When is the use of insulin mandatory: DKA, HHS, CKD, Pregnancy

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100 Years of Insulin Therapy: A long Successful Path

Disclosure

- Harry Jiménez MD, FACE

- I have no conflict with the information that I am going to give in this conference

Objectives

- Discuss the insulin use on DKA, HHS, CKD
- Review the use of insulin in pregnancy

DKA Triad

Diabetic Ketoacidosis (DKA) can occur in both type 1 & 2 diabetes mellitus.

- Overall Mortality rate is 0.2 – 2%
- It presents with three common characteristics:
  - Hyperglycemia: Blood glucose >250mg
  - Hyperketonemia: Plasma acetone positive
  - Metabolic Acidosis
    - PH <7.3
    - Anion gap >10 (Na +K) - (Cl +HC0)

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Classifying the Severity

	Mild	Moderate	Severe
Plasma Glucose	>250	>250	>250
Arterial pH	7.25 – 7.30	7.00 - <7.24	<7.0
Serum Bicarb	15 – 18	10 - <15	<10
Urine Ketone	Positive	Positive	Positive
Serum Ketone	Positive	Positive	Positive
Anion Gap	>10	>12	>12
Mental Status	Alert	Alert/Drowsy	Stuporous

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Etiology

- Inadequate insulin treatment or noncompliance.
- New onset diabetes (20-25%)
- Acute illness
  - Infection (30% to 40%)
  - CVA
  - Acute myocardial Infraction
  - Acute Pancreatitis
- Drugs
  - Clozapine or olanzapine
  - Cocaine
  - Lithium
  - Euglycemic DKA
    - SGLT2 Inhibitors
    - Insulin Pump
    - Pregnancy
    - Pancreatitis
  - Terbutaline
  - Steroids

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Laboratory Evaluation in DKA

- Blood test for glucose every 1 hour
- ABG
- Serum electrolytes every 2 - 4 hours
- Serum ketones (3-hydroxybetabutyrate)
- CBC
- Cultures
- Amylase
- Chest X-Ray

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Hyperglycemic Hyperosmolar Syndrome (HHS)

- Complication of type 2 diabetes
  - Adults
  - Obese adolescents
    - Early in the diagnostic of the condition
- When glucose cannot move into the cell, it accumulates in the bloodstream (leading to hyperglycemia and hyperosmolality)
- Since insulin is still produced in type 2 diabetes, it is sufficient to prevent lipolysis (which causes ketone byproducts)
- HHS does not cause ketoacidosis
- Overall Mortality up to 20%

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Hyperglycemic Hyperosmolar Syndrome (HHS)

- The serum osmolality is determined by the formula 2Na + Glucose /18 + BUN / 2.8. Osmolarity >320 mOsm/L
- The glucose level in HHS is usually above 600 mg/dL.
- Absence of significant ketoacidosis,
  - higher level of insulin with an associated lower level of glucagon
- Moderate to severe dehydration.
- Presence of neurological signs.

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Hyperglycemic Hyperosmolar Syndrome (HHS) Etiology

- Infection 50% – 60%
  - Respiratory
  - Gastrointestinal
  - Genitourinary
- Medicine
  - Thiazide
  - Beta Blocker
  - Steroid
  - Atypical antipsychotics
- CVD
  - Stroke
  - MI
- Obese diabetic adolescent

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Laboratory Evaluation in HHS

- Blood test for glucose every 1 hour
- ABG
- Serum electrolytes every 2 - 4 hours
- CBC
- Cultures
- Amylase
- Chest X-Ray
- EKG

