University of East Anglia

Norfolk and Norwich University Hospitals NHS
NHS Foundation Trust

Diabetes Related Emergencies – DKA and HHS – What is About to Change?

Prof Ketan Dhatariya MBBS MSc MD MS FRCP PhD
Consultant in Diabetes and Endocrinology
Norfolk and Norwich University Hospitals

JBDS-IP Joint British Diabetes Societies for Inpatient Care
Association of British Clinical Diabetologists
Endotext

Disclosures

- In the last 12 months I have received honoraria, travel or fees for advisory boards from
  - AstraZeneca
  - Novo Nordisk
  - Boehringer-Ingelheim
  - Eli Lilly
  - Abbott Diabetes
  - Menarini

Who is This Strange Man?

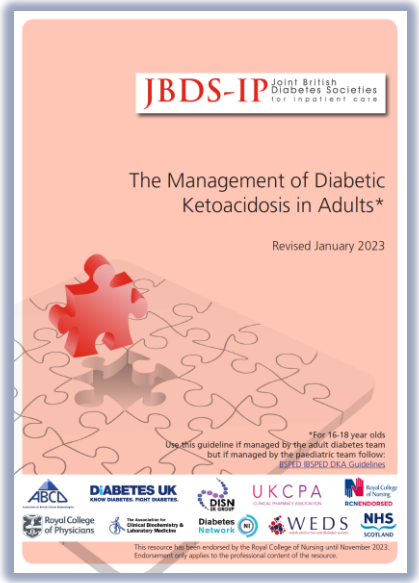
- I qualified in 1991
- I trained in D&E and G(I)M in London
- I did general practice for 2 years
- I did ITU / anaesthetics for a year
- I did research at Mayo Clinic for 2 years on DHEA
- I have been in Norwich since 2004
- Currently my other roles include
  - Chair of the Association of British Clinical Diabetologists
  - Chair of the Specialist Clinical Exam in D&E
  - Immediate Past Chair of the Joint British Diabetes Societies for Inpatient Care
  - Immediate Past-President of the Endocrine Section of the Royal Society of Medicine

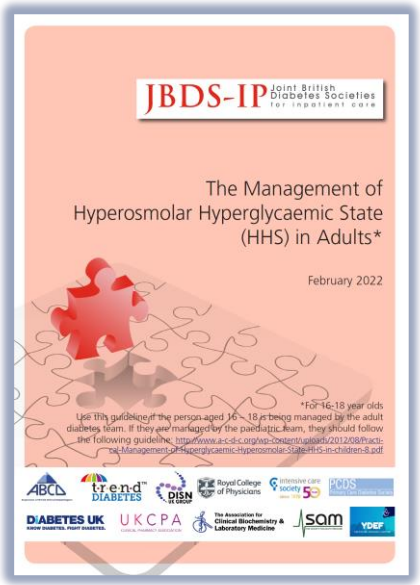
Before We Start – A Warning

- Much of what I am going to say in the next few minutes will change in October 2023
- There is a new global consensus document being written by ADA / EASD / JBDS / AACE / DTS
- However

Before We Start – Some Reassurance

- It will almost be the same as the UK JBDS documents on DKA and HHS





To find them type 'JBDS guidelines' into Google

Current Diagnostic Criteria – ADA and JBDS

	DKA		
	Mild (plasma glucose >250 mg/dl)	Moderate (plasma glucose >250 mg/dl)	Severe (plasma glucose >250 mg/dl)
Arterial pH	7.25–7.30	7.00 to <7.24	<7.00
Serum bicarbonate (mEq/l)	15–18	10 to <15	<10
Urine ketone	Positive	Positive	Positive
Serum ketone	Positive	Positive	Positive
Effective serum osmolality	Variable	Variable	Variable
Anion gap	>10	>12	>12
Mental status	Alert	Alert/drowsy	Stupor/coma

DIAGNOSIS:

Ketonaemia ≥ 3.0mmol/L **or** significant ketonuria (more than 2+ on standard urine sticks)

Blood glucose > 11.0mmol/L or known diabetes mellitus (200 mg/dL)

Bicarbonate (HCO_3^-) < 15.0mmol/L **and/or** venous pH < 7.3

ADA, American Diabetes Association; DKA, diabetic ketoacidosis; JBDS, Joint British Diabetes Societies.

