrs x48 hrs (blocks conversion of T4-T3)

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