DIABETIC KETOACIDOSIS

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DEFINITION

DKA is defined as the presence of ***all three*** of the following:

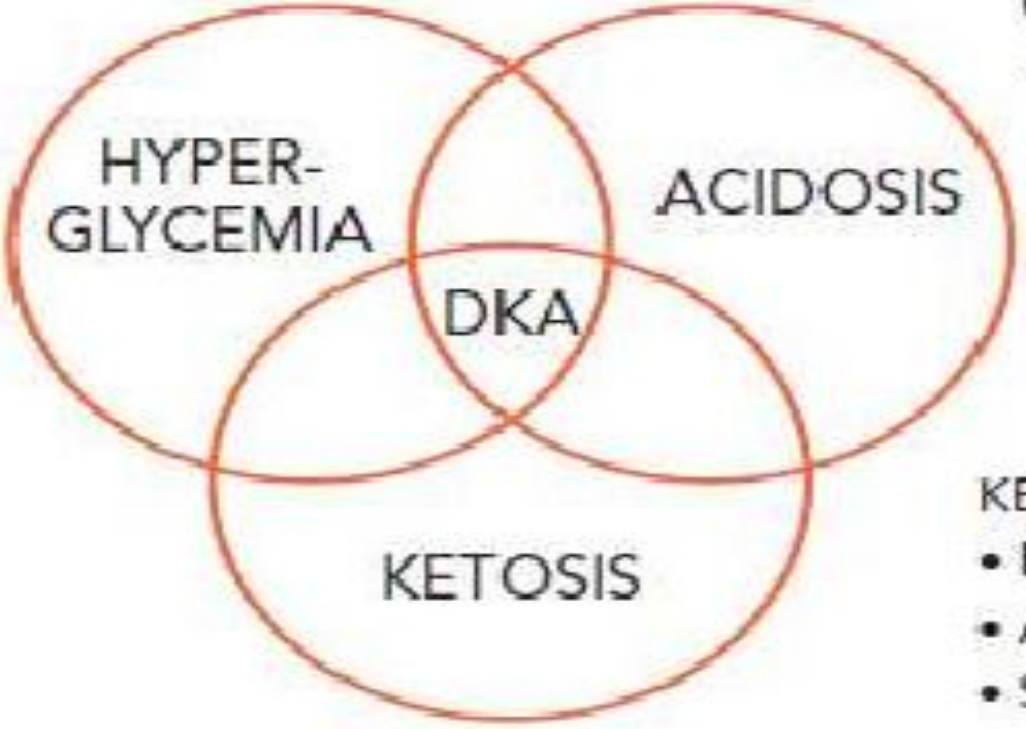
(i) Hyperglycemia (glucose >250 mg/dL)

(ii) Ketosis,

(iii) Acidemia (pH <7.3).

HYPERGLYCEMIC STATES
- Diabetes Mellitus
- Hyperosmolar Hyperglycemic State
- Impaired Glucose Tolerance
- Stress Hyperglycemia

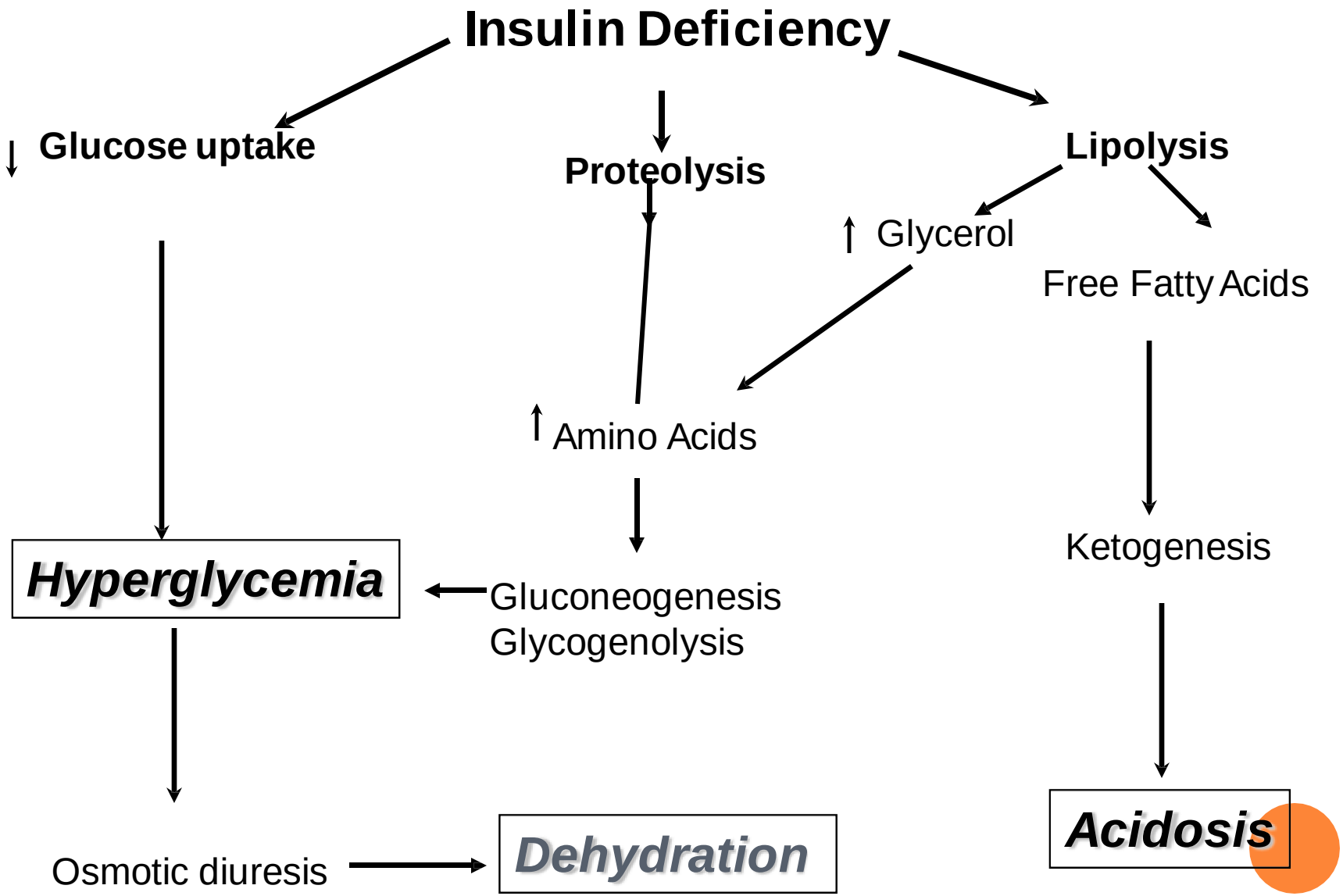
METABOLIC ACIDOTIC STATES
- Lactic Acidosis
- Hyperchloremic Acidosis
- Uremic Acidosis
- Drug-Induced Acidosis (eg, salicylates, methanol, ethylene glycol)



