Diabetic Ketoacidosis

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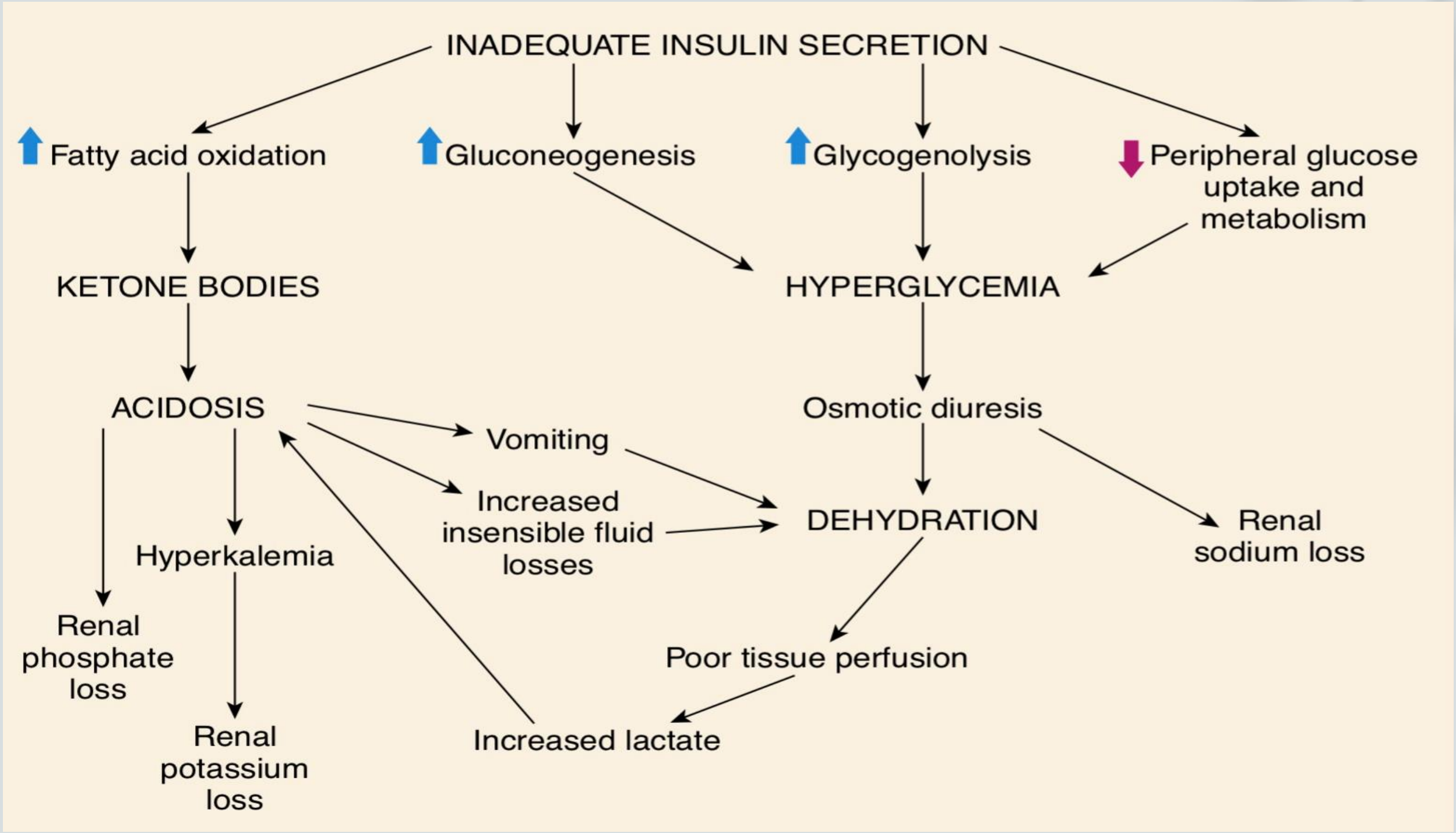
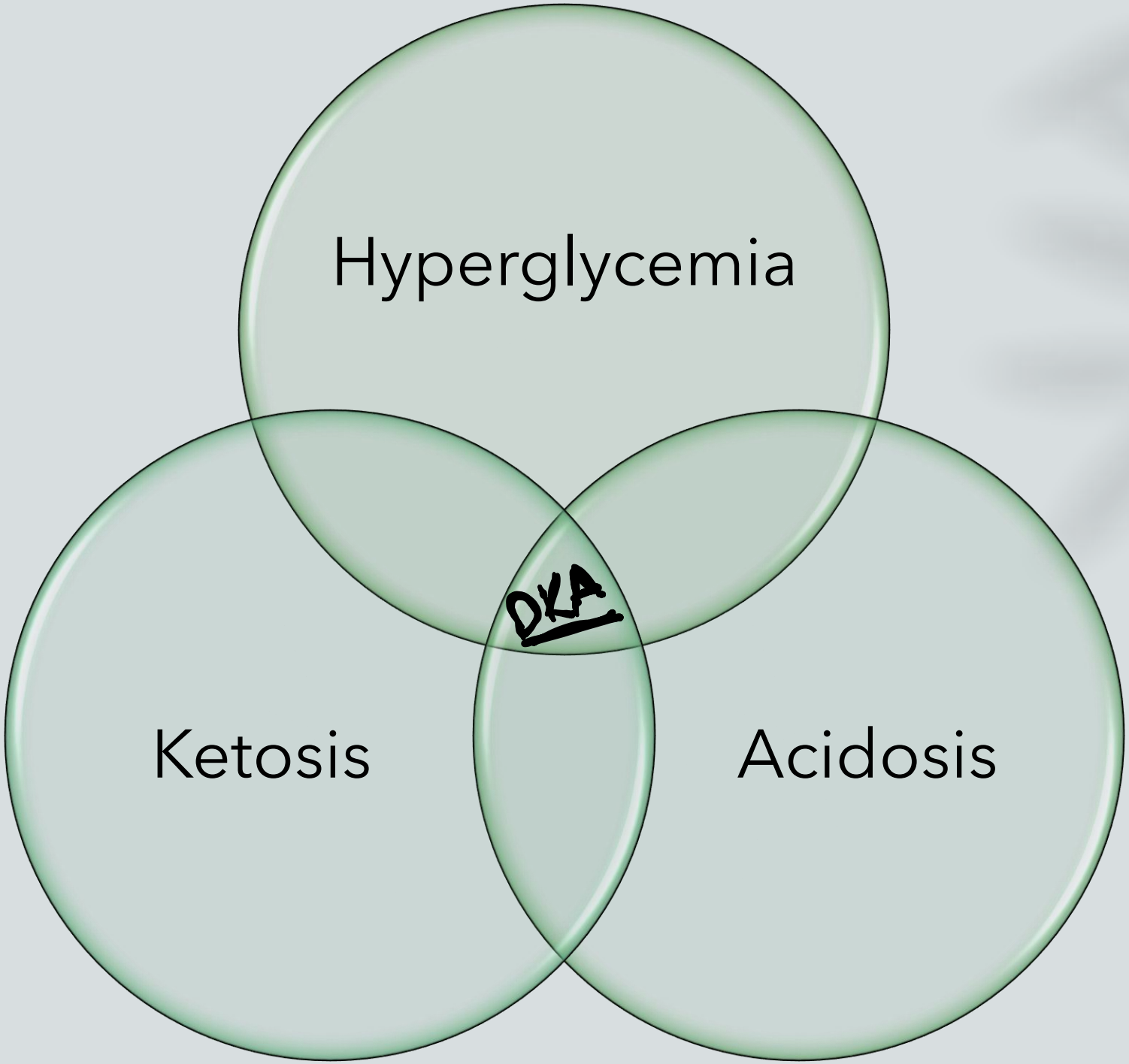
Definition

