Integrating Ketone and Glucose Monitoring for Optimized Diabetes Management

Ketone Monitoring Masterclass: **Ready-to-Use Toolkit**

Quick reference practice aids, at your fingertips, right in the clinic!

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Jennifer L. Sherr, MD, PhD

David Kerr, MBChB, DM, FRCP, FRCPE

Eda Cengiz, MD

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Integrating Ketone and Glucose Monitoring for Optimized Diabetes Management

The DKA Playbook: Applying Guidelines to Real-World Diagnosis

Stay up to date with the most recent guidelines for DKA

Diabetic ketoacidosis (DKA) can occur in individuals requiring intensive insulin therapy, regardless of diabetes type. Therefore, those with either type 1 or type 2 diabetes may be at risk.

Checking ketone levels is important, yet many clinicians, as well as people with diabetes, have suboptimal engagement with ketone testing.[1,2]

New 2024 American Diabetes Association consensus statement on DKA diagnostic criteria

Diagnosis should be based on the following three criteria:[3]

BLOOD GLUCOSE
Glucose ≥200 mg/dL (11.1 mmol/L) or prior history of diabetes

KETONES
β-hydroxybutyrate concentration ≥3.0 mmol/L or urine ketone strip ≥2

ACIDOSIS
pH <7.3 and/or bicarbonate concentration <18 mmol/L

ALL THREE ARE NEEDED FOR A DIAGNOSIS OF DKA

Types of ketone measurement methods[3]

Studies have shown the superiority of outcomes associated with measuring β-hydroxybutyrate in blood from capillary testing vs measuring acetoacetate using a nitroprusside reaction in urine or serum.[4]

KEY MESSAGES

- The risk and prevalence of DKA events is much greater in real-world practice than in clinical trial reports.
- The new 2024 American Diabetes Association consensus statement on hyperglycemic crises in adults with diabetes updated diagnostic criteria by reducing their definition of hyperglycemia in recognition of the wider range of glucose levels at presentation with DKA.[3]
- Remember, any type of ketone testing is better than no ketone testing! Educating your patients on the importance of testing is key!

References: 1. Albanese-O'Neil A, et al. *Diabetes Care*. 2017;40:e38-e39; 2. Hepprich M, et al. *BMJ Open Diabetes Res Care*. 2023;11:e003662; 3. Umpierrez GE, et al. *Diabetes Care*. 2024;47:1257-1275; 4. Laffel LM, et al. *Diabet Med*. 2006;23:278-284.

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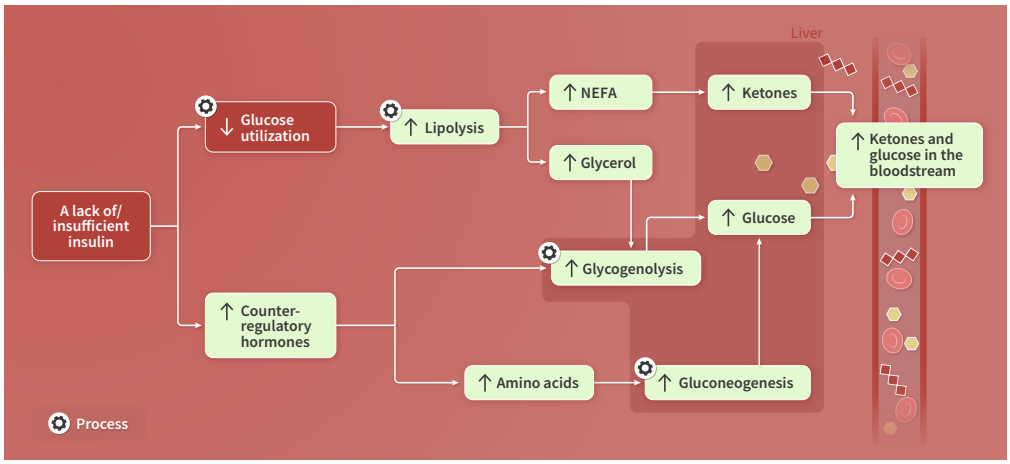
Pathways to Prevention: Understanding the Mechanisms Driving DKA

