How Sweet It Is: Managing Hyperglycemic Emergencies

PRESENTED BY

ROSEMARY TIMMERMAN, DNP, APRN, CCNS, CCRN-CSC-CMC

PROVIDENCE ALASKA MEDICAL CENTER

- No disclosures
- No COI

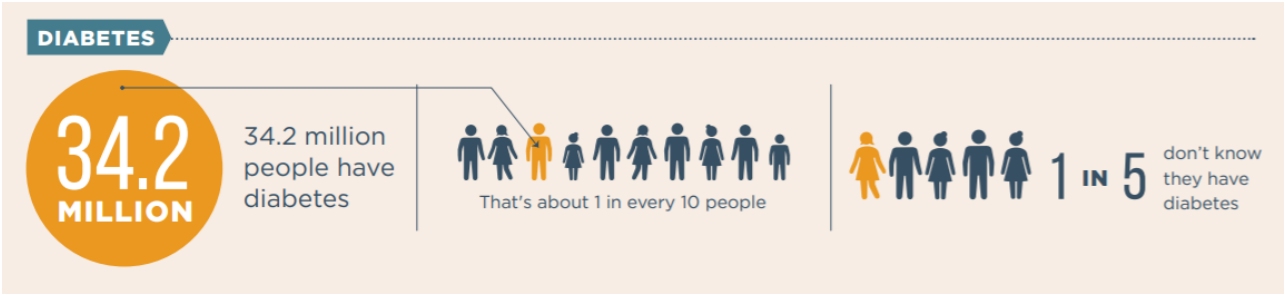
Learning Objectives

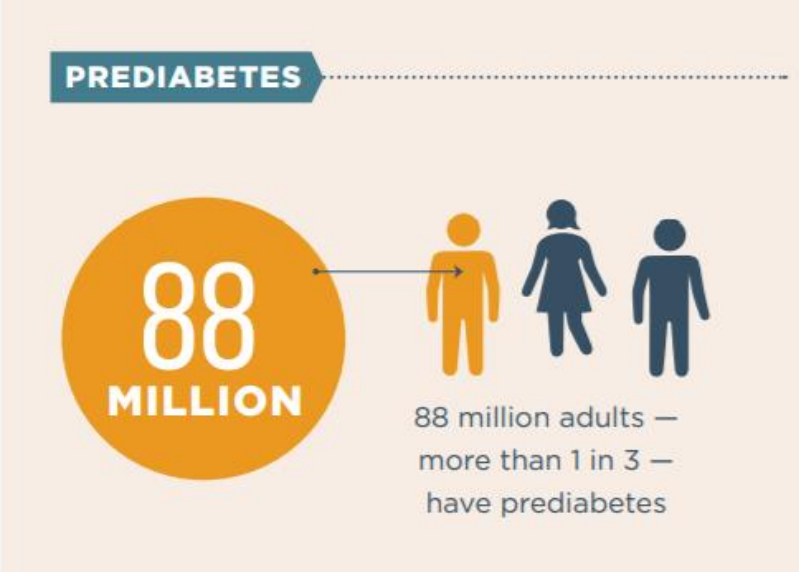
- **By the end of this presentation the learner will be able to:**
  - identify two precipitating risk factors leading to hyperglycemic emergencies.
  - compare and contrast the clinical presentation of a patient with DKA and a patient experiencing HHS.
  - list three critical interventions for the management of the patient with a hyperglycemic emergency.

A bit about.....

DM in US

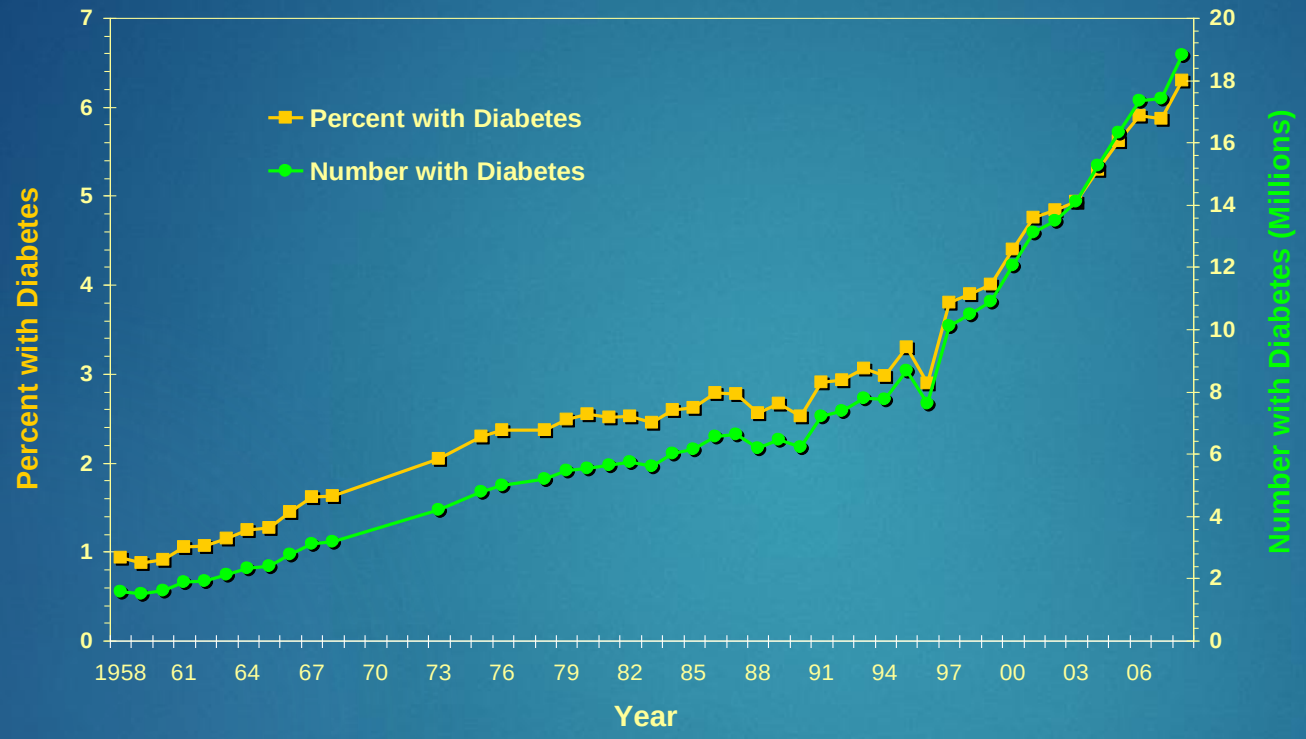
- 34.2 million
  - 10.5% of the population
    - 21.4% undiagnosed





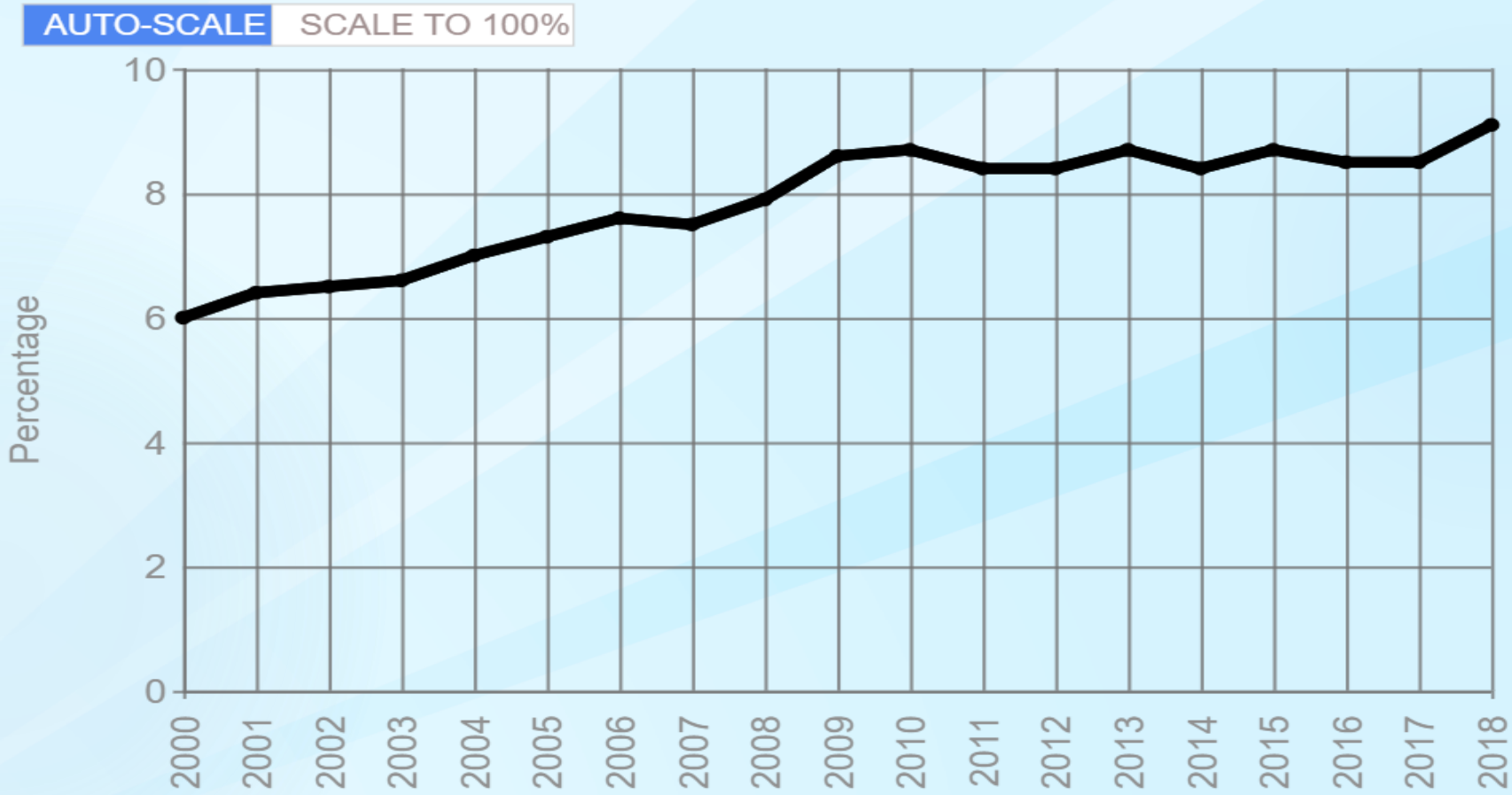
CDC, 2022

Number and Percentage of U.S. Population with Diagnosed Diabetes, 1958-2008



CDC's Division of Diabetes Translation. National Diabetes Surveillance System available at http://www.cdc.gov/diabetes/statistics