KETOTIC STATES
- Ketotic Hypoglycemia
- Alcoholic Ketosis
- Starvation Ketosis

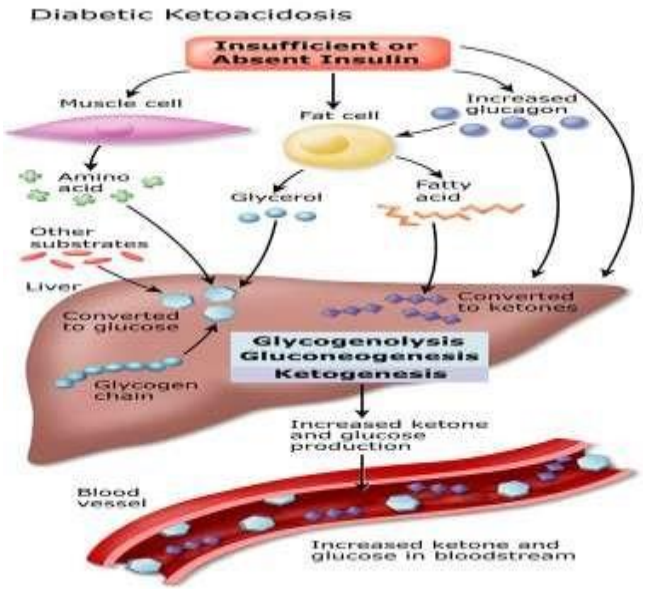
Figure 1. Diagnostic triad of diabetic ketoacidosis (DKA).
From Kitabchi AE. Diabetes mellitus. In: Glew RH, Peters SP, eds. *Clinical Studies in Medical Biochemistry*. New York, NY: Oxford University Press; 1987:102–117.

PATHOPHYSIOLOGY



Role of Insulin

- Required for transport of glucose into:
  - Muscle
  - Adipose
  - Liver
- Inhibits lipolysis



- Absence of insulin
  - Glucose accumulates in the blood.
  - Uses amino acids for gluconeogenesis
  - Converts fatty acids into ketone bodies : Acetone, Acetoacetate, β-hydroxybutyrate.

Diabetic Ketoacidosis

PRECIPITATING EVENTS

- **Infection(Pneumonia / UTI / Gastroenteritis / Sepsis)**
- **Inadequate insulin administration**
- Infarction(cerebral, coronary, mesenteric, peripheral)
- Drugs (cocaine)
- Pregnancy.

Harrison's Principle of internal medicine 20th edition

SYMPTOMS

- DKA can be the first presentation.
- Nausea/vomiting
- Thirst/polyuria
- Abdominal pain
- Shortnessof breath

PHYSICAL FINDINGS

- Tachycardia
- Dehydration/hypotension
- Tachypnea/kussmaul respirations/respiratory distress
- Fruity odour in breath.
- Abdominal tenderness(may resemble acute pancreatitis or surgical abdomen)
- Lethargy/obtundation/cerebral edema/possibly coma.

Differential Diagnosis of Ketosis and Anion Gap Acidosis

FEATURES	DIABETIC KETOACIDOSIS	ALCOHOL KETOACIDOSIS	STARVATION KETOACIDOSIS	URAEMIC ACIDOSIS	LACTIC ACIDOSIS
PH	↓	↓	↔	↓	↓
PLASMA GLUCOSE	↑	↔	↔	↔	↔
ANION GAP	↑	↑	↔	↑	↑
SERUM KETONES	↑ ↑	↑	↑	↔	↑
SERUM OSMOLALITY	↑	↔	↔	↑	↔

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DIAGNOSIS *INITIAL EVALUATION*

- Identify precipitating event leading to elevated glucose (pregnancy, infection, omission of insulin, myocardial infarction, central nervous system event)
- Assess hemodynamic status
- Examine for presence of infection
- Assess volume status and degree of dehydration
- Assess presence of ketonemia and acid-base disturbance

