Growing Expectations and New Perils in DKA Management
Financial Disclosures

• I receive a stipend as DM Director from Sharp.
Growing Expectations of Medical Cost Containment

Old Model:

- Length of Stay

New Model:

- Value based purchasing
How big is the problem?

- $250 Billion on Diabetes
- $180 Billion on Treatment
- $70 Billion on disability
- $2.4 Billion on DKA Treatment
- 30 million diabetics
- 150,000 admits/year
- McDonald’s Gross Annual Income $10 billion
How big is the problem?

Number (in Thousands) of Hospital Discharges with Diabetic Ketoacidosis listed as First Diagnosis, 1988-2009.

Data from CDC Diabetes Data & Trends
How good are we doing?

Average Length of Stay (LOS) in Days of Hospital Discharges with Diabetic Ketoacidosis, United States, 1988–2009

Length of Stay

3.4 days

Data from CDC Diabetes Data & Trends
How do we do?

Systemwide Sharp Numbers:

- DKA triggered powerplan
- 415 patients in 2015
- 32 spent > 3.5 d in icu
- 90 spent > 6 d in hospital
Length of DKA Hospital Stay Dilemma

- 35 yo diabetes naive male presented with dx of HHS, glucose of 1600.
- Spent 4 days in ICU,
- 6 days in hospital
- Had neurological symptoms of incoordination of hands prompting MRI and neurology evaluation
- To safely normalize glucose – 30 hours needed. (1500/50)
- Normalized Anion gap quickly, but
- 2 days to stabilize glucose after he began eating.
- Transition to SQ day 4.
- Trouble learning techniques
- Discharged to family
The blood compartment is not a storage location for Glucose!

- The entire normal glucose content of extracellular fluid is only 14 gm (50 Cal)!
- (140 dl x 100 mg/dl)
- That’s less Calories than an ampule of D50!
When does Severe Hyperglycemia Occur?  
(like over a 1000 mg/dl)

- Massive intake of glucose (The Juice Drinker)
- Massive Catabolism of Protein Stores (really really sick)
- Diminished Excretion (Renal Failure)
Have we reached a minimum physiologic limit in DKA length of stay?

1. Resuscitation.
2. Glucose Normalization.
3. Correction of anion gap and acidosis.
4. Titration of insulin dose anticipated to be used as outpatient.
5. Education of patient.

- Hours
- 1-2 days
- 1-2 days
- 1 day
- 2 days
The Nonadherent Patient with DKA

- 29 yo type 1 who stopped her insulin after a family argument.
- Not ill.
- Glucose 500
- Anion gap closed overnight.
- Home in 48 hrs.

- Blue Cross study 2008, over 15,000 members
- Diabetes medicine adherence over a year
- 73.9% adherent,
- 26.1% nonadherent
- Higher pharmacy costs $572
- 31% fewer hospitalizations
- Lower Overall Total Cost of care $1012
# Prolonged ICU stay

<table>
<thead>
<tr>
<th>Problem</th>
<th>Solution</th>
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<tr>
<td>Persistent Ketosis</td>
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<td>Lactic Acidosis</td>
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<td>Hypernatremia</td>
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Pathogenesis of Diabetic Ketoacidosis (DKA) and Hyperglycemic Hyperosmolar State (HHS)

Insulin Deficiency: Very low ----------- Relatively Low

Stress Hormones: Epi, Cortisol, Glucagon

Lipolysis

Ketogenesis

Ketoacidosis

Decreased Glucose Utilization

Glycogenolysis

Gluconeogenesis

Hyperglycemia

Hyperosmolarity

Dehydration

DKA

HHS
Case of a prolonged stay

- 24 yo with autism brought in for altered level of consciousness. Had decreased PO intake plus diarrhea, nausea and vomiting.
- No hx DM or kidney dz
- Hx of CAD + CHF with a stent placed a year ago.
- No alcohol, tobacco and ate a healthy diet with no sodas or excessive juice.
- Furosemide, HCTZ, spironolactone, lisinopril, metoprolol, hydralazine, oxcarbazepine, clonazepam, perphenazine.
- Obese, NAD,
- 102/53, 90s, afebrile
- Clear chest, nontender abdomen and no edema.
- Glucose 1515 and a Crn of 7.3, bicarb of 19.
## Case of a prolonged stay