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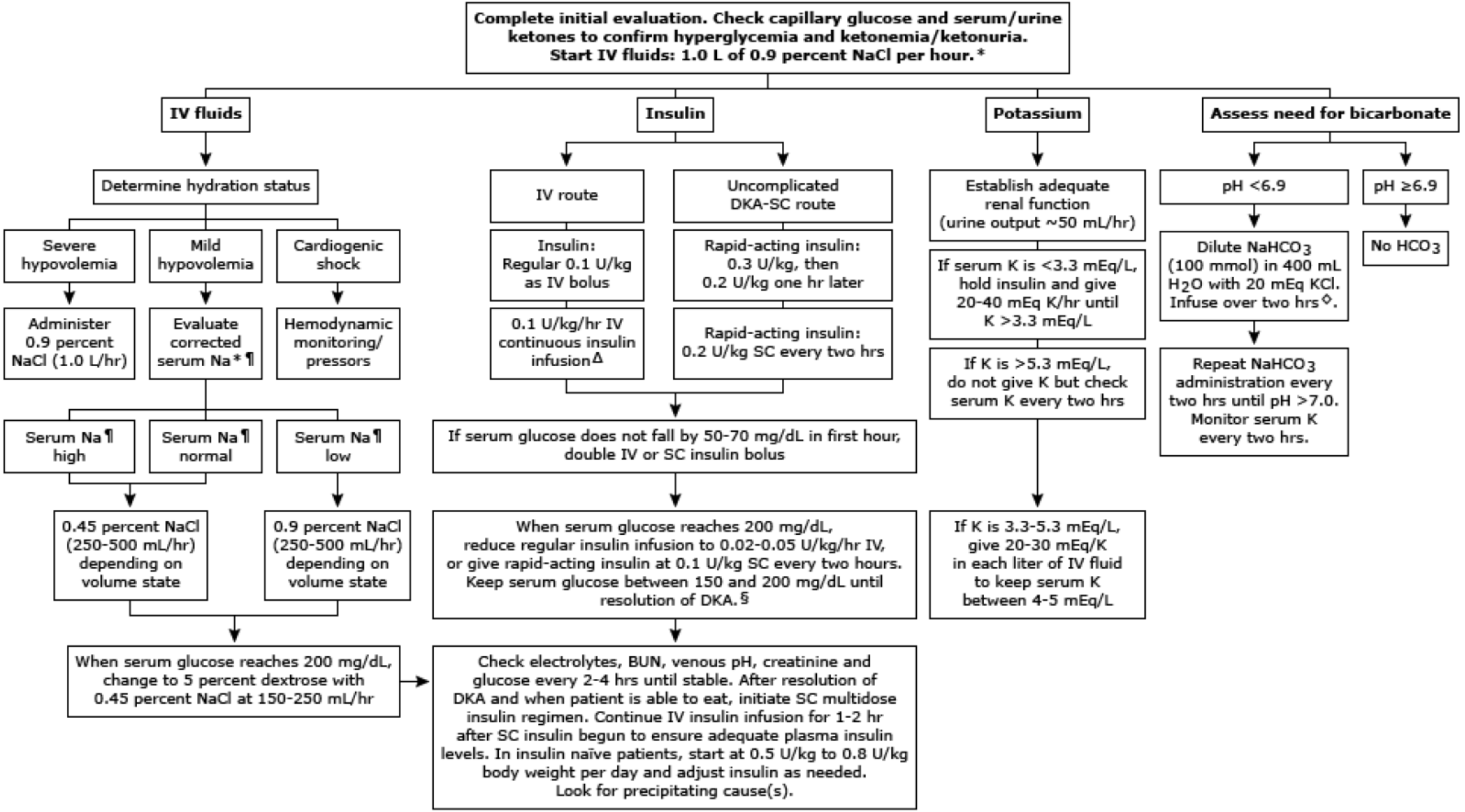
Complete initial evaluation. Check capillary glucose and serum/urine ketones to confirm hyperglycemia and ketonemia/ketonuria.
Start IV fluids: 1.0 L of 0.9 percent NaCl per hour.*
IV fluids
Determine hydration status
Severe hypovolemia
Mild hypovolemia
Cardiogenic shock
Administer 0.9 percent NaCl (1.0 L/hr)
Evaluate corrected serum Na*¶
Hemodynamic monitoring/ pressors
Serum Na¶ high
Serum Na¶ normal
Serum Na¶ low
0.45 percent NaCl (250-500 mL/hr) depending on volume state
0.9 percent NaCl (250-500 mL/hr) depending on volume state
When serum glucose reaches 200 mg/dL, change to 5 percent dextrose with 0.45 percent NaCl at 150-250 mL/hr
Insulin
IV route
Uncomplicated DKA-SC route
Insulin: Regular 0.1 U/kg as IV bolus
Rapid-acting insulin: 0.3 U/kg, then 0.2 U/kg one hr later
0.1 U/kg/hr IV continuous insulin infusionΔ
Rapid-acting insulin: 0.2 U/kg SC every two hrs
If serum glucose does not fall by 50-70 mg/dL in first hour, double IV or SC insulin bolus
When serum glucose reaches 200 mg/dL, reduce regular insulin infusion to 0.02-0.05 U/kg/hr IV, or give rapid-acting insulin at 0.1 U/kg SC every two hours. Keep serum glucose between 150 and 200 mg/dL until resolution of DKA.§
Check electrolytes, BUN, venous pH, creatinine and glucose every 2-4 hrs until stable. After resolution of DKA and when patient is able to eat, initiate SC multidose insulin regimen. Continue IV insulin infusion for 1-2 hr after SC insulin begun to ensure adequate plasma insulin levels. In insulin naïve patients, start at 0.5 U/kg to 0.8 U/kg body weight per day and adjust insulin as needed. Look for precipitating cause(s).
Potassium
Establish adequate renal function (urine output ~50 mL/hr)
If serum K is <3.3 mEq/L, hold insulin and give 20-40 mEq K/hr until K >3.3 mEq/L
If K is >5.3 mEq/L, do not give K but check serum K every two hrs
If K is 3.3-5.3 mEq/L, give 20-30 mEq/K in each liter of IV fluid to keep serum K between 4-5 mEq/L
Assess need for bicarbonate
pH <6.9
pH ≥6.9
Dilute NaHCO3 (100 mmol) in 400 mL H2O with 20 mEq KCl. Infuse over two hrs◇.
No HCO3
Repeat NaHCO3 administration every two hrs until pH >7.0. Monitor serum K every two hrs.

