Hyperglycemic Crises

First Principles in hyperglycemic syndromes

- What is causing hyperglycemia?
- How does DKA differ from HHS and other hyperglycemic syndromes;
 - Pathophysiology drives therapy
 - Choose the correct protocol

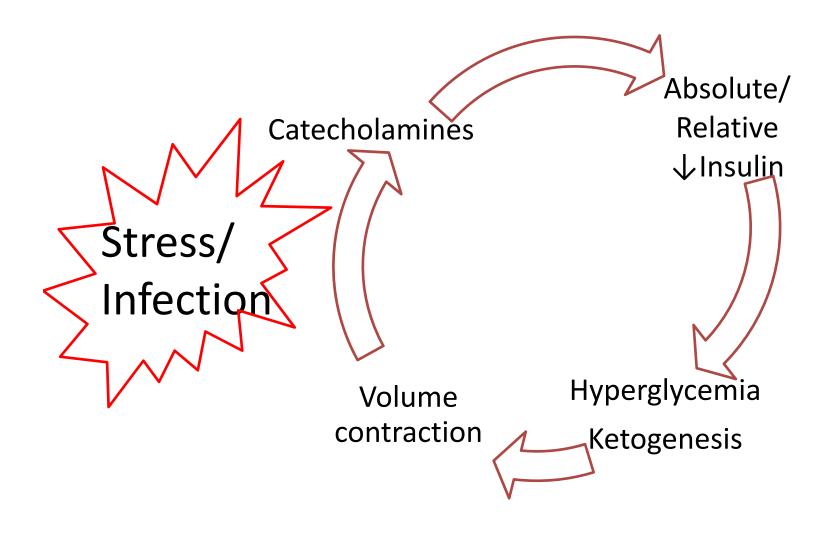
Pathogenesis of Decompensated Diabetic States

- Infection/stress/dehydration → Absolute or relative insulin deficiency
 - − ↑ Glucagon
 - ↑ Cortisol

 - ↑ Growth hormone
- Starvation $\rightarrow \uparrow$ lipolysis \rightarrow FFA to liver
- $\rightarrow \uparrow$ glucagon/insulin ratio \rightarrow ketogenesis
- $\rightarrow \uparrow$ gluconeogenesis and \downarrow glucose utilization
- Hyperosmolar states more common in patients with relative insulin deficiency

Pathogenesis of DKA

- Adipose tissue;
 ↓Insulin / ↑Epinephrine ⇒ ↑ FFA
- Liver;
 ↓Insulin / ↑Glucagon ⇒ ↑ Ketones



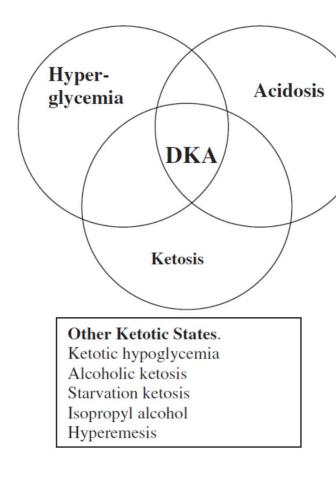
22 year old African-American woman presents with nausea, vomiting, weight loss, blurry vision. Multiple family members with diabetes. Ht 5'8", Wt 250 lbs. Acanthosis Nigricans on neck. Alert, abdominal pain+.

- ER Labs; Glucose 900 mg/dl
- β-OHB; 4.5 mmol/L
- pH 7.20 pCO₂ 20, pO₂ 105
- Na+ 125, K+ 4.5, Cl 90, HCO₃ 12, Cr 1.5, BUN 40
- Ca++ 9.0, Phos 5, Albumin 4
- WBC 15K, Hg 16, Lipase 600 (N < 140)
- Diagnosis: DKA vs HHS vs other

