



# SGLT2-I and Euglycemic DKA

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## Disclosures



- I am a speaker and advisory board member for Abiomed/J&J MedTech

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## Objectives



- Describe the presentation and pathophysiology of classic DKA
- Review the SGLT-2I medication class and its effects on glucose and Insulin metabolism
- Describe the presentation and pathophysiology of euglycemic DKA, especially as relates to SGLT-2I
- Discuss the diagnosis and treatment of euglycemic DKA

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## Diabetic Subtypes

- **Type 1DM**
  - Hyperglycemia via absolute insulin deficiency
  - Requires exogenous insulin administration
- **Type 2DM**
  - Hyperglycemia secondary to insulin resistance
  - Patient hyperinsulinemic at baseline



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## Acute Hyperglycemic Complications of DM

- **Diabetic Ketoacidosis**
  - Moderate hyperglycemia
  - Ketosis
  - Acidosis
  - Inadequate insulin to stay out of lipolysis and ketosis
- **Hyperosmolar Hyperglycemic State**
  - Severe hyperglycemia
  - Increased hyperosmolality
  - Minimal ketosis
  - Minimal acidosis
  - Adequate insulin to keep out of lipolysis and ketosis



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## Diabetic Ketoacidosis

- Hyperglycemia
- Ketosis
- Anion Gap Metabolic Acidosis



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## Diabetic Ketoacidosis

- Commonly associated with type 1 DM
  - Hyperglycemia secondary to absolute *insulin* deficiency
- Increased counter-regulatory hormone response
  - Glucagon, growth hormone, catecholamines, corticosteroids.
- Gluconeogenesis, proteolysis → hyperglycemia
- Glycogenolysis, lipolysis → ketosis
- Possible in type 2 DM (increasingly possible...)

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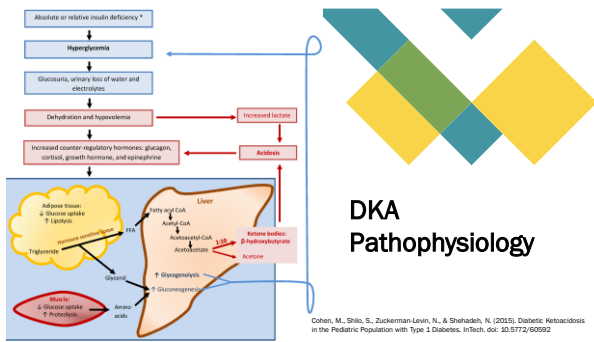
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## DKA Pathophysiology

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## Signs and Symptoms

- Nausea
- Vomiting
- Fatigue
- Anorexia
- Tachypnea
- Tachycardia
- Abdominal pain

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## Diabetic Ketoacidosis Diagnosis

- **D: glucose**  $\geq 200$ mg/dL or prior history of diabetes
- **K: Ketosis**
  - Beta-hydroxybutyrate level  $\geq 3$ mmol/L or
  - Urine ketones 2+ or higher
- **A: Metabolic acidosis**
  - pH  $< 7.3$  or
  - Bicarbonate concentration  $< 18$ mmol/L or
  - Both of the above

Umpierrez GE, Davis GM, ElSayed NA, et al. Hyperglycemic crises in adults with diabetes: a consensus report. *Diabetes Care* 2024; 47(8):1257-1275

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## SGLT-2 Inhibitors

- Canagliflozin
- Dapagliflozin
- Empagliflozin
- Ertugliflozin
- Bexagliflozin
- Sotaflozin

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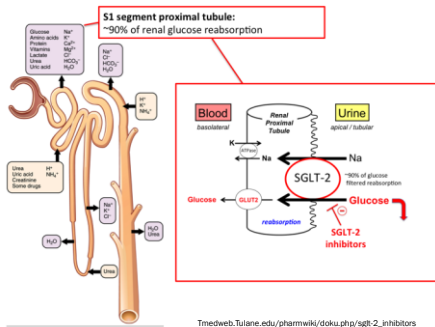
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## SGLT-2I




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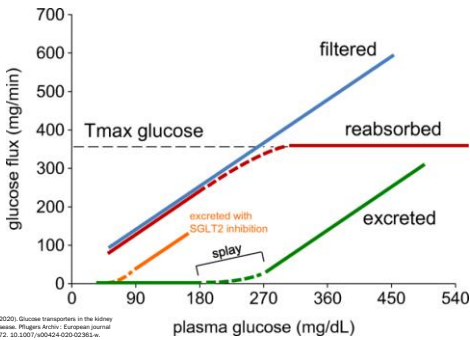
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## SGLT-2 Inhibitor Benefits