- Metabolic disorders due to acute **insulin insufficiency**
- If the **clinical features of new-onset DM1 are not detected**, diabetic ketoacidosis (DKA) will occur
- DKA may also occur in **patients with known DM1 if insulin injections are omitted or during an intercurrent illness when greater insulin requirements are unmet** in the presence of elevated concentrations of the counter-regulatory and stress hormones (glucagon, growth hormone [GH], cortisol, and catecholamines).


INADEQUATE INSULIN SECRETION
Fatty acid oxidation
Gluconeogenesis
Glycogenolysis
Peripheral glucose uptake and metabolism
KETONE BODIES
HYPERGLYCEMIA
ACIDOSIS
Osmotic diuresis
Vomiting
Increased insensible fluid losses
DEHYDRATION
Renal sodium loss
Hyperkalemia
Renal phosphate loss
Poor tissue perfusion
Renal potassium loss
Increased lactate


Hyperglycemia
DKA
Ketosis
Acidosis

DKA is present if

1. The arterial pH is below 7.3
2. The serum bicarbonate level is below 15 mEq/L
3. Ketones are elevated in serum or urine " ketonaemia or ketonuria"

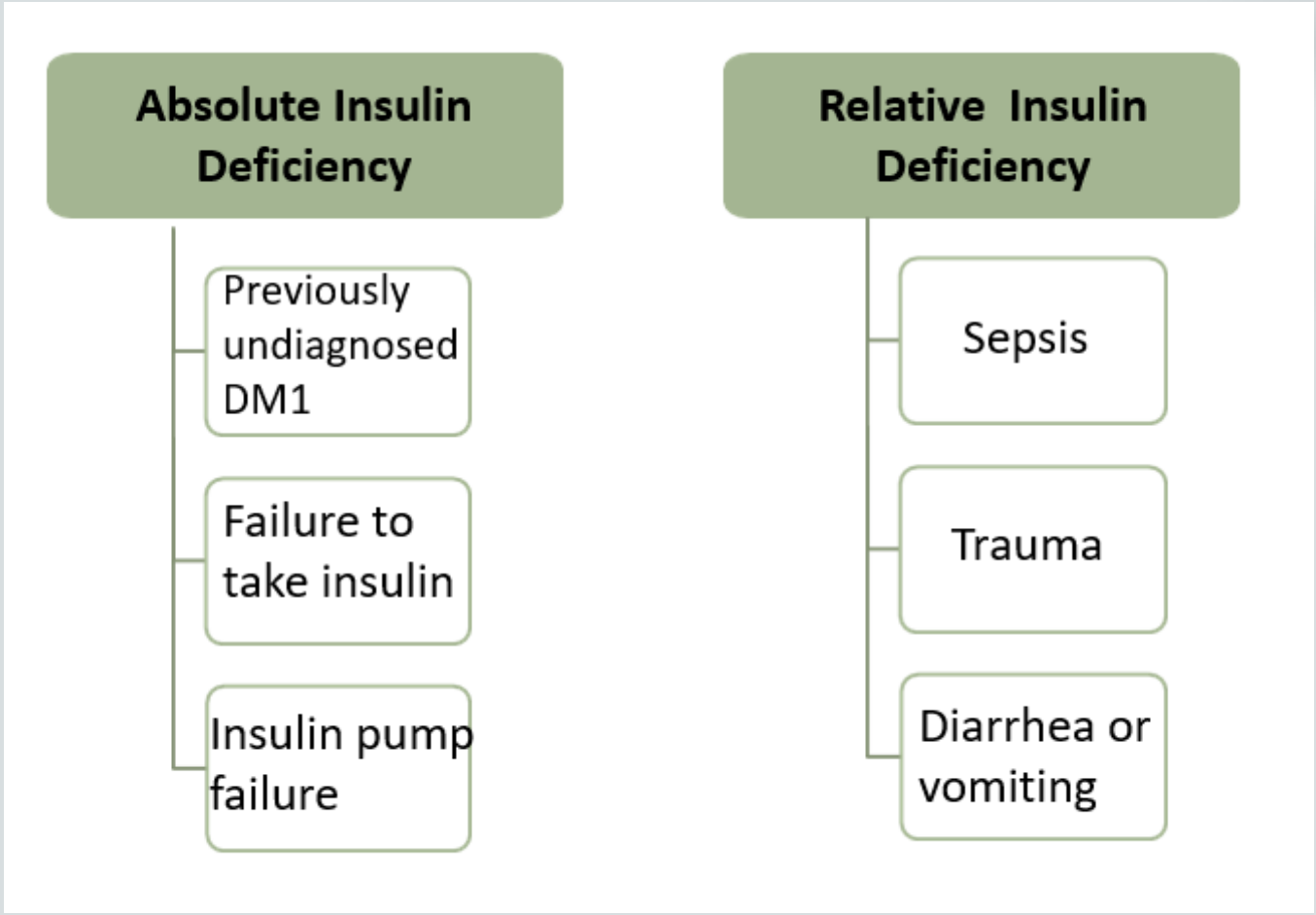
Pathophysiology & Clinical Presentation

In most cases ,DKA is caused by

- New onset of diabetes especially T1DM
- Omission of insulin injections, especially the long-acting component of a basal bolus regimen
- Interruption of insulin delivery in children using an insulin pump (Children who use an insulin pump can rapidly develop DKA when insulin delivery fails for any reason)
- Inadequate management of an infection (stress). Markedly reduce the doses of insulin ,for example ,during an intercurrent illness such as gastroenteritis

