DKA Pathway of Care
Fluid Resusitation in Adult Diabetic Ketoacidosis

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Team Work

DKA is a medical emergency with a significant morbidity and mortality. It should be diagnosed promptly and managed intensively

Institute for Safe Medication Practices

ISMP's List of *High-Alert* Medications

High-alert medications are drugs that bear a heightened risk of causing significant patient harm when they are used in error. Although mistakes may or may not be more common with these drugs, the consequences of an error are clearly more devastating to patients. We hope you will use this list to determine which medications require special safeguards to reduce the risk of errors. This may include strategies such as standardizing the ordering, storage, preparation, and administration of these products; improving access to information about these drugs; limiting access to high-alert medications; using auxiliary labels and automated alerts; and employing redundancies such as automated or independent double-checks when necessary. (Note: manual independent double-checks are not always the optimal error-reduction strategy and may not be practical for all of the medications on the list).

Classes/Categories of Medications
adrenergic agonists, IV (e.g., EPINEPHrine, phenylephrine, norepinephrine)
adrenergic antagonists, IV (e.g., propranolol, metoprolol, labetalol)
anesthetic agents, general, inhaled and IV (e.g., propofol, ketamine)
antiarrhythmics, IV (e.g., lidocaine, amiodarone)
antithrombotic agents, including: ■ anticoagulants (e.g., warfarin, low-molecular-weight heparin, IV unfractionated heparin) ■ Factor Xa inhibitors (e.g., fondaparinux) ■ direct thrombin inhibitors (e.g., argatroban, bivalirudin, dabigatran etexilate, lepirudin) ■ thrombolytics (e.g., alteplase, reteplase, tenecteplase) ■ glycoprotein IIb/IIIa inhibitors (e.g., eptifibatide)
cardioplegic solutions
chemotherapeutic agents, parenteral and oral
dextrose, hypertonic, 20% or greater
dialysis solutions, peritoneal and hemodialysis
epidural or intrathecal medications
hypoglycemics, oral
inotropic medications, IV (e.g., digoxin, milrinone)
insulin, subcutaneous and IV
liposomal forms of drugs (e.g., liposomal amphotericin B) and conventional counterparts (e.g., amphotericin B desoxycholate)
moderate sedation agents, IV (e.g., dexmedetomidine, midazolam)
moderate sedation agents, oral, for children (e.g., chloral hydrate)
narcotics/opioids ■ IV ■ transdermal ■ oral (including liquid concentrates, immediate and sustained-release formulations)
neuromuscular blocking agents (e.g., succinylcholine, rocuronium, vecuronium)
parenteral nutrition preparations
radiocontrast agents, IV
sterile water for injection, inhalation, and irrigation (excluding pour bottles) in containers of 100 mL or more
sodium chloride for injection, hypertonic, greater than 0.9% concentration

Specific Medications
epoprostenol (Flolan), IV
magnesium sulfate injection
methotrexate, oral, non-oncologic use
opium tincture
oxytocin, IV
nitroprusside sodium for injection
potassium chloride for injection concentrate
potassium phosphates injection
promethazine, IV
vasopressin, IV or intraosseous

Background

Based on error reports submitted to the ISMP National Medication Errors Reporting Program, reports of harmful errors in the literature, and input from practitioners and safety experts, ISMP created and periodically updates a list of potential high-alert medications. During October 2011–February 2012, 772 practitioners responded to an ISMP survey designed to identify which medications were most frequently considered high-alert drugs by individuals and organizations. Further, to assure relevance and completeness, the clinical staff at ISMP, members of our advisory board, and safety experts throughout the US were asked to review the potential list. This list of drugs and drug categories reflects the collective thinking of all who provided input.

ISMP
www.ismp.org

Typical Deficits in DKA

Water (ml/kg)	**100**
Sodium (mmol/kg)	**7 – 10**
Chloride (mmol/kg)	**3 – 5**
Potassium (mmol/kg)	**3 - 5**

Infusion solution	Advantages	Disadvantages
0.9% NaCl	• Decades of clinical experience • Readily available in clinical areas • Commercially available ready mixed potassium at required concentrations, 20mmol/L (0.15%) or 40mmol/L (0.3%) • Supports safe practice with injectable potassium (NPSA compliant	Hyperchloraemic metabolic acidosis which may cause renal arteriolar vasoconstriction leading to oliguria and a slowing of resolution of acidosis