- Improved glucose control in T2DM
- Improve long term outcomes in HFrEF
- Decreased major adverse cardiovascular events
- Slow progression of CKD

Felma A, Rasooli S, Devi S, Talha M, Wager F, Hase M, Khan MI, Iqbal AJ, Jaffer VM, Haider A, Shah S, Saeed F, Vameqi G, Khali M, Kumar S, Mohamed T. Evaluating the Cardiovascular Benefits of Sodium-Glucose Cotransporter-2 (SGLT-2) Inhibitors: Expanding Evidence Beyond Diabetes Management. *Currents*. 2023 Sep; 30:1501-1524. doi: 10.7759/cureus.46243. PMID: 37689537; PMCID: PMC10813932.



Valler, Volker. (2020). Glucose transporters in the kidney in health and disease. *Physiol. Acta - European journal of physiology*. 472. 33.1007/978-3-319-02392-4.

## SGLT-2I and Insulin

- Glucose spills into urine at lower plasma concentration
- Decrease in circulating insulin
  - Mild relative hypoinsulinemia
- Increased gluconeogenesis and FFA metabolism
- Increased baseline glucagon
  - Promotes ketogenesis
- Promotes negative fluid and sodium balance

Chow E, Clement S, Gang R. Euglycemic diabetic ketoacidosis in the era of SGLT-2 inhibitors. *BMC Diabet Res Clin*. 2023;11:e003666. <https://doi.org/10.1186/bmjdrc-2023-003666>



## Differential Diagnosis

- Alcoholic ketoacidosis
- Starvation ketosis
  - Milder ketosis
  - Higher bicarb
  - No acidosis
- Lactic Acidosis
- Other HAGMA



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## A Word of Caution

- pH Isn't everything
- Respirations compensate for metabolic acidosis
- Respiratory compensation in DKA can be profound
- Outstripping of compensation is precipitous



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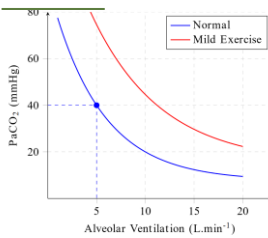
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## PCO2 vs Ventilation



Partone.litfl.com/dead\_space.html



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### A Classic ABG

- pH: 7.18
- pCO2: 28
- pO2: 124
- HCO3: 9



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### A Likely ABG

- pH: 7.32
- pCO2: 20
- pO2: 124
- HCO3: 7



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### Another Likely ABG

- pH: 7.32
- pCO2: 30
- pO2: 124
- HCO3: 15



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## Euglycemic DKA Management

- **Prevention**
  - Hold SGLT-2i 3 days prior to major surgery (esp cardiac)
  - Pause SGLT-2i in acute illness
  - Follow urine ketones on outpatient basis
  - Low threshold to check serum ketones in pts with nausea, vomiting, or malaise




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## Euglycemic DKA Management

- **Similar to Regular DKA**
  - Fluids
  - Potassium
  - Insulin




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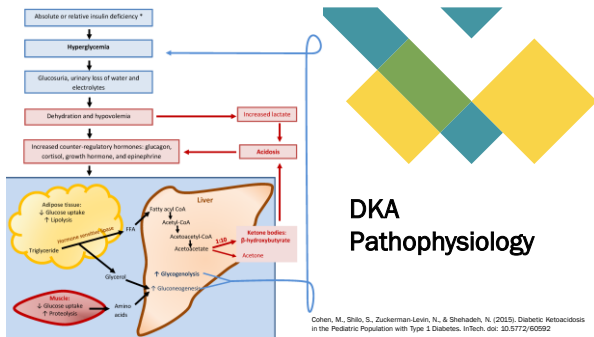
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## Insulin Management

- **Determine Severity of DKA**
  - How to determine?
  - Serum glucose?
  - pH?
  - Bicarb?
  - Respiratory compensation?



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## Insulin Management

- **Higher risk of relapsing into DKA if on SGLT-2i**
  - Our practice: observe in ICU 24hr after gap closure/resolution
    - Patient population specific



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## Insulin Management

- **Mild-moderate**
  - IV Dextrose
  - IV Insulin infusion 1.3U/hr
  - No initial bolus
- **Moderate-severe**
  - Hospital "DKA Protocol"
  - IV Dextrose
  - IV Insulin infusion 0.1U/kg/hr
  - No initial bolus



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