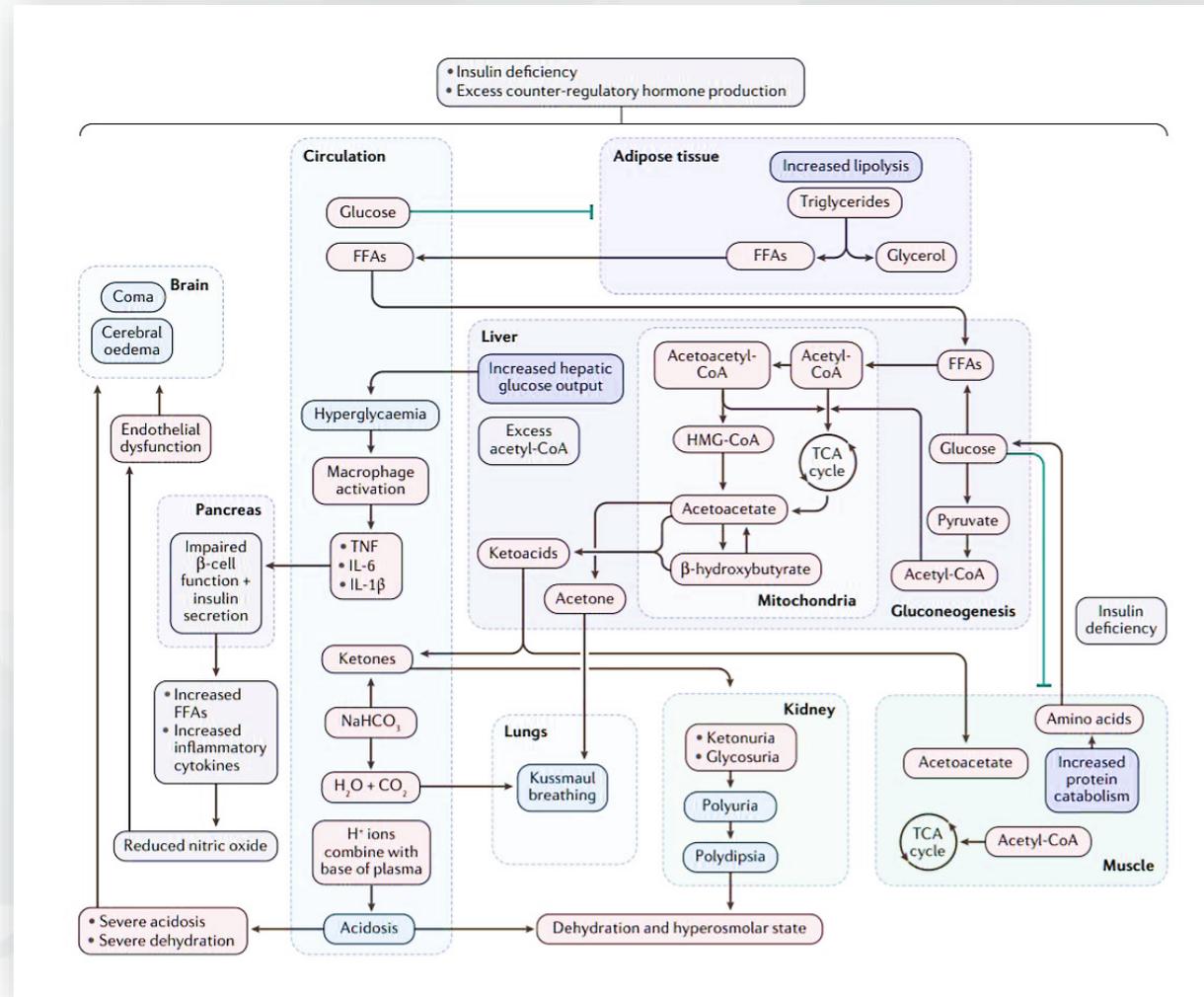


In the Range: Real Talk on Diabetes Monitoring Best Practices

Episode 1: DKA in Focus:
What the New Consensus Means for Practice

Presented by Cornerstone Medical Education and American Academy of CME.
Supported by an educational grant from Abbott Diabetes Care.

