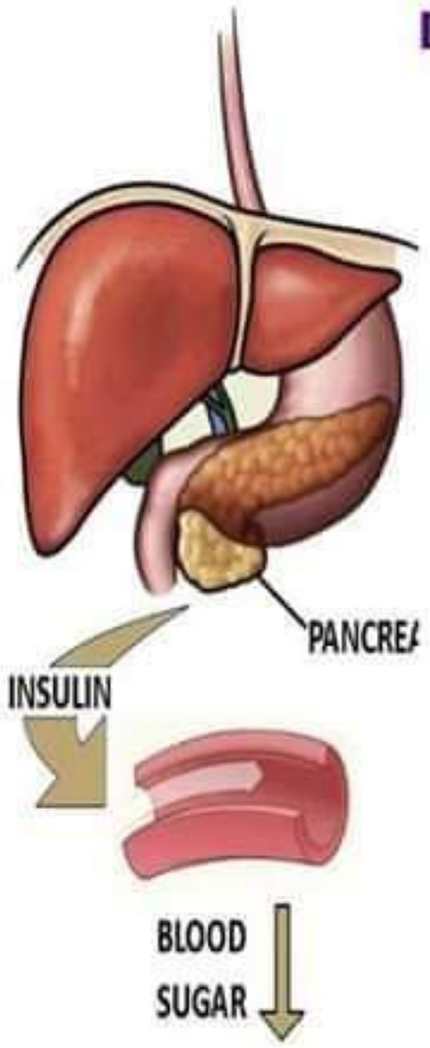
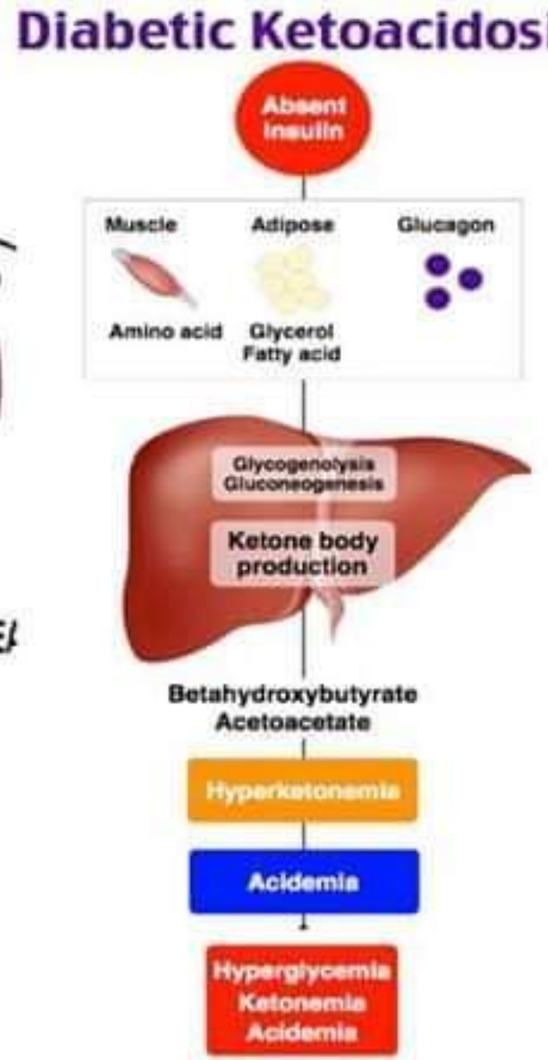
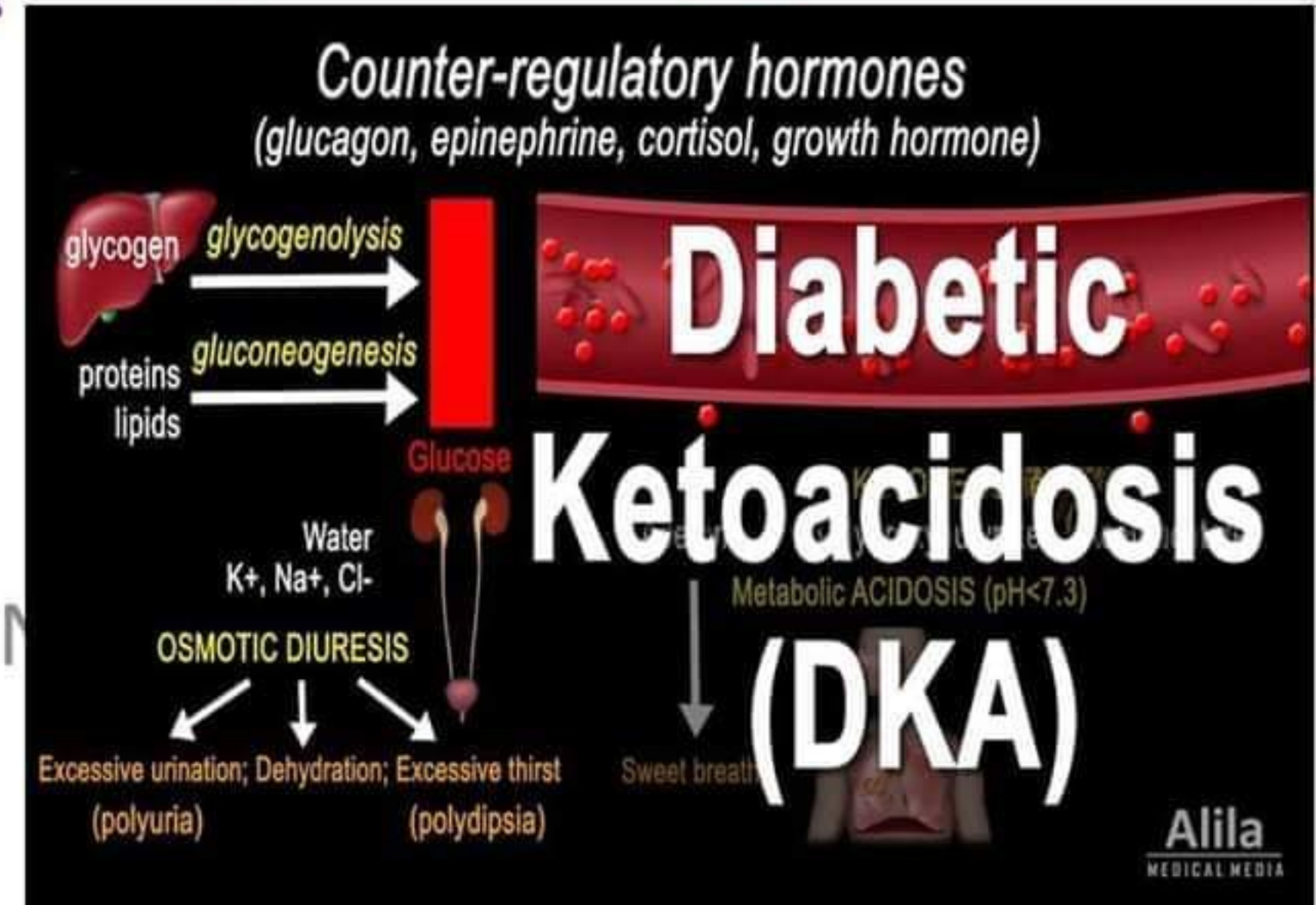
DIABETES KETOACIDOSIS







