

How Sweet It Is: Managing Hyperglycemic Emergencies

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PRESENTED BY

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PROVIDENCE ALASKA MEDICAL CENTER

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- ▶ No disclosures
- ▶ No COI

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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.

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A bit about.....



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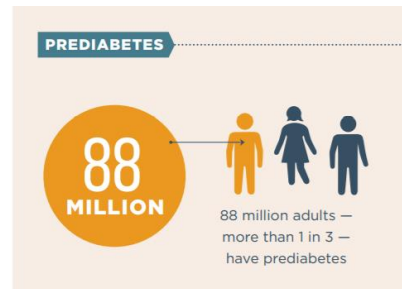
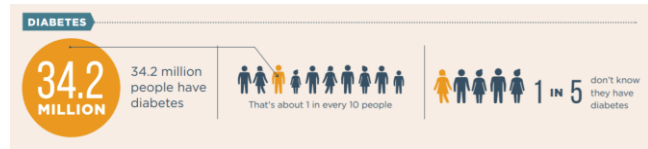
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DM in US

5

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

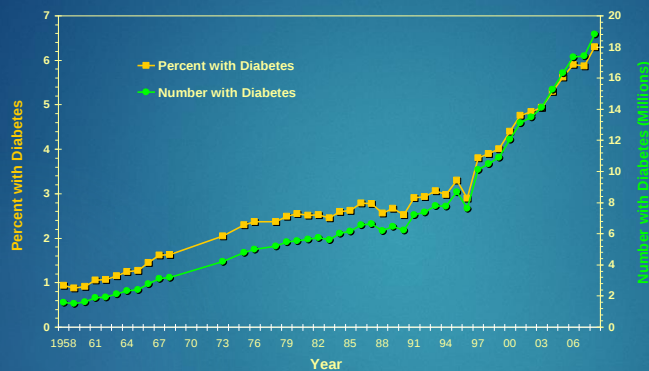
CDC, 2022



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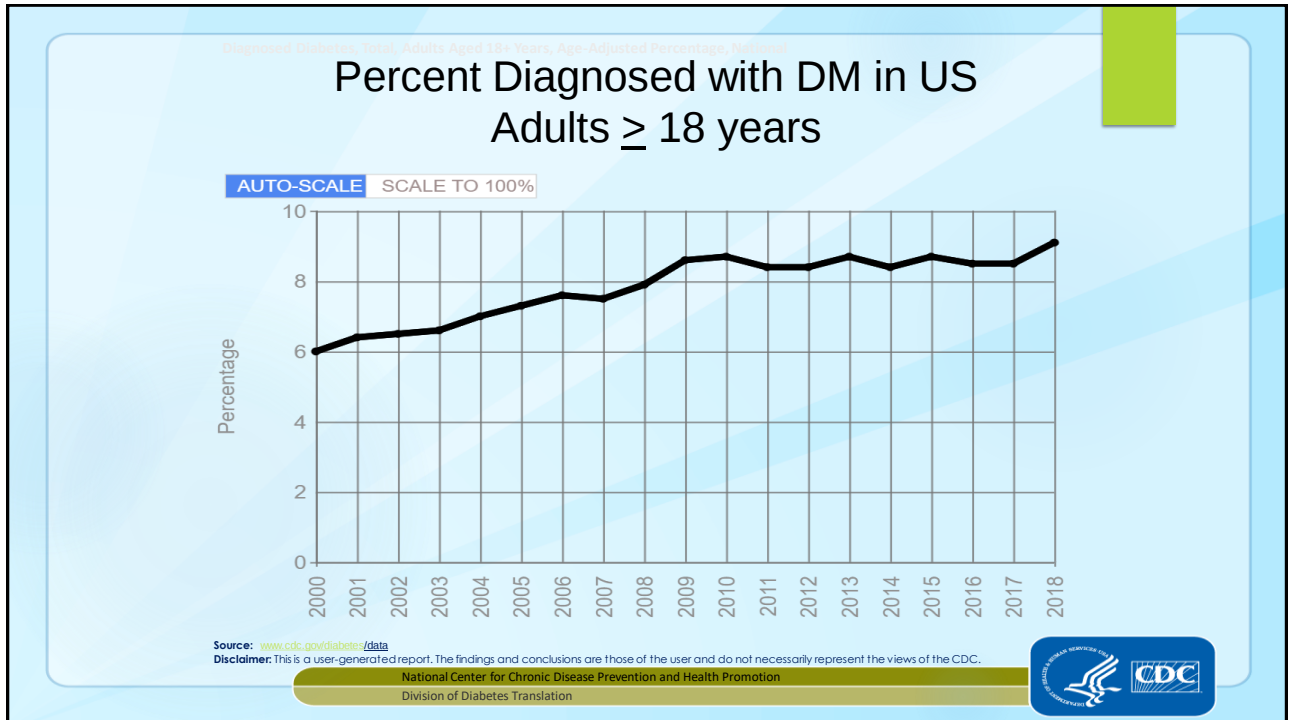
Number and Percentage of U.S. Population with Diagnosed Diabetes, 1958-2008