DIAGNOSIS *LAB INVESTIGATIONS*

- Complete blood count
- Serum ketones/ Urine ketones and sugar
- Calculate serum osmolality and anion gap
- Urinalysis and urine culture
- Consider blood culture
- Consider chest radiograph
- Acid-base assessment

LABORATORY VALUES IN DKA AND HHS

	DKA	HHS
Glucose,mg/dl	250-600	600-1200
Sodium meq/L	125-135	135-145
Potassium	Normal to↑	Normal
Osmolality mosm/kg	300-320	330-380
Plasma ketones	++++	+/-
Serum bicarbonate	<15meq/L	Normal to slightly ↓
Arterial pH	6.8-7.3	>7.3
Arterial pCO_2	20-30	Normal
Anion gap	↑	Normal to slightly↑

TYPICAL BODY DEFICIT OF WATER AND ELECTROLYTES

Total water (L)	6
Water (ml/kg)*	100
Na^+ (mEq/kg)*	7–10
Cl^- (mEq/kg)*	3–5
K^+ (mEq/kg)*	3–5
PO_4 (mEq/kg)*	5–7
Mg^{++} (mEq/kg)*	1–2
Ca^{++} (mEq/kg)*	1–2

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TREATMENT OF DKA

Initial hospital management

- Replace fluid and electrolytes
- IV Insulin therapy
- Watch for complications
- Treat causes

Once resolved

- Convert to home insulin regimen
- Prevent recurrence

PROTOCOL FOR MANAGEMENT OF ADULT PATIENTS WITH DKA

Initial evaluation: After history and physical examination, obtain arterial blood gases, complete blood count with differential, urinalysis, plasma glucose, BUN, electrolytes, chemistry profile, and creatinine levels STAT as well as an ECG. Chest X-ray and cultures as needed. Start IV fluid, 1.0 L of 0.9% NaCl per hour initially (15-20 ml/kg/hour).

Diagnostic criteria: DKA: blood glucose >250 mg/dl, arterial pH <7.3, bicarbonate <15 mEq/l, moderate ketonuria or ketonemia.

