# DIABETES type II & the euDKA trap

Tuan Tran, MD, PhD., Unit of Genetic & Genomic Medicine, Family Hospital, Da Nang.

# I. THE EUGLYCEMIC DIABETIC KETOACIDOSIS (euDKA) TRAP

The question was: Since a SGLT2 inhibitor continues to promote glucose excretion in the urine, how could the patient have ketosis in the first place?

This is an excellent question that gets to the heart of the "euglycemic" (near-normal sugar) mystery. To understand why ketosis happens while the drug is busy dumping sugar, we have to look at the **Insulin-to-Glucagon ratio**.

## 1.1. THE STARVATION IN THE MIDST OF PLENTY

SGLT2 inhibitors are so effective at clearing glucose through the urine (losing about 60–100 grams of glucose per day) that they lower circulating blood glucose levels.

When blood glucose levels drop, the body reacts in two ways:

- **Lowers Insulin:** The pancreas senses lower blood sugar and reduces insulin secretion.
- **Raises Glucagon:** The alpha cells in the pancreas increase the release of glucagon.

Even though the patient's blood sugar isn't "low" by emergency standards (e.g., 150 mg/dL), the **ratio of Insulin to Glucagon** drops significantly. This low ratio signals the body that it is in a "starvation state," even though there is actually sugar present.

## 1.2. THE TRIGGERING OF LIPOLYSIS

Because insulin (the "storage hormone") is low and glucagon (the "mobilization hormone") is high, the body begins a process called **lipolysis**:

1. **Fat Breakdown:** Adipose tissue releases free fatty acids into the bloodstream.
2. **Liver Uptake:** These fatty acids travel to the liver.
3. **Ketogenesis:** The liver converts these fatty acids into **ketone bodies** (acetoacetate and $\beta$-hydroxybutyrate) to be used as an alternative fuel source.

## 1.3. The "Masking" Effect

In a typical DKA case (without SGLT2 inhibitors), the kidneys eventually reach their "renal threshold" for glucose, but since the body can't get rid of it fast enough, the blood sugar climbs to 300, 500, or 800 mg/dL.

With an SGLT2 inhibitor, the "exit door" for glucose is wide open. The kidneys continue to dump glucose into the urine even as the liver is pumping out ketones. This keeps the blood glucose levels near normal, while the blood becomes increasingly acidic due to the buildup of ketones.

# Key Takeaway

**The Metabolic Trap:** SGLT2 inhibitors decouple the relationship between blood glucose levels and insulin demand. The patient enters ketosis not because they lack sugar, but because the **hormonal signaling** (Low Insulin/High Glucagon) incorrectly tells the liver that the body is starving.

### Standard DKA vs. Euglycemic DKA

| Feature | Standard DKA | Euglycemic DKA (The Trap) |
|---|---|---|
| **Blood Glucose** | **> 250 mg/dL (often > 500)** | **< 200 mg/dL** (often near-normal) |
| **Blood pH** | Acidic (< 7.3) | Acidic (< 7.3) |
| **Bicarbonate** | Low (< 18$ mEq/L) | Low (< 18$ mEq/L) |
| **Ketones** | Positive (Blood/Urine) | **Positive (Blood/Urine)** |
| **Primary Driver** | Absolute insulin deficiency | Relative insulin deficiency + Glucosuria |
| **Common Trigger** | **Infection, missed insulin doses** | **SGLT2i use, fasting, surgery, keto diet** |

# II. HOW TO AVOID THE euDKA TRAP?

To avoid the "euglycemic DKA" (euDKA) trap, management focuses on **clinical suspicion** rather than relying on glucose numbers. Since the lab results can be deceptive, clinicians and patients must follow a specific set of "sick day rules" and diagnostic protocols.

## 2.1. The "STICH" Protocol for Prevention

For patients taking SGLT2 inhibitors (Jardiance, Forxiga, etc.), many clinical guidelines recommend the **STICH** acronym to prevent the onset of ketosis:

- **S – STop** the SGLT2 inhibitor temporarily during acute illness (flu, COVID-19, vomiting).