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Prolonged Hospital Stay

Problem:
• Erratic blood sugars
• Inability to learn basic DM care techniques
• Abdominal Pain
• Narcotic Dependence
• Management of co-morbidities

Solution
• Diet education
• Social support and experienced educators
• Recognition of syndrome
• Psychiatric Advice
• Varies, must have early recognition.
Value Based Purchasing and DKA

- Poor Glycemic control Post CABG (old news)
- DKA as a Hospital Acquired condition
- DKA Readmission
- Prevention DKA
Hospital Acquired DKA

• Type 1 without basal insulin orders on admission
• Fail to restart insulin after hypoglycemic event
• Stopped Insulin drip and fail to start basal insulin.
• Stopped pump and fail to start basal insulin.
DKA/HHS Readmissions

**Problem**
- Understanding Disease
- Cost of Medication
- Access to Pharmacy
- Dexterity/Blindness
- Depression
- Isolation
- Misdiagnosis as type 2
- Under-treatment

**Solution**
- Education
- Preauthorization
- Case Management
- Training
- Psychiatry
- Day care
- Insulin after DKA/HHS
- Longer Training
Social Deprivation and DKA Deaths

- 628 pts over 5 years
- 96 had 1 admit DKA
- 111 had 2-5 admits
- 64 had >5
- Multiple admits had higher social deprivation score and more likely to take antidepressants.

- Mortality associated with single episode DKA = 5.2% over 4.1 yrs.
- Mortality associated with >5 episodes 23.4% over 2.4 yrs.

UK Study: Davenport *Diabetologia* 2016
Causes of Decompensation to DKA:

- New onset type 1 diabetes
- Acute major illness
- Omission of insulin in setting of reduced oral intake
- Malfunction of insulin pump
- Glucocorticoids
- Catecholamines: dopamine, norepinephrine, etc
- Atypical antipsychotics: Olanzapine, Clozapine, Resperidone, Quetiapine
- Recreational stimulants: Cocaine, amphetamines, caffeine
- Alcohol
- Na-Glucose Cotransporter 2 inhibitors, (SGLT-2I)
- Psychological or Social issues associated with Insulin
Diabulimia

• The deliberate underdosing of insulin in IDDM to lose weight.
• First reported 1983.
• Estimated in 14% of adolescent type I women.
• Risk of DKA
DKA with SGLT-2 Inhibitors

- 73 cases reviewed by FDA adverse event database
- 15 were Type 1 (not indicated)
- 44 were Type 2
- 14 unspecified
- Glucose from 90 to 1300
- Median of 211 mg/dl.
- Predisposing features were infection, reduced carbs or caloric intake, reduction in insulin, decrease in sulfonylurea or alcohol use.
SGLT-2 Inhibitors

- Decreased Ketone Body Excretion
- Sympathetic Activation
- Increased Lipolysis
- Increased Glucagon

Hypoglycemia
- Decreased Insulin
- Increased Ketogenesis

Osmotic Diuresis

α Cells Pancreas
- Increased Glucagon

DKA

Ketogenesis
Pathogenesis of Ketosis

Fatty acid Synthesis
Occurs with High Insulin and Low Glucagon

Low Insulin and High Glucagon
Decreases Malonyl CoA
Disinhibits CPT
And Fatty Acids are Transformed into Mitochondrion for Ketone Production

Cytosol

Fatty Acids

Acetyl-CoA

Citrate

Malonyl-CoA

CPT

Fatty Acid-CoA

Ketone Bodies

Mitochondrion

+Insulin
- Glucagon
+Glucagon

Low Insulin and High Glucagon
Decreases Malonyl CoA
Disinhibits CPT
And Fatty Acids are Transported into Mitochondrion for Ketone Production
Case of Euglycemic DKA

- 53 yo with hx of poorly controlled DM-2.
- Previously on Canagliflozin with good results, HgbA1c dropped from 15 to 9.5. Ran out of samples, 6 months ago.
- Rx authorization was approved and she restarted 1 month before presentation. HgbA1c 12.
- Was also taking metformin and a weekly injectable (GLP1 agonist).
- Had stopped Humalog when these 2 new meds were started.
- Developed malaise fatigue, headache, nausea, vomiting and presented to ER.