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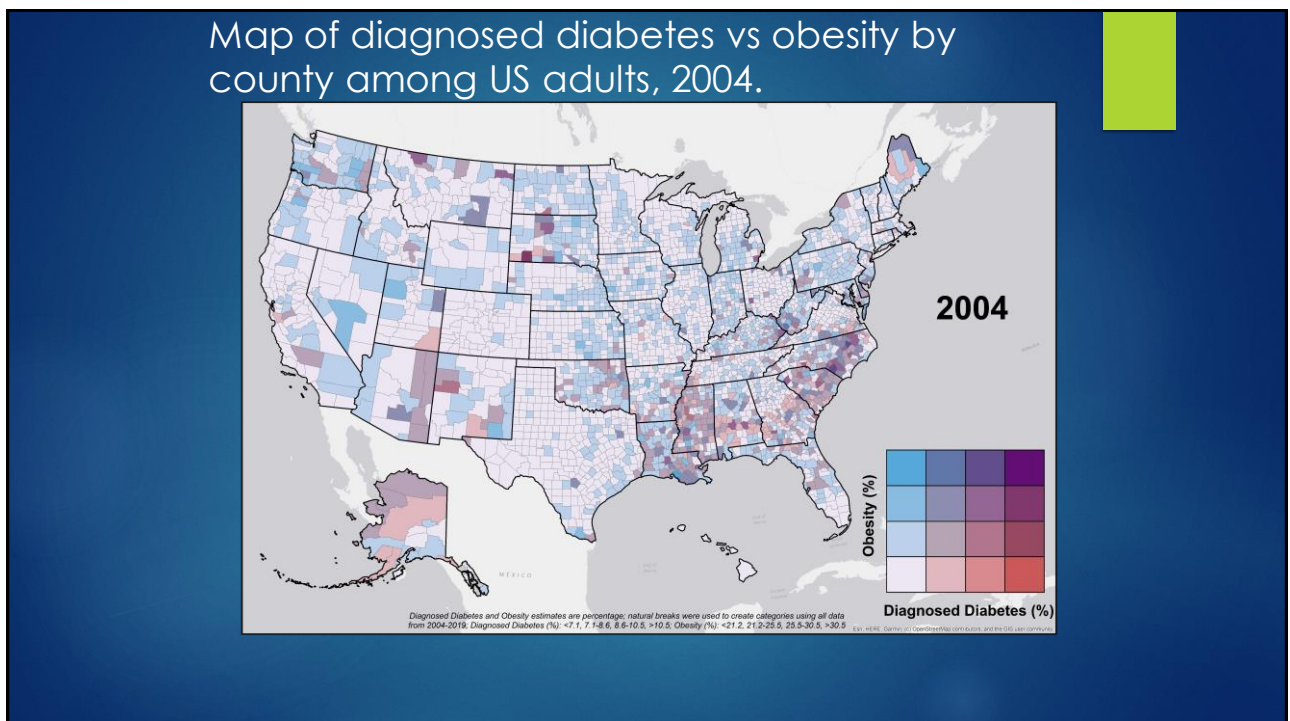


CDC's Division of Diabetes Translation. National Diabetes Surveillance System
available at <http://www.cdc.gov/diabetes/statistics>