Differences in DKA & HHS

- **DKA:**
- Correct acidosis
- Lower blood glucose
- Rehydrate
- Correct electrolytes
- Resolve cause

- **Criteria for resolved DKA:**
- **pH > 7.3**
- Bicarbonate ≥ 15 mEq/L
- Blood glucose **< 200** mg/dL
- Anion gap < 12
- Patient is able to eat

- **HHS:**
- Lower blood glucose
- Rehydrate
- Correct electrolytes
- Resolve cause

- **Criteria for resolved HHS:**
- BG **200 – 300** mg/dL
- Patient is able to eat

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DKA Nomogram

DIABETIC KETOACIDOSIS (DKA) NOMOGRAM – ADULT

Insulin regular (HUMULIN R, NovoLIN R) 50 Units in sodium chloride 0.9% 50 mL infusion

Start insulin drip at 0.1 units/kg/hr.

Target blood glucose (BG): 150 - 200 mg/dL until patient is mentally alert.

TITRATION INSTRUCTIONS:

BG change from Previous Value:		Insulin Infusion Rate Change & Calculation:
If BG is less than 70 mg/dL:		Stop insulin infusion. Repeat BG measurement STAT x1 to confirm. Call physician. Give 50 mL of D50W and recheck BG every 15 minutes until BG is greater than 100 mg/dL, then restart insulin infusion at 50% of previous rate by multiplying by infusion rate by 0.5 and resume every 1 hour BG measurements.
If BG is 70 – 149 mg/dL:		Decrease insulin infusion by multiplying by 0.5
If BG is 150 – 200 mg/dL:		
	If previous BG was greater than 200 mg/dL	Decrease insulin infusion by multiplying by 0.5
	If previous BG was less than or equal to 200 mg/dL	Continue same infusion rate. No change.
If BG is greater than 200 mg/dL:		
	If BG has increased from the previous value	Increase insulin infusion by multiplying by 1.5
	If BG has decreased by less than 50 mg/dL from the previous value	Increase insulin infusion by multiplying by 1.5
	If BG has decreased by 50 – 75 mg/dL from the previous value	Continue same infusion rate. No change.
	If BG has decreased by 76 – 100 mg/dL from the previous value	Decrease insulin infusion by multiplying by 0.75
	If BG has decreased by more than 100 mg/dL from the previous value	Decrease insulin infusion by multiplying by 0.5

