Management of Hyperglycemic Crises

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Case Vignette

- A 22-year-old woman with an 8-year history of type 1 diabetes is admitted to the hospital for management of a hyperglycemic crisis.
- She uses an insulin pump since 2 years ago. Her most recent HbA1c value was 7.2%.
- The night before admission her insulin pump malfunctioned overnight.
- Now, she has nausea, vomiting and abdominal pain.

Case Vignette (cont.)

- **P/E:**
  - She is awake and oriented but appears fatigued.
  - BT: 36.5°C; BP: 95/65 mmHg; PR: 110/min (regular)
  - Weight: 55 kg
  - Dry mucous membranes
  - Kussmaul respiration
  - Diffuse abdominal tenderness without rebound

Case Vignette (cont.)

- **Laboratory test results:**
  - pH: 6.9; bicarbonate: 10 mEq/L
  - Blood glucose: 268 mg/dL
  - BUN: 56 mg/dL; Cr: 2.6 mg/dL
  - Na: 135 mEq/L; K: 3.2 mEq/L; Cl: 108 mEq/L
  - Mg: 1.7 mg/dL; Ph: 3.6 mg/dL

Important Calculations

Case Vignette (cont.)

- **Anion gap**

  (Na+) – (Cl^- + $HCO3^-$): 17 mEq/L

- **<u>Effective</u> serum osmolality**

  2[measured Na+ (mEq/L)] + glucose (mg/dL)/18:

  285 mosm/mL

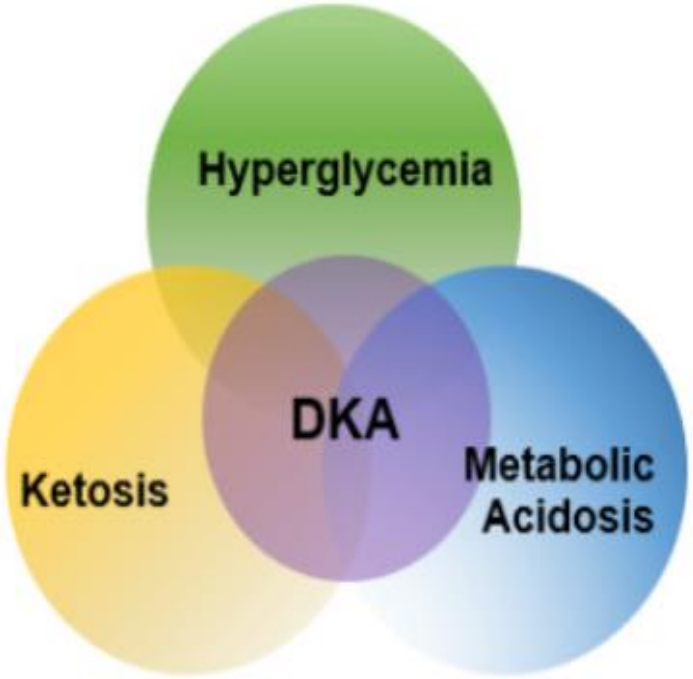
- **Corrected serum Na+**

  For each 100 mg/dL glucose >100 mg/dL, add 1.6 mEq:

  ~138 mEq/L

The triad of DKA

Other Hyperglycemic States:
- Diabetes Mellitus
- Non-ketotic Hyperosmolar Coma
- Stress Hyperglycemia
- Drug-induced Hyperglycemia



Other Ketotic States:
- Starvation Ketosis
- Alcoholic Ketosis

Other Metabolic Acidosis States:
- Normal Anion Gap Hyperchloremic Acidosis
  - Diarrhea
  - Renal Tubular Acidosis
  - Rapid Large Volume Saline Infusion
- High anion gap metabolic acidosis
  - Lactic acidosis (L- and D- lactate)
  - Salicylate
  - Ethylene Glycol, Methanol, Propylene
  - Renal Failure (Uremia)
  - Drug-induced Acidosis

Kitabchi AE, Wall BM. Med Clin North Am 1995;79(1):9-37.