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Definition and Diagnosis

Definition	Diagnosis
Biochemical triad of - ketonemia (ketosis) - hyperglycaemia - acidemia	≥ 3.0 mmol/L or ketonuria >2+ BG > 250 mg/dL Bicarbonate (HCO3-) < 15.0 mmol/L and/or pH<7.3

Assesment of Severity

- Blood ketone > 6 mml/L
- Bicarbonate < 5mmol/L
- Venous/arterial pH < 7.0
- Hypokalaemia on admission < 3.5mmol/L
- GCS <12 or abnormal AVPU scale

- Oxygen saturation below 92% on air*
- Systolic BP < 90mmHg
- Pulse > 100 or < 60 bpm
- Anion gap >16

[Anion Gap = $(Na^+ + K^+) – (Cl^- + HCO3^-)$]

* Assuming normal baseline respiratory function

Diagnostic criteria for DKA and HHS

	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

	HHS
	Plasma glucose >600 mg/dl
Arterial pH	>7.30
Serum bicarbonate (mEq/l)	>18
Urine ketone*	Small
Serum ketone*	Small
Effective serum osmolality†	>320 mOsm/kg
Anion gap‡	Variable
Mental status	Stupor/coma

Effective serum osmolality:
2measured Na (mEq/l) glucose (mg/dl)/18.

Anion gap: (Na) (Cl HCO3 (mEq/l)

Approach Consideration

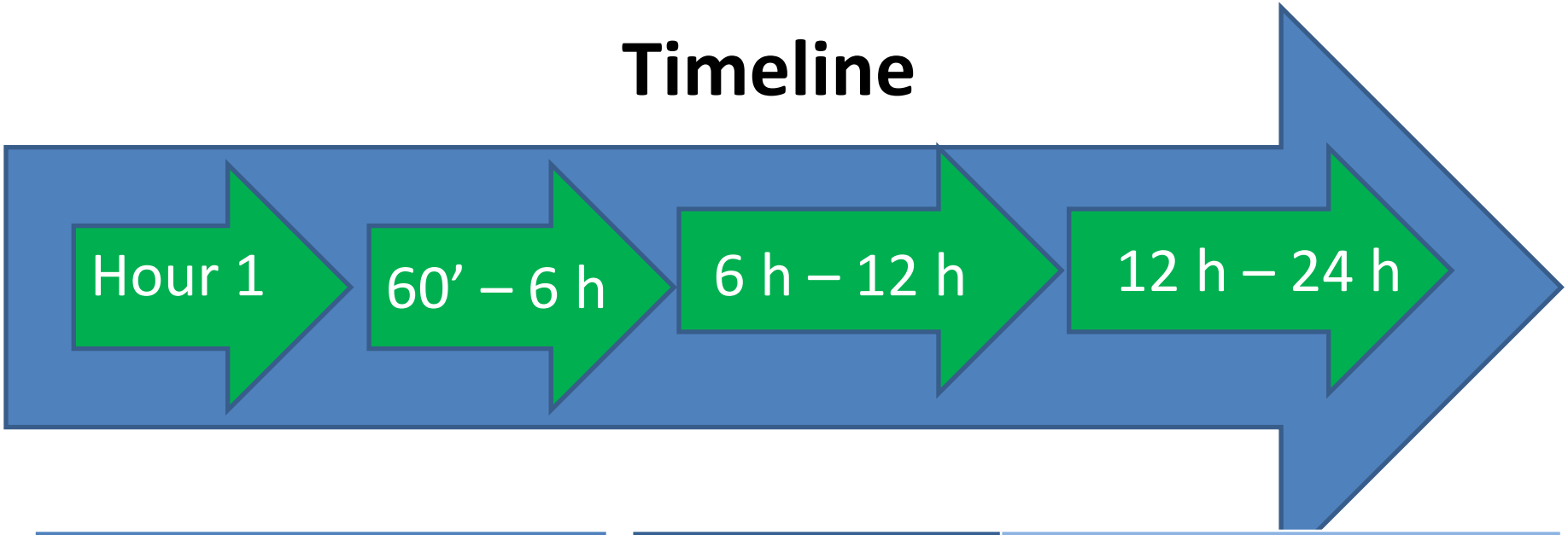
- Correction of fluid loss with IV fluid
- Correction of hyperglycaemia with insulin
- Correction of electrolyte disturbances, particularly potassium loss
- Correction acid-base balance
- Treatment concomittent disease/serious comorbidity

Hamdy O, Khardory R. Diabetic Treatment and Management approachConsideration, Correction of Fluid. Updated: February 08, 2018. MedScape