Pathophysiology

Imbalance between insulin & counter-regulatory hormones



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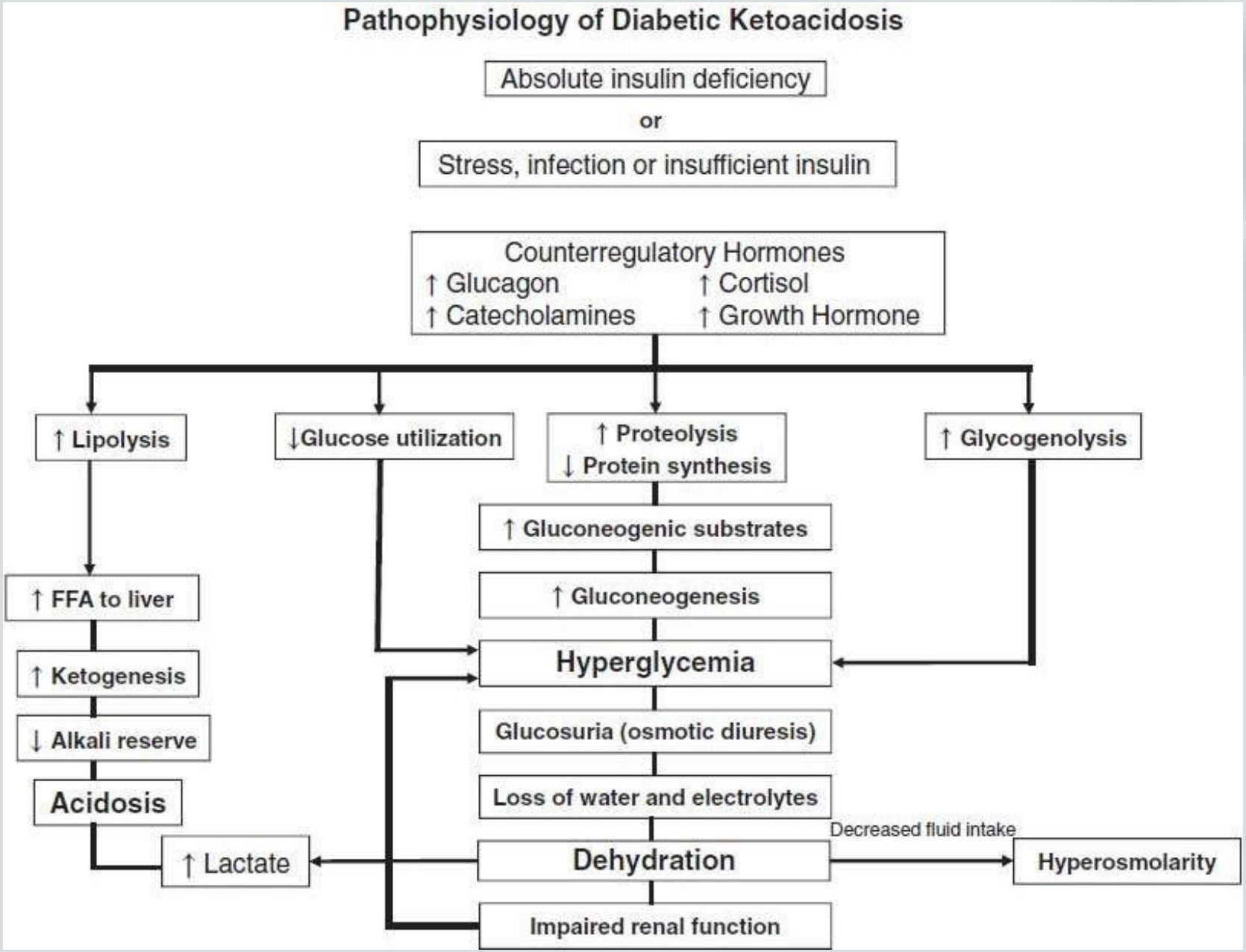


Signs and Symptoms of DKA

- Polyuria, polydipsia
  - Enuresis
- Dehydration
  - Tachycardia
  - Orthostasis
- Abdominal pain
  - Nausea
  - Vomiting

- Fruity breath
  - Acetone
- Kussmaul breathing
- Mental status changes
  - Combative
  - Drunk
  - Coma

Clinical Profile

- Check serum glucose to confirm hyperglycemia
- Check BMP for serum bicarbonate, anion gap, electrolytes, and renal function
- Check for the presence of ketones
  - **Urine ketones:** Standard urine dipstick assays detect acetoacetate and acetone but not beta-hydroxybutyrate
  - Serum beta-hydroxybutyrate
- Check blood gas analysis for pH
- Diagnostic workup to evaluate the underlying cause
  - HbA1c, CBC, ECG, infectious workup

Laboratory Studies Reveal

- Serum glucose concentrations ranging from 200 mg/dL to >1,000 mg/dL) *hyperglycemia*
- Arterial pH is below 7.30
- Serum bicarbonate concentration is less than 15 mEq/L
- Serum sodium concentrations may be elevated, normal, or low, depending on the balance of sodium and free water losses
- The measured serum sodium concentration is artificially low, however, because of hyperglycemia
- Hyperlipidemia also contributes to the decrease in measured serum sodium
- The level of blood urea nitrogen (BUN) can be elevated with prerenal azotemia secondary to dehydration
- The WBC count is usually elevated and can be left-shifted without implying the presence of infection. Fever is unusual and should prompt a search for infectious sources that may have triggered the episode of DKA