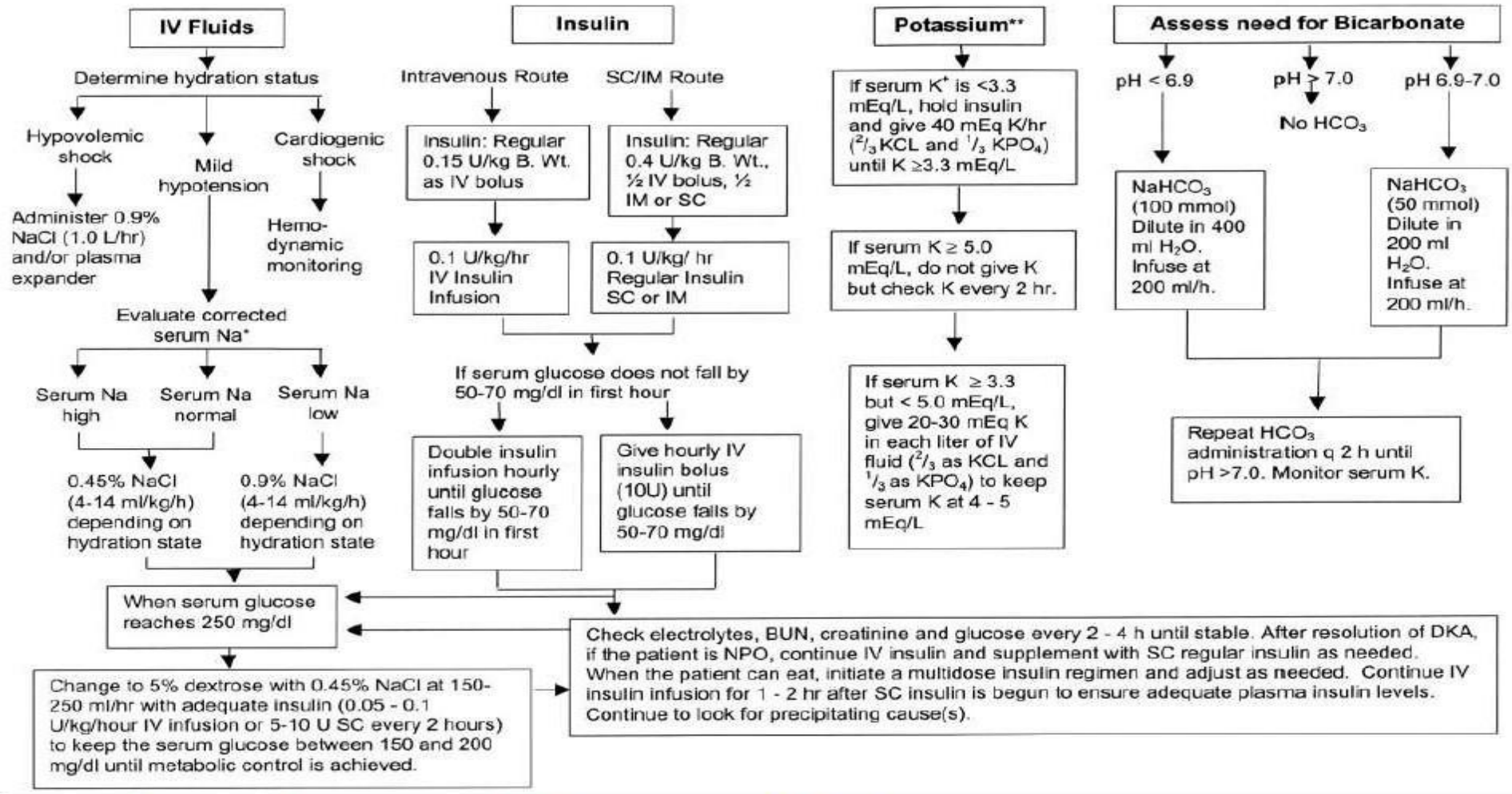


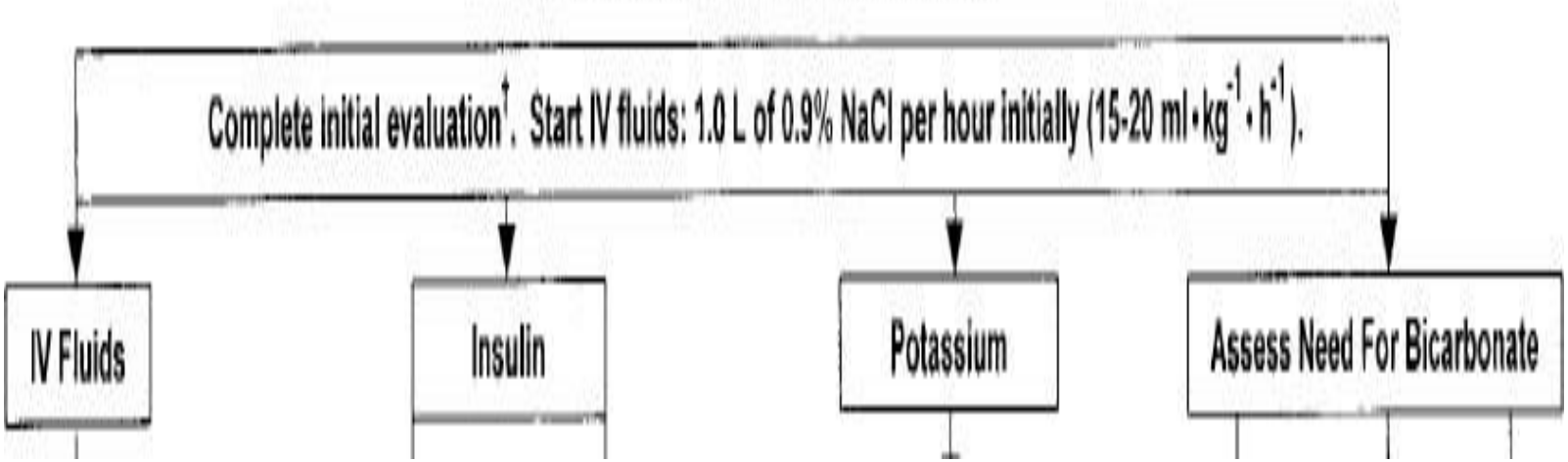
Figure 1. Protocol for Management of Adult Patients with Diabetic Ketoacidosis

*Serum Na^+ should be corrected for hyperglycemia (for each 100 mg/dl glucose above 100 mg/dl, add 1.6 mEq to sodium value for corrected serum sodium value).

**Upper limits for serum potassium may vary by laboratory.

Adapted with permission from reference 27.

Management of Adult Patients with DKA*



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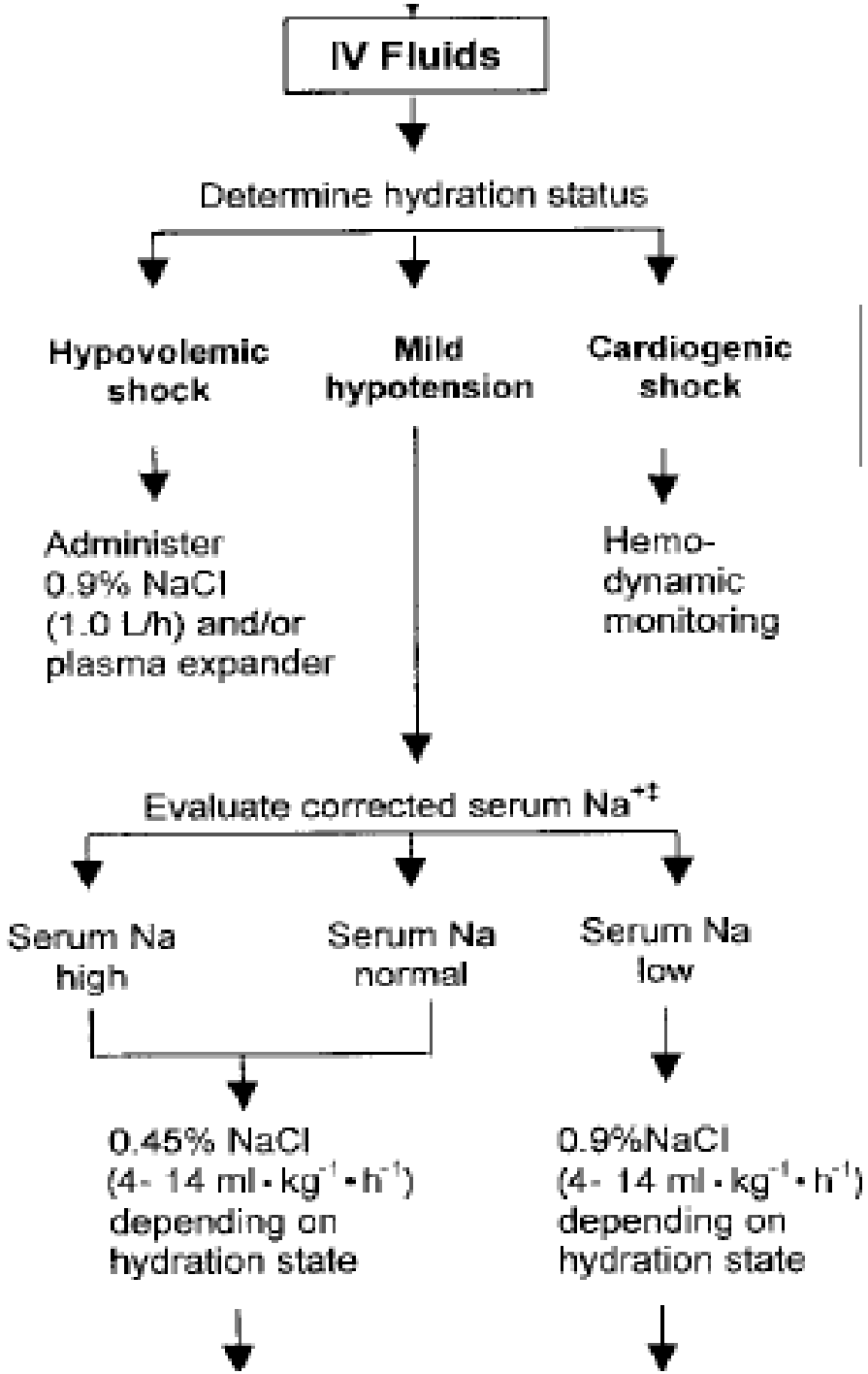