Physiology of Ketosis and Ketoacidosis

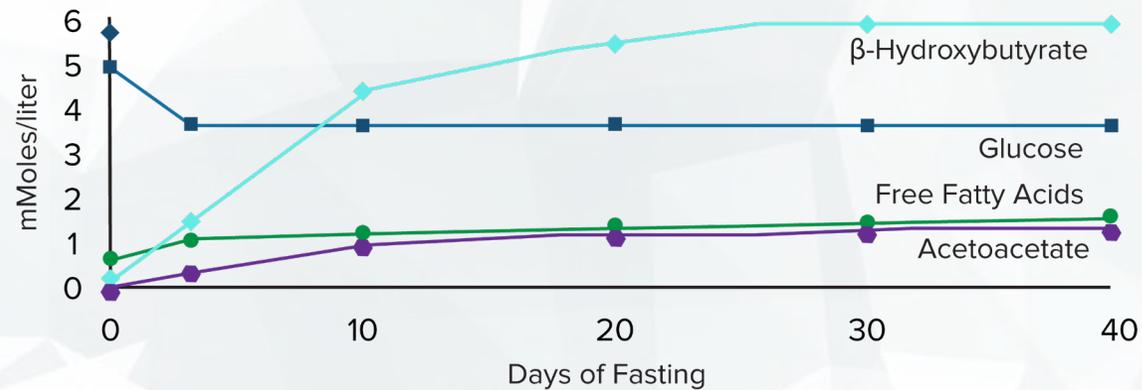


Ketones – Why Are They Important?

Levels of Circulating Substrates

Period of Observation	β -Hydroxybutyrate mM	Free Fatty Acids	Acetoacetate	Glucose mg/100 ml	Glycerol	Amino Acids	Lactate	Pyruvate
Post absorptive	0.01	0.5	0.01	80	0.06	4.5	0.6	0.1
After 1 week fast	4.0	1.5	1.0	65	0.1	4.5	0.6	0.1
After 4-5 week fast	6.0	1.5	1.5	65	0.1	3.5	0.6	0.1

Blood Glucose, Free Fatty Acids and Ketone Body Levels During Fast



Living Longer on Starvation Diets

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doi:10.1038/nature11432

Cell Metabolism

Short Article

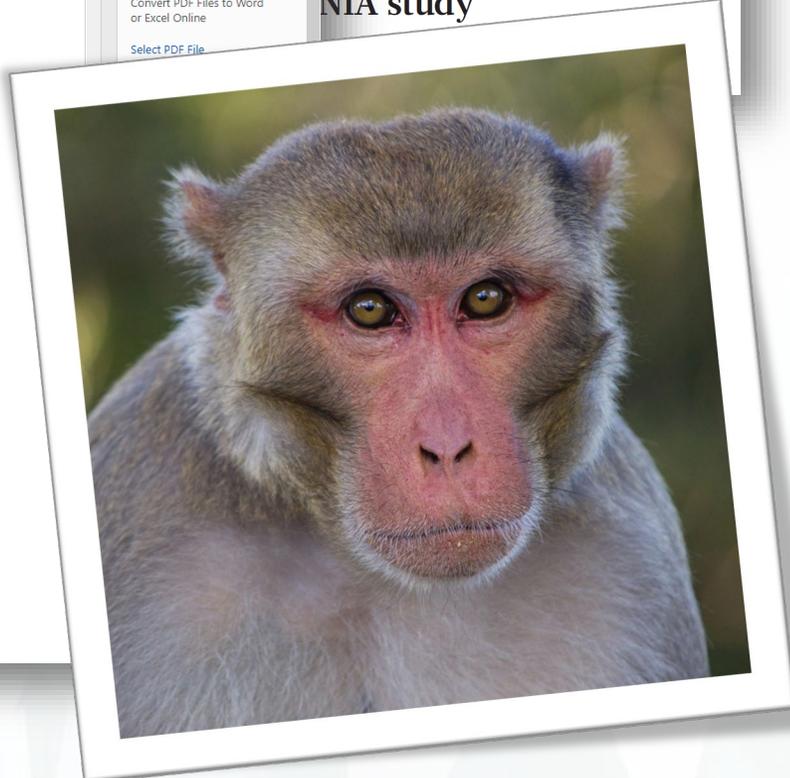
A Ketogenic Diet Extends Healthspan in Adult Mice

Megan N. Roberts,¹ Marita A. Wallace,² Alexey A. Tonouchi,¹ Gabriella Perez,¹ Elena Gutierrez-Casado,⁷ Shinichiro Kyoungmi Kim,⁵ Kevork Hagopian,¹ Marissa Z. McManus,¹ Jon J. Ramsey,^{1,9,*} and Jose Alberto Lopez-Dominguez,¹

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⁵Department of Public Health Sciences, School of Medicine
⁶Department of Physiology and Membrane Biology, School of Medicine, University of California, Davis, CA, USA
⁷Departamento de Biología Celular, Fisiología e Inmunología, Universidad de Córdoba, Córdoba, Spain
⁸Present address: Buck Institute for Research on Aging, Novato, CA, USA