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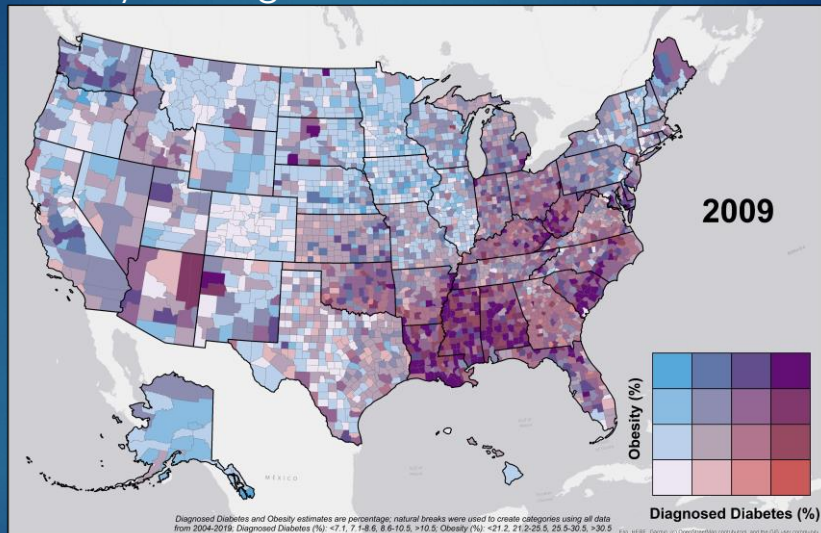


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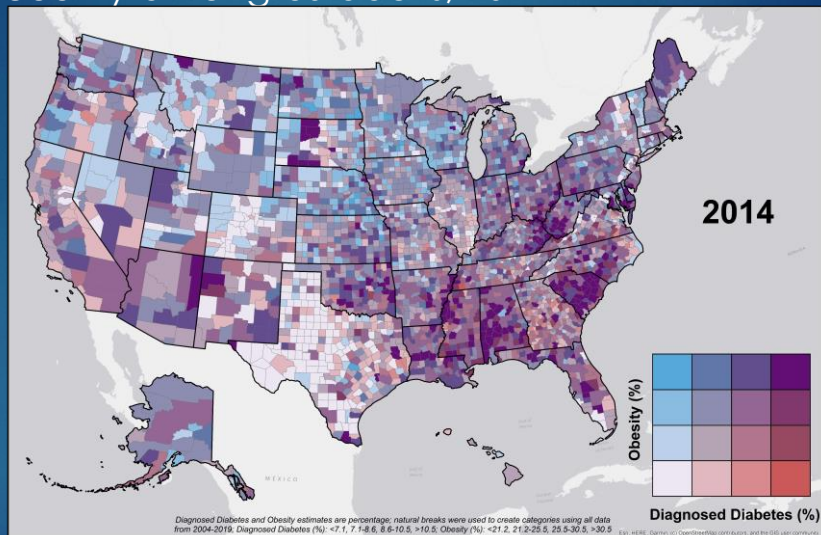
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Map of diagnosed diabetes vs obesity by county among US adults, 2009



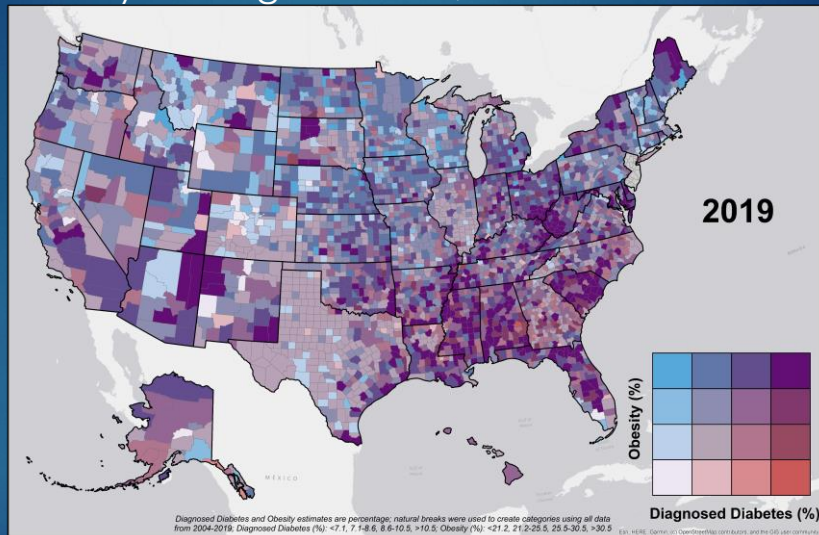
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Map of diagnosed diabetes vs obesity by county among US adults, 2014