Unpack the biochemical breakdown and patient-level risks fueling DKA

Over the past decade, the number of adults and children being diagnosed with diabetic ketoacidosis (DKA) has been rising despite advances in treatments for diabetes.[1]

The good news is that DKA is almost entirely preventable, and with improvements in technology and better understanding of the biochemical breakdown and patient-level risks driving DKA, primary care clinicians can play a major role in the early detection and prevention of DKA in both type 1 and type 2 diabetes.

The metabolic processes leading to DKA can be divided into two main categories:[2]



Insulin deficiency and lipolysis – DKA begins when there is insulin deficiency, allowing for uncontrolled lipolysis (the release of free fatty acids, which are immediately converted to ketone bodies), resulting in anion gap acidosis.

- This insulin deficiency can be absolute (e.g., not enough exogenous insulin is given) or relative (e.g., increased insulin needs during illness or stress are not met).
- In addition, due to this insulin deficiency, there is reduced peripheral uptake of glucose and increased endogenous glucose production, resulting in significant increases in blood glucose levels.

Increased counterregulatory hormones – in response to low insulin levels, the body releases counterregulatory hormones (glucagon, catecholamines [epinephrine and norepinephrine], cortisol, and growth hormone), leading to an increase in hepatic glucose production by the liver and less glucose uptake by muscles.

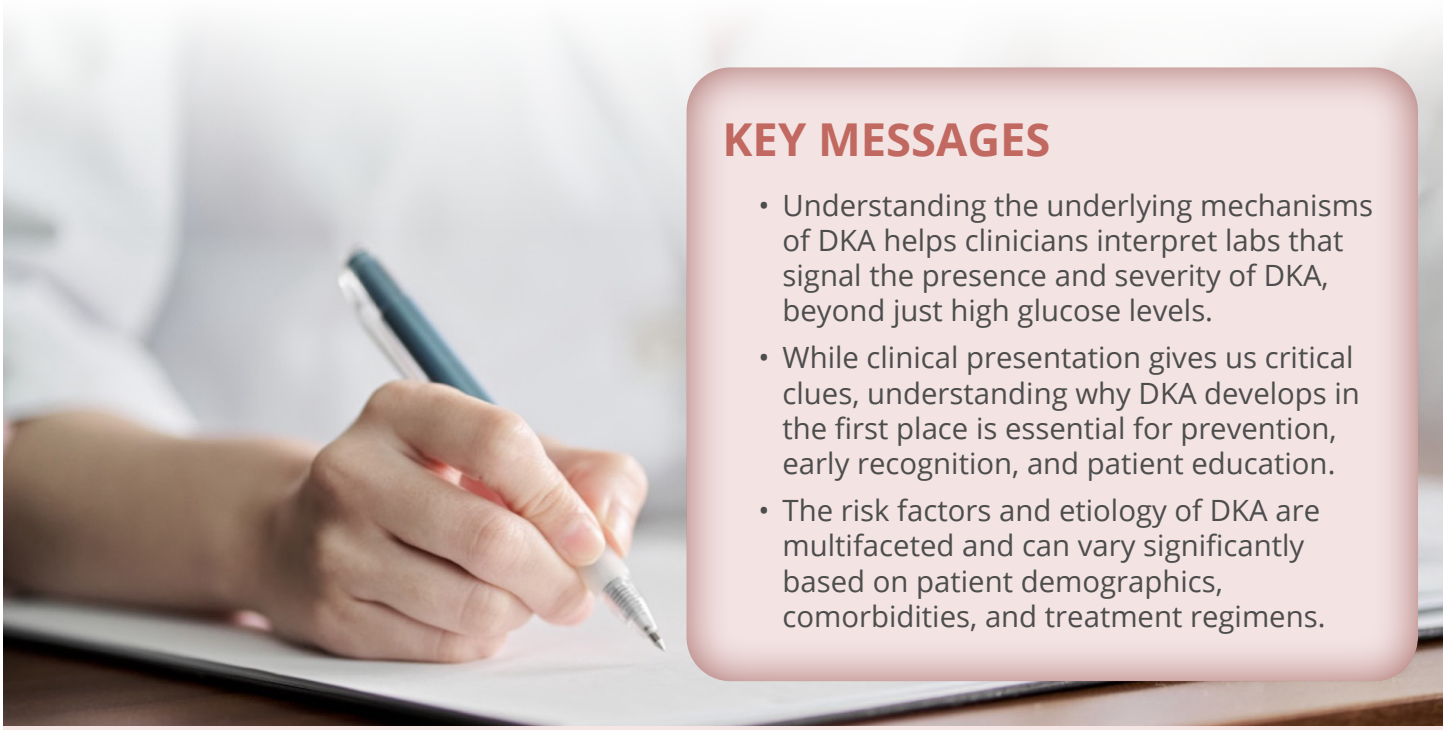
Key risk factors for DKA:

In the US, the leading risk factors for DKA in people with an established diagnosis of diabetes include suboptimal engagement with treatment (leading to insulin omission or under-dosing) and intercurrent infection or other illness.[3]

DKA is more common in adolescents and among individuals from a minority race or ethnicity.[4-6]

The use of sodium-glucose cotransporter 2 (SGLT-2) inhibitors is also associated with increased risk of DKA.[7]

In children, DKA most commonly occurs at the time of a diabetes diagnosis with children under the age of 5 years, and those who have difficulty accessing medical care have the highest rates of DKA at diabetes onset.[8]



KEY MESSAGES

- Understanding the underlying mechanisms of DKA helps clinicians interpret labs that signal the presence and severity of DKA, beyond just high glucose levels.
- While clinical presentation gives us critical clues, understanding why DKA develops in the first place is essential for prevention, early recognition, and patient education.
- The risk factors and etiology of DKA are multifaceted and can vary significantly based on patient demographics, comorbidities, and treatment regimens.

References: 1. McCoy RG. *Diabetes Care.* 2023;46:e69-e71. 2. Umpierrez GE, et al. *Diabetes Care*. 2024;47:1257-1275. 3. Umpierrez G, et al. *Nat Rev Endocrinol.* 2016;12:222-232. 4. Dhatariya KK. *Rev Diabet Stud*. 2016;13:217-225. 5. Randall L, et al. *Diabetes Care*. 2011;34:1891-1896. 6. Reid LA, et al. *Pediatr Diabetes*. 2022;23:982-990. 7. He Z, et al. *Acta Diabetol*. 2023;60:401-411. 8. Wolfsdorf J, et al. *Diabetes Care*. 2006; 29:1150-1159.

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Beyond the Strip: Innovations in Ketone Monitoring and Clinical Applications

Stay ahead of the curve—explore cutting-edge ketone monitoring systems and clinical trial insights shaping the future of patient care

Current methods for ketone measurement include urine, capillary blood, or breathalyzer testing, which all come with certain limitations:[1-3]

- Urine ketone strips, while inexpensive, only measure acetoacetate and not ß-hydroxybutyrate (BHB), making urine ketone testing unreliable for monitoring progression or resolution of diabetic ketoacidosis (DKA).
- Blood ketone monitors for BHB, while the preferred test for self-monitoring during illness and hyperglycemia, can be inconvenient, potentially painful, and relatively expensive.
- Breath analyzers, while convenient and less painful than finger sticks, do not measure BHB, are expensive, and lack an evidence base for their accuracy and dynamic range.