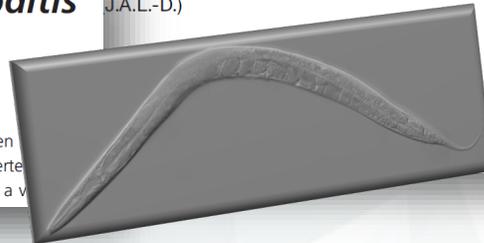
on health and survival in NIA study



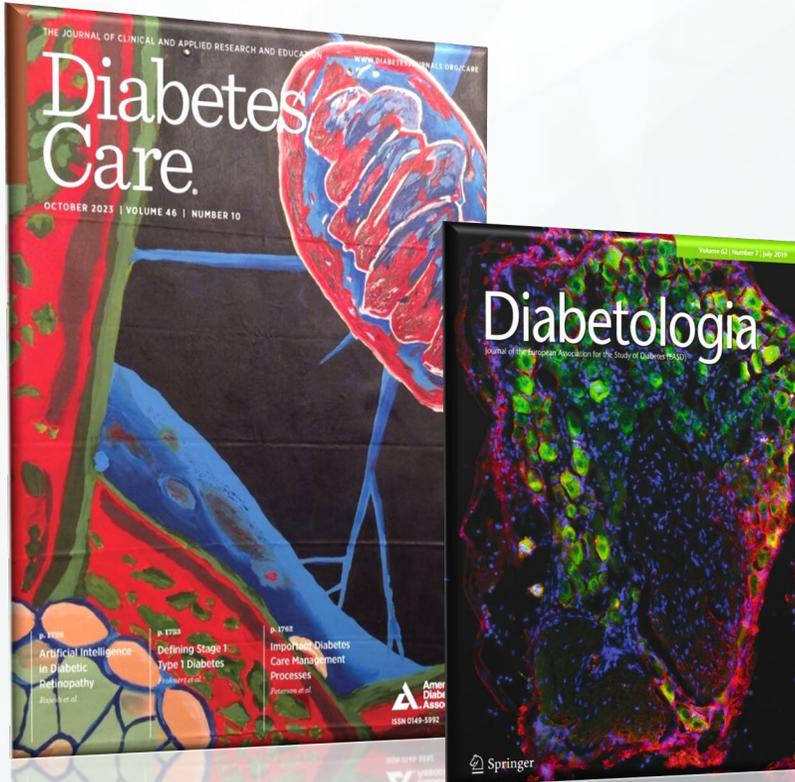
Dietary deprivation extends lifespan in *Caenorhabditis elegans*

Garrick D. Lee,¹ Mark A. Wilson,² Min Zhu,¹ Catherine A. Wolkow,² Rafael de Cabo,¹ Donald K. Ingram,^{1,3} and Sige Zou¹

dietary restriction (DR) (Masoro, 2005). DR has been shown to extend lifespan in many species, ranging from invertebrates to mammals. In addition, DR enhances resistance to a variety of stressors.



Consensus Report: Published August 2024



CONSENSUS REPORT

Hyperglycaemic crises in adults with diabetes: a consensus report

Guillermo E. Umpierrez¹  · Georgia M. Davis¹  · Nuha A. ElSayed^{2,3}  · Gian Paolo Fadini^{4,5}  ·
Rodolfo J. Galindo⁶  · Irl B. Hirsch⁷  · David C. Klonoff⁸  · Rozalina G. McCoy^{9,10}  · Shivani Misra^{11,12}  ·
Robert A. Gabbay^{2,3}  · Raveendhara R. Bannuru²  · Ketan K. Dhatariya^{13,14} 

Received: 28 March 2024 / Accepted: 29 March 2024 / Published online: 22 June 2024
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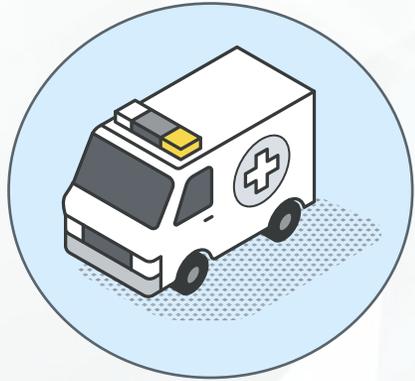
New DKA Diagnostic Criteria

DKA	Diabetes/hyperglycaemia	Glucose ≥ 200 mg/dl (11.1 mmol/l) or prior history of diabetes
	Ketosis	β -hydroxybutyrate ≥ 3.0 mmol/l or urine ketone strip 2+ or greater
	Metabolic Acidosis	pH < 7.3 and/or bicarbonate concentration < 18 mmol/l

Physiological vs Pathological

- It's the rate of appearance and the ability for renal and respiratory compensation for the drop in pH
- A rise of β hydroxybutyrate of ≥ 0.2 mmol/l/hr might be considered 'pathological'
- But there are currently no technologies available to allow prediction or prevention other than glucose meters that say 'Hi' and 'Check ketones' or point of care capillary ketone meters

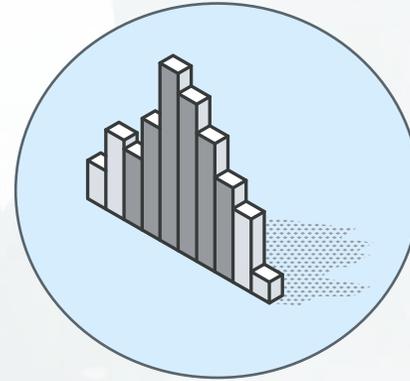
Any Age and Any Kind of Diabetes



Most common
hyperglycemic emergency
in persons living with
diabetes



DKA is a **leading**
cause of death among
children and adults
(< 58) with diabetes