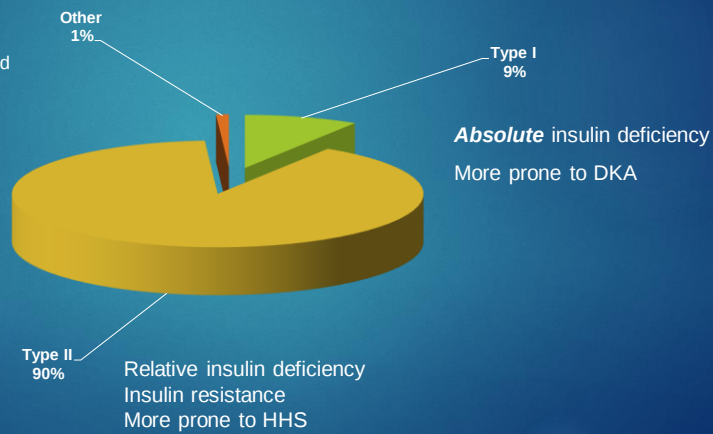
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Map of diagnosed diabetes vs obesity by county among US adults, 2019



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Diabetes Mellitus



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Reviews/Commentaries/ADA Statements
CONSENSUS STATEMENT

Hyperglycemic Crises in Adult Patients With Diabetes

ABBAS E. KITARCHI, PhD, MD¹
GUILLERMO E. UMPIERREZ, MD²

JOHN M. MILES, MD³
JOSEPH N. FISHER, MD⁴

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

DIABETES CARE, VOLUME 32, NUMBER 7, JULY 2009

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 Vellanki²

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



Guidelines

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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
Front. Clin Diabetes Healthc. 2022;2.

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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

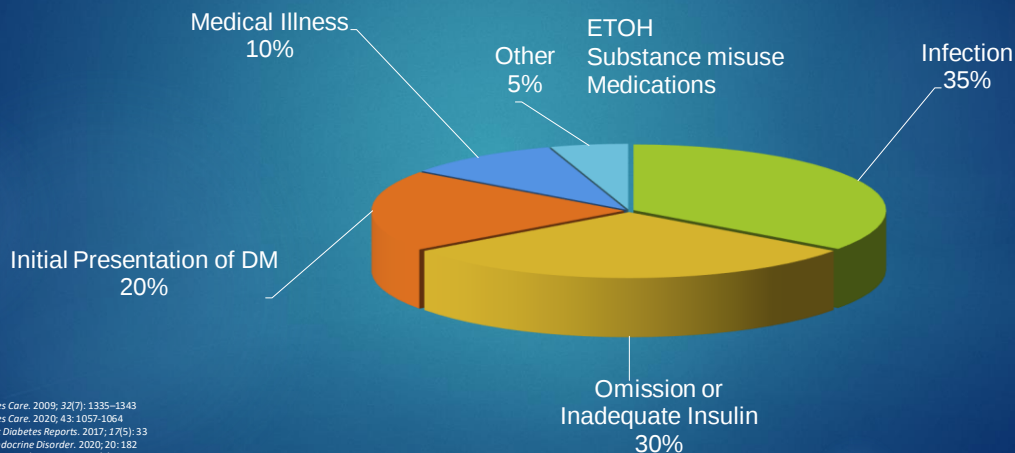
- Beta cells severely depleted
- Under stress of acute illness