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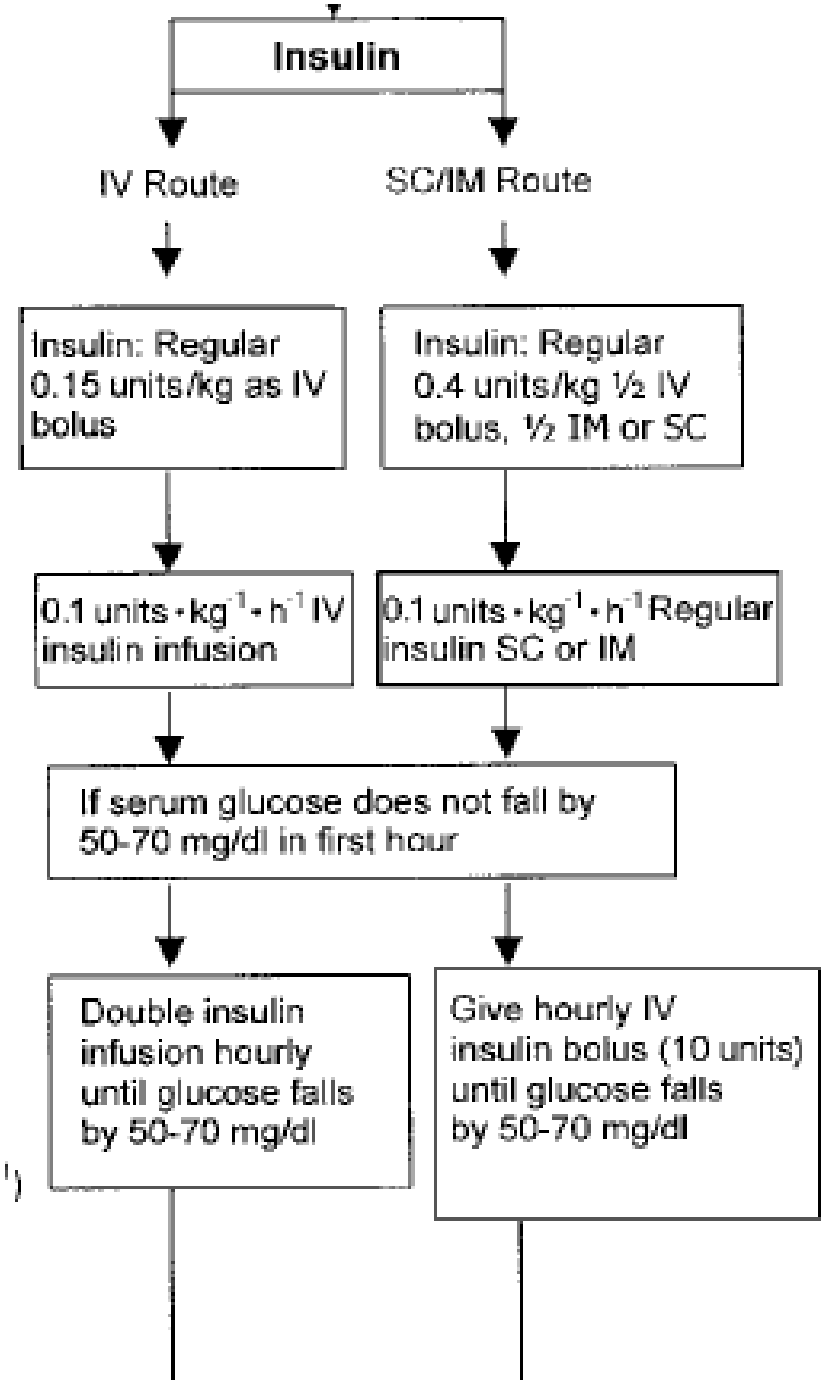