DO NOT stop the insulin infusion unless patient is hypoglycemic with blood glucose less than 70 mg/dL or by physician order.

Notify provider for initiation of immediate or long-acting subcutaneous insulin when DKA has resolved (e.g., pH greater than 7.3; bicarbonate greater than or equal to 15 mEq/L; glucose less than 200 mg/dL; and/or anion gap less than 12) AND patient is able to eat/tolerate enteral nutrition.

Discontinue insulin infusion 2 hours after initiation of intermediate or long-acting subcutaneous insulin.

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HHS Nomogram

HYPEROSMOLAR HYPERGLYCEMIA NOMOGRAM – ADULT

Insulin regular (HUMULIN R, NovoLIN R) 50 Units in sodium chloride 0.9% 50 mL infusion

Start insulin drip at 0.1 units/kg/hr.

Target blood glucose (BG): 200 – 300 mg/dL until patient is mentally alert.

TITRATION INSTRUCTIONS:

BG change from Previous Value:		Insulin Infusion Rate Change & Calculation:
If BG is less than 70 mg/dL:		Stop insulin infusion. Repeat BG measurement STAT x1 to confirm. Call physician. Give 50 mL of D50W and recheck BG every 15 minutes until BG is greater than 200 mg/dL, then resume every 1 hour BG measurements. Once BG is greater than 200 mg/dL, restart insulin infusion at 50% of previous rate by multiplying by 0.5.
If BG is 70 – 199 mg/dL:		Decrease insulin infusion by multiplying by 0.5
If BG is 200 – 300 mg/dL:		
	If previous BG was greater than 300 mg/dL	Decrease insulin infusion by multiplying by 0.5
	If previous BG was less than or equal to 300 mg/dL	Continue same infusion rate. No change.
If BG is greater than 300 mg/dL:		
	If BG has increased from the previous value	Increase insulin infusion by multiplying by 1.5
	If BG has decreased by less than 50 mg/dL from the previous value	Increase insulin infusion by multiplying by 1.5
	If BG has decreased by 50 – 75 mg/dL from the previous value	Continue same infusion rate. No change.
	If BG has decreased by 76 – 100 mg/dL from the previous value	Decrease insulin infusion by multiplying by 0.75
	If BG has decreased by more than 100 mg/dL from the previous value	Decrease insulin infusion by multiplying by 0.5

DO NOT stop the insulin infusion unless patient is hypoglycemic with blood glucose less than 70 mg/dL or by physician order.

Notify provider for initiation of immediate or long-acting subcutaneous insulin when HHS has resolved (e.g., glucose less than 300 mg/dL) and patient is able to eat/tolerate enteral nutrition.

Discontinue insulin infusion 2 hours after initiation of intermediate or long-acting subcutaneous insulin.