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
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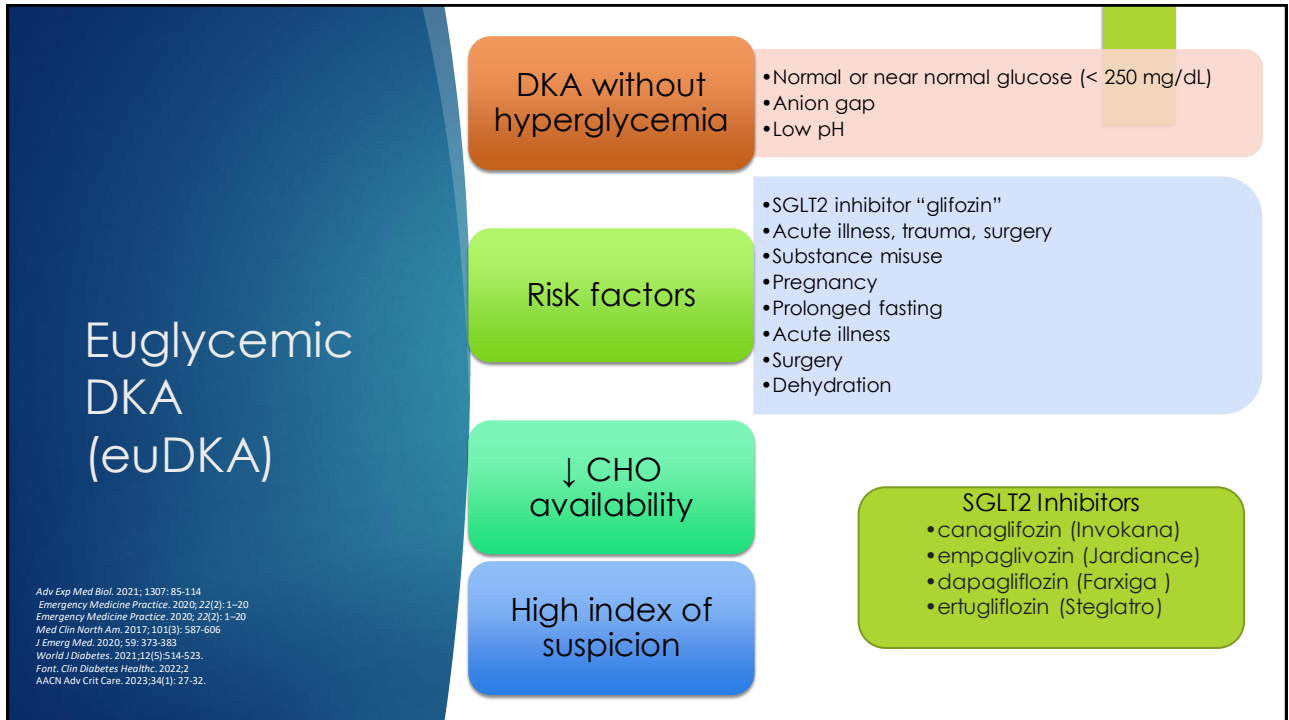
DKA Precipitating Factors

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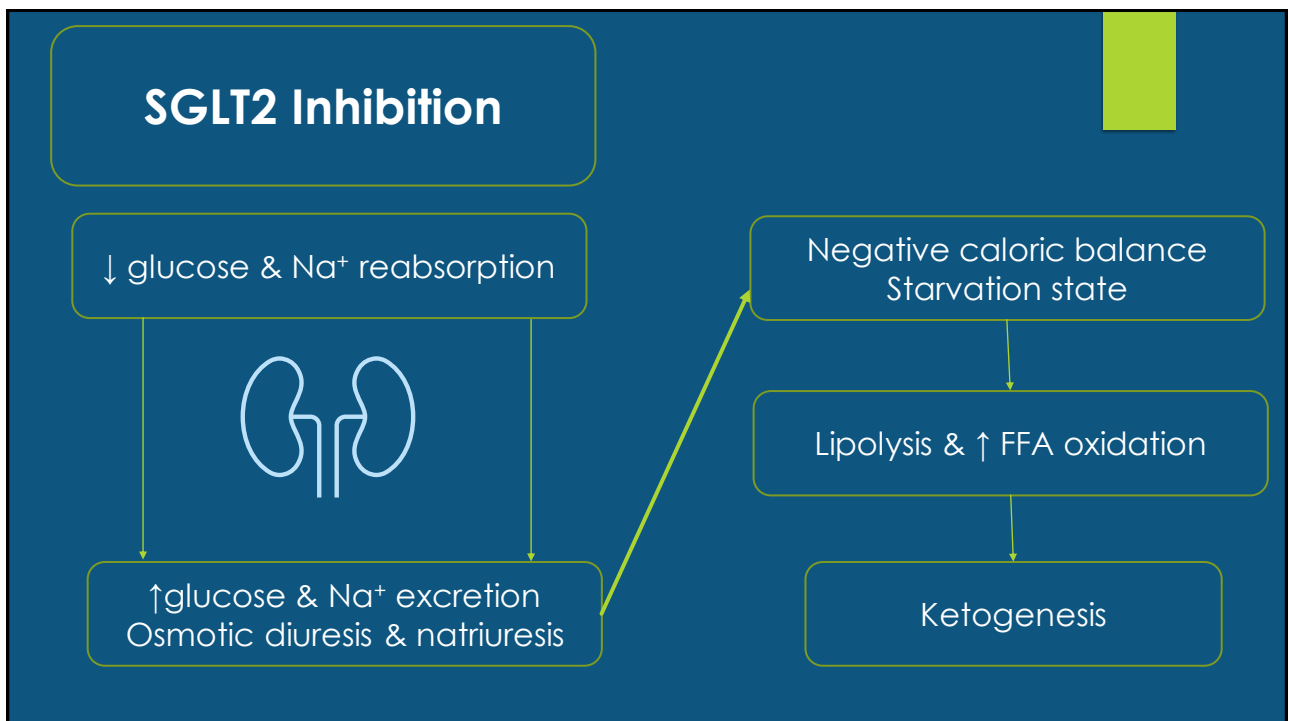