Classification of Diabetic Ketoacidosis

- The Severity of DKA depends on the degree of acidosis:
  - **Mild**
    - Venous pH - **<7.3**
    - HCO3 - **<15 mmol/L**
  - **Moderate**
    - Venous pH - **<7.2**
    - HCO3 - **<10 mmol/L**
  - **Severe**
    - Venous pH - **<7.1**
    - HCO3 - **<5 mmol/L**

Categories	Venous blood pH	Plasma bicarbonate (mM)
Mild	7.2–7.3	15
Moderate	7.1–7.2	10
Severe	≤7.1	≤5

Management of Diabetic Ketoacidosis

Emergency assessment

- Obtain vital signs
- Measure current weight
- Insert 2 peripheral IV lines (to obtain blood for laboratory evaluation from one, and give IV fluid therapy)
- Measure blood glucose and blood beta-hydroxybutyrate (BOHB) levels or urine acetoacetic acid concentration with urine test strips
- Measure venous PH, pCO2, glucose, electrolytes, serum urea nitrogen, and creatinine

Emergency assessment

- Assess level of dehydration
  - Mild 5%
    - You might skip the IV fluid bolus
  - Moderate 7%
    - Give 0.9% normal saline bolus (10 ml/kg over 30-60 minutes)
  - Severe (shock) 10% -- suggested by the presence of weak or impalpable peripheral pulses, hypotension or oliguria
    - Give 0.9% normal saline bolus (20ml/kg over 10-20 minutes)
- Assess level of consciousness (Glasgow Coma Scale)
  - In an unconscious patient start with ABCD
- Continuous cardiac monitor
  - Prolongation of the PR interval, T wave flattening and inversion, ST depression, prominent U waves, apparent long QT interval = hypokalaemia
  - Tall, peaked , symmetrical, hyperacute T waves and shortening of the QT interval = hyperkalaemia
- Admit the patient to PICU

PICU Admission

Main goals of treatment are

1. Replacement of fluid deficits
2. Correction of hyperglycemia
3. Correction of acidosis
4. Correction of electrolyte imbalance
   - Potassium
   - Phosphate
   - Sodium
5. Continuous monitoring
6. Identify & treat any precipitating events

PICU Admission

- **Fluid Replacement**
  - Calculate deficit & maintenance
    - To avoid rapid shifts in serum osmolality, start with 0.9% normal saline for the first 4-6 hours, the continue with 0.45% normal saline
    - There should be a concomitant increase in serum sodium concentration as the serum glucose concentration decreases (sodium should rise by 0.5 mmol/L for each 1 mmol/L decrease in glucose concentration

TABLE 1 Losses of fluid and electrolytes in diabetic ketoacidosis and maintenance requirements in normal children

	Average (range) losses per kg	24-hour maintenance requirements	
Water	70 mL (30-100)	*≤10 kg	100 mL/kg/24 h
		11-20 kg	1000 mL + 50 mL/kg/24 h for each kg from 11 to 20
		>20 kg	1500 mL + 20 mL/kg/24 h for each kg >20
Sodium	6 mmol (5-13)	2-4 mmol†	
Potassium	5 mmol (3-6)	2-3 mmol	
Chloride	4 mmol (3-9)	2-3 mmol	
Phosphate	0.5-2.5 mmol	1-2 mmol	

PICU Admission

- **Correction of Hyperglycemia**
  - Insulin therapy is essential to
    - Restore normal cellular metabolism
    - Supress lipolysis and ketogenesis
    - Normalize blood glucose concentration
  - Start insulin infusion at least 1 hour after starting fluid replacement
  - Fast acting soluble insulin as a continuous IV infusion (0.05 – 0.1 U/kg/hr)
    - The lower dose 0.05 U/kg/hr can be considered for children with pH > 7.15
    - If IV cannulation is not possible due to severe dehydration, we can administer IM insulin injection
  - Serum glucose should be decreased in a rate no faster than 100 mg/dL/ hr) to prevent cerebral oedema
  - 5% dextrose should be added to the IV fluid when plasma glucose falls to 250-300 mg/dL
  - When serum glucose concentration gets <200 mg/dL before correction of acidosis → glucose concentration in IV fluid should be increased but insulin infusion **should not** be decreased by more than half (should never be discontinued before resolution of acidosis)
  - Monitor pH and BOHB every 2 hours to ensure steady improvement of biochemical parameters