Kitabchi AE, *et al. Diabetes Care* 2009;32:1335–1343;

Association of British Clinical Diabetologists. Joint British Diabetes Societies (JBDS) for Inpatient Care Group. The management of diabetic ketoacidosis (DKA) in adults | ABCD (Diabetes Care) Ltd

Differences

Table 1 UK vs USA diagnostic criteria for DKA

		UK	USA		
			Mild	Moderate	Severe
"D"—a glucose concentration		>11.0 mmol/L (200 mg/dL) or a previous history of diabetes mellitus	>13.9 mmol/L (>250 mg/dL)	>13.9 mmol/L (>250 mg/dL)	>13.9 mmol/L (>250 mg/dL)
"K"—the presence of ketones		>3.0 mmol/L or significant (>2+) on standard urine ketone sticks	Urine or serum ketone positive	Urine or serum ketone positive	Urine or serum ketone positive
"A"—confirmation of an acidosis	pH	<7.3	7.25 to 7.30	7.00 to <7.24	<7.00
	Serum bicarbonate (mmol/L)	<15	15 to 18	10 to <15	<10
	Anion gap	Not applicable	>10	>12	>12

Dhatariya KK et al Curr Diab Rep 2017;17(5):33-39

2009 ADA Consensus Guideline

- No insistence on the ‘D’, the ‘K’, and the ‘A’ to diagnose DKA
- No clear acknowledgement of euglycaemic DKA
- No recommendation to use bedside ketone measurements to monitor and guide treatment
- No recommendation to continue long acting subcutaneous insulin

Guidelines for management of diabetic ketoacidosis: time to revise?

Dhatariya K et al Lancet Diab Endocrinol 2017;5(5):321-323

Diagnostic Criteria – DKA

- **The 'D'** – A blood glucose >200mg/dl (11.1mmol/l) **OR** a known history of diabetes
- **The 'K'** – A blood ketone concentration of >3.0mmol/l or >2+ on urine ketostix
- **The 'A'** – A pH <7.3 **AND/OR** a bicarbonate <18.0mmol/l

Euglycaemic DKA?

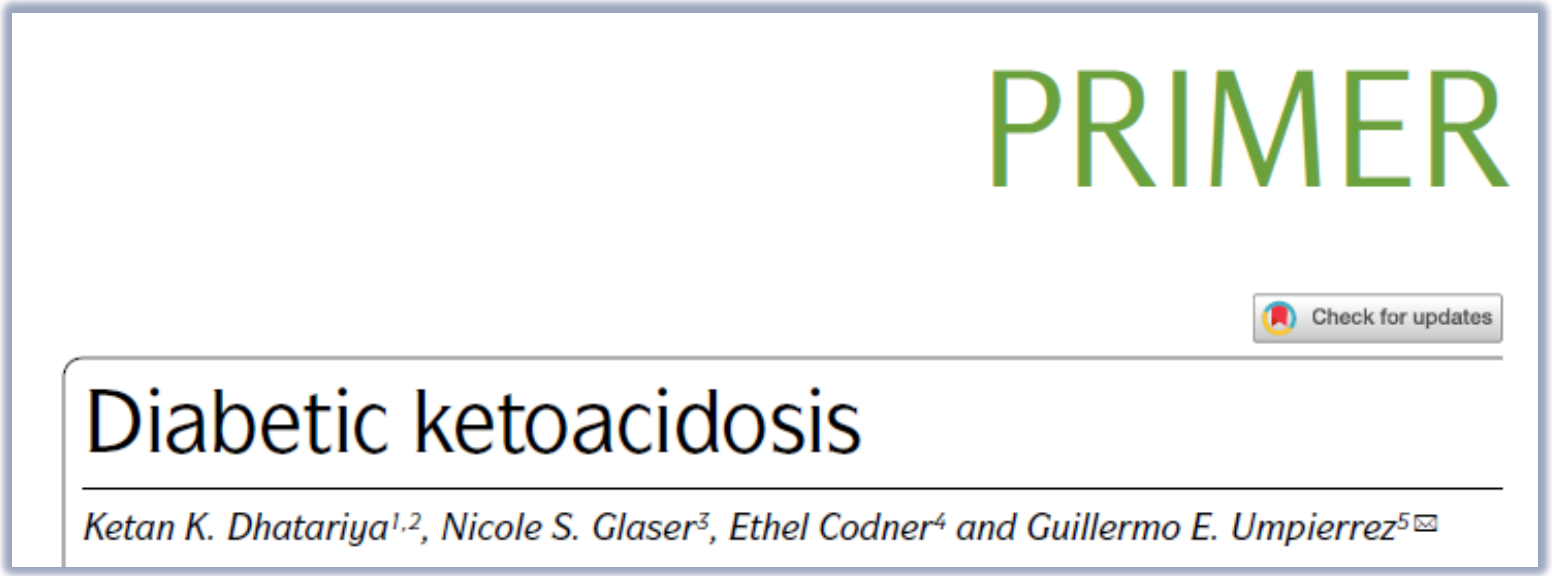
TABLE. Prevalence of Euglycemic Diabetic Ketoacidosis in People With Type 1 Diabetes in the United Kingdom[a]