Table 1 Diagnostic criteria for DKA and HHS					
	Mild DKA	Moderate DKA	Severe DKA	HHS	
Plasma glucose (mg/dL)	>250	>250	>250	>600	
pH	7.25-7.3	7.0-7.24	<7.0	>7.3	
Serum bicarbonate (mEq/L)	15–18	10–15	<10	>18	
Ketones (urine or serum)	Positive	Positive	Positive	Minimal or negative	
Anion gap	>10	>12	>12	Variable	
Osmolality (mOsm/kg)	Variable	Variable	Variable	>320	
Mental status	Alert	Alert/drowsy	Stupor/coma	Stupor/coma	

Data from Kitabchi AE, Umpierrez GE, Miles JM, et al. Hyperglycemic crises in adult patients with diabetes. Diabetes Care 2009;32(7):1335–43.

Other Hyperglycemic States Uncontrolled DM HHS Stress hyperglycemia



Other Metabolic Acidotic States Lactic acidosis

Hyperchloremic acidosis Salicylism

Adapted from ref 19

Fig. 2 - Differential diagnosis of DKA. Data adapted from ref [19].

Table 3 – Laboratory evaluation of metabolic acidosis and coma.											
	Starvation or high fat intake	DKA	Lactic acidosis	Uremic acidosis	Alcoholic ketosis (starvation)	Salicylate intoxication	Methanol or ethylene glycol intoxication	Hyperosm- olar coma	Hypoglycemic coma	Rhabdomyolysis	Isoproproply alcohol
pН	Normal	↓	↓	Mild↓	↓↑	↓ ↑	↓	Normal	Normal	Mild ↓ may be ↓↓	Normal
Plasma glucose	Normal	1	Normal	Normal	↓ or normal	Normal or \downarrow	Normal	↑↑ >500 mg/dl	↓↓ <30 mg/dl	Normal	1
Glycosuria	Negative	++	Negative	Negative	Negative	Negative †	Negative	++	Negative	Negative	Negative
Total plasma ketones*	Slight ↑	↑ ↑	Normal	Normal	Slight to moderate ↑	Normal or	Normal	Normal or slight ↑	Normal or slight ↑	Normal	1
Anion gap	Slight ↑	†	↑	Slight ↑	1	1	1	Normal	Normal or slight	† †	$\uparrow \uparrow$
Osmolality	Normal	†	Normal	1	Normal	Normal	† †	↑↑ >330 mOsm/kg	Normal	Normal or slight ↑	1
Uric Acid	Mild (starvation)	1	Normal	Normal	1	Normal	Normal	Normal	Normal	1	Normal
Miscellaneous	False- positive	May give lactate for ethylene glycol	Serum >200 >7 mmol/l	BUN mg/dl	salicylate	Serum levels positive	Serum positive		hemoglobinuria	Myoglobinuria	

DKA vs HHS

- Etiology:
 - New onset ~ 20%
 - Non-adherence ~ 50% (recurrent DKA ~ 80%)
 - Infection ~ 15%
 - Other ~ 15%
 - stroke, MI, pancreatitis, medication effect (steroids), pregnancy, SGLT-2, insulin pump malfunction, antipsychotics (olanzapine, risperidone)
- Mortality:
 - -<1% in DKA
 - 5-16% HHS

Formulas

- Anion gap= (Na + K)- (bicarb + chloride).
 Abnormal > 12. [abnormal > 10 if K+ not included]
- Osmolar gap. Measured osmoles calculated osmoles.
- Calculated osmoles = 2(Na) + K + (BUN/2.8) + (glu/18)
- Corrected Na = Measured Na + {1.6 x [glu -100]/100}.
- Arterial pH = $6.97 + (0.0163 \times bicarbonate)$
- If corrected Na is normal range, then low measured Na is due to osmotic shifting. If corrected Na is below normal range, then Na is truly low due to osmotic diuresis. If measure Na is in the normal range without correction in the setting of significant hyperglycemia, this is likely due to loss free H20.
- Note: Pseudohyponatremia due to chylomicronemia

Characterization of Diabetes

- Beta cell reserve: "β-"
 - C-Peptide in face of glucose > 200 mg/dl
- Autoimmunity: "A+"
 - GAD antibody [ZnT8 antibody]
 - Islet cell antibody
 - Anti-insulin antibody (Pedi only)
- HLA
 - DR3/DR4 + other genetic traits
- MODY genes