Diagnostic criteria for DKA and HHS

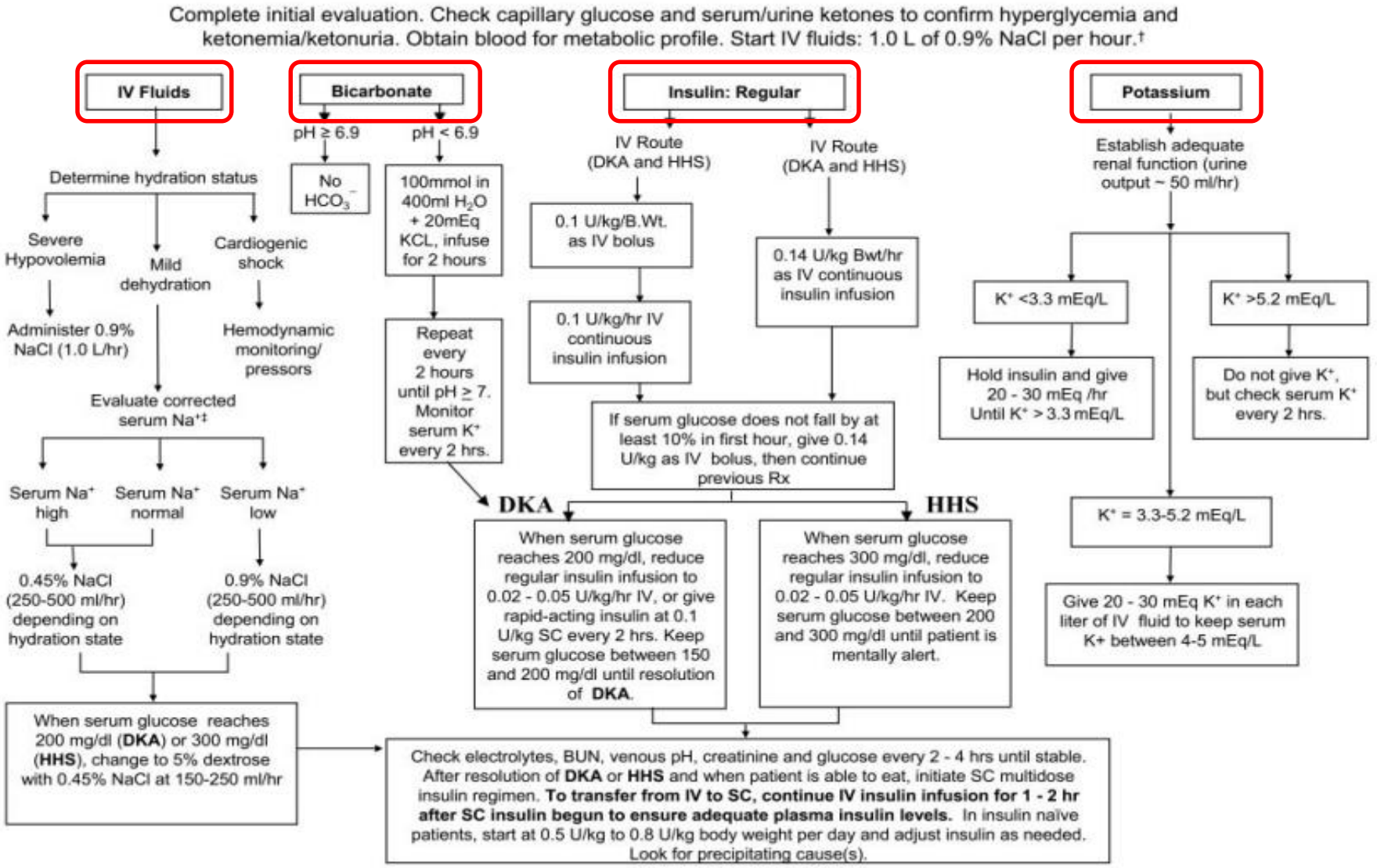
	DKA			HHS
	Mild (plasma glucose >250 mg/dl)	Moderate (plasma glucose >250 mg/dl)	Severe (plasma glucose >250 mg/dl)	Plasma glucose >600 mg/dl
Arterial pH	7.25–7.30	7.00 to <7.24	<7.00	>7.30
Serum bicarbonate (mEq/l)	15–18	10 to <15	<10	>18
Urine ketone*	Positive	Positive	Positive	Small
Serum ketone*	Positive	Positive	Positive	Small
Effective serum osmolality†	Variable	Variable	Variable	>320 mOsm/kg
Anion gap‡	>10	>12	>12	Variable
Mental status	Alert	Alert/drowsy	Stupor/coma	Stupor/coma

*Nitroprusside reaction method. †Effective serum osmolality: 2[measured Na^+ (mEq/l)] + glucose (mg/dl)/18. ‡Anion gap: $(Na^+) - [(Cl^- + HCO_3^-$ (mEq/l)].