	Number	Admission glucose <11.0 mmol/L (200 mg/dL)[1]	Admission glucose <13.9 mmol/L (250mg/dL)[2]	Admission glucose <16.7 mmol/L (300 mg/dL)[3]
National survey (2014)[4]	277	6	14	23
Local audit (2015)[5]	57	4	4	6
	334	10	18	29
		3.0%	5.4%	8.7%

[a]Data from a national survey[4] and local audit.[5] Data are divided into different thresholds of "euglycemia."

Munro JF et al BMJ 1973;2(5866):578-5880
Kitabchi AE et al Diab Care 2009;32(7):1335-1343
Dhatariya K et al Diab Med 2016;33(2):252-260
Macfarlane J et al Mayo Clin Proc 2019;94(9):1909-1910

If Anyone is Interested



Dhatariya K et al Nature Rev Dis Primers 2020;6:40

HHS - Fewer Differences

Table 2 UK vs USA diagnostic criteria for HHS

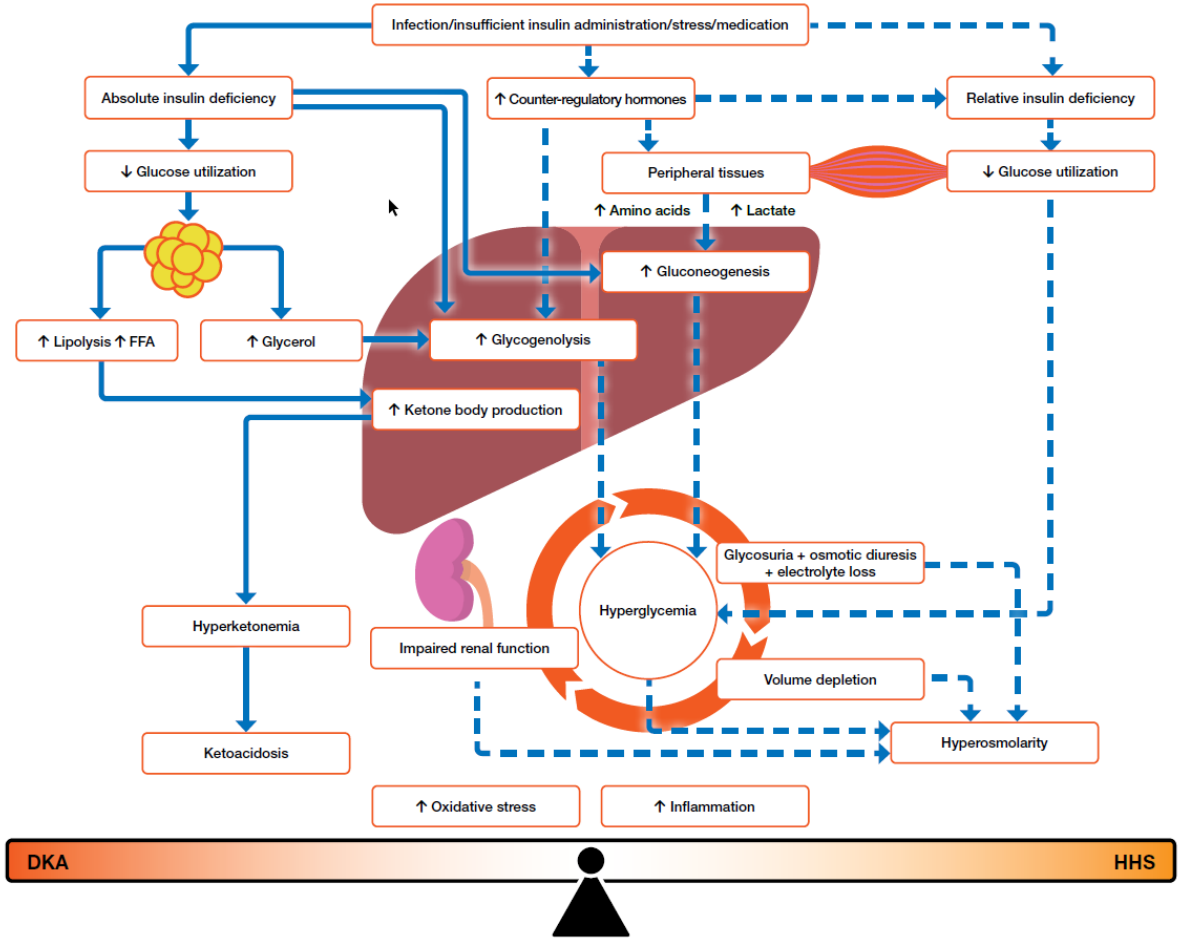
		UK	USA
Hyperglycemia		>30 mmol/L (540 mg/dL)	>33.3 mmol/L (600 mg/dL)
Hyperosmolarity		>320 mOsm/kg	>320 mOsm/kg
	Calculation	2 × Na (mmol/L) + glucose (mmol/L) + urea (mmol/L)	2 × Na (meQ/L) + glucose (mg/dL)/18 + blood urea nitrogen (mg/dL)]/2.8
Lack of acidosis	Ketones	Low	Low
	pH	>7.3	>7.3
	Bicarbonate	>15 mmol/L	>20 mmol/L
Mental status changes		Present	Present