PICU Admission

- **Correction of Acidosis**
  - Insulin therapy decreases production of free fatty acids and protein catabolism and enhance glucose usage in target tissues
  - **Bicarbonate therapy should be avoided** (paradoxical increase in CNS acidosis caused by increased diffusion of carbon dioxide across BBB → cerebral oedema
  - **Note:** as acidosis is corrected, urine ketone concentrations may appear to rise
    - due to conversion of beta-hydroxybutyrate wo acetoacetate which is detected in urine ketone assay

PICU Admission

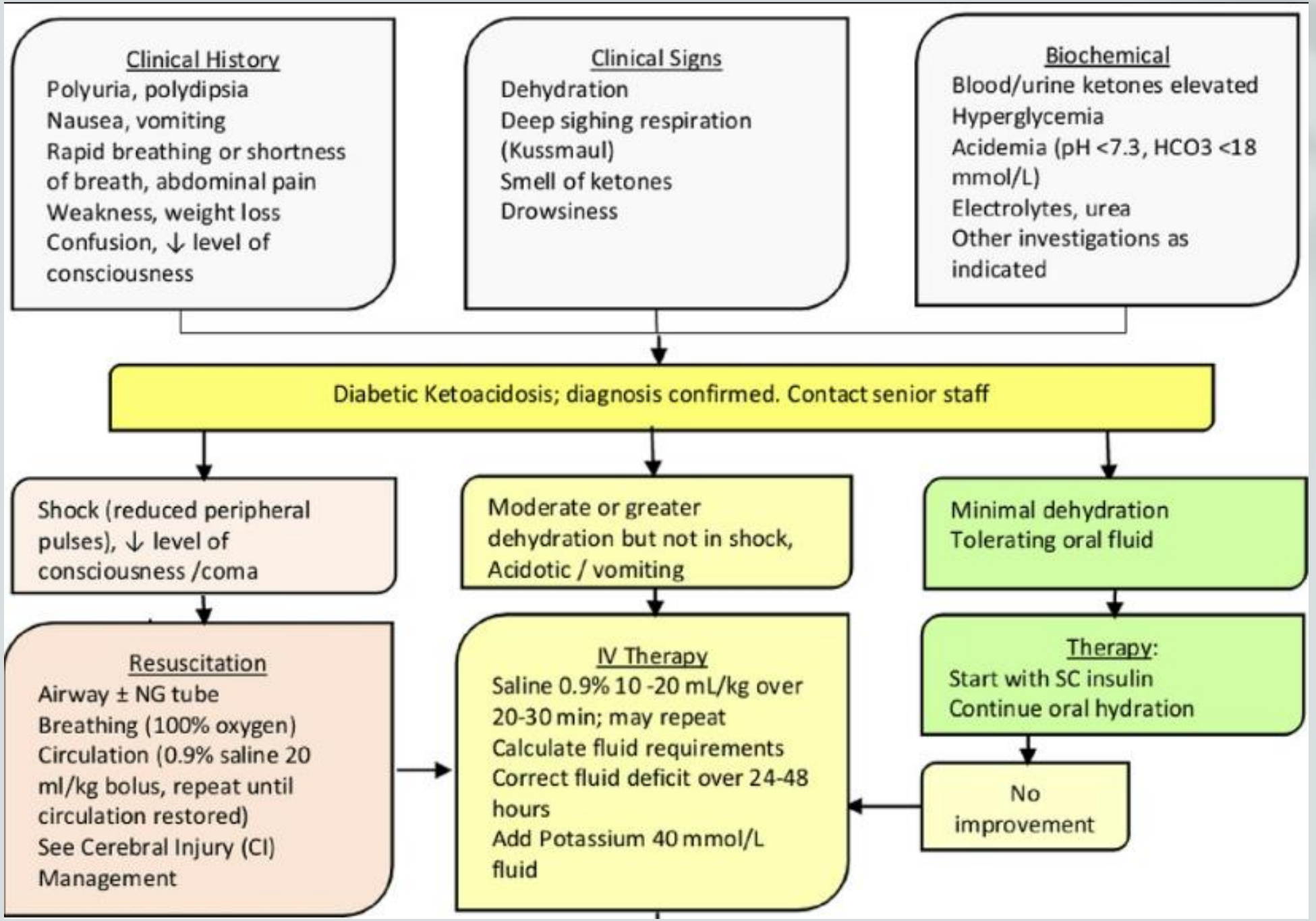
- **Correction of Electrolyte Imbalance (Potassium)**
  - Potassium (which can be high, normal or low)
    - Serum potassium can decrease rapidly as insulin and then glucose therapy improves acidosis → potassium is exchanged for intracellular hydrogen ions
    - If high potassium (>5.5 mmol/L) – no need to start potassium replacement
    - If potassium is normal or low (<5.5 mmol/L) – potassium replacement should be started when adequate urine output is shown
  - It is recommended to give 50% of replacement as potassium chloride and the other 50% as potassium phosphate at 20-40 mEq/L
    - For example: give 20 mmol/L potassium chloride (or 20 mmol/L potassium acetate) with 20 mmol/L potassium phosphate
  - The maximum recommended rate of intravenous potassium replacement is usually 0.5 mmol/kg/hr