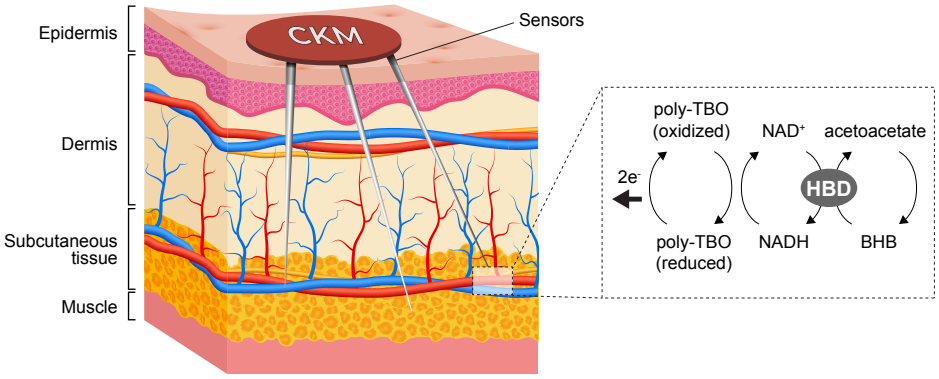
Therefore, continuous ketone monitors (CKMs), an emerging technology that offers real-time tracking of ketone levels, are under development to improve early detection of clinically significant ketosis and ketoacidosis, which will allow for timely intervention and improved metabolic control.[1]

CKMs detect BHB in interstitial fluid (ISF) rather than in blood or urine.[4]

Two types of CKM sensors have been proposed so far:

- **Electrochemical sensors:** measure ketone levels in ISF using enzymatic reactions that generate an electrical signal proportional to ketone concentration.[4]
- **Optical sensors:** optical methods analyze changes in light absorption caused by ketone bodies.[7]

Schematic illustration of continuous monitoring of BHB in ISF using a microneedle sensor[5,6]



β-hydroxybutyrate dehydrogenase (HBD) reduces NAD+ into NADH and oxidizes BHB to acetoacetate. NADH is in turn oxidized at the electrode surface to generate a current proportional to BHB concentration.

CKM=continuous ketone monitor; HBD=β-hydroxybutyrate dehydrogenase; Poly-TBO=electropolymerized toluidine blue O.

Recent studies have demonstrated the feasibility of CKMs:

- A combined continuous glucose monitor (CGM) and CKM system using subcutaneous electrochemical sensors that measure BHB levels is currently under development and has received US Food and Drug Administration (FDA) breakthrough device designation.[4,8]
- Another device measuring ISF ketone levels includes a microneedle sampling method with a sensor array. A pilot study demonstrated the ability of this sensor to detect BHB levels with similar correlation trends to standard blood BHB profiles.[6]
- An implantable near-infrared spectroscopy sensor measuring optical transmittance in ISF was well tolerated and produced accurate measurements of ketones, as well as glucose, lactate, and ethanol, in an early feasibility study (GLOW, NCT04782934).[7]

Populations likely to benefit most from CKMs include:[9]

- Children with type 1 diabetes (T1D)
- Pregnant women with T1D
- Individuals with recurrent DKA
- Individuals on SGLT inhibitors or low-carbohydrate diets
- Individuals performing high-intensity exercise
- Individuals with diabetes living in rural areas, away from emergency rooms/hospitals
- Individuals fasting for procedures

KEY MESSAGES

- Current methods for ketone measurement, including urine, capillary blood, and breathalyzer testing, all come with certain limitations.
- Integrating CKMs with traditional glycemic control measures, such as CGMs, holds substantial promise for improving metabolic safety and treatment precision in diabetes management.
- Ongoing research and technological improvements are expected to address current challenges, paving the way for the integration of CKMs into standard diabetes management protocols.