Syndromes of Ketosis-Prone Diabetes Mellitus

Ashok Balasubramanyam, Ramaswami Nalini, Christiane S. Hampe, and Mario Maldonado

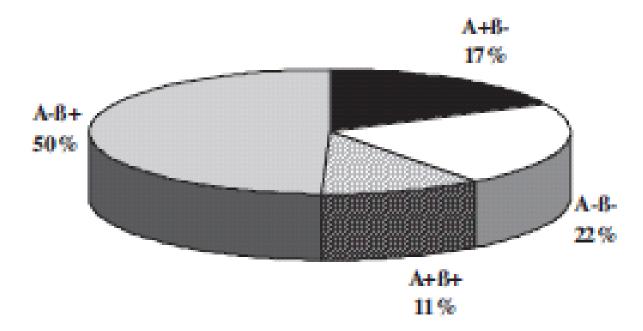


Fig. 1. Frequency distribution of patients in the four Aβ groups in a multiethnic adult U.S. urban population. [Reproduced with permission from M. Maldonado et al.: J Clin Endocrinol Metab 88:5090— 5098, 2003 (1). Copyright The Endocrine Society.]

Presentation- signs

Dehydration (hypovolemia by dry mucus membranes, decreased skin turgor, or by hypotension)

- Ketone breath (fruity odor)(acetoacidic acid -> converted to acetone -> removed via lungs)
- Kussamaul breathing (deep regular sigh respirations

Approach

- 1) Confirm diagnosis.
 - Usually blood glucose >250-300. Beware of euglycemic DKA.
 - pH < 7.3 (met acidosis w an anion gap)</p>
 - Elevation in serum ketones > 3.
- 2) Initiate treatment in a 3 pronged manner.
 - Insulin deficient- supply insulin.
 - Fluid depleted- supply fluids.
 - Electrolyte derangements- correct.

- What rate do you start IVFs and what kind?
- When do you transition IVFs and what kind?
- How much IVF does the average DKA patient require?

IV Fluids - 1

• Fluids:

- Average DKA patient is 5-8L depleted upon presentation.
- Give 1-2L NS bolus in 1st hour (usually done in ER but double check them!)
- Goal is to replace ½ fluid deficit within first 8 hrs.
- Don't forget about urine loss
- Generally over hours 2-4, infuse NS at rate of 500 cc/hr
- Technically when bp is stable and UOP is adequate, rate can be reduced to 250 cc/hr.
- Type of fluid is changed to 1/2NS usually when bp and UOP are stable, or when Na > 155

IV Fluids- 2

- Add 5% D5 to fluid when glucose < 250. (hormonal axis leading to hyperglycemia has not normalized and patient will experience worsening DKA without continued insulin).
- Continue glucose administration until ketosis (not ketonuria) clears and patient is able to tolerate po.
- If glucose < 150 and pt is still ketotic, can change fluids to D10% or D20%.
- Fluid replacement alone:
 - Expands intravascular compartment as well as interstitial compartment (improves perfusion),
 - Leads to reduction in serum glucose levels alone (by as much as 25%)
 - Leads to less circulating hormones producing hyperglycemia

- What rate do you start insulin?
- How fast should serum glucose fall?
- Is it possible for serum glucose to fall too rapidly?
- When can you stop IV insulin?
- What are situations when you would delay starting insulin?

Research question: use of long acting insulin?

Insulin-1

Insulin:

- Prime tubing with insulin.
- Begin IV regular insulin infusion at rate 0.14 U/kg/hr (if no bolus).
- IV regular insulin has a half life of 7-8 minutes. No interruptions should occur in drip (including transfer from ED to ICU) due to short half life.
- Goal serum glucose fall 50-70 mg/dL (~ 10%) in 1st hr.
- Adjust infusion rate until glucose is falling this much hourly.
- If rate of glucose decline > 100 mg/dL/hr, decrease rate of insulin administration to avoid cerebral edema.
- Continue infusion until serum ketosis (not ketonuria) resolves (< 3 mmol. If glucose, bicarbonate, anion gap have resolved but serum ketosis remains, pt will remain highly resistant to insulin, should consider continuing protocol until ketosis resolves.