INTRODUCTION

- **Diabetic ketoacidosis** (**DKA**) is a potentially life-threatening complication in people with diabetes mellitus. It happens predominantly in those with type 1 diabetes, but it can occur in those with type 2 diabetes under certain circumstances.
- DKA results from a shortage of insulin; in response the body switches to burning fatty acids and producing acidic ketone bodies that cause most of the symptoms and complications

DEFINATION

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

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

(ii) Ketosis,

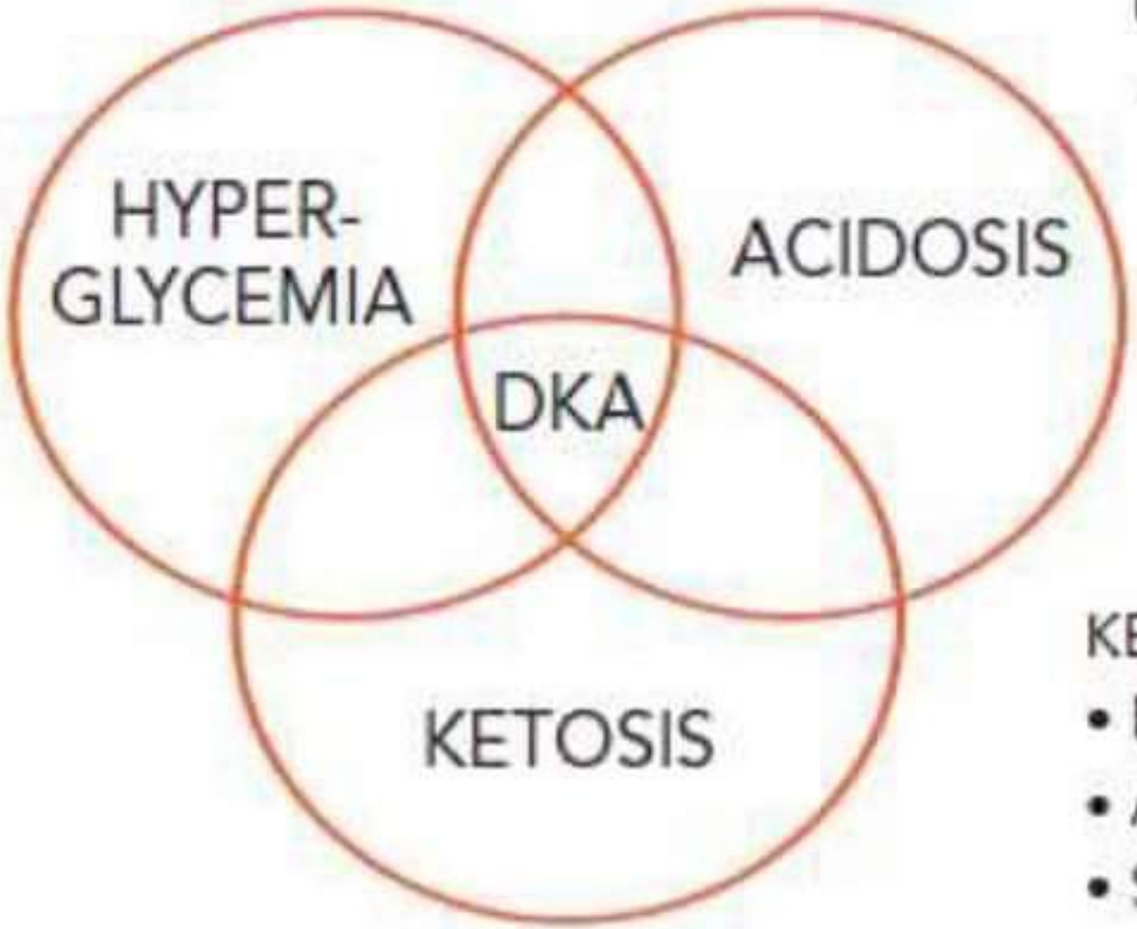
(iii) Acidemia (pH <7.3).