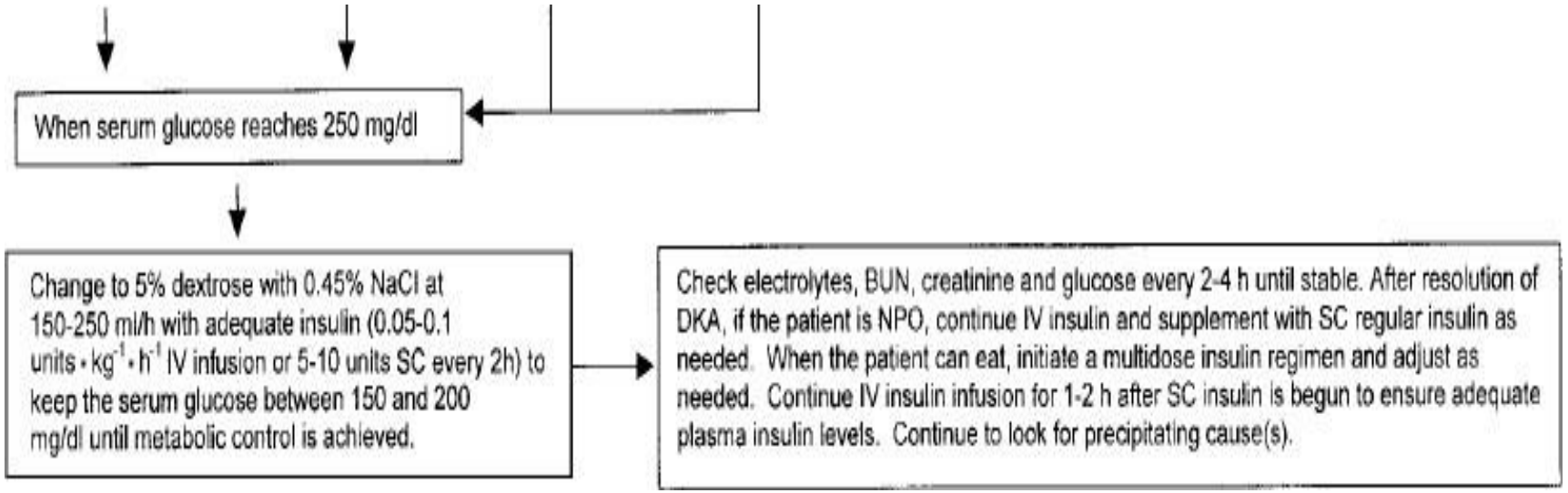
When serum glucose reaches 250 mg/dl
Change to 5% dextrose with 0.45% NaCl at 150-250 ml/h with adequate insulin (0.05-0.1 units • kg^{-1} • h^{-1} IV infusion or 5-10 units SC every 2h) to keep the serum glucose between 150 and 200 mg/dl until metabolic control is achieved.
Check electrolytes, BUN, creatinine and glucose every 2-4 h until stable. After resolution of DKA, if the patient is NPO, continue IV insulin and supplement with SC regular insulin as needed. When the patient can eat, initiate a multidose insulin regimen and adjust as needed. Continue IV insulin infusion for 1-2 h after SC insulin is begun to ensure adequate plasma insulin levels. Continue to look for precipitating cause(s).

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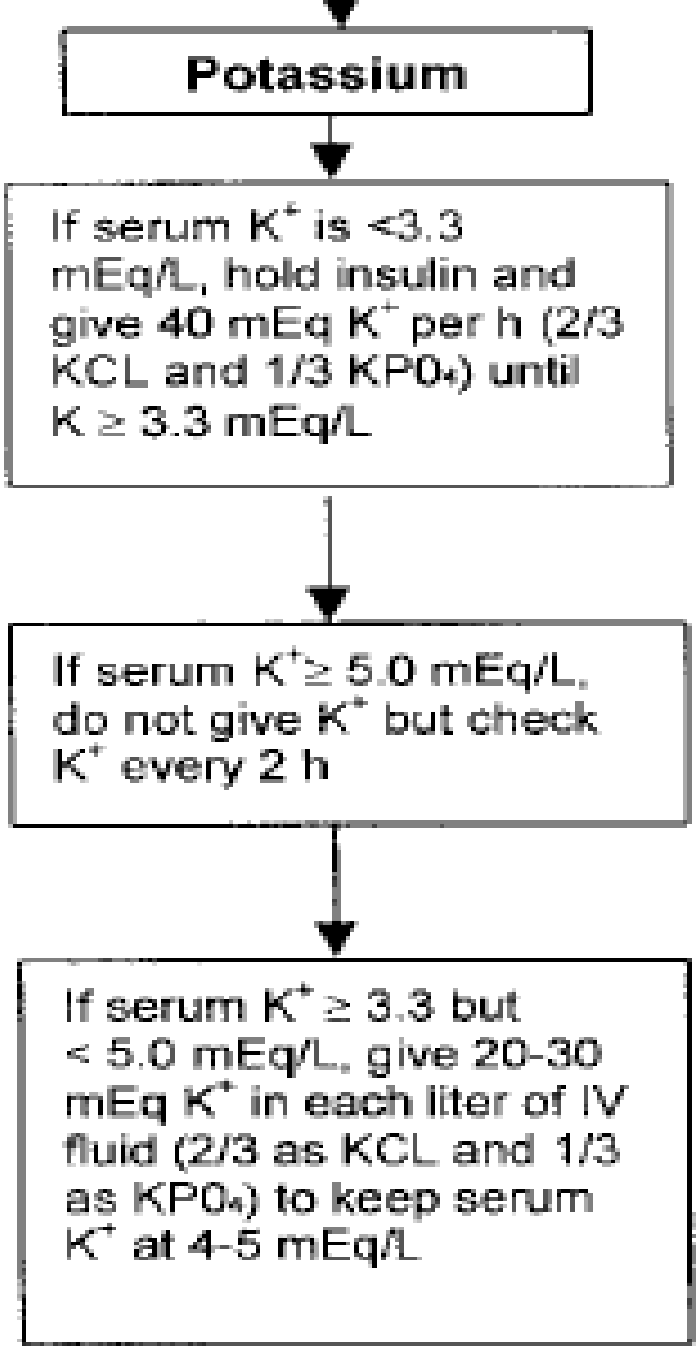