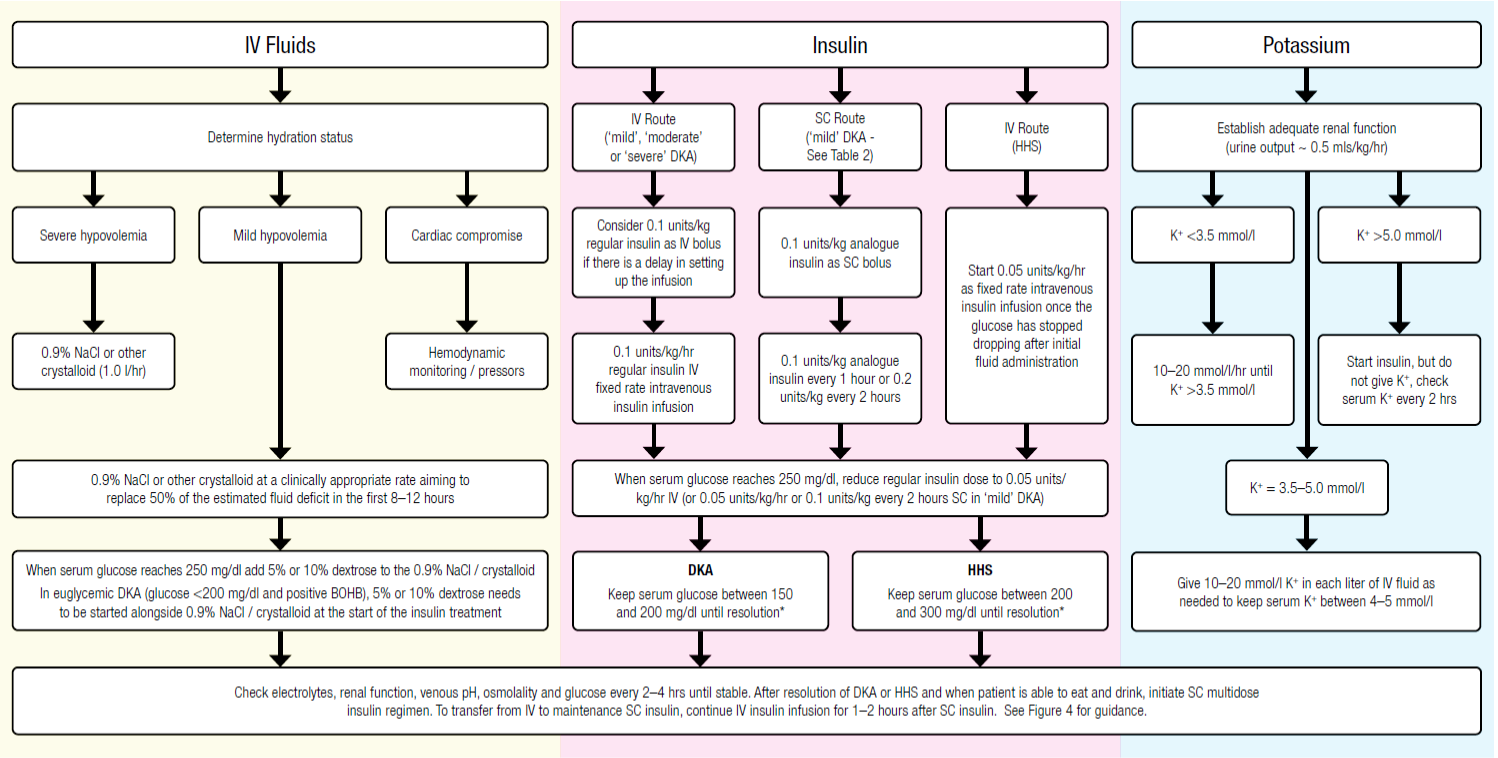
- No unified diagnostic criteria
- HHS and DKA frequently occur together – treat as DKA
- No clear criteria for resolution