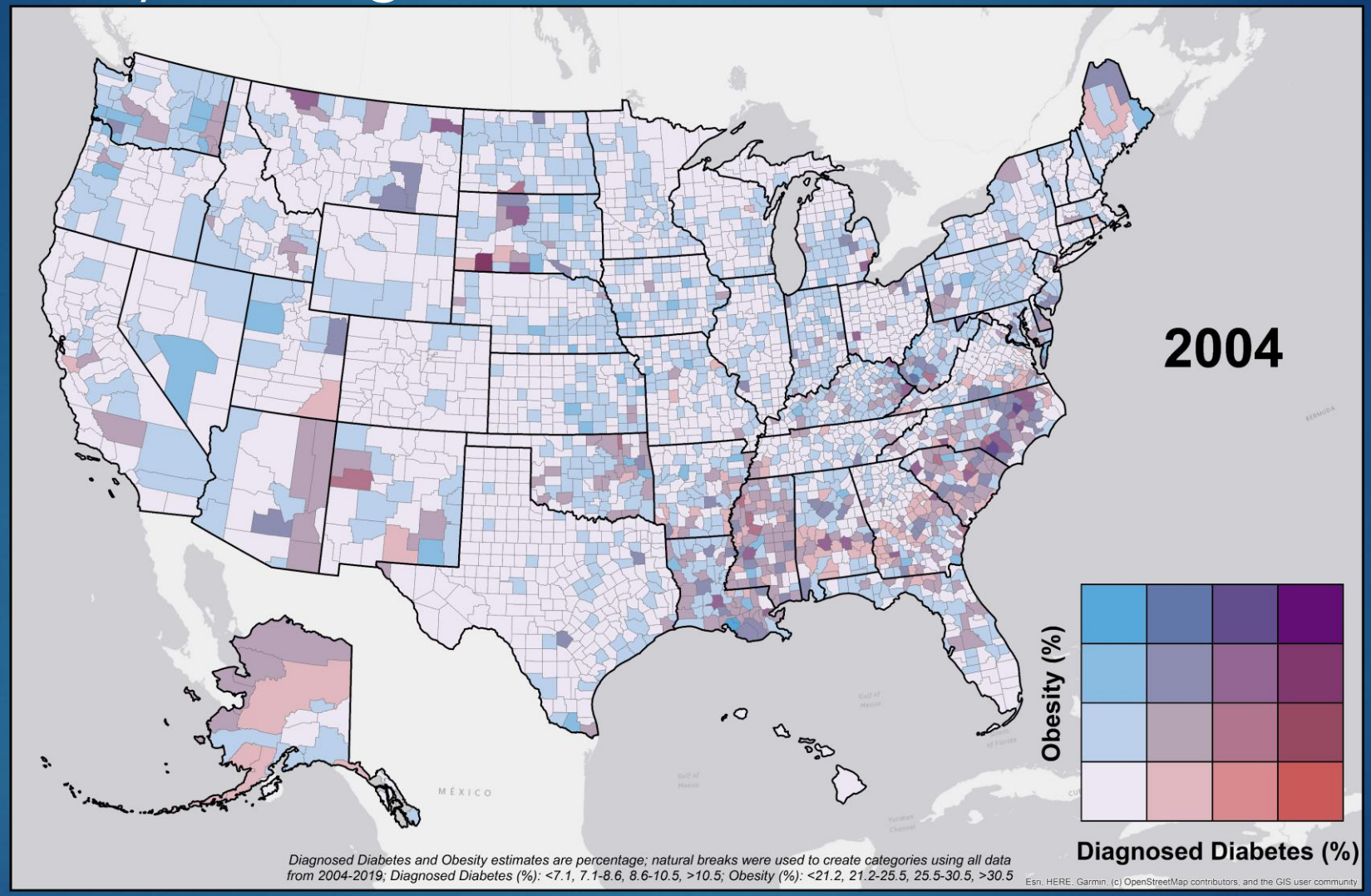
Percent Diagnosed with DM in US Adults ≥ 18 years



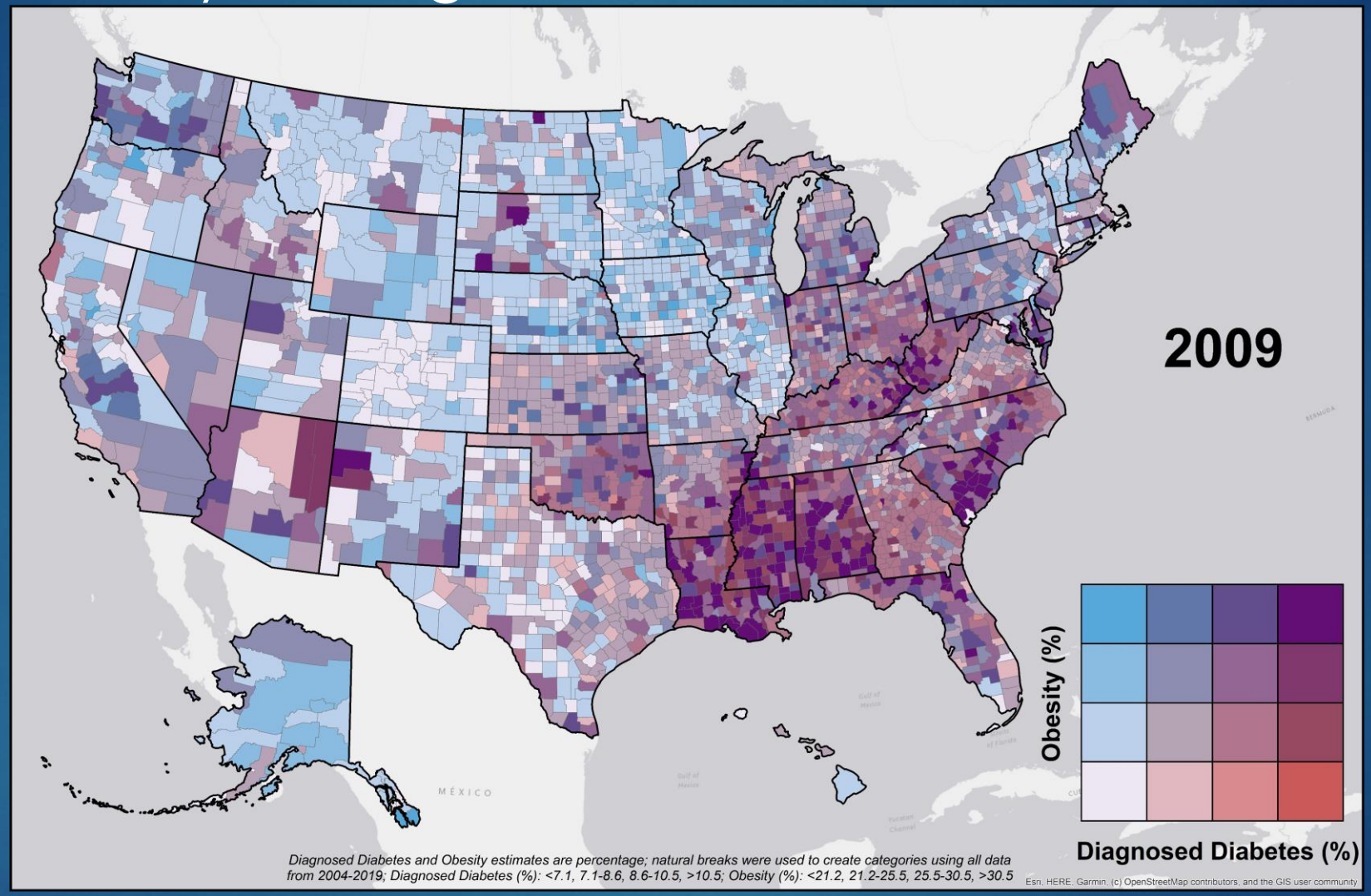
Source: www.cdc.gov/diabetes/data

Disclaimer: This is a user-generated report. The findings and conclusions are those of the user and do not necessarily represent the views of the CDC.