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Diagnostic Criteria for GDM

- Test should be done on the 24-28 weeks of gestation
  - The diagnostic test (100 gm 3-hour OGTT)

Fasting	95 mg/dL
1 hour	180 mg/dL
2 hour	155 mg/dL
3 hour	140 mg/dL

One Value exceeding any of these threshold is diagnostic for GDM

Carpenter / Coustan 2017

Gestational Diabetes Mellitus (GDM) Monitoring

- Before breakfast
- At one or at two hours post prandial after each meal
- Self-Monitoring of Blood Glucose (SMBG) 4 times a day
- Continuous Glucose Monitoring (CGM)

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Gestational diabetes mellitus: Glycemic control and maternal prognosis Sept 2021

Gestational Diabetes Mellitus (GDM) Treatment

- Minimize maternal and neo-natal morbidity
  - ↓ preeclampsia
  - ↓ birth weight > 4000g
  - ↓ shoulder dystocia

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Gestational diabetes mellitus: Glycemic control and maternal prognosis Sept 2021

Gestational Diabetes Mellitus (GDM) Treatment

- 70% will be controlled with medical nutrition plus exercise therapy
  - Dietitian evaluation and follow up
- 30% will need pharmacotherapy
  - Metformin
  - Glyburide
  - Insulin* (1st Choice)
    - 0.7 units to 2 units per kilogram

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Gestational diabetes mellitus: Glycemic control and maternal prognosis Sept 2021

Gestational Diabetes Mellitus (GDM) Treatment

- Insulin Treatment Criteria
  - Fasting and post prandial hyperglycemia
  - By sonogram
    - Fetal AC > 75th percentile
    - Fetal EFW ≥ 90th percentile
- Insulin Treatment Goals
  - Fasting blood glucose concentration: < 95 mg/dL
  - One-hour postprandial blood glucose concentration: < 140 mg/dL
  - Two-hour postprandial glucose concentration: < 120 mg/dL

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ADA and American College of Obstetric 2021

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Gestational Diabetes Mellitus (GDM) Treatment

- NPH 10 to 20 units plus 6 to 10 units (lispro or aspart) before breakfast
- If postprandial glucose level are elevated post lunch add 6 to 10 units of rapid acting insulin
- If postprandial glucose level are elevated post dinner add 6 to 10 units of rapid acting insulin
- If the fasting glucose level are elevated and postprandial glucose on targeted range add intermediate insulin at bedtime or with dinner

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Gestational diabetes mellitus: Glycemic control and maternal prognosis Sept 2021

Gestational Diabetes Mellitus (GDM) Treatment

- If only the fasting blood concentration is high use 0.2 unit/kg
  - NPH, Insulin Glargine or detemir given before bedtime or before dinner
- If only postprandial blood glucose concentration are high
  - 6 to 10 units of aspart or lispro before meals
- If both postprandial and pre-prandial blood glucose are high start insulin 0.9 units/kg or 1.0 units/kg
  - In the morning two-third of basal inulin plus one-third rapid acting insulin
  - In the evening one-third of the total dose half basal and half rapid acting insulin

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Diabetes CKD
Insulin Physiology

- Increase insulin resistance
- Reduce Hepatic Insulin Metabolism
- Reduce insulin clearance
- Reduce insulin synthesis