- 133/87, afebrile
- Exam
- Glucose 263
- Anion gap 25
- Wbc 9.3
- BUN 45, Crn 1.2 (previously 0.7)
- UA 6-10 wbc, + ketones
- CT head negative

- Discharged with Rx Ciprofloxacin for dx UTI/Pyelonephritis

- Readmitted 1 day later with
- pH 7.23, Bicarb 12, AG 45
- Glucose of 363
Can we predict who will get DKA?

- Type 1 adults
- 255 with episode DKA
- 1755 without DKA
- Relative Risks:
  - Duration DM - 0.98
  - HgbA1c - 1.25
  - Psychiatric Dx - 1.98
  - Gastroparesis - 4.13

Butalia, *Diabetic Medicine*, 2013
In-Hospital Mortality of DKA/HHS

- Generally quoted at 2-5%
- Remarkably stable over time.
- Advanced age, mechanical ventilation and bedridden state are greatest risk factors.
- HHS felt to be worse
Case of a Reluctant Patient

- 89 yo with long hx DM developed CKD and was taken off glyburide and metformin. Started nateglinide.
- Polyuria, polydipsia.
- Didn’t check sugars, tired of sticking his fingers.
- Hx prostatic obstruction and incontinence.
- Losartan, HCTZ, fesoteridine, imipramine, amlodipine.

- Thirsty, nad, 140/70, HR in 90s, afebrile.
- Exam unremarkable.
- Na 127, K 5.3, Gluc 1070,
- BUN 62, Crn 2.5, Bicarb 26
- UA showed >100 wbc’s

- Admitted to ICU, but signed out AMA a few hours later.
- Got a Rx for antibiotics and he took his nateglinide.
- Doing fine 5 years later.
Prevention is better than management, so...

- Eat right
- Check your sugar
- Take your insulin
Vomiting Pregnant Type 1

- 24 yo DM-1
- Pregnant 11 weeks
- N/V x 3 days
- Abdominal pain

- 7.45/98/33/32
- Na 131
- K 3.1
- Cl 75
- HCO3 31
- BUN 42
- Crn 1.0
- Glucose 400
- Anion Gap 25
- Acetone Large
Vomiting Pregnant Type 1

Diagnosis
• ER: DKA
• OB: DKA
• Medicine: Not DKA
• Dehydrated

Management
• Regular insulin 5 units IVP
• 1 liter NS
• She refused additional aspart sq due to falling glucose.
• 18 h post original lab was started on D5W at 30 and an insulin drip.
Vomiting Pregnant Type 1
Vomiting Pregnant Type 1

Criticism
• This was DKA
• Hidden or Masked Acidosis
• Concomitant Metabolic Alkalosis from Vomiting
• Common presentation
• Inadequate IVF rate
• Needed more Glucose, Potassium
• Best managed by insulin drip
Abdominal Pain and Renal Failure

- 61 yo with DM-2
- On Metformin
- 2 days abdominal pain
- hypotensive

- 6.89/51/27/5
- Glucose 575
- Na 129
- K 6
- Cl 85
- CO2 6
- BUN 21
- Crn 1.7
- Acetone neg
- Lactate 18
- Anion Gap 38
- Phos 10
- Troponin 0.7
Abdominal Pain and Renal Failure

**Diagnosis**
- ER: DKA v HHS, septic shock, NSTEMI
- Medicine: same
- Cardiology: same

**Management**
- IV bicarbonate
- IV insulin
- Vanco, Zosyn
- IVF
- Heparin
Abdominal Pain and Renal Failure

Criticism

• Not DKA
• Lactic acidosis
• Mortality >90%
Chest Pain

• 56 yo with DM-2
• 5 days of chest pain
• Shortness of breath
• Hypotensive
• Oliguric

• 7.31/67/40/19
• Glucose 356
• Na 136
• K 4
• Cl 96
• CO2 20
• Anion Gap 20
• Acetone neg
• Troponin 0.12
Chest Pain

**Diagnosis**
- ER NSTEMI, not DKA
- Medicine DKA, NSTEMI, Pneumonia
- Cardiology delayed intervention due to DKA

**Management**
- Saline bolus
- Heparin and NTG
- DKA protocol
- Worsened anion gap and hypoxia with treatment
- Lactic acid returned at 6.5
- Fluids stopped, then restarted due to Dx of DKA.
Chest Pain

Criticism

• Not DKA
• Cardiogenic shock
• Lactic acidosis
• IVF not appropriate in CHF or oliguria
• Delayed intervention