1%–13% annual
prevalence of DKA
in adults with T1D
across countries

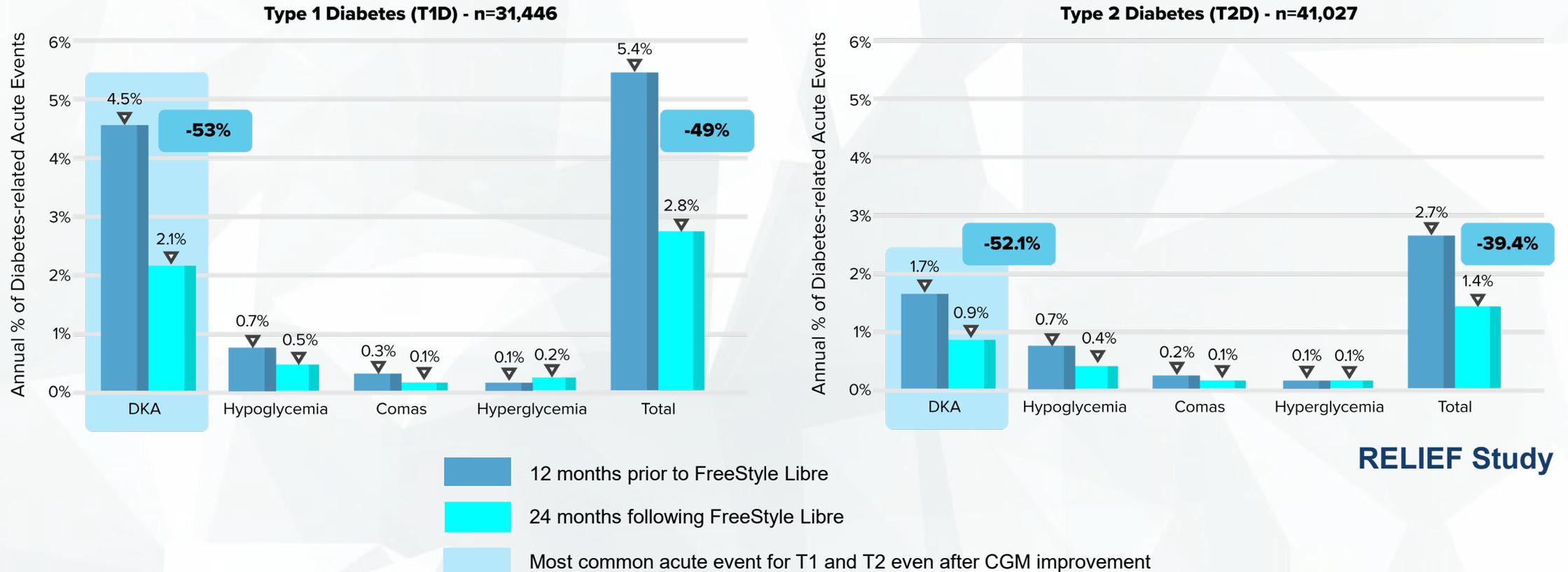


 **Hospitalization for**
DKA: 1 in 5 cases
attributed to T2D

 **Higher mortality for**
T2D (0.85%) with
DKA than T1D (0.2%)

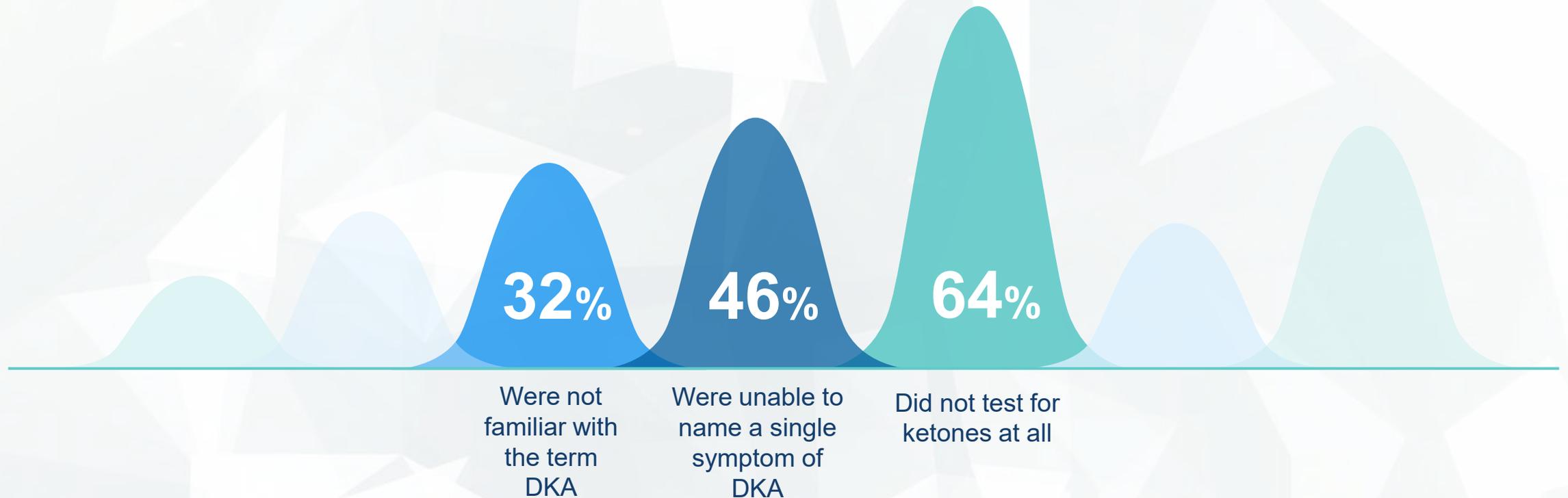
FSL Users Have ~ 50% Decreased Acute Events