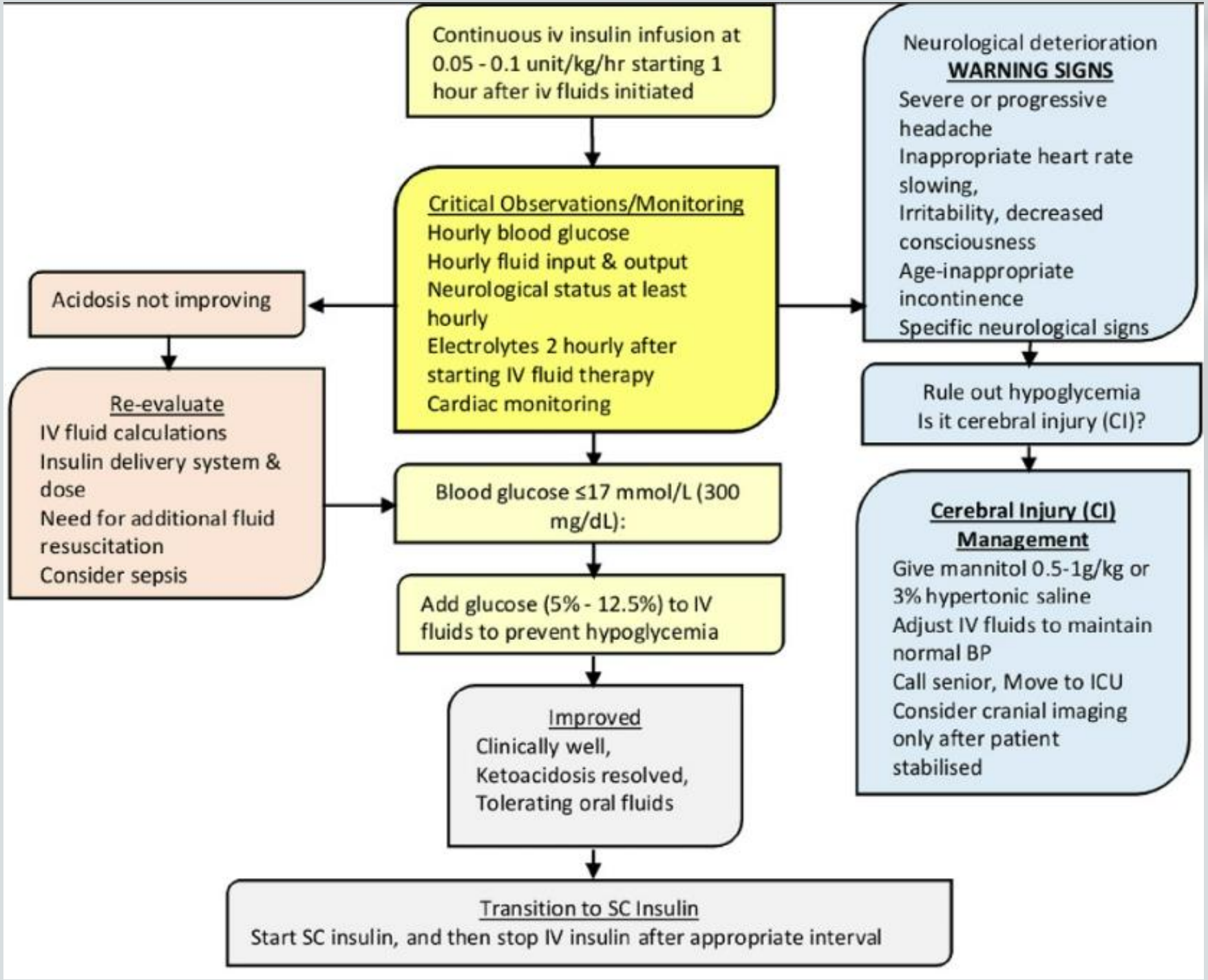
PICU Admission

- **Correction of Electrolyte Imbalance (Phosphate)**
  - Phosphate depletion occurs in DKA due to osmotic diuresis and a shift of intracellular phosphate to the ECF as a result of metabolic acidosis, but it is rare
  - Potassium phosphate can be used to alleviate phosphate levels
  - Monitor serum calcium and magnesium concentrations during phosphate infusion to avoid hypocalcemia