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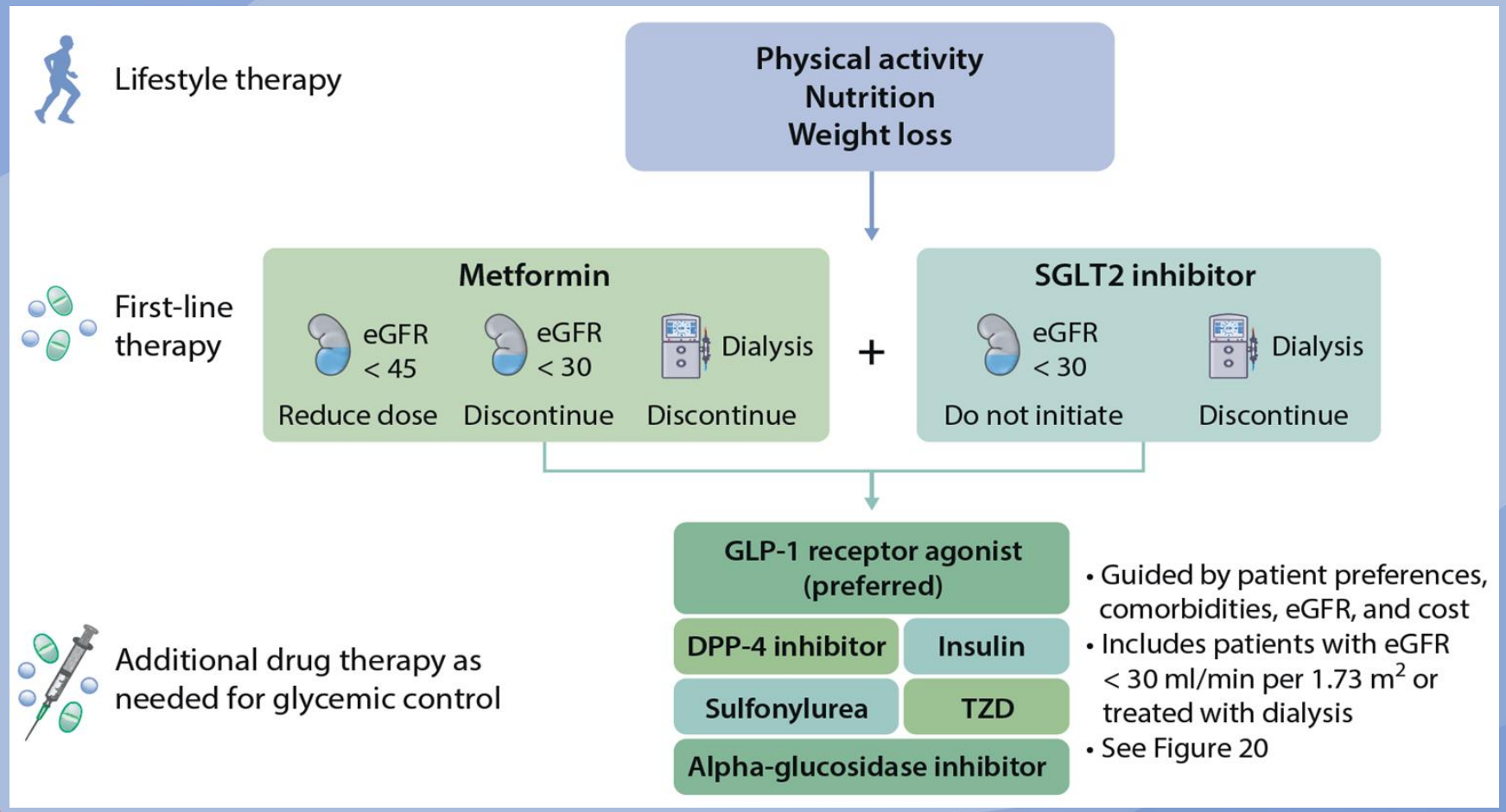
Treatment algorithm for selecting antihyperglycemic drugs for patients with T2D and CKD



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Diabetes CKD

- Insulin
  - When GFR <45 ml/dL insulin clearance is decrease
  - GRF > 45 mL/min → no dose adjustment
  - GFR 10 mL/min to 45 mL/min → 25% reduction
  - GFR < 10 mL/min → 50% reduction

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Insulin in patients on hemodialysis

- Long-acting Insulin 0.1 u/kg
- Insulin resistance diminishes after the start od dialysis
- Half-life of insulin is prolonged
- The potential for hypoglycemia with both oral and insulin increases in the presence of CKD
- Self-monitoring of blood glucose concentration is imperative.
- Insulin requirement often decreases by ~30%
- Glargine has been shown to reduce hypoglycemia in hemodialysis patients (0.1 units /kg to start)
- CGM

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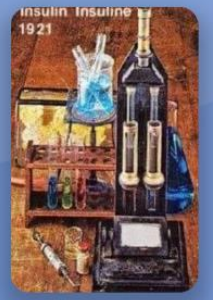
CGM in Diabetes CKD

- CKD-4
- CKD-5
- Patients in dialysis
- When clinical course is not concordance with A1c results



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