DKA, diabetic ketoacidosis
HHS, hyperglycemic hyperosmolar state

Kitabchi AE, et al. Diabetes Care 2009;32(7):1335-43.
Gosmanov AR, et al. Endotext NCBI Bookshelf 2021.

Protocol for the management of adult patients with DKA or HHS



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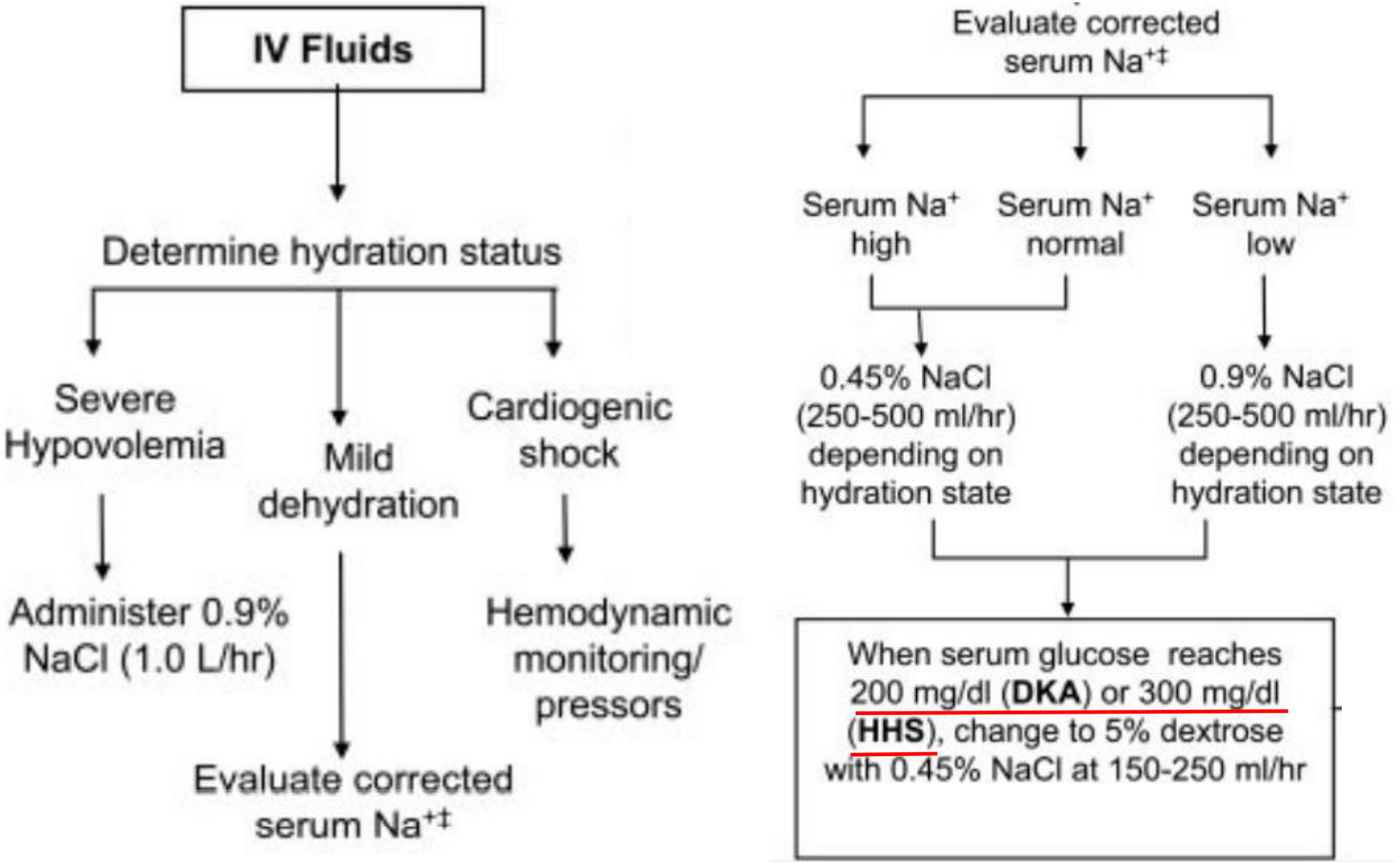