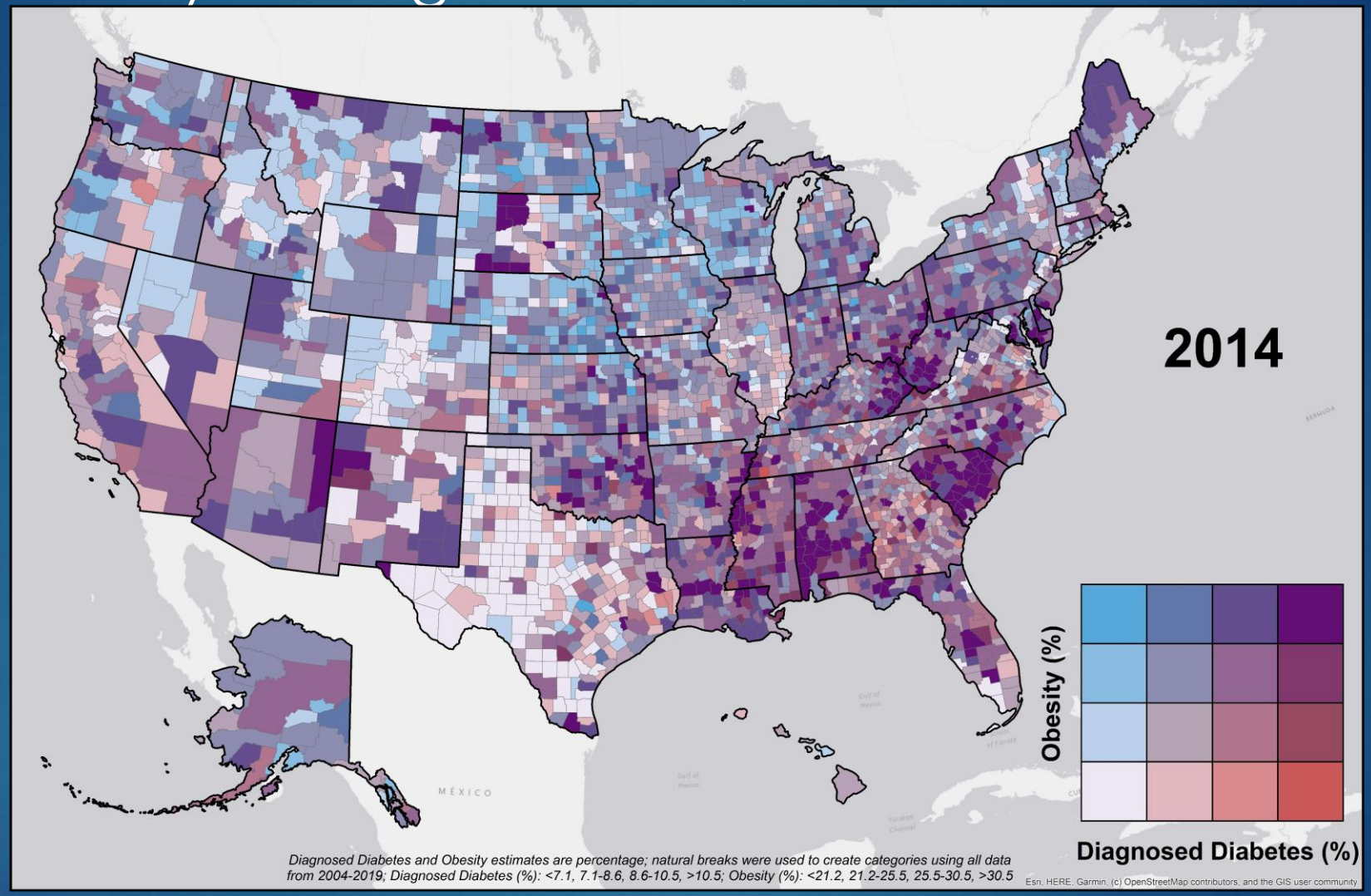
Map of diagnosed diabetes vs obesity by county among US adults, 2004.



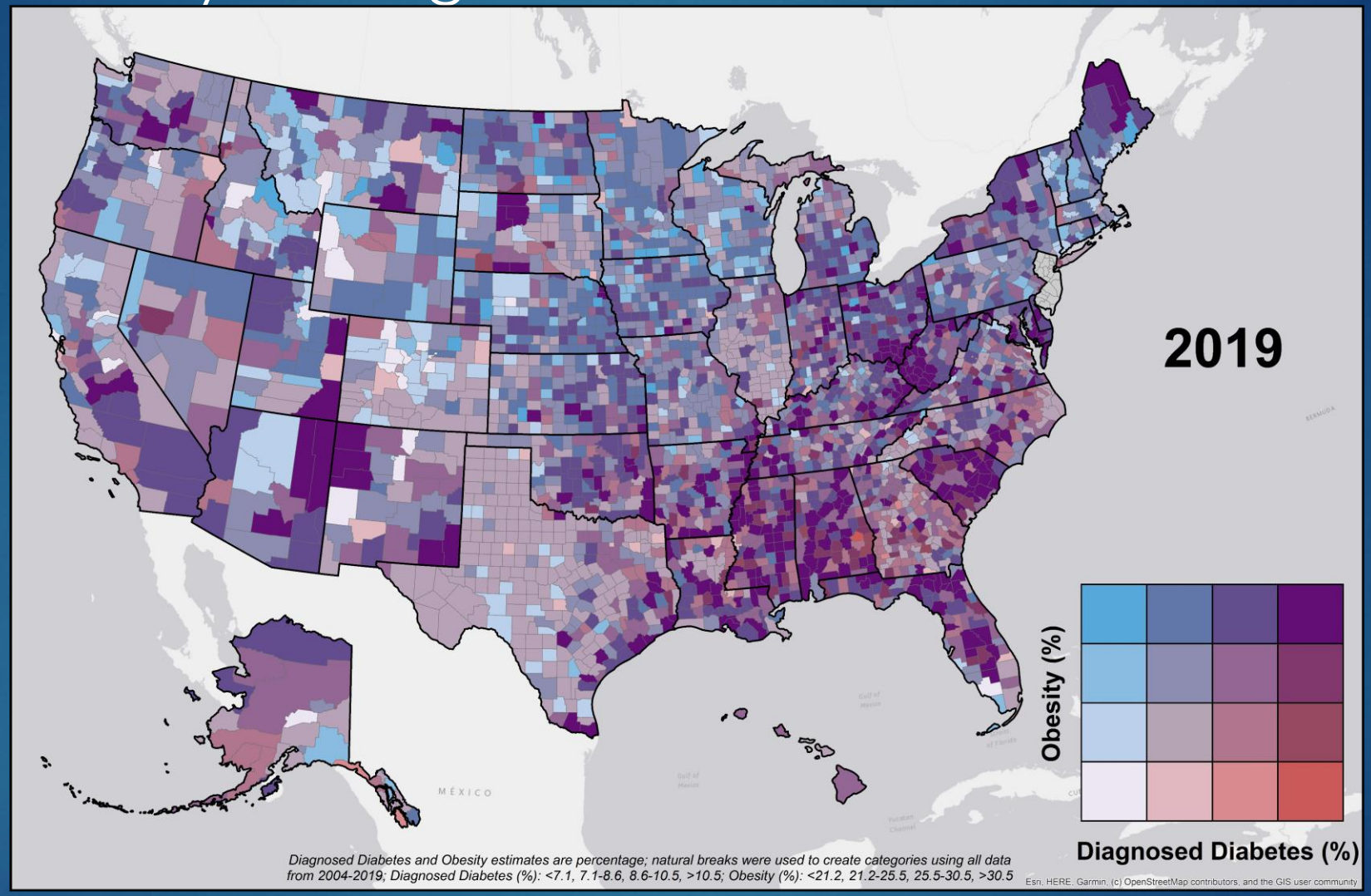
Map of diagnosed diabetes vs obesity by county among US adults, 2009



Map of diagnosed diabetes vs obesity by county among US adults, 2014



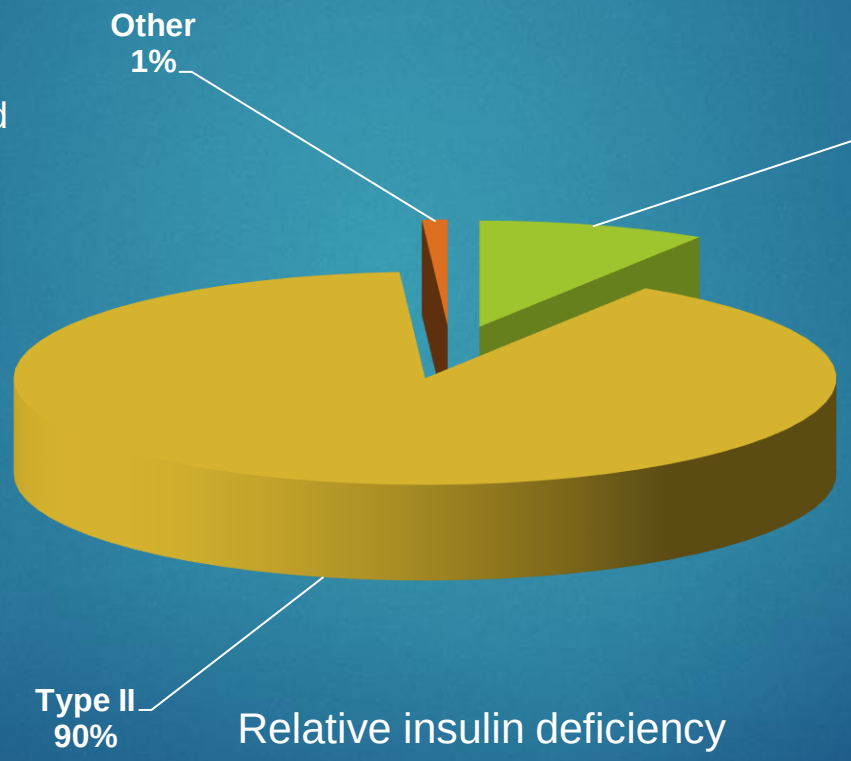
Map of diagnosed diabetes vs obesity by county among US adults, 2019



Diabetes Mellitus

Gestational

Steroid-induced



Absolute insulin deficiency

More prone to DKA

Relative insulin deficiency
Insulin resistance
More prone to HHS

Guidelines

Reviews/Commentaries/ADA Statements
CONSENSUS STATEMENT

Hyperglycemic Crises in Adult Patients With Diabetes

ABBAS E. KITABCHI, PHD, MD[1]
GUILLERMO E. UMPIERREZ, MD[2]
JOHN M. MILES, MD[3]
JOSEPH N. FISHER, MD[1]