Serious Complications of DKA and their Treatment

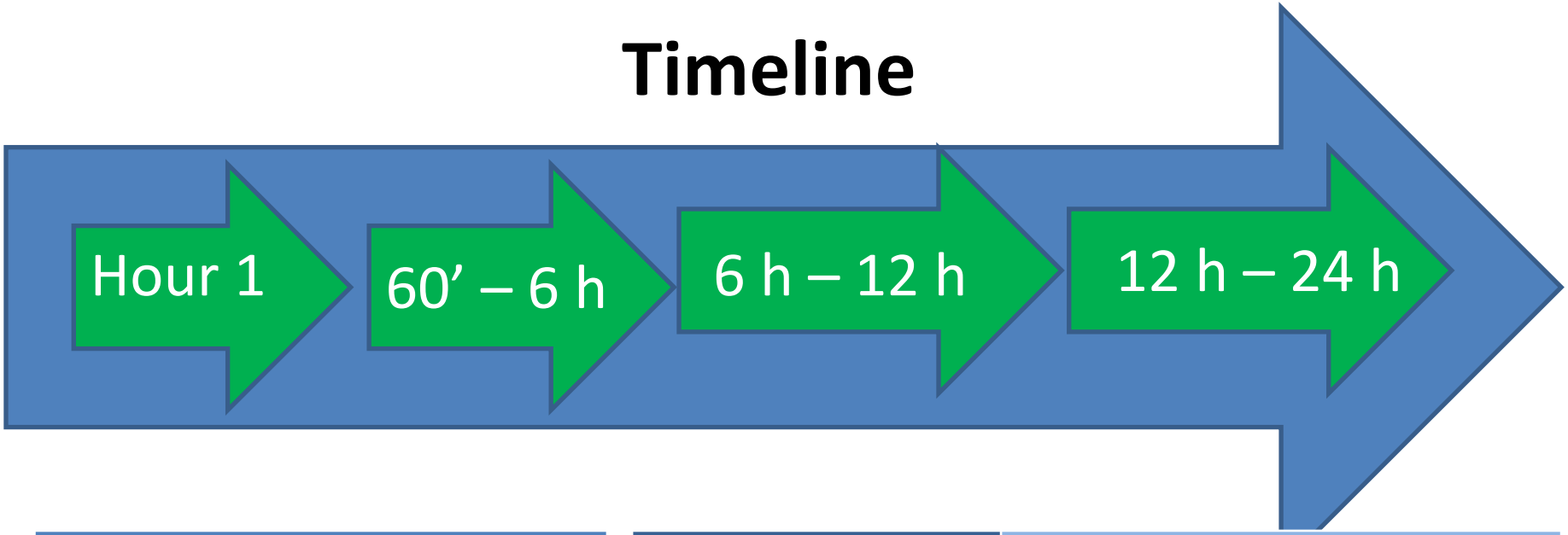
- **Hypokalaemia and hyperkalaemia**
- **Hypoglycaemia**
- **Cerebral oedema**
- **Pulmonary oedema**

Timeline



T = 0 **I.V fluids commene**	**Action 1**
Aims Commence IV 0.9% NaCL Commence FRIII Monitoring regime - BG hourly - Ketone hourly - K+ 2 hourly (at least) Clinical/biochemicalassessment	Action 2
	Action 3
Diabetes Specialist Team	Action 4

Timeline



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Time Line

Hour 1 (0 to 60 minutes)

Action 1: IV access and initial investigation

- Rapid ABC (Airway, Breathing, Circulation)
- Large bore IV, commence IV fluid replacement
- Clinical assessment
- [illegible]

Full Clinical Investigation

- Blood ketones
- Capillary blood glucose
- Venous plasma glucose
- Urea and electrolytes
- Venous blood gases
- Full blood count
- Blood cultures
- ECG
- Chest radiograph if clinically indicated
- Urinalysis and culture
- Continuous cardiac monitoring

Time Line

Hour 1 (0 to 60 minutes)

Action 2: Restoration of circulating volume

Assessment the severity of dehydration using pulse and BP (90 mmHg as aguide)

Systolic BP < 90 mmHg on admission

Give 500 – 1000 ml of 0.9% sodium chloride solution over10-15 minutes

If no improvement consider involving critical care team

Once SBP > 90 mmHg follfow luid replacement as shown below

CAUTION !!!