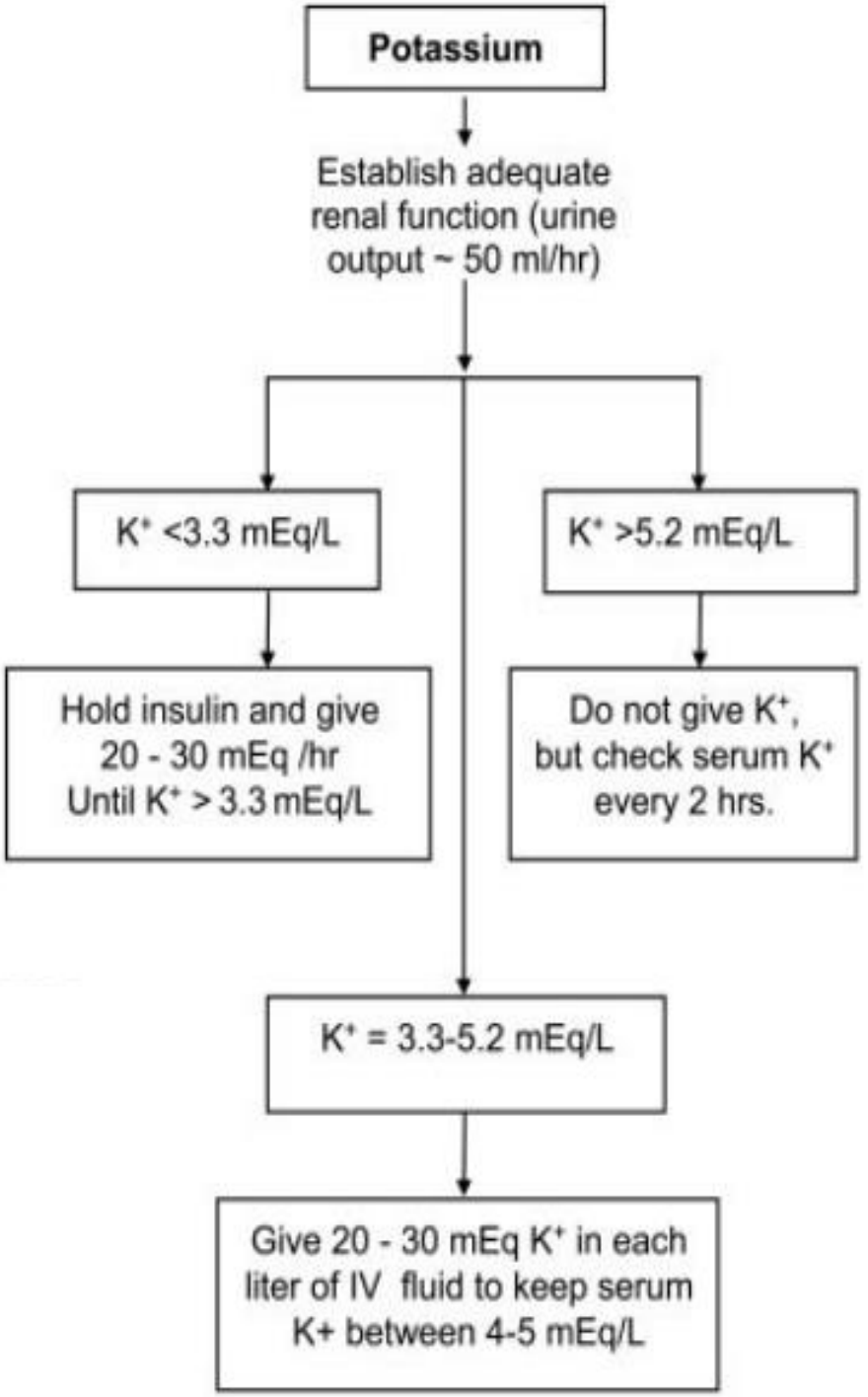
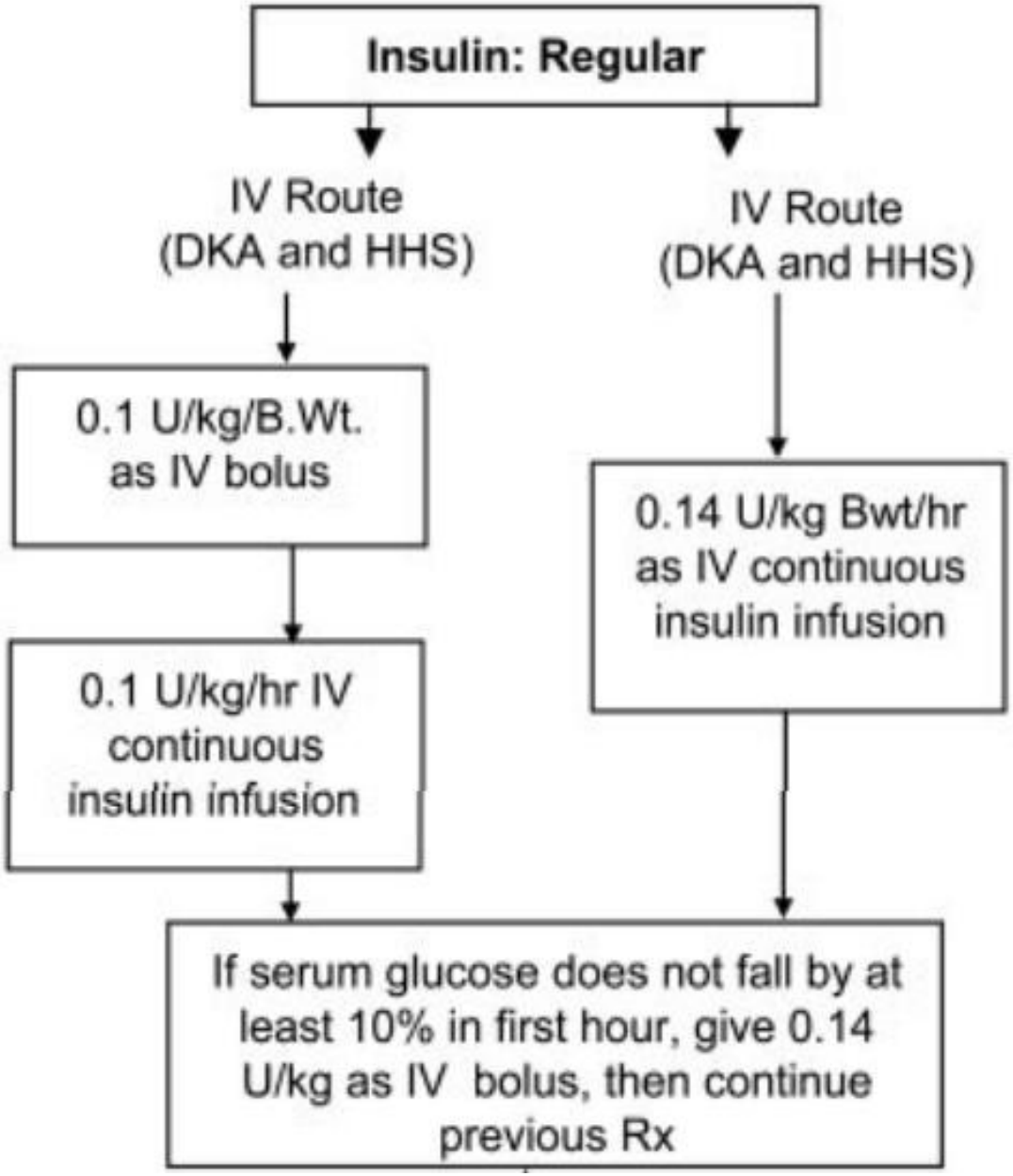
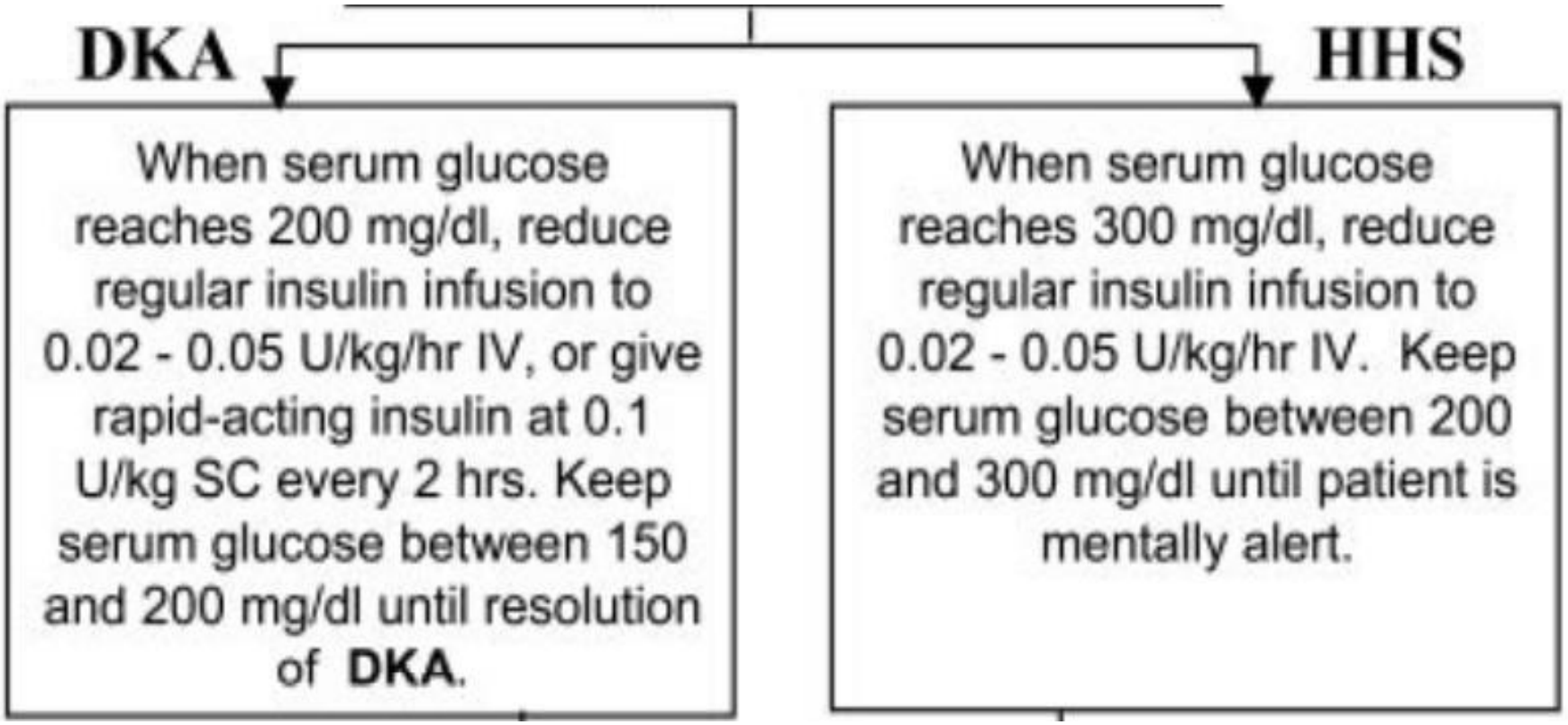