DIABETES CARE, VOLUME 32, NUMBER 7, JULY 2009

glucose utilization by peripheral tissues (12–17). This is magnified by transient insulin resistance due to the hormone im-

Curr Diab Rep (2017) 17: 33
DOI 10.1007/s11892-017-0857-4

HOSPITAL MANAGEMENT OF DIABETES (A WALLIA AND JJ SELEY, SECTION EDITORS)

Treatment of Diabetic Ketoacidosis (DKA)/Hyperglycemic Hyperosmolar State (HHS): Novel Advances in the Management of Hyperglycemic Crises (UK Versus USA)

Ketan K. Dhatariya[1,3] · Priyathama Vellanki[2]

Diabetes care. 2009; *32*(7): 1335–1343
Current Diabetes Reports. 2017; *17*(5): 33

Pathogenesis of Hyperglycemic Emergencies

- **Inadequate insulin**
  - Decreased insulin production - Undiagnosed DM
  - Failure to administer enough insulin
  - Increased insulin requirements
- **Concomitant elevation of counter-regulatory hormones**
  - Glucagon
  - Catecholamines
  - Cortisol
  - Growth hormone
  - Produced during periods of physical stress
  - Gluconeogenesis - increased hepatic glucose production

Diabetes care. 2009; *32*(7): 1335–1343
Current Diabetes Reports. 2017; *17*(5): 33
Frontiers in Endocrinology. 2017; 8(106): 1-13
Font. Clin Diabetes Healthc. 2022;2.

Diabetic Ketoacidosis

Definition

- Inadequate insulin
- Hyperglycemia
- Accumulation of ketones

Mortality ~ 1 - 9% in experienced centers

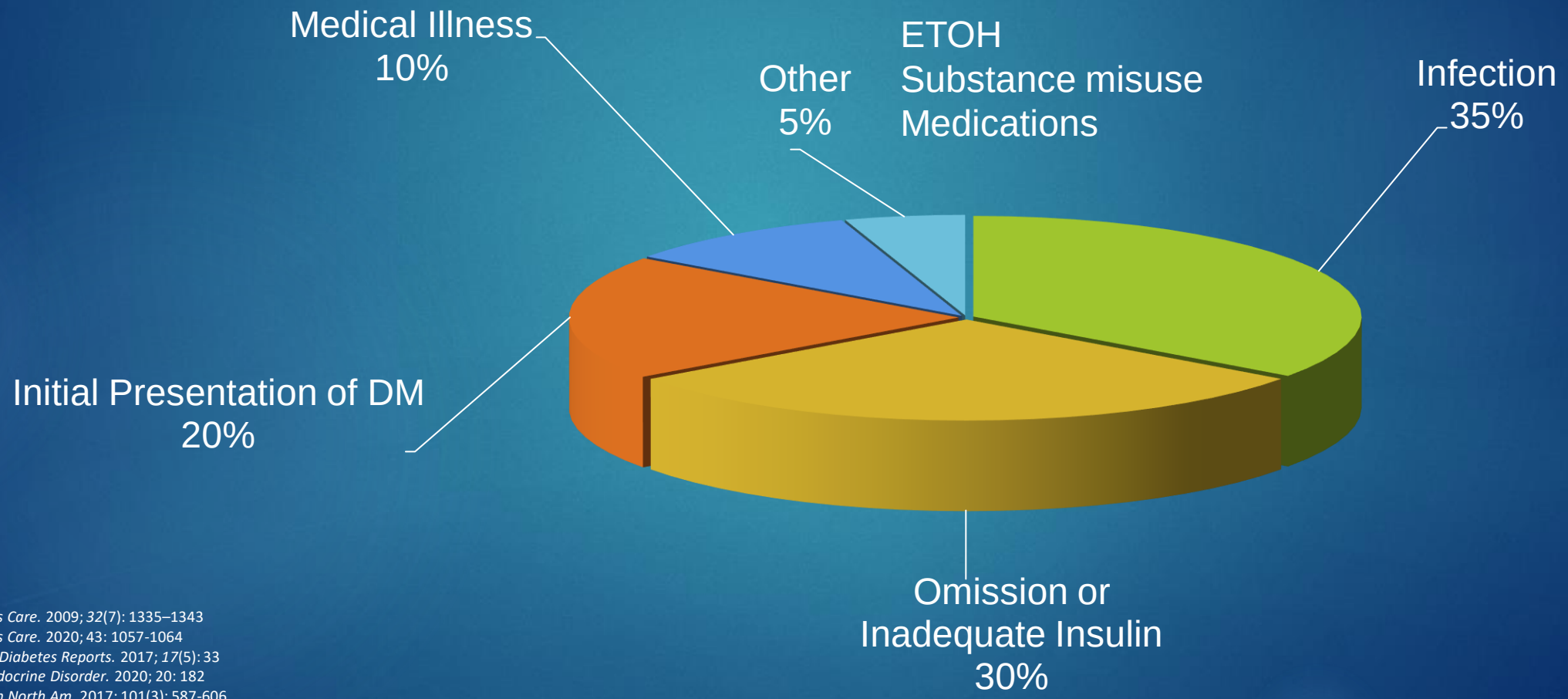
More common in people with Type I DM

Can occur in people with Type II DM

- Beta cells severely depleted
- Under stress of acute illness

Diabetes Care. 2009; *32*(7): 1335–1343
Diabetes Care. 2020; 43: 1057-1064
Current Diabetes Reports. 2017; *17*(5): 33
BMC Endocrine Disorder. 2020; 20: 182
Frontiers in Endocrinology. 2017; 8(106): 1-13
J Emerg Med. 2020; 59: 373-383
Font. Clin Diabetes Healthc. 2022;2

DKA Precipitating Factors



Diabetes Care. 2009; *32*(7): 1335–1343
Diabetes Care. 2020; 43: 1057-1064
Current Diabetes Reports. 2017; *17*(5): 33
BMC Endocrine Disorder. 2020; 20: 182
Med Clin North Am. 2017; 101(3): 587-606
J Emerg Med. 2020; 59: 373-383
Font. Clin Diabetes Healthc. 2022;2.

Euglycemic DKA (euDKA)

DKA without hyperglycemia

- Normal or near normal glucose (< 250 mg/dL)
- Anion gap
- Low pH

Risk factors

- SGLT2 inhibitor "glifozin"
- Acute illness, trauma, surgery
- Substance misuse
- Pregnancy
- Prolonged fasting
- Acute illness
- Surgery
- Dehydration

↓ CHO availability

High index of suspicion

SGLT2 Inhibitors

- canaglifozin (Invokana)
- empaglivozin (Jardiance)
- dapagliflozin (Farxiga)
- ertugliflozin (Steglatro)

Adv Exp Med Biol. 2021; 1307: 85-114
Emergency Medicine Practice. 2020; *22*(2): 1–20
Emergency Medicine Practice. 2020; *22*(2): 1–20
Med Clin North Am. 2017; 101(3): 587-606
J Emerg Med. 2020; 59: 373-383
World J Diabetes. 2021;12(5):514-523.
Font. Clin Diabetes Healthc. 2022;2
AACN Adv Crit Care. 2023;34(1): 27-32.

SGLT2 Inhibition

↓ glucose & Na^+ reabsorption

↑glucose & Na^+ excretion
Osmotic diuresis & natriuresis

Negative caloric balance
Starvation state

Lipolysis & ↑ FFA oxidation

Ketogenesis

HHS

- Previously known as HHNK, HHNC
- Less common than DKA
- Mortality rate 5 – 20%
- Mean age of onset – 7th decade of life

Adv Exp Med Biol. 2021; 1307: 85-114
Diabetes Care. 2009; *32*(7): 1335–1343
Diabetes Care. 2020; 43: 1057-1064
Current Diabetes Reports. 2017; *17*(5): 33
BMC Endocrine Disorder. 2020; 20: 182
J Emerg Med. 2021; 61: 365-375
Font. Clin Diabetes Healthc. 2022;2

HHS Precipitating Factors

Inadequate insulin secretion

- Usually with type 2 diabetes
- Onset slow as beta cell function diminishes
- 20% have no Hx DM – delays recognition

Often in older adults in LTC facility

- Chronically ill or disabled
- Altered thirst mechanism
- Lack of ability to take care of themselves

Acute illness - stress response – most common

Medications

Adv Exp Med Biol. 2021; 1307: 85-114
Diabetes Care. 2009; *32*(7): 1335–1343
Diabetes Care. 2020; 43: 1057-1064
Current Diabetes Reports. 2017; *17*(5): 33
BMC Endocrine Disorder. 2020; 20: 182
Med Clin North Am. 2017; 101(3): 587-606
J Emerg Med. 2021; 61: 365-375
Font. Clin Diabetes Healthc. 2022;2.