Acute diabetes events before and after FreeStyle Libre systems in 74,011 FSL users with T1 or T2D 2015-2018*



DKA Unawareness

Multinational, multicenter survey of endocrine outpatient clinic patients with average duration of T1D of 22 years (N=333)



No Self-Monitoring

< 20%

Test ketone levels,
even when glucose is
> 16.7 mmol/L for
1 hour or more

38%

Never test ketones
when nauseated
and/or vomiting

45%

Never test ketone
levels when they
detect a fever

Monitoring Ketoneuria in People with Diabetes: Preliminary Findings from Real-World Studies

- Real-world assessment of ketones in individuals living with type 1 and type 2 diabetes
- Data taken from Freestyle Libre and fingerstick ketone measures
- 3,023,587 ketone tests performed among 165,108 readers from 89 countries
- Most (87%) of readings were in normal range
- Few (1.8%) readings were above the threshold of $>3.0\text{mmol/L}$

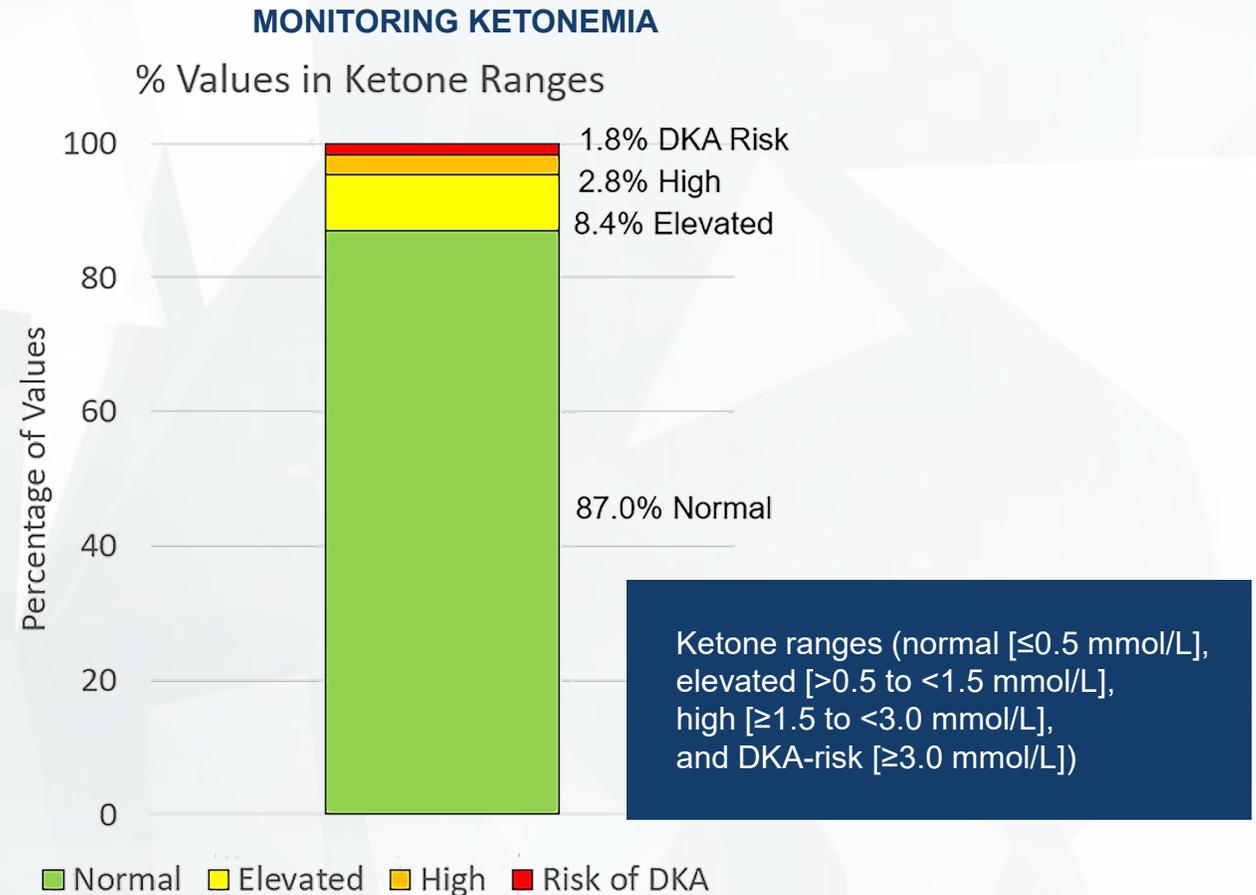


FIG. 1. Ketone test values for all participants ($n = 3,023,587$)

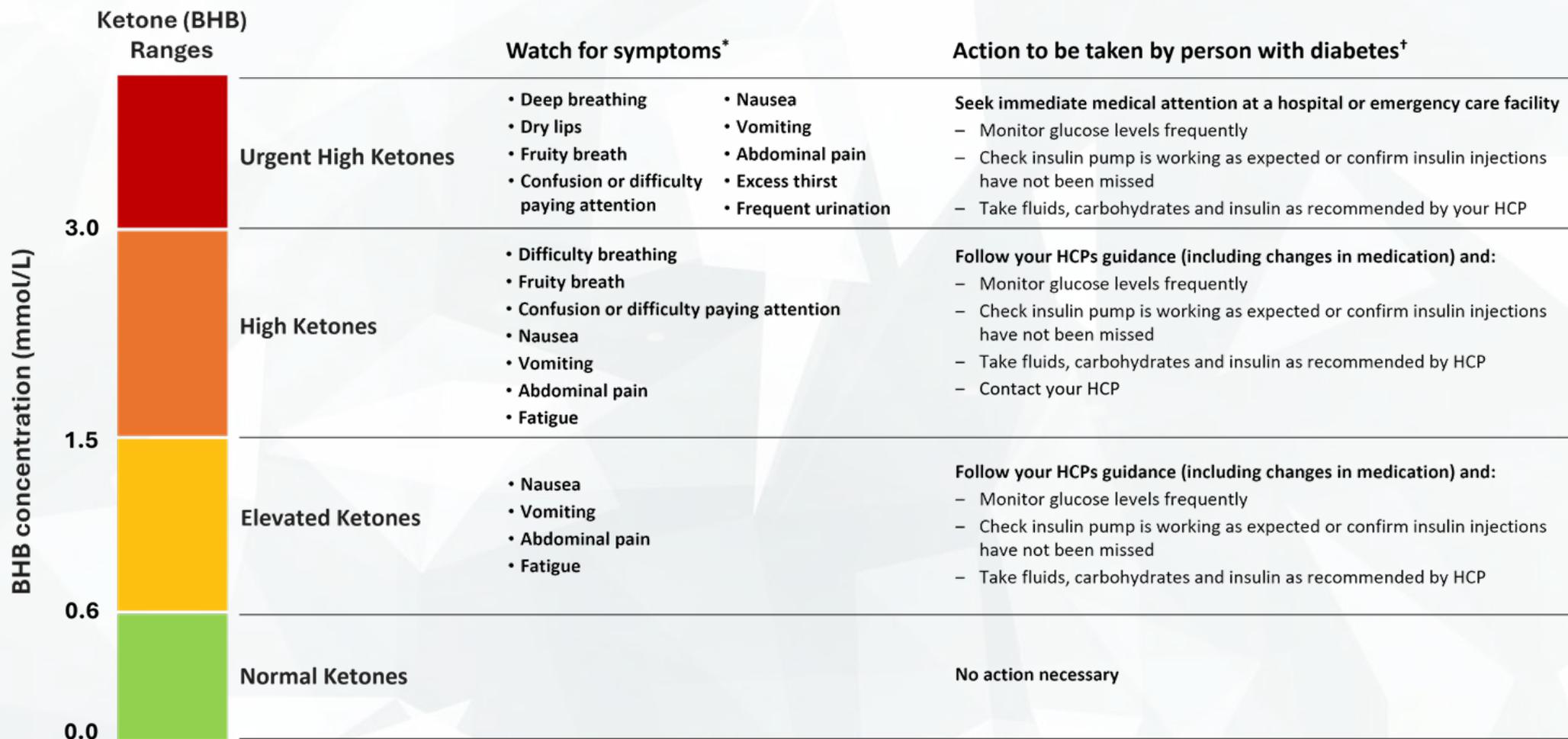
Suggested Use



Continuous ketone monitoring for people with diabetes: international expert recommendations on the application of a new technology