IV Fluids
Determine hydration status
Severe Hypovolemia
Mild dehydration
Cardiogenic shock
Administer 0.9% NaCl (1.0 L/hr)
Evaluate corrected serum Na+‡
Hemodynamic monitoring/ pressors
Evaluate corrected serum Na+‡
Serum Na+ high
Serum Na+ normal
Serum Na+ low
0.45% NaCl (250-500 ml/hr) depending on hydration state
0.9% NaCl (250-500 ml/hr) depending on hydration state
When serum glucose reaches 200 mg/dl (DKA) or 300 mg/dl (HHS), change to 5% dextrose with 0.45% NaCl at 150-250 ml/hr

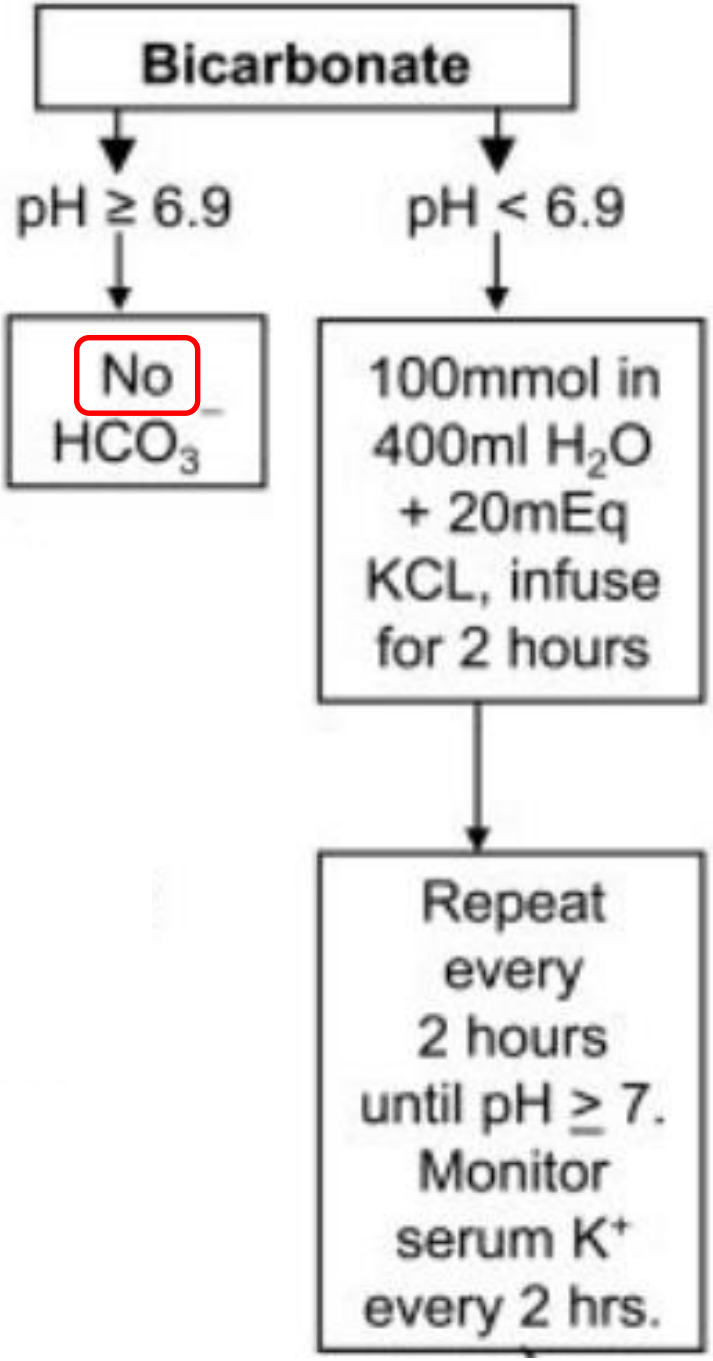

Potassium
Establish adequate renal function (urine output ~ 50 ml/hr)
K+ <3.3 mEq/L
K+ >5.2 mEq/L
Hold insulin and give 20 - 30 mEq /hr Until K+ > 3.3 mEq/L
Do not give K+, but check serum K+ every 2 hrs.
K+ = 3.3-5.2 mEq/L
Give 20 - 30 mEq K+ in each liter of IV fluid to keep serum K+ between 4-5 mEq/L


Insulin: Regular
IV Route
(DKA and HHS)
IV Route
(DKA and HHS)
0.1 U/kg/B.Wt.
as IV bolus
0.14 U/kg Bwt/hr
as IV continuous
insulin infusion
0.1 U/kg/hr IV
continuous
insulin infusion
If serum glucose does not fall by at least 10% in first hour, give 0.14 U/kg as IV bolus, then continue previous Rx



BS 150-200 mg/dL

BS 200-300 mg/dL


Bicarbonate
pH ≥ 6.9
pH < 6.9
No HCO_3^-
100mmol in 400ml H_2O + 20mEq KCL, infuse for 2 hours
Repeat every 2 hours until pH ≥ 7. Monitor serum K^+ every 2 hrs.