Young people age 18 – 25 years
Elderly
Pregnant
Heart or kidney failure
Other serious comorbidity

Systolic BP on Admission ≥ 90mmHg

Fluid replacement regimen for a previously well 70kg adult

Fluid	Volume
0.9% sodium chloride 1L *	1000ml over 1st hour
0.9% sodium chloride 1L with potassium chloride	1000ml over next 2 hours
0.9% sodium chloride 1L with potassium chloride	1000ml over next 2 hours
0.9% sodium chloride 1L with potassium chloride	1000ml over next 4 hours
0.9% sodium chloride 1L with potassium chloride	1000ml over next 4 hours
0.9% sodium chloride 1L with potassium chloride	1000ml over next 6 hours
Re-assessment of cardiovascular status at 12 hours is mandatory, further fluid may be required	

0.9% NaCL Solution or Hartmann's Solution for resuscitation

Infusion solution	Advantages	Disadvantages
0.9% sodium chloride	• Decades of clinical experience • Readily available in clinical areas • Commercially available ready mixed with potassium at required concentrations, 20mmol/L (0.15%) or 40mmol/L (0.3%) • Supports safe practice with injectable potassium (NPSA compliant (NPSA alert 2002))	• Hyperchloraemic metabolic acidosis which may cause renal arteriolar vasoconstriction leading to oliguria and a slowing of resolution of acidosis
Compound sodium	• Balanced crystalloid with minimal tendency to hyperchloraemic metabolic acidosis	• Insufficient potassium if used alone • Not commercially available with adequate pre-mixed potassium. Potassium addition in general clinical areas is unsafe. (NPSA alert 2002) • Unfamiliar and not routinely kept on medical wards

Time Line

Hour 1 (0 to 60 minutes)

Action 3: Potassium Replacement

Hypokalaemia and hyperkalaemia are life threatening conditions and are common in DKA. Serum potassium is often high on admission (although total body potassium is low) but falls precipitously upon treatment with insulin.

Regular monitoring is mandatory

Potassium Replacement

Potassium level at first 24 h	K+ replacement in mmol/L of infusion solution
> 5.5	Nil
3.5 – 5.5	40
< 3.5	Senior review

Time Line

Hour 1 (0 to 60 minutes)

Action 4: Commence a FRIII (fixed rate intravenous insulin infusion)

If pregnant use her present weight
Start FRIII via infusion pump
Use human (Actrapid, Humulin R, Insuman R) soluble insulin
Infusion at fixed rate of 0.1 unit/kgBW/hr
Continue Long-acting basal analogue (R/Levemir,R/Lantus, R/Tresiba, R/Glargine 300)

Prepared by Hospital Farmacy
49.5 ml NS + 0.5 ml RI
1 unit RI/1 mlNS

Potassium Replacement

Potassium level at first 24 h	K+ replacement in mmol/L of infusion solution
> 5.5	Nil
3.5 – 5.5	40
< 3.5	Senior review

Time Line

60 minutes to 6 hours

Aims: Commence a FRIII (fixed rate intravenous insulin infusion)

Clear blood ketone and suppressed ketogenesis
Achieve a rate of fall of ketone s of 0.5 mmol/L/hr
Bicarbonate shoul rise by 3.0 mmol/L/hr (If ketone measurement is not available)
Maintain serum K+ in the normal range
Avoid hypoglycaemia

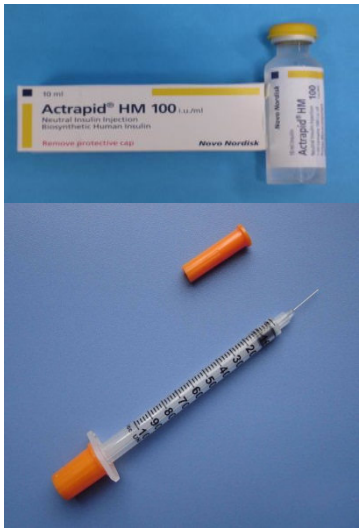
Action 1: Re-assess patient, monitor vital sign

Initially, reviewd patient's response hourly (adequate progress ? Keton ? Glucose?)
Consider urine catheterisation if incontinen tor anuric (anuric by 60 minutes)
Consider NG tube insertion (if persistently vomiting or obtunded)
If the oxygen saturation falls, perform arterial BG measurement and repeat Chest XR
Maintai n an accurate fluid balance (urine output > 0.5 ml/kgBW/hr)
Give low molecular weigt heparin
Continue cardiac monitoring