PICU Admission

- **Monitoring**
  - Vital signs hourly
  - Level of consciousness hourly
  - Fluid input and output hourly
  - Gluco-check hourly
  - Venous blood gases every 2 hours
  - Serum electrolytes and KFT every 2-4 hours
  - Measure body weight every morning


Clinical History
Polyuria, polydipsia
Nausea, vomiting
Rapid breathing or shortness of breath, abdominal pain
Weakness, weight loss
Confusion, ↓ level of consciousness
Clinical Signs
Dehydration
Deep sighing respiration (Kussmaul)
Smell of ketones
Drowsiness
Biochemical
Blood/urine ketones elevated
Hyperglycemia
Acidemia (pH <7.3, HCO3 <18 mmol/L)
Electrolytes, urea
Other investigations as indicated
Diabetic Ketoacidosis; diagnosis confirmed. Contact senior staff
Shock (reduced peripheral pulses), ↓ level of consciousness /coma
Moderate or greater dehydration but not in shock, Acidotic / vomiting
Minimal dehydration
Tolerating oral fluid
Resuscitation
Airway ± NG tube
Breathing (100% oxygen)
Circulation (0.9% saline 20 ml/kg bolus, repeat until circulation restored)
See Cerebral Injury (CI) Management
IV Therapy
Saline 0.9% 10 -20 mL/kg over 20-30 min; may repeat
Calculate fluid requirements
Correct fluid deficit over 24-48 hours
Add Potassium 40 mmol/L fluid
Therapy:
Start with SC insulin
Continue oral hydration
No improvement


Continuous iv insulin infusion at 0.05 - 0.1 unit/kg/hr starting 1 hour after iv fluids initiated
Critical Observations/Monitoring
Hourly blood glucose
Hourly fluid input & output
Neurological status at least hourly
Electrolytes 2 hourly after starting IV fluid therapy
Cardiac monitoring
Acidosis not improving
Re-evaluate
IV fluid calculations
Insulin delivery system & dose
Need for additional fluid resuscitation
Consider sepsis
Blood glucose ≤17 mmol/L (300 mg/dL):
Add glucose (5% - 12.5%) to IV fluids to prevent hypoglycemia
Improved
Clinically well,
Ketoacidosis resolved,
Tolerating oral fluids
Transition to SC Insulin
Start SC insulin, and then stop IV insulin after appropriate interval
Neurological deterioration
WARNING SIGNS
Severe or progressive headache
Inappropriate heart rate slowing,
Irritability, decreased consciousness
Age-inappropriate incontinence
Specific neurological signs
Rule out hypoglycemia
Is it cerebral injury (CI)?
Cerebral Injury (CI) Management
Give mannitol 0.5-1g/kg or 3% hypertonic saline
Adjust IV fluids to maintain normal BP
Call senior, Move to ICU
Consider cranial imaging only after patient stabilised

Complications of Therapy

- Cerebral oedema
- Hypokalaemia
- Hyperchloremic acidosis
- Hypoglycaemia
- Inadequate rehydration

Complications of Therapy

- **Cerebral Oedema**
  - It is the major cause of mortality and morbidity, accounts for 60%-90% of all DKA deaths
  - Risk of cerebral oedema increases in
    - Younger age
    - New onset diabetes
    - Longer duration of symptoms
    - Increased serum urea nitrogen at presentation
    - Severe acidosis at presentation
    - Bicarbonate treatment for correction of acidosis
    - A marked early decrease in serum effective osmolality
      - Administration of insulin in the first hour of fluid treatment
    - Greater volumes of fluid given in the first 4 hours (more than it should)

Complications of Therapy

- **Cerebral Oedema (Signs & Symptoms)**
  - Onset of headache after beginning treatment or progressively worsening headache
  - Change in neurological status
  - New onset neurological signs
  - Cushing's triad (hypertension, bradycardia, and respiratory depression)
    - A late but important sign of increased ICP
  - Decreased O2 saturation

Complications of Therapy

- **Cerebral Oedema (Treatment)**
  - Adjust fluid administration rate as needed to maintain normal blood pressure
  - Elevate the head of the bed to 30 and keep the head in the midline position
  - Mannitol administration (0.5-1 g/kg) IV over 10-15 minutes
    - Effect of mannitol should be apparent after 15 minutes
    - Expected to last about 120 minutes
  - Hyperosmotic normal saline (3% NS) should be readily available at bedsite
    - Dose: 2.5-5 mL/kg over 10-15 minutes
    - May be given if mannitol is not available or if no response to mannitol within 15-30 minutes
  - If necessary, the dose can be repeated after 30 minutes