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)



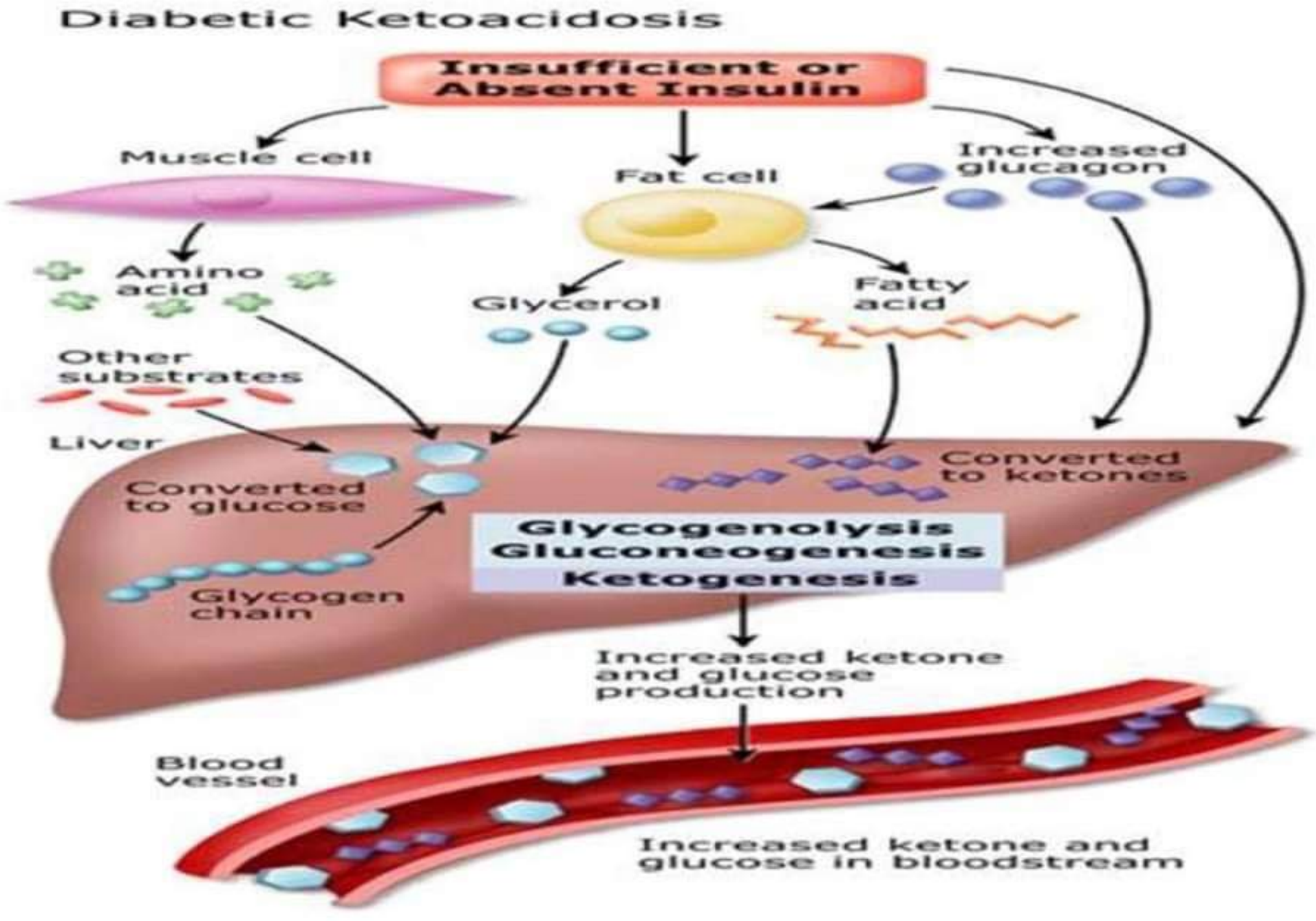
KETOTIC STATES

- Ketotic Hypoglycemia
- Alcoholic Ketosis
- Starvation Ketosis

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



SYMPTOMS

•DKA can be the first presentation.

•Nausea/vomiting

•Thirst/polyuria

•Abdominal pain

•Shortness of breath

PHYSICAL FINDINGS

•Tachycardia

•Dehydration/hypotension

•Tachypnea/kussmaul respirations/respiratory distress

•Fruity odour in breath.