Medications

- Affect blood glucose levels
  - Thiazides
  - Phenytoin
  - Glucocorticoids
  - Beta blockers
  - Calcium channel blockers
  - Catecholamines
  - Loop diuretics
  - Quetiapine (Seroquel)
  - Risperidone
  - Olanzapine

Adv Exp Med Biol. 2021; 1307: 85-114
Diabetes Care. 2009; *32*(7): 1335–1343
Diabetes Care. 2020; 43: 1057-1064
Current Diabetes Reports. 2017; *17*(5): 33
BMC Endocrine Disorder. 2020; 20: 182
Am Fam Phys. 2017; 96:729-736.
Med Clin North Am. 2017; 101(3): 587-606

8 I's

- **Insulin**: deficiency/insufficiency
- **Iatrogenic**: steroids, thiazides, atypical antipsychotics
- **Infection**: most common
- **Ischemia**: gut, foot
- **Infarction**: ACS, stroke
- **Inflammation**: acute pancreatitis, cholecystitis
- **Intoxication**: alcohol, cocaine
- Infant on board

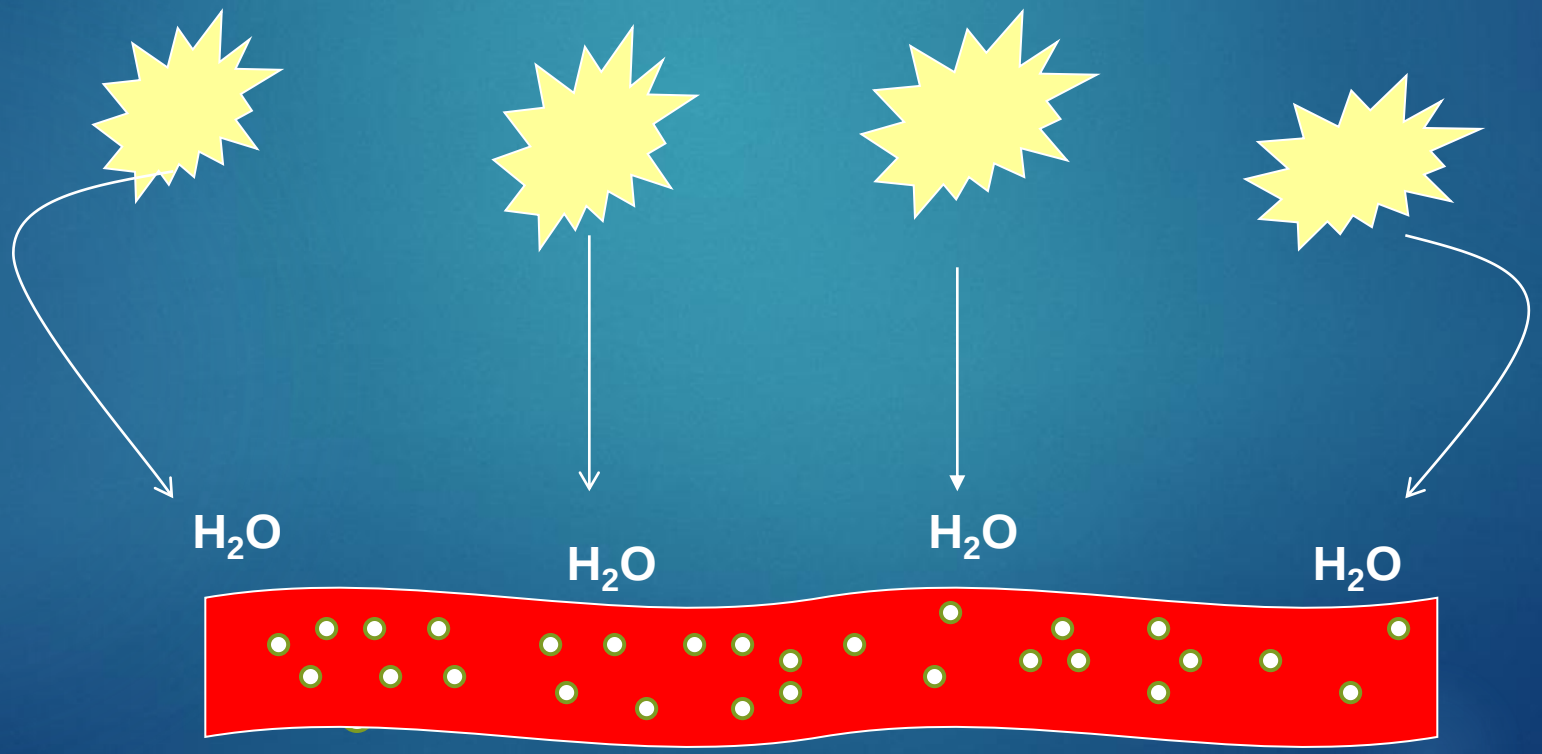
Adv Exp Med Biol. 2021; 1307: 85-114

Pathophysiology

High serum glucose level → osmotic gradient → fluid moves out of cells & interstitial space → osmotic diuresis

Dehydration

Electrolyte loss



Adv Exp Med Biol. 2021; 1307: 85-114
Frontiers in Endocrinology. 2017; 8(106): 1-13
Emergency Medicine Practice. 2020; *22*(2): 1–20
Emergency Medicine Practice. 2020; *22*(2): 1–20
J Emerg Med. 2020; 59: 373-383
J Emerg Med. 2021; 61: 365-375
Font. Clin Diabetes Healthc. 2022;2

Serum Sodium

- Usually present with a low serum Na^+
  - Pseudo-hyponatremia
  - Sodium-poor intracellular fluid moves into vascular space
- Normal or increased serum Na^+ indicates profound dehydration

Diabetes care. 2009. *32*(7), 1335–1343
Current Diabetes Reports. 2017, *17*(5), 33
Frontiers in Endocrinology. 2017, 8(106), 1-13
J Emerg Med. 2020; 59: 373-383
J Emerg Med. 2021; 61: 365-375

Corrected Serum Na^+

- Add 1.6 mEq to Na^+ value for each 100 mg/dL glucose over 100
- Example: Blood glucose = 600 mg/dL

  Serum Na^+ = 130

  - Corrected serum Na^+ = 1.6 X 5 = 8

    130 + 8 = 138

Am Fam Phys. 2017; 96:729-736.
J Emerg Med. 2020; 59: 373-383
J Emerg Med. 2021; 61: 365-375

DKA Pathophysiology

Inadequate insulin

- Cells are starving

Gluconeogenesis

- Breakdown of protein and fat
- Protein breakdown
  - ↑ urea production → ↑ osmotic diuresis & dehydration

Release of free fatty acids

- Unrestrained hepatic fatty acid oxidation
- Ketone body production
  - Acetoacetate
  - B-hydroxybutyrate
  - Acetone
- Metabolic acidosis

Adv Exp Med Biol. 2021; 1307: 85-114
Frontiers in Endocrinology. 2017; 8(106): 1-13
J Emerg Med. 2020; 59: 373-383
Font. Clin Diabetes Healthc. 2022;2.

DKA Pathophysiology

- Dehydration →
- ↓ perfusion →
- Tissue hypoxia
- Anaerobic metabolism →
- Lactic acid production
- Worsening metabolic acidosis

Diabetes care. 2009. *32*(7), 1335–1343
Current Diabetes Reports. 2017, *17*(5), 33
Frontiers in Endocrinology. 2017, 8(106), 1-13
J Emerg Med. 2020; 59: 373-383
Font. Clin Diabetes Healthc. 2022;2.

DKA Pathophysiology

- Anion Gap – presence & severity of metabolic acidosis

$$[Na^+ - (Cl^- + HCO_3^-)]$$

Normal = 7 – 9 mEq/L

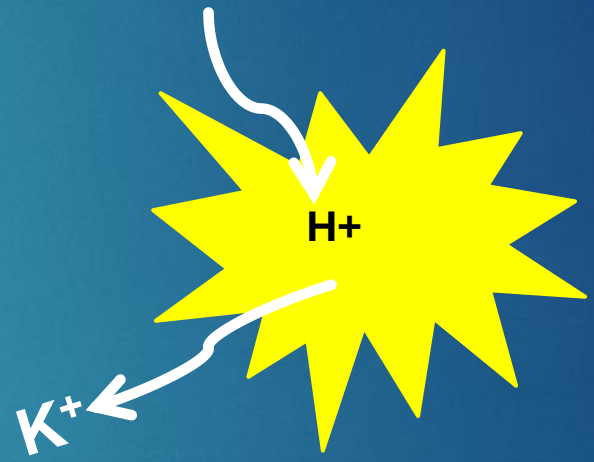
> 10 - 12 mEq/L indicates the presence of excess organic acids (ketone bodies)

Metabolic acidosis

DKA → Anion Gap > 20 mEq/L

Serum Potassium

- May be falsely elevated
- Movement of K^+ out of cells
  - Solute drag
  - Acidosis → H^+ shift
- Total body K^+ may be low
- Watch K^+ as acidosis resolves



Adv Exp Med Biol, 2021; 1307: 85-114
Frontiers in Endocrinology, 2017; 8(106): 1-13
Med Clin North Am. 2017; 101(3): 587-606

Criteria for DKA

	Mild	Moderate	Severe
D: glucose level	> 250 mg/dL	> 250 mg/dL	> 250 mg/dL
K: presence of ketones	Urine or serum +	Urine or serum +	Urine or serum +
A: acidosis	7.25 – 7.30	7.0 to < 7.24	< 7.0
Anion gap	>10	>12	> 12
Mental status	Alert	Alert or drowsy	Stupor/coma

Diabetes Care. 2009; *32*(7): 1335–1343
Current Diabetes Reports. 201;, *17*(5): 33
Frontiers in Endocrinology. 2017; 8(106): 1-13
J Emerg Med. 2020; 59: 373-383
Font. Clin Diabetes Healthc. 2022;2

HHS Pathophysiology

- Relative insulin deficiency
- Insulin resistance
- Increased production of glucose
  - Stress of acute illness
- Occurs slowly over days
- Extreme hyperglycemia
  - Usually > 600 mg/dL

Diabetes care. 2009; *32*(7): 1335–1343
Current Diabetes Reports. 2017; *17*(5): 33
Frontiers in Endocrinology. 2017; 8(106): 1-13
J Emerg Med. 2021; 61: 365-375 .
Font. Clin Diabetes Healthc. 2022;2