Ketan Dhatariya, Richard M Bergenstal*, Mohammed Al-Sofiani, Anastasia Albanese-O'Neill, Tadej Battelino, Kelly Close, Christophe De Block, Sanjoy Dutta, Rodolfo J Galindo, Amin GhavamiNejad, Ahmad Haidar, Julie Heverly, Davida Kruger, Lori M Laffel, Julianne Lally, David M Maahs, Claudio Maffeis, Chantal Mathieu, Eden Miller, Medha Munshi, Rimei Nishimura, Kirsten Nørgaard, Tal Oron, David N O'Neal, Monica Oxenreiter, Bruce A Perkins, Moshe Phillip, Eric Renard, Jonathan Rosen, Mauro Scharf, Jennifer Sherr, Carol Wysham, Thomas Danne*

Suggested Thresholds



Suggested Graphics

Orientation	Interpretation
	Ketones are rising faster than 0.4 mmol/L/h
	Ketones are changing slowly , less than or equal to 0.4 mmol/L/h
	Ketones are falling faster than 0.4 mmol/L/h

Suggested Actions

STOP DKA considerations for bolus insulin and CHO			
Continuous ketone concentration (mmol/L)	Blood glucose meter / CGM value (check every hour)*		
	4.0-8.0 mmol/L (70-150 mg/dL)	8.1-14.0 mmol/L (151-250 mg/dL)	>14 mmol/L (>250 mg/dL)
<0.6 Normal	<ul style="list-style-type: none"> No extra insulin Usual bolus to cover CHO + usual correction 		<ul style="list-style-type: none"> 5-10% TDD supplemental insulin or usual correction bolus Usual bolus to cover CHO
0.6–1.5 Elevated Ketonemia <i>Consider rate of change arrow</i>	<ul style="list-style-type: none"> 5% TDD supplemental insulin + usual bolus to cover CHO 30 - 45 g CHO every 2-4 hours 	<ul style="list-style-type: none"> 10% TDD supplemental insulin or 1.5x correction bolus Usual bolus to cover CHO 30 g CHO every 2-4 hours 	<ul style="list-style-type: none"> 10% TDD supplemental insulin or 1.5x correction bolus Usual bolus to cover CHO every 2-4 hours
1.6–2.9 High Impending DKA <i>Consider rate of change arrow</i>	<ul style="list-style-type: none"> 10% TDD supplemental insulin + usual bolus to cover CHO 30 - 45 g CHO every 2-4 hours 	<ul style="list-style-type: none"> 20% TDD supplemental insulin or 2x correction bolus Usual bolus to cover CHO 30 - 45 g CHO every 2-4 hours 	<ul style="list-style-type: none"> 20% TDD supplemental insulin or 2x correction bolus Usual bolus to cover CHO every 2-4 hours
≥3.0 Urgent High Probable DKA	<ul style="list-style-type: none"> 10% TDD supplemental insulin + usual bolus to cover CHO 30 - 45 g CHO every 2-4 hours 	<ul style="list-style-type: none"> 20% TDD supplemental insulin or 2x correction bolus Usual bolus to cover CHO 30 - 45 g CHO every 2-4 hours 	<ul style="list-style-type: none"> 20% TDD supplemental insulin or 2x correction bolus Usual bolus to cover CHO every 2-4 hours

DKA is likely if ketones remain ≥3 mmol/L (Continuous Ketone System Alarm) despite supplemental insulin

Potentials

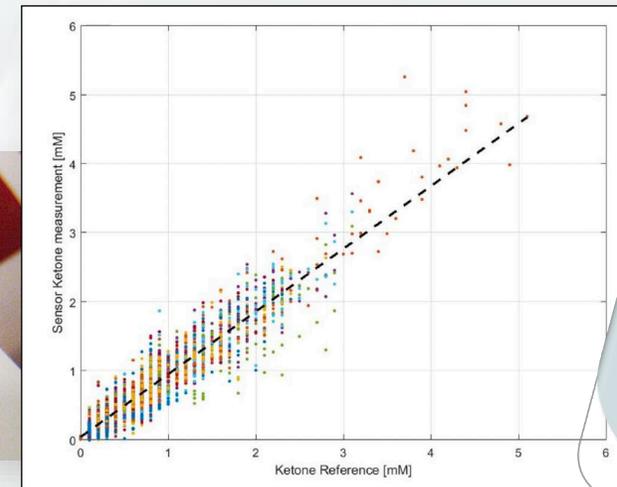
There are several!

- Helping to identify a rise in ketones allowing the implementation of sick day rules
- Early warning of pump/infusion set failure
- Preventing acute illness/hospital admission
- High risk people may get most benefits – recurrent DKA, poor social circumstance, meal insecurity, homeless, etc
- Fewer pieces of ‘kit’ to carry about
- Developing an AID algorithm that incorporates ketones/sick day rules

Challenges & Unknowns

There are several!