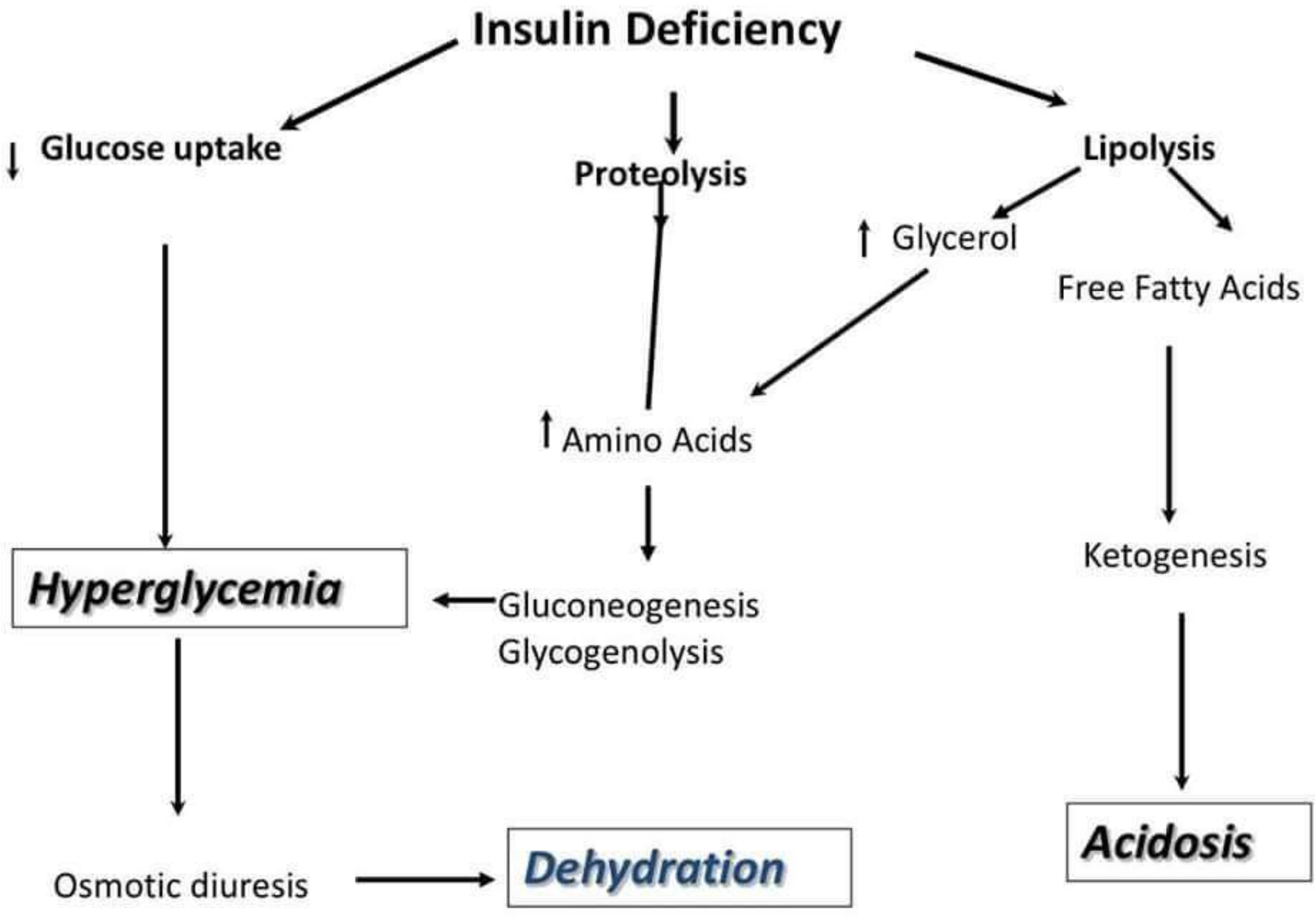
•Abdominal tenderness(may resemble acute pancreatitis or surgical abdomen)

•Lethargy/obtundation/cerebral edema/possibly coma.

ETIOLOGY

- Diabetic patients
- Infection: Pneumonia/UTI/Gastroenteritis/sepsis
- Inadequate insulin administration
- Infarction: cerebral, coronary, mesenteric, peripheral
- Drugs: cocain
- Pregnancy

PATHOPHYSIOLOGY



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PATHOPHYSIOLOGY

- Diabetic ketoacidosis arises because of a lack of insulin in the body.
- The lack of insulin and corresponding elevation of glucagon leads to increased release of glucose by the liver(a process that is normally suppressed by insulin) from glycogen via glycogenolysis and also through gluconeogenesis.
- High glucose levels spill over into the urine, taking water and solutes (such as sodium and potassium) along with it in a process known as osmotic diuresis.
- This leads to polyuria, dehydration, and compensatory thirst and polydipsia.

- The absence of insulin also leads to the release of free fatty acids from adipose tissue (lipolysis), which are converted through a process called beta oxidation, again in the liver, into ketone bodies (acetoacetate and β-hydroxybutyrate).
- β-Hydroxybutyrate can serve as an energy source in the absence of insulin-mediated glucose delivery, and is a protective mechanism in case of starvation.

- The ketone bodies, however, have a low pKa and therefore turn the blood acidic (metabolic acidosis).
- The body initially buffers the change with the bicarbonate buffering system, but this system is quickly overwhelmed and other mechanisms must work to compensate for the acidosis.
- One such mechanism is hyperventilation to lower the blood carbon dioxide levels (a form of compensatory respiratory alkalosis).