Dhatariya KK et al Curr Diab Rep 2017;17(5):33-39

Diagnostic Criteria – HHS

- **Hyperglycemia** – a glucose of >600mgdl (33.3mmol/l)
- **Hyperosmolality** - Calculated effective serum osmolality >300 mosml/l (calculated as [2xNa^+ (mmol/l) + glucose (mmol/l)]), **OR** total osmolality >320 mosml/l [(2xNa^+ (mmol/l) + glucose (mmol/l) + urea (mmol/l)]
- **Absence of significant ketonemia** – plasma ketones of <3.0mmol/l or <2+ on standard urine ketone sticks
- **Absence of acidosis** – a pH>7.3 and serum bicarbonate of >15mmol/l


Infection/insufficient insulin administration/stress/medication
Absolute insulin deficiency
↑ Counter-regulatory hormones
Relative insulin deficiency
↓ Glucose utilization
Peripheral tissues
↓ Glucose utilization
↑ Amino acids
↑ Lactate
↑ Gluconeogenesis
↑ Lipolysis ↑ FFA
↑ Glycerol
↑ Glycogenolysis
↑ Ketone body production
Glycosuria + osmotic diuresis + electrolyte loss
Hyperglycemia
Hyperketonemia
Impaired renal function
Volume depletion
Ketoacidosis
Hyperosmolarity
↑ Oxidative stress
↑ Inflammation
DKA
HHS



*Definitions of resolution (use clinical judgement and do not delay discharge or level of care if these are not met):

- **DKA:** Plasma ketone < 0.6 mmol/l and venous pH > 7.3 or bicarbonate > 18 mmol/l
- **HHS:** Calculated serum osmolality falls to < 300 mosm/Kg and urine output is > 0.5 ml/kg/hr, and cognitive status is back to the baseline state, and glucose is < 250 mg/dl

150 mg/dl = 8.3 mmol/l
200 mg/dl = 11.0 mmol/l
250 mg/dl = 13.9 mmol/l
300 mg/dl = 16.6 mmol/l

Bicarbonate should only be considered if pH is <7.0

Phosphate should not be given unless there is muscle weakness, respiratory compromise and a phosphate <1.0 mmol/l

Treatment – Fluids

- Fluids started ASAP (usually 0.9% sodium chloride but increasing evidence for balanced crystalloid)

Treatment – Insulin

- DKA
  - 0.1units/Kg/hr started when the diagnosis is made and reduced to 0.05units/Kg/hr when the glucose drops to <14mmol/l
- HHS
  - 0.05units/Kg/hr started when the glucose stops dropping after initial fluid resuscitation
    - There is a comment on whether continuing sc basal insulin should be continued – it should be *considered*

Potassium

- Insulin treatment should not be started unless the potassium is >3.5mmol/l

Definition of Resolution – DKA

- pH >7.3 or bicarbonate >18
- Plasma ketones <0.6mmol/l
- Avoid using anion gap

Definition of Resolution – HHS

- Glucose <250mg/dl (13.9mmol/l)
- Osmolality <300mOsmol/Kg
- Hypovolaemia corrected (urine output ≥0.5ml/kg/h)
- Cognitive status is back to the pre-morbid state

In Summary

- Guidelines for DKA and HHS exist but are (subtly) different in places
- The ADA Consensus document is quite outdated and a new global consensus document is out in October 2023
- There remain gaps in the evidence for what we do, but for the time being, these documents seem to work well

University of East Anglia

Norfolk and Norwich University Hospitals NHS
NHS Foundation Trust

Diabetes Related Emergencies – DKA and HHS – What is About to Change?

www.norfolkdiabetes.com

ketan.dhatariya@nnuh.nhs.uk

@ketandhatariya

@ABCDiab

@JBDSIP

JBDS-IP Joint British Diabetes Societies for Inpatient Care

Association of British Clinical Diabetologists

Endotext