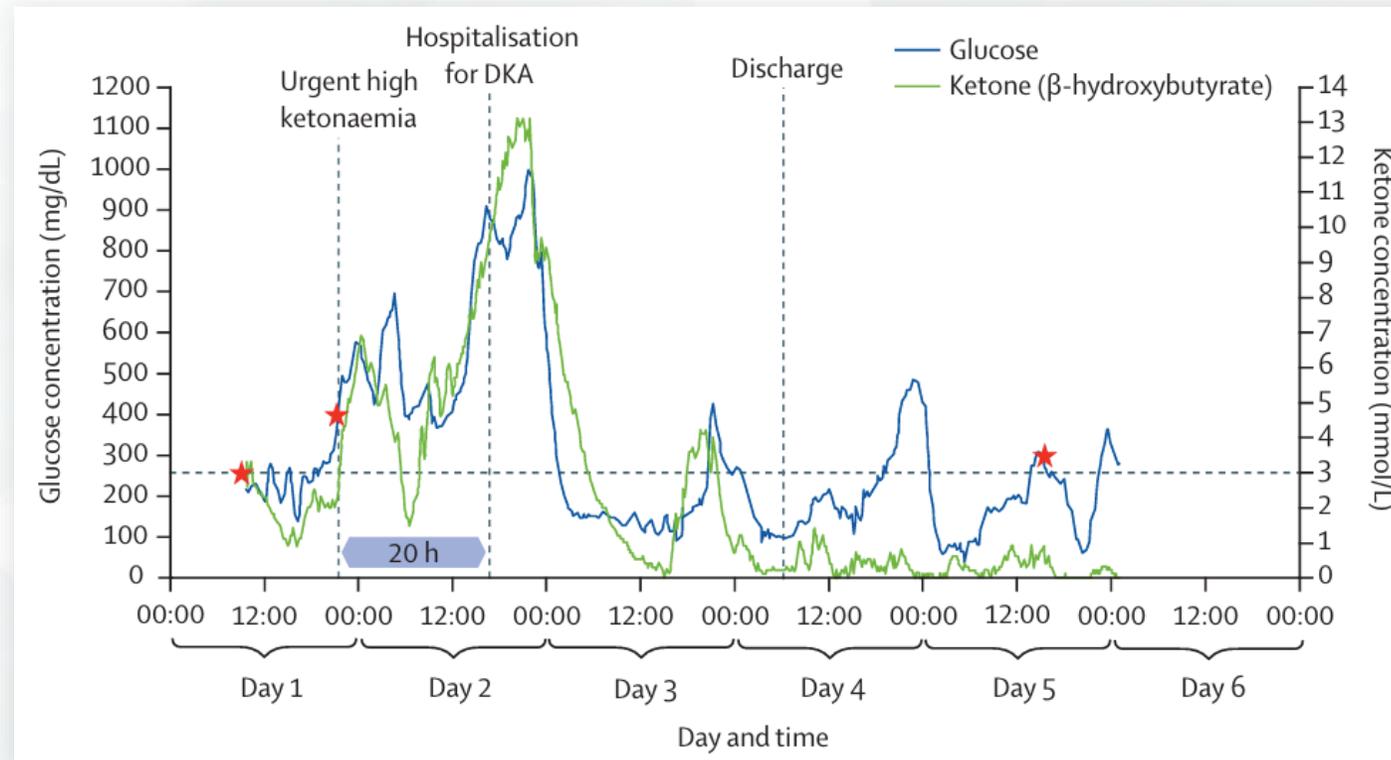
- Education of people with diabetes – what do the numbers mean?
- Education of health care professionals – what do the numbers mean?
- When does physiological become pathological?
- Are there significant differences between blood/capillary and interstitial fluid?
- T1DM vs T2DM
- How to manage euglycaemic ketonaemia/DKA
- Reimbursement?



Interprofessional Team Overview in DKA Care

- Nurse coordinators
- Social workers
- Psychologists
- Dietitians
- Advanced practice providers
- School nurses
- Pharmacists
- Diabetes care and education specialists

Case Study: A 14-year-old girl with T1D enrolled in a study using a blinded glucose/ketone sensor



An urgent high ketone level (≥ 3.0 mmol/L) was measured 20 h before hospitalization with full clinical symptoms of DKA. Resolution of DKA can be seen with initiation of an insulin drip following admission, with a slight elevation in glucose and ketones towards the end of the treatment period.

Key Takeaways

- Ketones are an evolutionary adaptation to prolonged starvation
- Their presence can be beneficial or harmful – depending on the rate of appearance in the circulation
- Continuous ketone measurement seems to be the next logical step in the management of type 1 diabetes, and incorporation into an AID system seems likely
- Challenges remain but the potential for benefit is huge



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Means for Practice



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Supported by an educational grant from Abbott Diabetes Care.