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

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LAB INVESTIGATION

- Serum glucose levels
- Serum electrolyte levels (eg, potassium, sodium, chloride, magnesium, calcium, phosphorus)
- Bicarbonate levels
- Amylase and lipase levels
- Urine dipstick
- Ketone levels
- Serum or capillary beta-hydroxybutyrate levels
- ABG measurements
- CBC count
- BUN and creatinine levels
- Urine and blood cultures if intercurrent infection is suspected
- ECG (or telemetry in patients with comorbidities)

IMAGING TESTS

Radiologic studies that may be helpful in patients with DKA include the following:

- Chest radiography: To rule out pulmonary infection such as pneumonia
- Head CT scanning: To detect early cerebral edema; use low threshold in children with DKA and altered mental status
- Head MRI: To detect early cerebral edema (order only if altered consciousness is present

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.

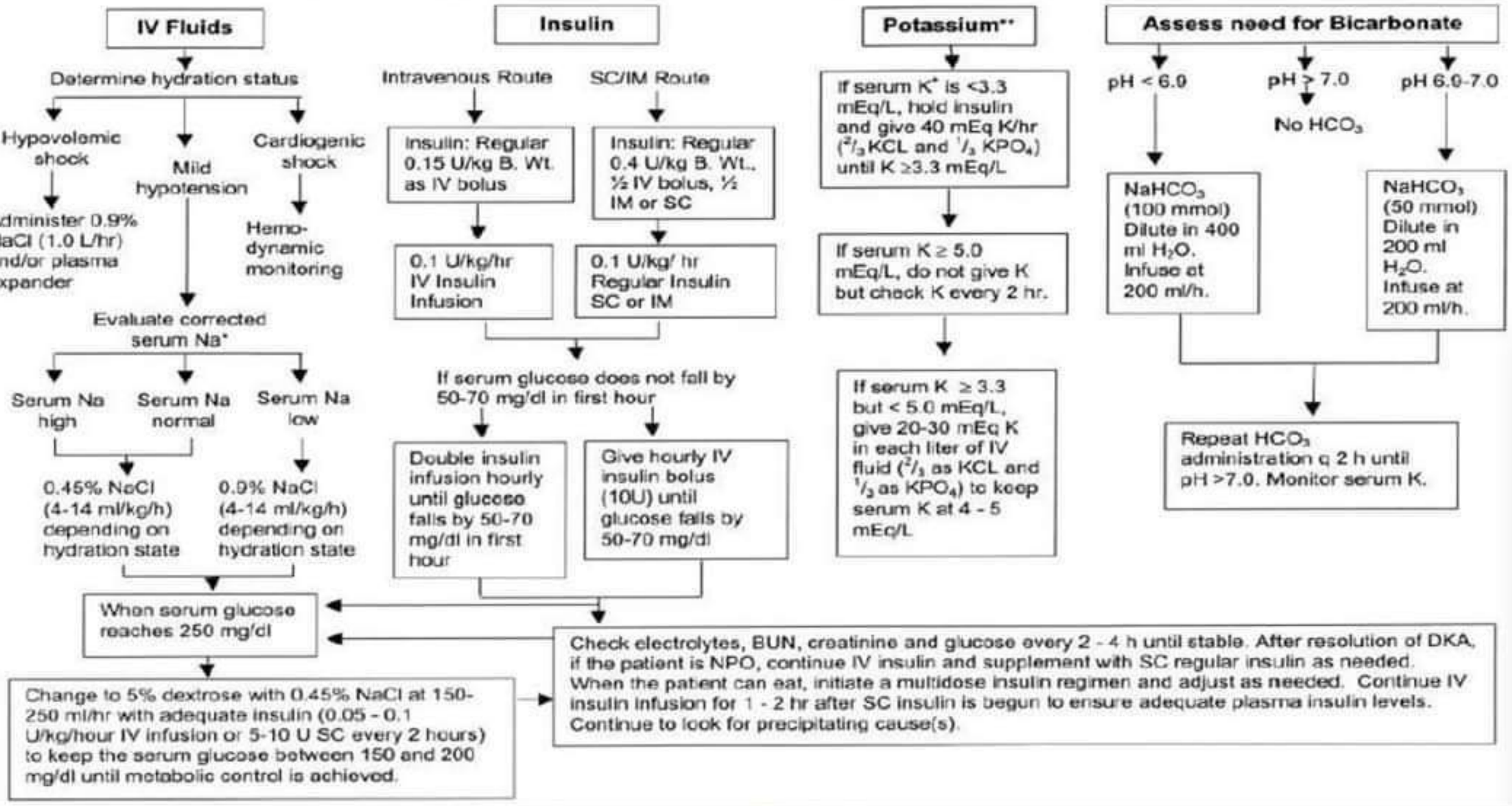


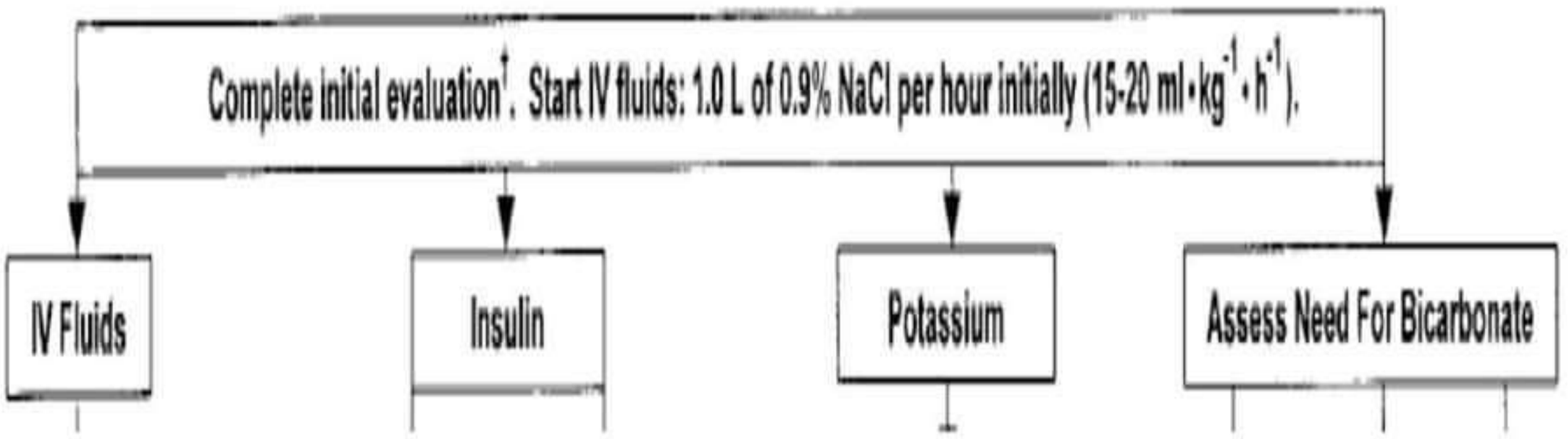
Figure 1. Protocol for Management of Adult Patients with Diabetic Ketoacidosis

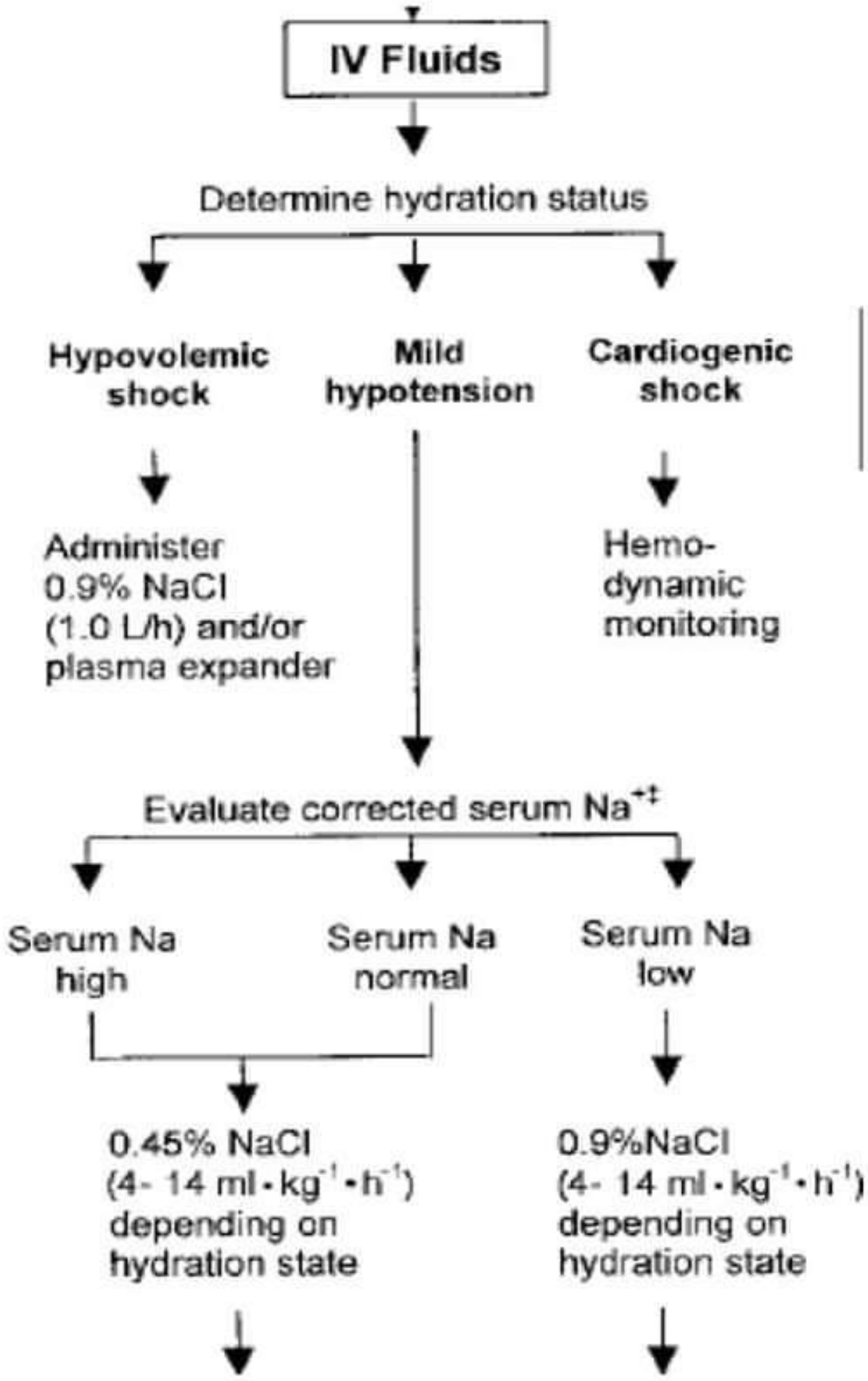
*Serum Na^+ should be corrected for hyperglycemia (for each 100 mg/dl glucose above 100 mg/dl, add 1.6 mEq to sodium value for corrected serum sodium value).