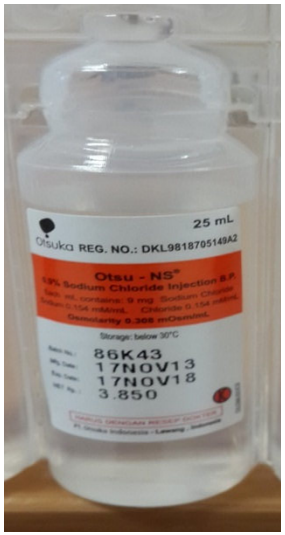
Prescribing and Commencing Continuous Intravenous Insulin Infusion

- Most commonly 1 unit regular human insulin (Actrapid/Humulin R) per 1 ml of 0.9% saline
  - 50 units regular insulin- insulin syringe
  - Made up to 50 mls with 0.9% saline
- Delivered via a syringe driver
- Stop any oral anti-hyperglycaemics or GLP-1 agonists
- Stop any short- or intermediate-acting insulin

Intravenous insulin infusion



50 units regular human insulin
(Actrapid/Humulin R)

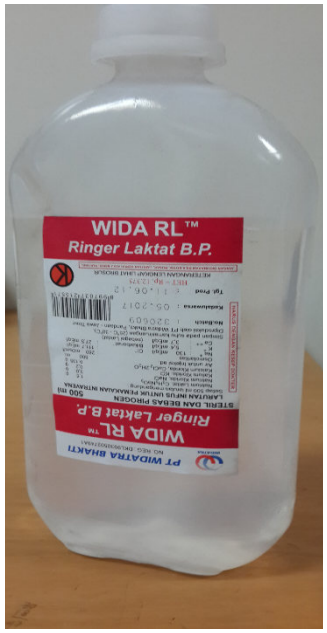


49.5 mls 0.9% NaCl

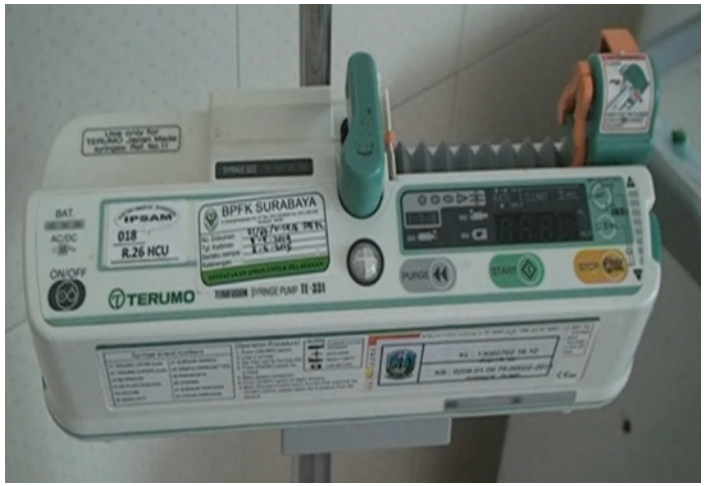
Syringe driver

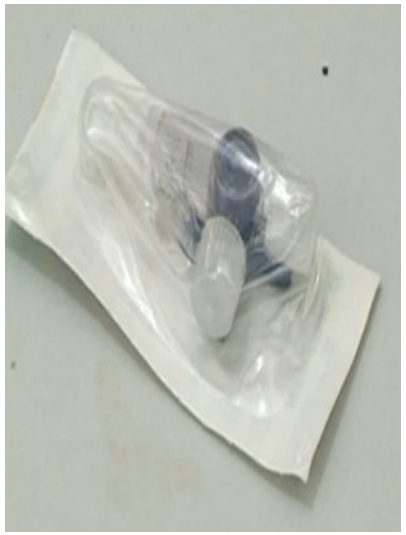
50 units of regular human insulin must be measured using an insulin syringe and made up to 50mls with 0.9% sodium chloride

Intravenous fluids



Syringe pump





2-or 3-tailed device with non-return valves

- Accompanying fluids via the same intravenous cannula as insulin
- Additional fluids via a separate cannula may be needed
  - According to clinical situation
- Close monitoring (i.e. at least daily) of potassium needed when patient receiving IV insulin
  - Potassium supplementation via IV fluids will be necessary for the majority of patients