HHS Pathophysiology

Increased serum osmolality

Severe osmotic diuresis

Profound dehydration

Altered mental status

- 25 – 50% comatose

Ketosis and acidosis is mild or absent

- Enough insulin to prevent lipolysis and ketosis

Diabetes care. 2009; *32*(7): 1335–1343
Current Diabetes Reports. 2017; *17*(5): 33
Frontiers in Endocrinology. 2017; 8(106): 1-13
J Emerg Med. 2021; 61: 365-375
Font. Clin Diabetes Healthc. 2022;2

Diagnostic Criteria for HHS

- Blood glucose > 600mg/dL
  - Average ~ 1000 mg/dL
- Arterial pH >7.3
- Serum HCO_3^- >15 mEq/L
- Serum osmolality > 320 mOsmol/kg
  - May be as high as 380
- Absent or mild ketonuria
- Mental status change

Diabetes care. 2009; *32*(7): 1335–1343
Current Diabetes Reports. 2017; *17*(5): 33
Frontiers in Endocrinology. 2017; 8(106): 1-13
J Emerg Med. 2021; 61: 365-375
Diab Med. 2020; 37(12): 2001–2008
Font. Clin Diabetes Healthc. 2022;2

DKA versus HHS

- DKA
  - Blood sugar >300 mg/dl; average 600 mg/dl
  - Evolves over 24 hours
  - Metabolic acidosis
    - HCO_3^- <15 mEq/L
    - pH < 7.3
  - Kussmaul's respirations
  - Acetone excreted in lungs
    - Fruity breath
  - Ketones in urine and blood

- HHS
  - Blood sugar >600 mg/dl; average 1000 mg/dL
  - Higher serum osmolarity
    - > 320 mOsm
    - Altered LOC
  - More electrolyte imbalances
  - Evolves over days to weeks
  - More "normal" ABGs
    - pH > 7.30
  - Ketosis absent or mild

Diabetes care. 2009; *32*(7): 1335–1343
Current Diabetes Reports. 2017; *17*(5): 33
Frontiers in Endocrinology. 2017; 8(106): 1-13
J Emerg Med. 2020; 59: 373-383
J Emerg Med. 2021; 61: 365-375

euDKA Pathophysiology

Diagnosis

- Blood glucose < 250 mg/dL
- Anion gap
- pH < 7.3
- Serum bicarbonate < 18 mgEq/L;
- Ketosis

Precipitating factors

- SGLT2 inhibitors
- Substance misuse
  - ↓ CHO intake, liver dysfunction
- Pregnancy
  - Hypoinsulinemia & resp. alkalosis→ loss HCO_3^-
- Prolonged fasting

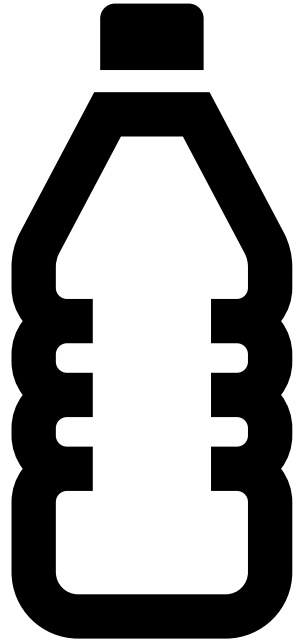
Treatment:

- High index of suspicion
- IV Dextrose with insulin

Adv Exp Med Biol. 2021; 1307: 85-114
Emergency Medicine Practice. 2020; *22*(2): 1–20
Emergency Medicine Practice. 2020; *22*(2): 1–20
Med Clin North Am. 2017; 101(3): 587-606
J Emerg Med. 2020; 59: 373-383
World J Diabetes. 2021;12(5):514-523.
CMAJ. 2018;190:3766-8.
Font. Clin Diabetes Healthc. 2022;2.
AACN Adv Crit Care. 2023;34(1): 27-32.

Clinical Manifestations: Physical Exam

- Dehydration
  - Polyuria
  - Polydipsia
  - Tachycardia
  - Poor skin turgor
  - Dry buccal mucosa
  - Sunken eyeballs
  - Orthostatic hypotension
  - Hypotension
  - Prolonged capillary refill
  - Weakness



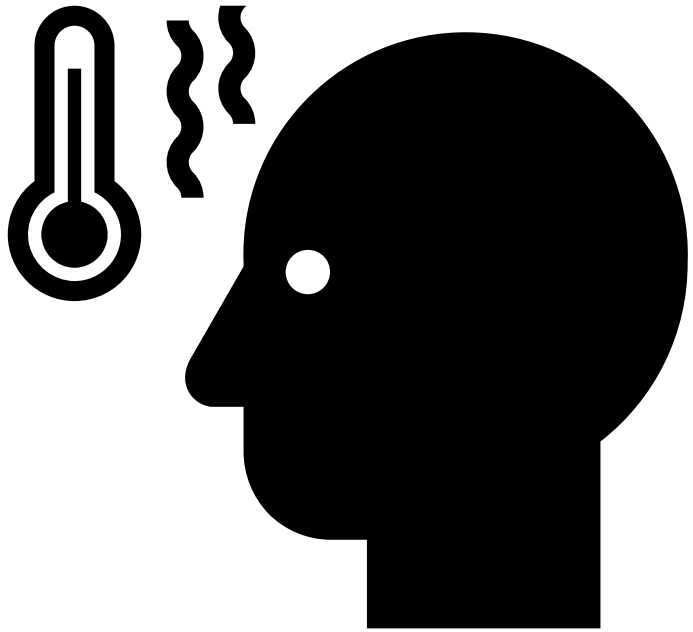
Clinical Manifestations: Physical Exam

- Abdominal pain
  - More common with DKA
  - Correlates with severity of acidosis
  - Ketone have paralytic effect on smooth muscles
  - Relieved with reversal of dehydration
  - Consider other intra-abdominal pathology

Diabetes care. 2009; *32*(7): 1335–1343
Current Diabetes Reports. 2017; *17*(5): 33
Frontiers in Endocrinology. 2017; 8(106): 1-13
Emergency Medicine Practice. 2020; *22*(2): 1–20
Emergency Medicine Practice. 2020; *22*(2): 1–20
J Emerg Med. 2020; 59: 373-383

Clinical Manifestations: Physical Exam

- Frequently afebrile
- Altered LOC
  - Cellular dehydration in CNS
  - More common with HHS
  - Confusion, somnolence, coma
  - Focal neurological signs (hemiparesis)
  - Seizures
  - Consider other neuro pathology if serum osmo is < 320 mOsm/kg



Emergency Medicine Practice. 2020; *22*(2): 1–20
J Emerg Med. 2020; 59: 373-383
J Emerg Med. 2021; 61: 365-375

euDKA Clinical Manifestations

NAUSEA

VOMITING

ABDOMINAL PAIN

FATIGUE

HYPERVENTILATION OR KUSSMAUL BREATHING

SOMNOLENCE OR CONFUSION

World J Diabetes. 2021;12(5):514-523.
CMAJ. 2018;190:E766-8.

Diagnostic Testing

- Serum glucose
- Chemistry panel
  - Na & K
  - Anion gap
- Serum β-OHB
- ABGs
  - Venous pH correlates
- Serum osmolality
- BUN/Cr
- Hgb A_1C

Diabetes Care,.2009; *32*(7): 1335–1343
Current Diabetes Reports. 2017; *17*(5): 33
Frontiers in Endocrinology. 2017; 8(106): 1-13
Emergency Medicine Practice. 2020; *22*(2): 1–20
J Emerg Med. 2020; 59: 373-383
J Emerg Med. 2001; 61: 365-375

Look for Causative Factors

CBC
- Mild leukocytosis due to ketosis
- > 25,000 or >50% bands highly suggestive of infection

Lipase & amylase

CT scan

CXR if pneumonia suspected

Blood, sputum, & urine cultures

UA & cultures

Cardiac enzymes

12-lead EKG

Emergency Medicine Practice. 2020; *22*(2): 1–20
Med Clin North Am. 2017; 101(3): 587-606
J Emerg Med. 2020; 59: 373-383
J Emerg Med. 2021; 61: 365-375

Respiratory Support

A

B

C

D

↓ LOC

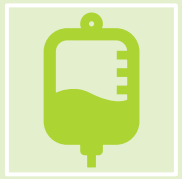
Protect airway from aspiration

Intubation & mechanical ventilation

Severe cases – usually HHS	Until metabolic derangements normalized	Avoid periods of apnea	Can result in worsening acidosis for DKA

Diabetes Care. 2009; *32*(7): 1335–1343
Adv Exp Med Biol. 2021; 1307; 85-114
Current Diabetes Reports. 2017; *17*(5): 33
Frontiers in Endocrinology. 2017; 8(106): 1-13
J Emerg Med. 2020; 59: 373-383
J Emerg Med. 2021; 61: 365-375

Fluid Replacement



Severe dehydration

Fluid deficit up to **6** liters DKA

9 -12 liters with HHS

Aggressive fluid replacement

Goals

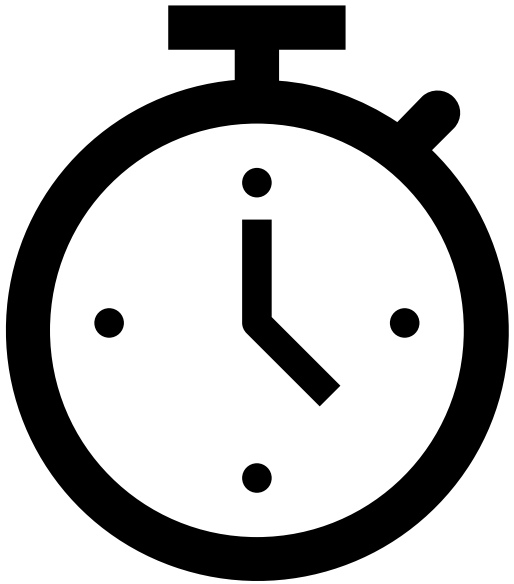
Reverse extracellular volume depletion

Restore renal perfusion

Diabetes care. 2009.;*32*(7): 1335–1343
Current Diabetes Reports. 2017; *17*(5): 33
Adv Exp Med Biol, 2021; 1307: 85-114
Emergency Medicine Practice. 2020; *22*(2): 1–20
Font. Clin Diabetes Healthc. 2022;2

Fluid Replacement

- IV fluid
  - Lowers blood glucose independent of insulin
  - Reverses hypotension
  - Improves tissue/organ perfusion
- Replace ½ fluid deficit over 1st 8 hours
- Then 2nd ½ over next 16 hours



Diabetes Care. 2009; *32*(7): 1335–1343
Adv Exp Med Biol. 2021; 1307: 85-114
Current Diabetes Reports. 2017; *17*(5): 33
Frontiers in Endocrinology. 2017; 8(106): 1-13
Am Fam Phys. 2017; 96:729-736.
Emergency Medicine Practice. 2020; *22*(2): 1–20
J Emerg Med. 2020; 59: 373-383
J Emerg Med. 2021; 61: 365-375
Font. Clin Diabetes Healthc. 2022;2
Font. Clin Diabetes Healthc. 2022;2.