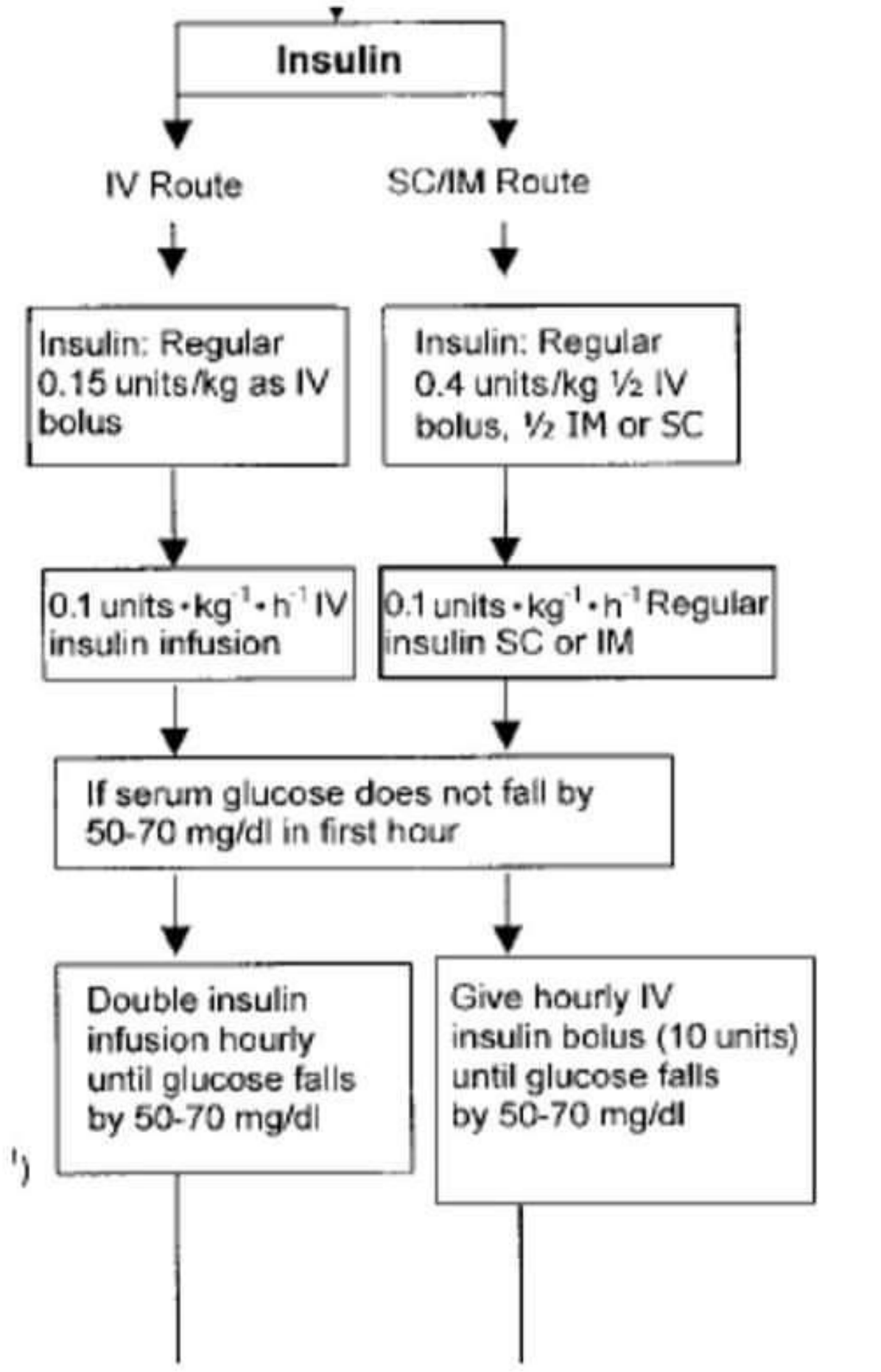
**Upper limits for serum potassium may vary by laboratory.

Adapted with permission from reference 27.

Management of Adult Patients with DKA*




IV Fluids
Determine hydration status
Hypovolemic shock
Mild hypotension
Cardiogenic shock
Administer 0.9% NaCl (1.0 L/h) and/or plasma expander
Hemo-dynamic monitoring
Evaluate corrected serum Na*‡
Serum Na high
Serum Na normal
Serum Na low
0.45% NaCl (4- 14 ml • kg⁻¹ • h⁻¹) depending on hydration state
0.9%NaCl (4- 14 ml • kg⁻¹ • h⁻¹) depending on hydration state


Insulin
IV Route
SC/IM Route
Insulin: Regular 0.15 units/kg as IV bolus
Insulin: Regular 0.4 units/kg ½ IV bolus, ½ IM or SC
0.1 units • kg⁻¹ • h⁻¹ IV insulin infusion
0.1 units • kg⁻¹ • h⁻¹ Regular insulin SC or IM
If serum glucose does not fall by 50-70 mg/dl in first hour
Double insulin infusion hourly until glucose falls by 50-70 mg/dl
Give hourly IV insulin bolus (10 units) until glucose falls by 50-70 mg/dl

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).