Insulin - 2

- Glucose levels should be monitored hourly.
- Target serum glucose initially 250 mg/dL.
- Insulin replacement alone-
 - Gluconeogensis and ketone production in the liver are halted.
 - Lipolysis of adipose tissue is halted.
- Delay insulin replacement for:
 - Severely hypotensive patients. As insulin administration can lead to dramatic intravascular shift which can precipitate vascular collapse. Fluids first!
 - Severely hypokalemic patients. As insulin administration can lead to dramatic intravascuar shift, and cardiac arrythymias can occur with significant hypokalemia.

 Which electrolytes might merit replacement before administering insulin?

Table 2 Potassium repletion in DKA and HHS		
Serum Potassium (mEq/L)	Repletion	
>5.3	No repletion, repeat in 1 h.	
4.0-5.3	Add 10 mEq/L KCl/h to IV fluids.	
3.5-<4.0	Add 20 mEq/L KCl/h to IV fluids.	
<3.5	Hold insulin. Add 20–60 mEq/L/h to IV fluids, place on continuous cardiac monitor.	

Data from McNaughton CD, Self WH, Slovis C. Diabetes in the emergency department: acute care of diabetes patients. Clin Diabetes 2011;29(2):51–9.

Electrolytes

• Electrolytes:

- Bicarbonate:
 - Generally does not need replacement.
 - Can consider if pH < 6.9 or bicarb < 5. Can replete by adding it to fluid 1-2 amps of bicarbonate in fluid. When pH reaches 7.0, stop, to avoid late alkalosis.
- Phosphorus:
 - Repletion not normally required.
 - If phosphate < 1 or symptomatic, give 30-60 mM over 24 hrs.
 - ratio 2/3 potassium chloride : 1/3 potassium phosphate
 - Watch for hypocalcemia, hypomagnesium while repleting phosphate.
 - Symptoms of hypophosphatemia include: lethargy, depression, diarrhea, hemolytic anemia from lack of 2,3-diphosphoglycerate

HHS Treatment

- Generally fluid administration is greater:
 - If patient is hypotensive, give 2L fluid in first hour, rather than 1L.
 - Serium osm < 320, give 2-3L bolus of NS in 1st hr. (rather than 1-2L)
 - If serum osm > 320, some suggest:
 - Give 1.5L hypotonic saline for 1st hr.
 - 1 L of hypotonic saline for 2nd and 3rd hrs.
 - 500-750 cc of hypotonic saline for 4th hr.
 - Thus after 4 hrs = 4.5 L or more of hypotonic saline.
 - Continue hypotonic saline administration until serum osm < 320.
 - However, this strategy is controversial as in these patients even normal saline tends to be hypotonic.
- Insulin is less important than fluid administration:
 - Patients tend to be quite sensitive to insulin. Can start insulin at 0.05 U/kg rather than 0.1 U/kg.
 - In severe hypotension, do not start insulin. This will exacerbation hypotension and will not have effective delivery of insulin until circulating volume is improved.
 - Fall of glucose not tracked as closely. Goal is to have decrease over 2-4 hrs. If this does not occur, double insulin infusion rate. (rather than decrease by 50-70 every hour)
 - When glucose falls < 250, can add D5 to IVFs or can ½ rate of insulin administration. (in DKA must add D5 cannot stop insulin infusion!)
- Complications:
 - Thrombosis more common. MUST have heparin prophylaxis.
 - Also DIC, rhabdomyolysis more common than DKA.