- **T – Test** for ketones (blood or urine) if feeling unwell, regardless of blood sugar.
- **I – Insulin** should never be stopped entirely in Type 1s; in Type 2s, insulin might need to be started or increased if ketones are present.
- **C – Carbohydrates** should be consumed to provide a glucose source, which allows for higher insulin dosing to "shut off" ketone production.
- **H – Hydration** is critical to flush out ketones and maintain kidney perfusion.

## 2.2. Clinical Management: Diagnostic Shifts

In the ER or clinic, the "trap" is avoided by changing the diagnostic threshold.

- **Trust the pH, not the Glucose:** If a patient on an SGLT2i feels "off" (nausea, fatigue, rapid breathing), a **Venous Blood Gas (VBG)** or **Anion Gap** calculation is mandatory. You are looking for metabolic acidosis, even if the finger-stick glucose is only 140 mg/dL.
- **Direct Ketone Testing:** Urine ketone strips are okay, but **Blood $\beta$-hydroxybutyrate** testing is the gold standard. A level > 0.6 mmol/L is a warning; > 3.0 mmol/L is a medical emergency.

## 2.3. Surgical & High-Risk Precautions

The most common "traps" occur around surgery or extreme diet changes.

- **The "3-Day Rule":** Most major associations (like the ADA) now recommend stopping SGLT2 inhibitors **3 to 4 days before scheduled surgery**. This allows the "renal exit door" to close and the insulin/glucagon ratio to normalize before the stress of surgery.
- **Avoid Keto Diets:** Patients on SGLT2 inhibitors should be strictly advised against "Very Low Carb" or Ketogenic diets. Combining a keto diet (which naturally raises ketones) with a drug that promotes ketosis is a recipe for euDKA.

## 2.4. The Off-Switch:

MY TAKE: To stop ketosis, we must stop the liver from making ketones. The only 'off-switch' for the liver's ketone factory is **Insulin**. But to give Insulin safely, the patient needs **Glucose** in their system so they don't crash. Therefore, the treatment for euDKA is often giving **Insulin + Intravenous Dextrose** simultaneously.

## 2.5. Summary Table

| Aspect | Standard DKA | Euglycemic DKA (The Trap) |
|---|---|---|
| **Glucose Level** | Very High (> 250 mg/dL) | **Near Normal (< 200 mg/dL)** |
| **Cause** | Absolute Insulin deficiency | **Low Insulin/High Glucagon Ratio** |
| **Primary Danger** | Dehydration + Acidosis | **Delayed Diagnosis (The Trap)** |
| **Key Test** | Finger-stick Glucose | **Blood Ketones & pH (VBG)** |

# III. References:


1. Jensen, Simon K.; Heide-Jørgensen, Uffe, et al. SGLT2 inhibitors vs GLP-1 receptor agonists for kidney outcomes in individuals with type 2 diabetes. *JAMA Intern Med*. 2026 Jan 20. https://pubmed.ncbi.nlm.nih.gov/41557360/
2. American Diabetes Association Professional Practice Committee for Diabetes*. **1. Improving Care and Promoting Health in Populations: Standards of Care in Diabetes-2026.** *Diabetes Care*. 2026 Jan;49(Suppl 1):S1-S6. https://pubmed.ncbi.nlm.nih.gov/41358887/
3. Dutta, S., et al. (2022). Euglycemic diabetic ketoacidosis associated with SGLT2 inhibitors: A systematic review and quantitative analysis. *Journal of Family Medicine and Primary Care*, *11*(3), 927. https://doi.org/10.4103/jfmpc.jfmpc_644_21
4. Gajewska, A., et al. (2024). SGLT2 Inhibitors in Kidney Diseases—A Narrative Review. *Internation. J. of Molecu. Sciences*, *25*(9). https://doi.org/10.3390/ijms25094959
5. Gandecka-Pempera, A., et al. (2025). Severe euglycemic ketoacidosis following combined therapy with GLP-1 receptor agonist and SGLT-2 inhibitor, refractory to standard treatment: A case report. *Frontiers in Endocrinology*, *16*, 1649270. https://www.frontiersin.org/journals/endocrinology/articles/10.3389/fendo.2025.1649270/full