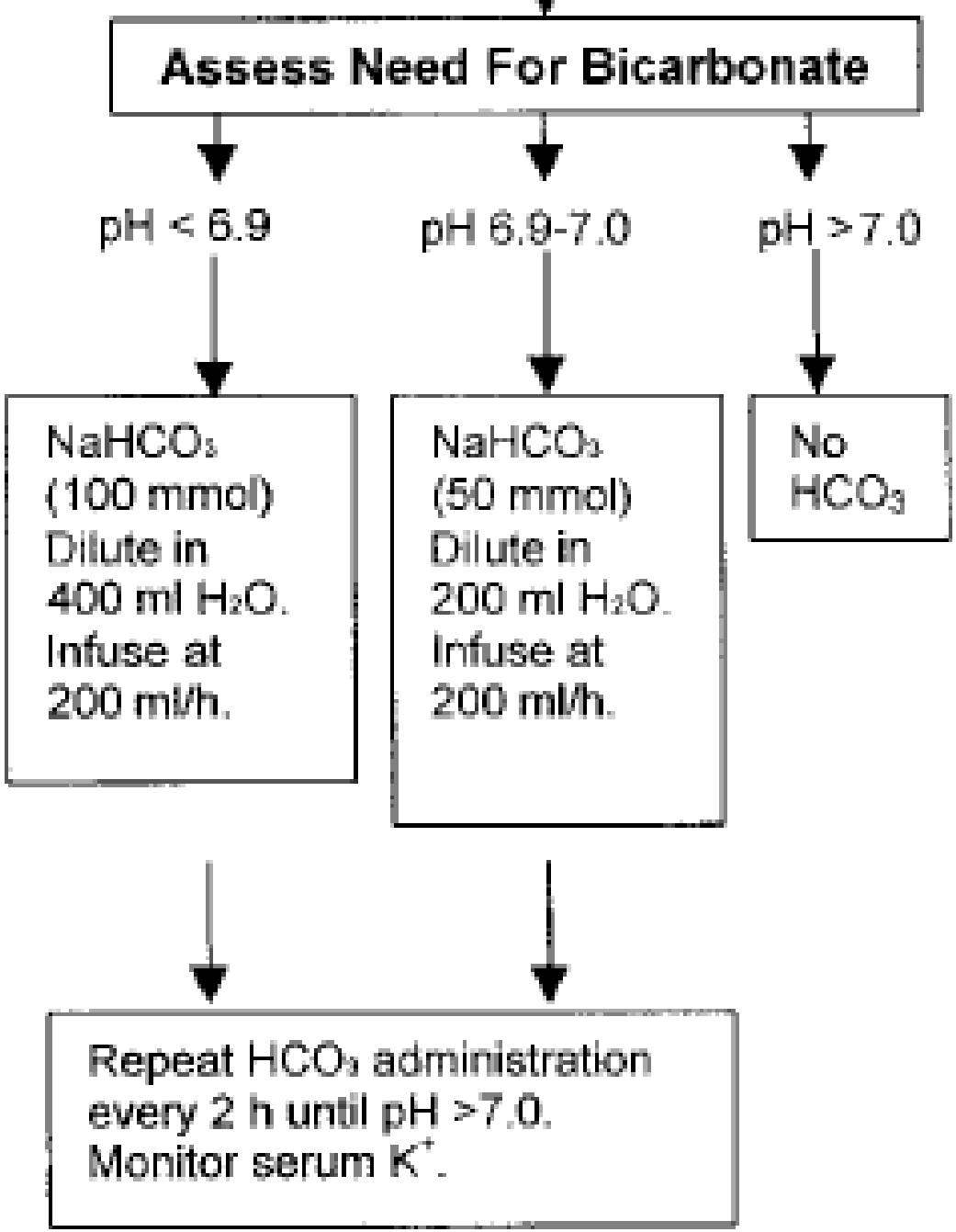
Assess Need For Bicarbonate
pH < 6.9
pH 6.9-7.0
pH >7.0
NaHCO3 (100 mmol) Dilute in 400 ml H2O. Infuse at 200 ml/h.
NaHCO3 (50 mmol) Dilute in 200 ml H2O. Infuse at 200 ml/h.
No HCO3
Repeat HCO3 administration every 2 h until pH >7.0. Monitor serum K+.

FLUID REPLACEMENT

- Administer NS as indicated to maintain hemodynamic status, then follow general guidelines:

  - NS for first 4 hr.
  - Consider half NS thereafter.
  - Change to D5 half NS when blood glucose ≤250 mg/dL.

FLUID REPLACEMENT *CONTD…*

Hours	Volume
1st half-hour to 1 hour	1 L
2nd hr	1 L
3rd hr	500 mL– 1 L
4th hr	500 mL– 1 L
5th hr	500 mL– 1 L
Total 1st 5 hr	3.5 - 5 L
6th–12th hr	250– 500 mL/hr

May need to adjust type and rate of fluid administration in the elderly and in patients with congestive heart failure or renal failure.