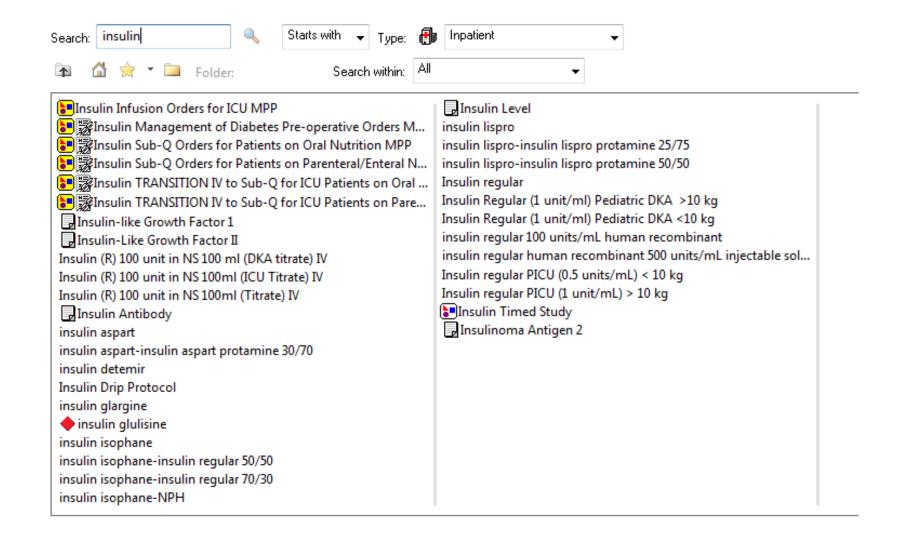
- Glucose 500 mg/dl
- ↓Serum ketones
- Na+ 155, K+ 3.9, Cl 105, HCO₃ 15, AG
- Cr 1.1, BUN 26
- Ca++ 8.5, Phos 2.5, Albumin 4

- Glucose 350 mg/dl
- ↓Serum ketones
- Na+ 155, K+ 3.0, Cl 115, HCO₃ 12, AG
- Cr 1.1, BUN 26
- Ca++ 8.0, Phos 2.0

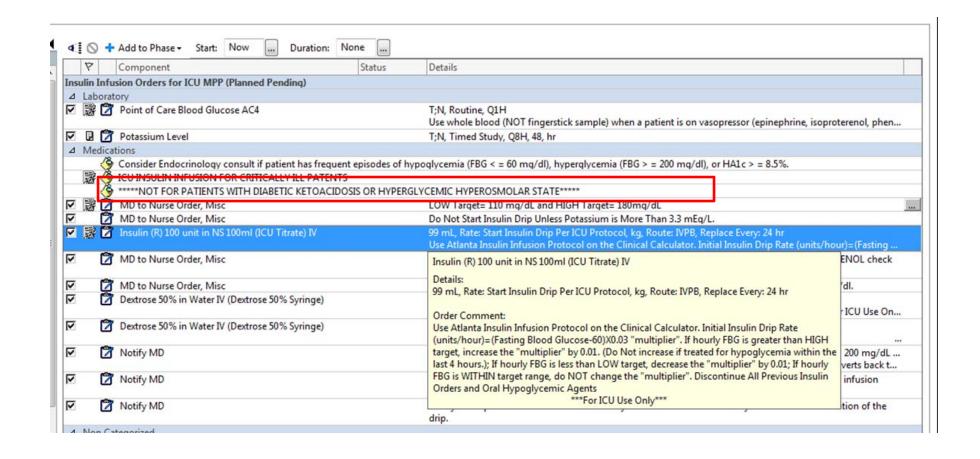
- Glucose 200 mg/dl
- ↓Serum ketones
- Na+ 148, K+ 3.0, Cl 120, HCO₃ 12, AG
- Cr 0.9, BUN 18
- Ca++ 8.0, Phos 2.0

- Glucose 200 mg/dl
- Neg Serum ketones
- Na+ 140, K+ 3.4, Cl 115, HCO₃ 15, AG
- Cr 0.6, BUN 10
- Ca++ 8.0, Phos 2.0
- Hungry, clinically improved