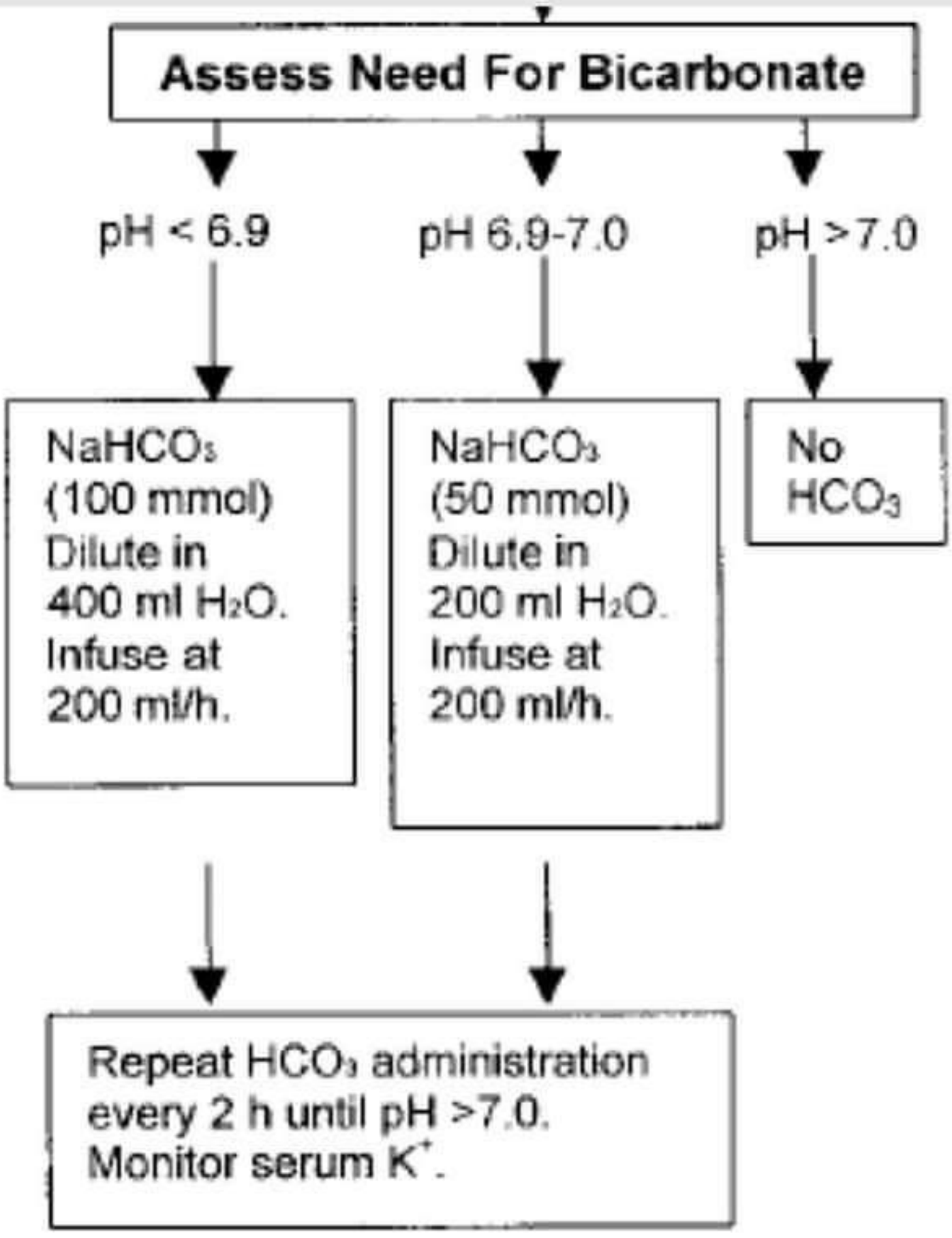
Potassium

If serum K^+ is <3.3 mEq/L, hold insulin and give 40 mEq K^+ per h (2/3 KCL and 1/3 KPO_4) until $K \geq 3.3$ mEq/L

If serum $K^+ \geq 5.0$ mEq/L, do not give K^+ but check K^+ every 2 h

If serum $K^+ \geq 3.3$ but < 5.0 mEq/L, give 20-30 mEq K^+ in each liter of IV fluid (2/3 as KCL and 1/3 as KPO_4) to keep serum K^+ at 4-5 mEq/L

Diabetes Spectrum Volume 15, Number 1, 2002



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.

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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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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.

Williams textbook of endocrinology 10th edition p 454

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 .

Williams textbook of endocrinology 10th edition p456

BICARBONATE

- Clinical trials do not support the routine use of bicarbonate replacement

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

Williams textbook of endocrinology 10th edition p456

BICARBONATE *CONTD*...

- ❑ However in presence of severe acidosis ph<6.9,in hemodynamic instability with ph<7.1 and hyperkalemia 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].

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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

Williams textbook of endocrinology 10th edition p 456

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.

Williams textbook of endocrinology 10th edition p455

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

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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