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HHS

Adv Exp Med Biol. 2021; 1307: 85-114
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Font. Clin Diabetes Healthc. 2022;2

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Previously known as HHNK,
HHNC

Less common than DKA

Mortality rate 5 – 20%

Mean age of onset – 7th
decade of life

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HHS Precipitating Factors

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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

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Medications

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► Affect blood glucose levels

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

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Med Clin North Am. 2017; 101(3): 587-606

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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

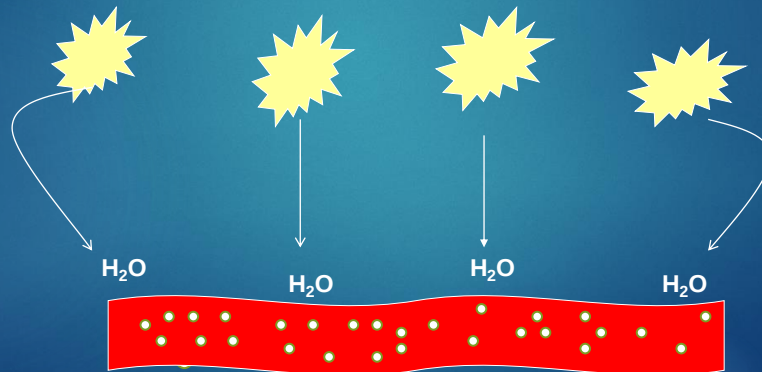
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Pathophysiology

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

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Dehydration
Electrolyte loss



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

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- ▶ 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

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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⁺ = $1.6 \times 5 = 8$
 $130 + 8 = 138$

Am Fam Phys. 2017;96:729-736.
J Emerg Med. 2020; 59: 373-383
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DKA Pathophysiology

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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

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DKA Pathophysiology

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

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DKA Pathophysiology

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- ▶ Anion Gap – presence & severity of metabolic acidosis

$$[\text{Na}^+ - (\text{Cl}^- + \text{HCO}_3^-)]$$

Normal = 7 – 9 mEq/L

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

Metabolic acidosis

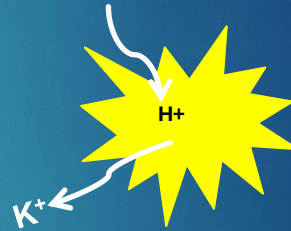
DKA → Anion Gap > 20 mEq/L

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Serum Potassium

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- ▶ May be falsely elevated
- ▶ Movement of K^+ out of cells
 - ▶ Solute drag
 - ▶ Acidosis $\rightarrow$ 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): S87-606

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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

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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

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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

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Diagnostic Criteria for HHS

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Blood glucose > 600mg/dL

• Average ~ 1000 mg/dL

Arterial pH >7.3

Serum HCO_3^- >15 mEq/L

Serum osmolality > 320 mOsm/kg

• May be as high as 380

Absent or mild ketonuria

Mental status change

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Diab Med. 2020; 37(12): 2001-2008
Front. Clin Diabetes Healthc. 2022;2

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DKA versus HHS

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- 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 osmolality
 - ▶ > 320 mOsm
 - ▶ Altered LOC
 - ▶ More electrolyte imbalances
 - ▶ Evolves over days to weeks
 - ▶ More "normal" ABGs
 - ▶ pH > 7.30
 - ▶ Ketosis absent or mild

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euDKA Pathophysiology

Adv Exp Med Biol. 2021;1307:85-114.
Emergency Medicine Practice. 2020;22(2):1-20.
Med Clin North Am. 2017;101(8):587-606.
J Emerg Med. 2020;59:379-383.
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.