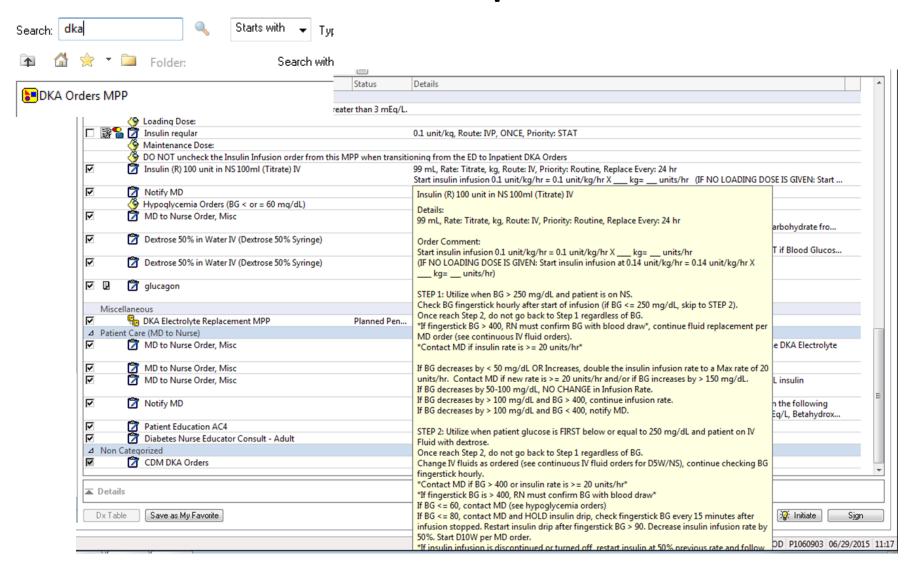
MHH



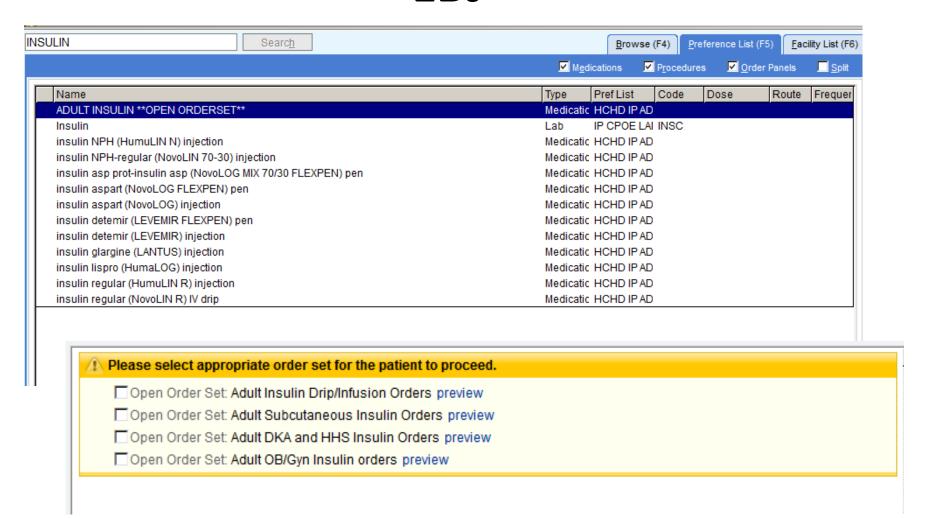
MHH – Atlanta protocol



MHH – DKA protocol



LBJ



LBJ – insulin DKA

	For blood glucose < 100 mg/dl, consider using Dextrose 10 % + 0.9 % NaC	
	 0.9% NaCl infusion STAT (if not cardiac compromised or susceptible to fluid overload, recommend 15-20 ml/kg/hr) 	Intravenous, ONCE Starting today For 1 Doses, STAT
П	0.9% NaCl infusion (maintenance)	Intravenous, CONTINUOUS Starting today For 30 Days, Routine
	D5W -0.9 % NaCl infusion (when Blood Glucose is less than 200 mg/dL)	Intravenous, CONTINUOUS Starting today For 30 Days, Routine
П	■ D5W-LR infusion (when Blood Glucose is less than 200 mg/dL)	Intravenous, CONTINUOUS Starting today For 30 Days, Routine
	□ D10W - 0.9 % NaCl infusion (when Blood Glucose falls to less than	Intravenous, CONTINUOUS Starting today For 30 Days, Routine
П	100 mg/dL)	
ľ	Insulin Orders	
	Please remember to Discontinue all previous insulin orders and/or oral diabet	etes medications
	Recommended titrations are based on fingerstick blood glucose (BG), and	performed by nursing
	OKA/HHS Nursing Guidelines URL: http://hhintranet02/departme	nts/pharmacydept/epic/smartsets/guidance/DKA_HHS_NursingGuidelines.p
	Give one-time dose of specified Regular Insulin IV push prior to	IV Push, ONCE Starting today For 1 Doses, Routine
П	initiating insulin infusion (suggest 0.1 unit/kg)	
П	Start hourly infusion of Regular Insulin at specified rate (suggest 0.1	Intravenous, AS DIRECTED For 30 Days, Routine
П	unit/kg/hr)	•