Fluid Replacement

- 0.9% NS
  - Initial resuscitation
  - Replaces extracellular fluid
  - Start at 15 – 20 ml/kg/hr
    - 1 – 1.5 L in 1st hour
  - Then 4 – 14 ml/kg/hr until BP normalizes

- 0.45% NS
  - When serum Na^+ normalizes
  - Replaces intracellular fluids

Diabetes Care. 2009; *32*(7): 1335–1343
Adv Exp Med Biol. 2021; 1307: 85-114
Current Diabetes Reports. 2017; *17*(5): 33
Frontiers in Endocrinology. 2017; 8(106): 1-13
Am Fam Phys. 2017; 96:729-736.
Am Fam Phys. 2017; 96:729-736
J Emerg Med. 2020; 59: 373-383
J Emerg Med. 2021; 61: 365-375
Font. Clin Diabetes Healthc. 2022;2

Insulin Therapy Goal

Interrupt ketosis

Restores normal glucose uptake by cells

Steady ↓ in serum glucose of 50 – 75 mg/dL per hour

- Blood glucose should not fall too fast or too far
- Sudden and rapid lowering allows water to move very rapidly back into the cells
- Lead to vascular collapse
- Early volume replacement before

Diabetes Care. 2009; *32*(7): 1335–1343
Current Diabetes Reports. 2017; *17*(5): 33
Frontiers in Endocrinology. 2017; 8(106): 1-13
J Emerg Med. 2020; 59: 373-383
J Emerg Med. 2021; 61: 365-375
Font. Clin Diabetes Healthc. 2022;2

Insulin Therapy

Initial IV bolus: 0.15 Units/kg regular insulin

Insulin infusion: 0.1 Units/kg/hr

- Short ½ life
- Titrate to achieve a steady decrease in blood glucose
- If serum $K^+ < 3.3$ hold insulin it is ≥ 3.5

Subcutaneous insulin

- Mild DKA

Diabetes Care. 2009; *32*(7): 1335–1343
Current Diabetes Reports. 2017; *17*(5): 33
Frontiers in Endocrinology. 2017; 8(106): 1-13
Am Fam Phys. 2017; 96:729-736.
Emergency Medicine Practice. 2020; *22*(2): 1–20
Med Clin North Am. 2017; 101(3): 587-606
J Emerg Med. 2020; 59: 373-383
J Emerg Med. 2021; 61: 365-375
Font. Clin Diabetes Healthc. 2022;2

Insulin Therapy

Monitor

Monitor blood glucose hourly & prn

Glucose

When blood glucose approaches

- 250 for DKA
- 300 mg/dL for HHS
- Add dextrose to IV fluid
- ¯ insulin infusion to 0.02 – 0.05 Units/kg/hr

Adjust

Adjust insulin to maintain blood glucose

- 150 – 200 mg/dL in DKA
- 250 – 300 mg/dL in HHS

Resolve

While dehydration & ketosis resolve

Diabetes Care. 2009; *32*(7): 1335–1343
Current Diabetes Reports. 2017; *17*(5): 33
Frontiers in Endocrinology. 2017; 8(106); 1-13
Emergency Medicine Practice. 2020; *22*(2): 1–20
J Emerg Med. 2020; 59: 373-383
J Emerg Med. 2021; 61: 365-375
Font. Clin Diabetes Healthc. 2022;2

Insulin Therapy

Transition to subcutaneous insulin

- After resolution of hyperglycemia, dehydration, hypotension, & acidosis
- Regain baseline mental status
- When able to take oral diet
- Overlap 1 – 2 hour overlap for long-acting insulins

Known diabetics may return to previous regimen if it was controlling blood glucose

Multi-dose insulin for insulin-naïve patients

Use combination of long and short-acting insulins

- Basal-bolus regimens
- Proposed as more physiologic

Diabetes Care. 2009; *32*(7): 1335–1343
Current Diabetes Reports. 2017; *17*(5): 33
Frontiers in Endocrinology. 2017; 8(106): 1-13
Med Clin North Am. 2017; 101(3): 587-606
J Emerg Med. 2020; 59: 373-383
J Emerg Med. 2021; 61: 365-375

Electrolyte Replacement

K^+ loss with diuresis

- May ↓ even further with insulin therapy & correction of acidosis
  - K^+ moves into cells
- Total K^+ deficit as high as 600 mEq

Start K^+ replacement after 1st liter of IV fluid replacement

- 20 mEq/liter if serum level 3.5 – 5.5
- 40 mEq/liter if serum level < 3.5
- May also require IVPB

Hold insulin <3.3
Stop K^+ > 5.2

Diabetes Care. 2009; *32*(7): 1335–1343
Current Diabetes Reports. 2017; *17*(5): 33
Frontiers in Endocrinology. 2017; 8(106): 1-13
Med Clin North Am. 2017; 101(3): 587-606
J Emerg Med. 2020; 59: 373-383
J Emerg Med. 2021; 61: 365-375

Electrolyte Replacement

- KPO_4^- Replacement
  - If PO_4^- < 1 mg/dL
  - Cardiac dysfunction
  - Respiratory depression
  - Anemia
- Add 20 – 30 mEq KPO_4^- to replacement fluids

Diabetes Care. 2009; *32*(7): 1335–1343
Current Diabetes Reports. 2017; *17*(5): 33
Frontiers in Endocrinology. 2017; 8(106): 1-13
Emergency Medicine Practice. 2020; *22*(2): 1–20
J Emerg Med. 2020; 59: 373-383
J Emerg Med. 2021; 61: 365-375
Font. Clin Diabetes Healthc. 2022;2

Acidosis Correction

$NaHCO_3^-$ usually not administered

- Fluid replacement & insulin administration will interrupt the ketotic cycle

$NaHCO_3^-$ may cause CNS acidosis if too aggressive

- Bicarb combines with H^+
- Dissociates to CO_2 and H_2O
- CO_2 diffuses freely through the blood-brain barrier causing cerebral acidosis and depression

Diabetes Care. 2009; *32*(7): 1335–1343
Current Diabetes Reports. 2017; *17*(5): 33
Frontiers in Endocrinology. 2017; 8(106): 1-13
J Emerg Med. 2020; 59: 373-383
J Emerg Med. 2021; 61: 365-375
Font. Clin Diabetes Healthc. 2022;2

Acidosis Correction

- $NaHCO_3^-$ if pH < 7.0
- Replace slowly
- Only correct to pH 7.0
- Replace K^+ concurrently to prevent hypokalemia
- Kidneys will conserve HCO_3^- once fluid & electrolyte imbalances are corrected

Diabetes Care. 2009; *32*(7): 1335–1343
Current Diabetes Reports. 2017; *17*(5): 33
Frontiers in Endocrinology. 2017; 8(106): 1-13
Emergency Medicine Practice. 2020; *22*(2): 1–20
Emergency Medicine Practice. 2020; *22*(2): 1–20
Med Clin North Am. 2017; 101(3): 587-606
J Emerg Med. 2020; 59: 373-383
J Emerg Med. 2021; 61: 365-375

Cerebral Edema

Pathophysiology is poorly understood

Rapid fall in blood glucose → **Cerebral Edema** → Coma Death (21-24%)

Fluid moves rapidly into cells of CNS

Lower blood glucose slowly

Perform neuro assessment hourly & prn

Diabetes Care. 2009; *32*(7): 1335–1343
Adv Exp Med Biol. 2021; 1307: 85-114
Current Diabetes Reports. 2017; *17*(5): 33
Frontiers in Endocrinology. 2017; 8(106): 1-13
Emergency Medicine Practice. 2020; *22*(2): 1–20
Current Neur and Neuroscience Reports. 2021; 21: 21
Med Clin North Am. 2017; 101(3): 587-606
J Emerg Med. 2020; 59: 373-383
J Emerg Med. 2021; 61: 365-375
Font. Clin Diabetes Healthc. 2022;2

Cerebral Edema

- Symptoms:
  - Headache
  - Lethargy
  - Gradual ↓ in LOC
  - Cranial nerve palsies
  - Seizures
  - Pupil changes
  - Bradycardia
  - Elevation in BP
  - Respiratory arrest

- Treatment
  - Mannitol
  - HTS

Adv Exp Med Biol. 2021; 1307: 85-114
Med Clin North Am. 2017; 101(3): 587-606

Cerebral Edema

- Prevention
  - Avoid excessive hydration and rapid reduction of plasma osmolarity
    - Max reduction 3 mOsm/kg H_2O per hour
  - Gradually lower serum glucose
  - Maintain blood glucose 250 – 300 mg/dL until serum osmolality is normalized and mental status improved