Check electrolytes, BUN, venous pH, creatinine and glucose every 2 - 4 hrs until stable. After resolution of **DKA** or **HHS** and when patient is able to eat, initiate SC multidose insulin regimen. **To transfer from IV to SC, continue IV insulin infusion for 1 - 2 hr after SC insulin begun to ensure adequate plasma insulin levels.** In insulin naïve patients, start at 0.5 U/kg to 0.8 U/kg body weight per day and adjust insulin as needed. Look for precipitating cause(s).

- **Criteria for resolution of ketoacidosis:**

  Blood glucose <200 mg/dL and two of the following criteria:

  Serum bicarbonate ≥15 mEq/L

  Venous pH >7.3

  Calculated anion gap ≤12 mEq/L

- **Criteria for resolution of HHS:**

  Normal osmolality and regain of normal mental status

Kitabchi AE, et al. Diabetes Care 2009;32(7):1335-43.

Important Points

Some points

- During treatment of DKA, hyperglycemia is corrected faster than ketoacidosis.
- Rapid correction of hyperglycemia can precipitate the development of cerebral edema.
- Insulin therapy, correction of acidosis, and volume expansion decrease serum potassium concentration.
- Phosphate concentration decreases with insulin therapy. Serum phosphate <1 mg/dL: careful phosphate replacement and calcium monitoring
- Hypomagnesemia may develop during DKA therapy.

Some points

- Bicarbonate therapy for DKA offers no advantage in improving cardiac or neurologic functions or in the rate of recovery of hyperglycemia and ketoacidosis.

- Keep in mind deleterious effects of bicarbonate therapy:

  Increased risk of hypokalemia

  Decreased tissue oxygen uptake

  Cerebral edema

  Development of paradoxical CNS acidosis

Some points

- Many patients with DKA who develop hypoglycemia during treatment do not experience adrenergic manifestations of sweating, nervousness, fatigue, hunger, and tachycardia.

- Hyperchloremic non-anion gap acidosis, which is seen during the recovery phase of DKA, is self-limited with few clinical consequences.

Some points related to laboratory

- Leukocytosis
- Hypertriglyceridemia
- Hyperamylasemia
- False positive values for lipase
- Artificial elevation of serum creatinine

Some points related to laboratory

- Most of the laboratory tests for ketone bodies use the nitroprusside method, which detects acetoacetate, but not β-hydroxybutyrate (β-OHB). Additionally, since β-OHB is converted to acetoacetate during treatment, the serum ketone test may remain positive for a prolonged period suggesting erroneously that ketonemia is deteriorating; therefore, the follow-up measurement of ketones during the treatment by nitroprusside method is not recommended.

Some points related to laboratory

- The levels of β-hydroxybutyrate of ≥3.8mmol/L (≥3.0mmol/L in children) measured by a specific assay: highly sensitive and specific for DKA diagnosis

- Measurement of serial levels of blood beta-hydroxybutyrate can be useful adjunct to monitor the resolution of DKA. The expected fall in β-OHB with the adequate insulin dosing is 1mmol/L/hr; a lower decrease in blood β-OHB may suggest inadequate insulin provision.

Gosmanov AR, et al. Endotext NCBI Bookshelf 2021.

Euglycemic Diabetic Ketoacidosis

Diagnostic criteria for euglycemic DKA

- Relative euglycemia (< 250 mg/dL)
- Acidosis (pH < 7.30, bicarbonate <18 mEq/L)
- Ketosis

(preferably serum beta-hydroxybutyrate >3 mmol/L if available; serum acetoacetate or urine ketones can be utilized)

Long B, et al. Am J Emerg Med 2021;44:157-160.

Conditions associated with euglycemic DKA

- Anorexia/fasting state (pre-operative)
- Gastroparesis
- Glycogen storage disease
- Infection/sepsis
- Insulin pump use
- Intoxication/Ingestion (alcohol, cocaine)
- Intraabdominal pathology (gastroenteritis, pancreatitis, etc.)
- Ketogenic diet
- Liver disease
- Pregnancy
- Renal disease
- Self-treatment with insulin for DKA prior to presentation
- SGLT2 inhibitor use
- Surgery

Long B, et al. Am J Emerg Med 2021;44:157-160.

Thanks for your patience