П	☐ Insulin REGULAR bolus if blood glucose does not decrease by 75	IV Push, PRN For 30 Days, Other, Only give when blood glucose does not
П	mg/dL in one hour	decrease by 75 mg/dL in one hour, Routine
П	✓ If BG does not decrease by 75 mg/dL in any hour, give bolus Regular	IV Push, PRN For 30 Days, Other, Routine
	Insulin with no rate change	
	Potassium Replacement	
	It is recommended to select potassium supplementation order below that I	
	Orders that have more than 20 mEq of KCI per liter will have to be prepared	d by the inpatient pharmacy and delivered. You may enter an order with >
١,	20 mEq KCl in the search field at the bottom of this order set.	
П	✓ If potassium <= 3.3 mEq/L give KCl as needed (limit 10 mEq per hour)	10 mEq, Intravenous, PRN For 30 Days, Other, See administration
	peripherally)	instruction, Routine
	✓ If potassium is 3.3 to 5.3 mEq/L give KCl as needed (limit 10 mEq.)	10 mEq, Intravenous, PRN For 30 Days, Other, See administration
П	per hour peripherally)	instruction, Routine
П	Potassium > 5.3 mEq/L: recheck potassium in 2 hours and change	Routine, UNTIL DISCONTINUED, Starting today, DKA/HHS Protocol: If
П	all IVs to solutions without KCI added	Potassium > 5.3 mEq/L: recheck potassium in 2 hours and change all IVs
	=ti	to solutions without KCl added
	potassium chloride (KLOR-CON) 20 mEq oral packet	Oral, ONCE For 1 Doses, Routine
	Medications	

Hypoglycemia Medication Orders Hypoglycemia Management Protocol

URL: http://hhintranet02/departments/pharmacydept/epic/smartsets/guidance/Hypoglycemia