References: 1. Umpierrez GE, et al. *Diabetes Care*. 2024;47:1257-1275; 2. Dhatariya KK, et al. *Nat Rev Dis Primers*. 2020;6:40; 3. Nguyen KT, et al. *J Diabetes Sci Technol*. 2022;16:689-715; 4. Alva S, et al. *J Diabetes Sci Technol*. 2021;15:768-774; 5. Cengiz E, Tamborlane WV. *Diabetes Technol Ther*. 2009;11(Suppl 1):S11-S16; 6. Moonla C, et al. *ACS Sens*. 2024;9:1004-10137. 7. De Ridder F, et al. *PLoS One*. 2024;19(5):e0301041; 8. https://abbott.mediaroom.com/2022-06-03-Abbott-Announces-Development-of-Novel-Continuous-Glucose-Ketone-Monitoring-System; 9. Kong YW, et al. *Diabetes Obes Metab*. 2024;26(Suppl 7):47-58.

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The Ketone Conversation: Removing Barriers and Rethinking Monitoring

Solutions, strategies, and patient empowerment for proactive diabetes management

Many barriers exist to poor patient utilization of ketone testing, including:[1]

Inadequate patient education[1-3]

- **Lack of awareness:** some individuals may not fully understand the importance of ketone testing, especially in preventing diabetic ketoacidosis (DKA).
- **Misinterpretation:** individuals might not recognize the symptoms that warrant ketone testing, such as nausea, vomiting, or abdominal pain.
- **Neglect:** in some cases, individuals might forget or neglect to test for ketones, especially if they are managing multiple aspects of their diabetes care.

Lack of access to testing supplies[1,4]

- **Cost:** blood ketone meters and strips can be thought to be expensive, making regular testing less accessible for some individuals.

Inconvenience of frequent monitoring[5]

- **Cumbersome testing:** testing for ketones can be seen as cumbersome, requiring either urine strips or blood meters.

While the barriers to ketone monitoring are real and multifaceted, they are not insurmountable. With targeted strategies and thoughtful communication, ketone testing can be made more accessible, actionable, and routine.

Practical, evidence-based approaches to help overcome the above barriers to testing include:

Normalizing ketone education[6-8]

- Identify patients at risk of DKA and integrate ketone education during visits.
- Use intake forms and team-based approaches to initiate conversations.
- Teach when, why, and how to test—most people cannot rely on smell to detect ketosis.
- Review glucose/ketone logs and provide structured education and sick-day plans.
- Begin education at diagnosis and reinforce it annually or as needed.

Prescribing proactively[7,8]

- Provide easy-to-access handouts and up-to-date testing supplies.
- Personalize testing options based on patient preference and access.
- Use behavioral and peer-support interventions for patients with recurrent DKA.
- Incorporate telemedicine and emergency support for patients at risk of DKA.
- Stay informed about upcoming tools like continuous ketone monitors (CKMs).

KEY MESSAGES

- Testing for ketones can be life and cost saving. However, current evidence suggests that ketone testing is done infrequently and not at a time when it could have the most benefit.
- Primary care physicians should provide clear guidance on when and how to check ketones, including the need to obtain supplies in the event of ketosis becoming a reality.
- Small changes in education and follow-up can greatly improve ketone testing and help prevent DKA. Do not assume that patients remember everything—keep revisiting the topic!

References: 1. Nguyen KT, et al. *J Diabetes Sci Technol*. 2022;16:689-715; 2. Verhoeff N, et al. *Diabetes*. 2024;73(Suppl 1):552-P; 3. Ebekozien O, et al. *Diabetes Obes Metab*. 2024;26(Suppl 1):3-13; 4. Dhatariya K, et al. *Diabet Med*. 2016;33:269-270; 5. Umpierrez GE, et al. *Diabetes Care*. 2024;47:1257-1275; 6. Huang J, et al. *J Diabetes Sci Technol*. 2024;18:714-726; 7. Ehrmann D, et al. *Lancet Diabetes Endocrinol*. 2020;8:436-446; 8. Phelan H, et al. *Pediatr Diabetes*. 2022;23:912-925.