Diabetes Care. 2009; *32*(7): 1335–1343
Adv Exp Med Biol. 2021; 1307: 85-114
Current Diabetes Reports. 2017; *17*(5): 33
Am Fam Phys. 2017; 96:729-736.
Am Fam Phys. 2017; 96:729-736.
J Emerg Med. 2020; 59: 373-383
J Emerg Med. 2021; 61: 365-375

Resolution of Hyperglycemic Emergency

- DKA
  - Blood glucose < 200 mg/dL
  - Serum HCO_3^- ≥ 15 mEq/L
  - pH > 7.30
  - Calculated anion gap < 12 mEq/L
- HHS
  - Normal serum osmolality
  - Regain normal mental status

Diabetes Care. 2009; *32*(7): 1335–1343
Adv Exp Med Biol. 2021; 1307: 85-114
Current Diabetes Reports. 2017; *17*(5): 33
Frontiers in Endocrinology. 2017; 8(106): 1-13
J Emerg Med. 2020; 59: 373-383

Diabetic Sick Day Management

Usual basal insulin or oral anti-diabetic agents	Liberal fluid intake	Easily digestible CHO if unable to eat normal diet	Have family member check on them q 4 hrs	Early consultation with PCP
		• Custard, pudding, cream soup, toast • Gelatin, broth, juice, soda		

Adv Exp Med Biol. 2021; 1307: 85-114

Diabetic Regimen Adherence

- Complex issues
  - Knowledge deficit
  - Health beliefs
  - Culture
  - Mental health
  - Substance misuse
  - Financial resources
  - Insurance
  - Social support
- Consultations
  - Social services
  - Psychiatry
  - Discharge planner
  - Spiritual care
  - Registered Dietician

Summary

- Fluids, insulin, & electrolytes
  - How much?
  - How fast?
- Treat underlying illnesses
- Sick day management

References

- Aldhaeefi, M., Alldardeer, N. F., Alkhani, N., Alqarni, S. M., Alhammad, A. M., & Alshyaya, A. I. (2022) . Updates in the management of hyperglycemic crisis. Frontiers in Clinical Diabetes and Healthcare, 2,820728 . https://doi.org/10.3389/fcdhc.2021.82072
- Andes LJ, Cheng YJ, Rolka DB, Gregg EW, & Imperatore G. (2020). Prevalence of prediabetes among adolescents and young adults in the United States, 2005-2016. *JAMA Pediatrics*,174(2):e194498. doi:10.1001/jamapediatrics.2019.4498
- American Diabetes Association (2021). 15. Diabetes Care in the Hospital: *Standards of Medical Care in Diabetes-2021*. *Diabetes care*, *44*(Suppl 1), S211–S220. https://doi.org/10.2337/dc21-S015
- Benoit, S. R., Hora, I., Pasquel, F. J., Gregg, E. W., Albright, A. L., & Imperatore, G. (2020). Trends in Emergency Department Visits and Inpatient Admissions for Hyperglycemic Crises in Adults With Diabetes in the U.S., 2006-2015. *Diabetes Care*, *43*(5), 1057–1064. https://doi.org/10.2337/dc19-2449
- Blank, S. P., Blank, R. M., Ziegenfuss, M. D., & Australian and New Zealand Intensive Care Society (ANZICS) Centre for Outcomes & Resource Evaluation (CORE) for the ANZICS CORE Committee (2020). The importance of hyperosmolarity in diabetic ketoacidosis. *Diabetic Medicine : a Journal of the British Diabetic Association*, *37*(12), 2001–2008. https://doi.org/10.1111/dme.14277
- CDC. (2022)DM: The Facts, Stats, and Impacts of Diabetes. www.cdc.gov/diabetes
- Cruz-Flores, S. (2021). Neurological complications of endocrine emergencies. Current Neurology and Neuroscience Reports, 21, 21. doi: 10.1007/s11910-021-01105-2
- Dhatariya, K. K., & Vellanki, P. (2017). Treatment of Diabetic Ketoacidosis (DKA)/Hyperglycemic Hyperosmolar State (HHS): Novel Advances in the Management of Hyperglycemic Crises (UK Versus USA). *Current Diabetes Reports*, *17*(5), 33. https://doi.org/10.1007/s11892-017-0857-4
- Dingle, H. E., & Slovis, C. (2020). Diabetic hyperglycemic emergencies: a systematic approach. *Emergency Medicine Practice*, *22*(2), 1–20.
- Fan, W. (2017). Epidemiology in diabetes mellitus and cardiovascular disease. Cardiovascular Endocrinology, 6, 8-16. doi: 10.1097/XCE.0000000000000116
- Fayfman, M., Pasquel, F. J., & Umpierrez, G. E. (2017). Management of Hyperglycemic Crises: Diabetic Ketoacidosis and Hyperglycemic Hyperosmolar State. *The Medical clinics of North America*, *101*(3), 587–606. https://doi.org/10.1016/j.mcna.2016.12.011
- Karslioglu French, E., Donihi, A. C., & Korytkowski, M. T. (2019). Diabetic ketoacidosis and hyperosmolar hyperglycemic syndrome: Review of acute decompensated diabetes in adult patients. *BMJ (Clinical research ed.)*, *365*, l1114. https://doi.org/10.1136/bmj.l1114
- Kitabchi, A. E., Umpierrez, G. E., Miles, J. M., & Fisher, J. N. (2009). Hyperglycemic crises in adult patients with diabetes. *Diabetes Care*, *32*(7), 1335–1343. https://doi.org/10.2337/dc09-9032
- Klinkner, G., & Steingraber-Pharr, M. (2023). Euglycemic diabetic ketoacidosis associated with SGLT2 inhibitor therapy: A case report. *AACN Advanced Critical Care*, *34*(1), 27–32. https://doi.org/10.4037/aacnacc2023830
- Long, B., Willis, G. C., Lentz, S., Koyfman, A., & Gottlieb, M. (2020). Evaluation and Management of the Critically Ill Adult With Diabetic Ketoacidosis. *The Journal of emergency medicine*, *59*(3), 371–383. https://doi.org/10.1016/j.jemermed.2020.06.059
- Long, B., Willis, G. C., Lentz, S., Koyfman, A., & Gottlieb, M. (2021). Diagnosis and Management of the Critically Ill Adult Patient with Hyperglycemic Hyperosmolar State. *The Journal of Emergency Medicine*, *61*(4), 365–375. https://doi.org/10.1016/j.jemermed.2021.05.008
- Muneer, M., & Akbar, I. (2021). Acute Metabolic Emergencies in Diabetes: DKA, HHS and EDKA. *Advances in Experimental Medicine and Biology*, *1307*, 85–114. https://doi.org/10.1007/5584_2020_545
- Nasa, P., Chaudhary, S., Shrivastava, P. K., & Singh, A. (2021). Euglycemic diabetic ketoacidosis: A missed diagnosis. *World journal of diabetes*, *12*(5), 514–523. https://doi.org/10.4239/wjd.v12.i5.514
- Nhoung, H. K., Goyal, M., Cacciapuoti, M., Day, H., Hashemzadeh, T., Magee, M., & Jarris, Y. S. (2020). Food Insecurity and Insulin Use in Hyperglycemic Patients Presenting to the Emergency Department. *The Western Journal of Emergency Medicine*, *21*(4), 959–963. https://doi.org/10.5811/westjem.2020.4.45918
- Stoner G. D. (2017). Hyperosmolar Hyperglycemic State. *American Family physician*, *96*(11), 729–736.
- Tran, T., Pease, A., Wood, A. J., Zajac, J. D., Mårtensson, J., Bellomo, R., & Ekinci, E. (2017). Review of Evidence for Adult Diabetic Ketoacidosis Management Protocols. *Frontiers in Endocrinology*, *8*, 106. https://doi.org/10.3389/fendo.2017.00106
- Wolf, R. A., Haw, J. S., Paul, S., Spezia Faulkner, M., Cha, E., Findley, M. K., Khan, F., Markley Webster, S., Alexopoulos, A. S., Mehta, K., Alfa, D. A., & Ali, M. K. (2019). Hospital admissions for hyperglycemic emergencies in young adults at an inner-city hospital. *Diabetes Research and Clinical Practice*, *157*, 107869. https://doi.org/10.1016/j.diabres.2019.107869
- Wolf, R. A., Haw, J. S., Paul, S., Spezia Faulkner, M., Cha, E., Findley, M. K., Khan, F., Markley Webster, S., Alexopoulos, A. S., Mehta, K., Alfa, D. A., & Ali, M. K. (2019). Hospital admissions for hyperglycemic emergencies in young adults at an inner-city hospital. *Diabetes research and clinical practice*, *157*, 107869. https://doi.org/10.1016/j.diabres.2019.107869
- Wu, X. Y., She, D. M., Wang, F., Guo, G., Li, R., Fang, P., Li, L., Zhou, Y., Zhang, K. Q., & Xue, Y. (2020). Clinical profiles, outcomes and risk factors among type 2 diabetic inpatients with diabetic ketoacidosis and hyperglycemic hyperosmolar state: A hospital-based analysis over a 6-year period. *BMC Endocrine Disorders*, *20*(1), 182. https://doi.org/10.1186/s12902-020-00659-5
- Zhang, L., & Tamilia, M. (2018). Euglycemic diabetic ketoacidosis associated with the use of a sodium-glucose cotransporter-2 inhibitor. *CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne*, *190*(25), E766–E768. https://doi.org/10.1503/cmaj.171319

Questions?

THANK YOU FOR YOUR ATTENTION!

ROSEMARY.TIMMERMAN@PROVIDENCE.ORG