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

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Clinical Manifestations: Physical Exam

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



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Clinical Manifestations: Physical Exam 37

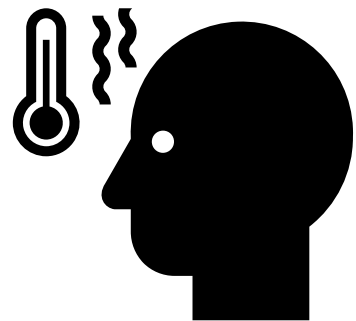
- ▶ Abdominal pain
 - ▶ More common with DKA
 - ▶ Correlates with severity of acidosis
 - ▶ Ketone have paralytic effect on smooth muscles
 - ▶ Relieved with reversal of dehydration
 - ▶ Consider other intra-abdominal pathology

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Clinical Manifestations: Physical Exam 38

- ▶ 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
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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.

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Diagnostic Testing

Serum glucose

Chemistry panel

- Na & K
- Anion gap

Serum β -OHB

ABGs

- Venous pH correlates

Serum osmolality

BUN/Cr

Hgb A₁C

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Look for Causative Factors

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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

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Respiratory Support

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↓ 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

A
B
C
D

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Fluid Replacement

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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

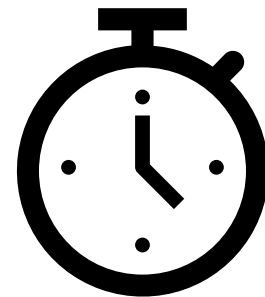
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Fluid Replacement

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



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Fluid Replacement

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▶ 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



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Insulin Therapy Goal

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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

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Insulin Therapy

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Initial IV bolus: 0.15 Units/kg regular insulin

Insulin infusion: 0.1 Units/kg/hr

- Short $\frac{1}{2}$ 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



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Font. Clin Diabetes Healthc. 2022;2

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Insulin Therapy

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Monitor

Monitor blood glucose hourly & prn

Glucose

When blood glucose approaches

- 250 for DKA
- 300 mg/dL for HHS
- Add dextrose to IV fluid
- $\bar{=}$ 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

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Insulin Therapy

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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

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Electrolyte Replacement

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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

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Frontiers in Endocrinology. 2017; 8(106): 1-13
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J Emerg Med. 2020; 59: 373-383
J Emerg Med. 2021; 61: 365-375

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Electrolyte Replacement

- ▶ KPO_4^- Replacement
 - ▶ If $\text{PO}_4^- < 1 \text{ mg/dL}$
 - ▶ 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: 372–383
 J Emerg Med. 2021; 61: 365–375
 Front. Clin Diabetes Healthc. 2022;2

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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: 372–383
 J Emerg Med. 2021; 61: 365–375
 Front. Clin Diabetes Healthc. 2022;2

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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
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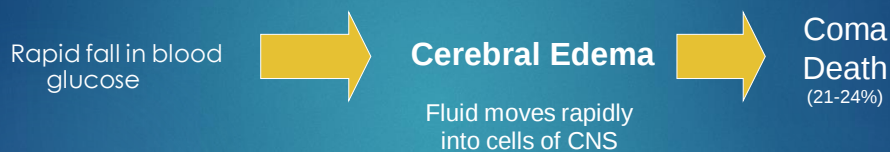


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Cerebral Edema

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Pathophysiology is poorly understood



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
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J Emerg Med. 2020; 59: 373-383
J Emerg Med. 2021; 61: 365-375
Font. Clin Diabetes Healthc. 2022;2

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Cerebral Edema

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- ▶ 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

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Cerebral Edema

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- ▶ Prevention
 - ▶ Avoid excessive hydration and rapid reduction of plasma osmolarity
 - ▶ Max reduction 3 mOsm/kg H₂O 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: 379-383
J Emerg Med. 2021; 61: 365-375

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Resolution of Hyperglycemic Emergency

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- ▶ DKA
 - ▶ Blood glucose < 200 mg/dL
 - ▶ Serum $\text{HCO}_3^- \geq 15$ 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

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Diabetic Sick Day Management

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Usual basal insulin
or oral anti-
diabetic agents



Liberal fluid intake



Easily digestible
CHO if unable to
eat normal diet

- Custard, pudding, cream soup, toast
- Gelatin, broth, juice, soda

Have family
member check on
them q 4 hrs



Early consultation
with PCP



Adv Exp Med Biol. 2021; 1307: 85–114

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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



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Summary

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

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Questions?

THANK YOU FOR YOUR ATTENTION!

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