Time Line

60 minutes to 6 hours

Action 2: Re-assess patient, monitor vital sign

- Measure **blood ketones and CBG hourly**
- Review patient's response to FRIII (ketone and CBG falls) hourly
- Blood ketone falling should be >0.5 mmol/L/hr, if not achieved- increase isulin infusion rate by 1.0 unit/hr
- If blood ketone measurement is not available, Use venous bicarbonate (rising > 3.0 mmol/L/hr) alternatively
- CBG should fall 50 (40 – 60) mg /dL/hr if not increase insulin infusion rate by 1.0 unit/hr
- Measure venous BG for pH, bicarbonate, and K+ at 60 minutes, 2 hourly
- Continue FRIII until the ketone is < 0.6 mmol/L, pH > 7.3 and/or HCO3- > 18 mmol/L
- If the glucose falls < 250 mg/dL, commence D 10% 125 ml/hr alongside NS solution
- Monitor and replace K+ (it may fall rapidly)

Time Line

60 minutes to 6 hours

Action 3: Identify and treat precipitating factors

Review patient's response to FRIII hourly (adequate progress ? Keton ? HCO^-, Glucose)

Action 4: Identify and treat precipitating factors

Patients presenting with newly diagnosed type 1 diabetes should be given human NPH insulin or Lantus® or Levemir®, at a dose of 0.25 units/Kg subcutaneously once daily to mitigate against rebound ketosis when they are taken off the FRIII

Time Line

6 to 12 hours

Aim:

- Ensure that clinical and biochemical parameters are improving
- Continue IV fluid replacement
- Continue insulin administration
- Assess for complications of treatment e.g. Fluid overload, cerebral oedema
- Continue to treat precipitating factors as necessary
- Avoid hypoglycaemia

Action 1: Re-assess patient, monitor vital signs

- If the patient is not improving then seek senior advice
- Ensure a referral has been made to the specialist diabetes team

Action 2: Review biochemical and metabolic parameters

- At 6 hours check the venous pH, bicarbonate, potassium, as well as blood ketones and glucose

Time Line

6 to 12 hours

Action 2: Resolution of DKA

- Ketones < 0.6mmol/L and
- Venous pH > 7.3 (do not use bicarbonate)
- Transfer to subcutaneous insulin if the patient is eating and drinking normally

Time Line

12 to 24 hours

Expectation: By 24 hours the ketonaemia and acidosis should have resolved

Aim:

- Ensure that the clinical and biochemical parameters are improving or have normalised
- Continue IV fluids if the patient is not eating and drinking
- If the patient is not eating and drinking and there is no ketonaemia move to a VRIII as per local guidelines
- Re-assess for complications of treatment e.g. fluid overload, cerebral oedema
- Continue to treat any precipitating factors as necessary
- Transfer to subcutaneous insulin if the patient is eating and drinking normally (SC insulin is started before the IV insulin is discontinued)

Action 1: Re-assess patient, monitor vital signs

Action 2: Review biochemical and metabolic parameters

- **At 12 hours check venous pH, bicarbonate, potassium, as well as blood ketones and glucose**
- **Resolution of DKA is defined as blood ketones < 0.6mmol/L, and venous pH > 7.3**

Conversion to Subcutaneous Insulin

- Patient is eating and drinking normally
- Subcutaneous insulin is started before the IV insulin is discontinued
- Give the subcutaneous fast acting insulin at a meal and discontinue IV insulin one hour later

Criteria for Discharge

- Metabollically stable and clinically well
- No vomited within 24 hours
- Eating and drinking
- CBG less than 360 mg/dL
- Seen by a member of Diabetes Specialist Team
- Has own CBG meter and able to use Ketostix effectively
- Information leaflets given
- Appointment made for follow-up

NB: **ketonuria alone should not prevent discharge**

AUDIT

Audit standards for the management of the adult patient with diabetic ketoacidosis

Purpose of these audit standards

- Maximise patient safety and quality of care
- Support professional best practice
- Deliver enhanced patient satisfaction
- Reduce Trust operating costs (litigation, complaint procedures)
- Contribute to improved financial performance (reduced length of stay)

Institutional Standards:	
Indicator	Standard

- **Institutional Accountability and Integrity**
- **Department of Health 'Never Event' Standard**
- **Additional Best Practice Tariff Standards**

Terima Kasih
10 November 2018

"Every beginning ends something."
Paul Valery, French Poet

Transitions starts with an ending, go through a period of uncertainty and end with a new beginning...

Neither the old ways nor the new ways seems to be working. This is the dangerous time, where anxiety rises and motivation falls

There will be more illness, but it will also be a more creative time; redefine it and use it constructively