INSULIN MANAGEMENT

- Regular insulin 10 U i.v. stat (for adults) or 0.15 U/kg i.v. stat.
- Start regular insulin infusion 0.1 U/kg per hour or 5 U per hour.
- Increase insulin by 1 U per hour every 1–2 hr if less than 10% decrease in glucose or no improvement in acid-base status.
- Decrease insulin by 1–2 U per hour (0.05–0.1 U/kg per hour) when glucose ≤250 mg/dL and/or progressive improvement in clinical status with decrease in glucose of >75 mg/dL per hour.
- Do not decrease insulin infusion to <1 U per hour.

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INSULIN MANAGEMENT *CONTD…*

- Maintain glucose between 140 and 180 mg/dL.
- If blood sugar decreases to <80 mg/dL, stop insulin infusion for no more than 1 hr and restart infusion.
- If glucose drops consistently to <100 mg/dL, change i.v. fluids to D10 to maintain blood glucose between 140 and 180 mg/dL.
- Once patient is able to eat, consider change to s.c. insulin:
- Overlap short-acting insulin s.c. and continue i.v. infusion for 1–2 hr.
- For patients with previous insulin dose: return to prior dose of insulin.
- For patients with newly diagnosed diabetes: full-dose s.c. insulin based on 0.6 U/kg per day.

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TREATMENT OF DKA
FLUIDS AND ELECTROLYTES

- Sodium replacement
  - Calculate effective serum sodium
  - Serum sodium + 1.6 (blood glucose-100)/100
  - isotonic saline (0.9% NaCl) is infused at a rate of 15–20 ml ·/ kg/ body wt /· h or greater during the 1st hour (~1–1.5 l in the average adult). Subsequent choice for fluid replacement depends on the state of hydration, serum electrolyte levels, and urinary output.
  - In general, 0.45% NaCl infused at 4–14 ml / kg/ h is appropriate if the corrected serum sodium is normal or elevated; 0.9% NaCl at a similar rate is appropriate if corrected serum sodium is low.

POTASSIUM REPLACEMENT

- Do not administer potassium if serum potassium >5.5 mEq/L or patient is anuric.
- Use KCl but alternate with KPO4 if there is severe phosphate depletion and patient is unable to take phosphate by mouth.
- Add i.v. potassium to each liter of fluid administered unless contraindicated.

POTASSIUM REPLACEMENT *CONTD…*

Serum K (mEq/L)		Additional K required
<3.5 - 4.0	-	40 mEq/L
3.5–4.5	-	20 mEq/L.
4.5–5.5	-	10 mEq/L
>5.5	-	Stop K infusion

PHOSPHATE

- Hypophasphatemia may develop during increased glucose usage

- If serum level <1mg/dl then phosphate supplementation considered and monitor for hypocalcemia and hypomagnesemia

- No benefit demonstrated in RCT .

BICARBONATE

- Clinical trials donot support the rouine use of bicarbonate replacement

- HCO3 replacement and rapid reversal of acidosis can impair cardiac function, reduce tissue oxygenation and promote hypokalemia and hypocalcemia.

BICARBONATE *CONTD…*

- However in presence of sevare acidosis ph<6.9,in hemodynamic instability with ph<7.1 and hyperkaemia with ecg finding bicarbonate therapy considered .

- In the presence of severe acidosis (arterial pH <6.9), the ADA advises bicarbonate [50 mmol/L (meq/L) of sodium bicarbonate in 200 mL of sterile water with 10 meq/L KCl per hour for 2 h until the pH is >7.0].

TREATMENT OF DKA
GLUCOSE ADMINISTRATION

- Plasma glucose reaches 250 mg/dl in DKA or 300 mg/dl in HHS,
- Decrease the insulin infusion rate to 0.05–0.1 unit/kg/h (3–6 units/h),
- Add dextrose (5–10%) to the intravenous fluids.
- Maintain the above glucose values until acidosis in DKA or mental obtundation and hyperosmolarity in HHS are resolved

MONITORING

- Flow sheet mantained tabulating mental status, vital signs,insulin dose,fluid and electrolyte administered and urine output

- Capillary glucose 1-2hrly,electrolytes especially K+,bicarbonate and phosphate) and anion gap every 4 hrly for first 24 hr

- Monitor BP,pulse respiration fluid intake and output every 1-4 h

ONCE DKA RESOLVED…

- Most patients require 0.5-0.6 units/kg/day
- highly insulin resistant patients
  - 0.8-1.0 units/kg/day

- Give ***subcutaneous*** insulin at least 2 hours prior to weaning insulin infusion.

COMPLICATIONS OF DKA

- Shock
  - If not improving with fluids r/o MI
- Vascular thrombosis
  - Severe dehydration
  - Cerebral vessels
  - Occurs hours to days after DKA
- Pulmonary Edema
  - Result of aggressive fluid resuscitation
- Cerebral Edema
  - First 24 hours
  - Mental status changes
  - May require intubation with hyperventilation

Strategies to Prevent Diabetic Ketoacidosis

- Diabetic education
- Blood glucose monitoring
- Sick-day management
- Home monitoring of ketones or beta-hydroxybutyrate
- Supplemental short-acting insulin regimens
- Easily digestible liquid diets when sick
- Reducing, rather than eliminating, insulin when patients are not eating
- Guidelines for when patients should seek medical attention
- Case monitoring of high-risk patients
- Special education for patients on pump management

Thankyou