LBJ – insulin gtt

Addit insulin iniusion/Dnp Guidance	URL. http://minimanetoz/departments/pharmacydep/repic/smartsets/guidance/Addit
	Insulin Drip Guidance.pdf
General	
Notify Physician	
✓ Notify physician	Routine, UNTIL DISCONTINUED, Starting today
	Physician pager number:
E ALCO I CO	Notify physician BEFORE starting insulin if serum potassium is 3.3 mEq/L or lower
Notify physician	Routine, UNTIL DISCONTINUED, Starting today Physician pager number:
	Notify physician if blood glucose reverts to higher than 200 mg/dL x 2 consecutive
	tests after patient is at target blood glucose level
Nursing Assessment	toolo ditor patient is at target blood glacood level
POCT Glucose	Routine, 1 TIME, Starting today, between 15 and 30 minutes after treatment of
	hypoglycemia
	Routine, AS PER ORDER COMMENT, Starting today, every hour until blood
	glucose remains in target for 4 consecutive hours, then fingerstick glucose every 2
	hours
POCT Glucose	Routine, EVERY 1 HOUR, Starting today, if blood glucose is above target
Labs	
Common Labs	
☐ Hemoglobin A1C	Routine, AM DRAW, Starting tomorrow For 1 Occurrences, with next blood draw
	(once per hospital admission)
Medications	
Medication Orders	
Discontinue all previous insulin orders and oral diabetes medications	
Select Target BG range based on guidance from linked dosing charts	
insulin regular human 100 Units in 0.9% NaCl 100 mL IV drip	Intravenous, TITRATABLE-SEE ADMIN INSTR. Starting today For 30 Days, Routine
If TPN interrupted, immediately start 10% Dextrose in 0.45 % NaCl @ 1 ml/hr	at 100 mL/hr, Intravenous, AS DIRECTED, Routine
☐ If TPN interrupted, immediately start 10% Dextrose in 0.225 % NaCl @	100 at 100 mL/hr, Intravenous, AS DIRECTED, Routine
ml/hr	
Hypoglycemia Management Orders	
Hypoglycemia Management Protocol	URL: http://hhintranet02/departments/pharmacydept/epic/smartsets/guidance/Hypoglycemia Management.pdf
dextrose 50 % injection	IV Push, PRN For 30 Days, Other, See Admin Instruction, Routine

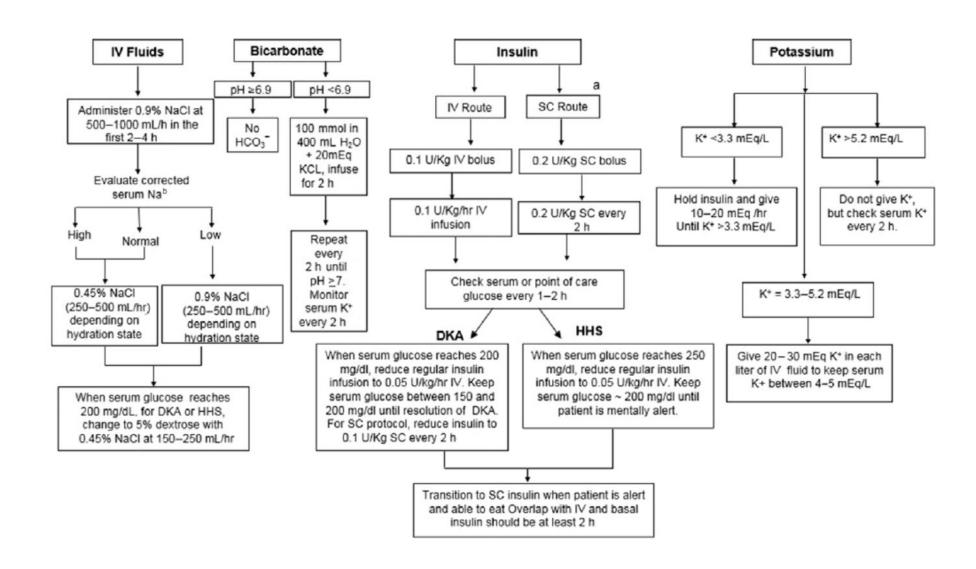
Mild DKA Pilot

Eligibility Criteria	Exclusion Criteria
1. Blood glucose > 250 mg/dL	 Age ≥ 80 years
2. $pH > 7.25$	2. Altered Mental Status
3. HCO3 > 15	3. Acute Myocardial Infarction
4. BOHB or serum ketones < 3	4. Congestive Heart Failure
	(NYHA Class III or IV)
	5. Pregnancy
	6. EGFR < 45 ml/min
	7. MAP < 65
	8. Severe Pancreatitis
	9. Anasarca

Insulin Aspart/Lispro

Initial Bolus	0.3 units/kg SC x 1 dose (max dose of 30 units)
Blood glucose ≥ 250 mg/dL	0.2 units/kg SC every 2 hours (max dose of 20 units)
Blood glucose is < 250 mg/dL	0.1 units/kg SC every 2 hours (max dose of 10 units)

Fayfman et al



 How do you determine insulin dose when transitioning from iv insulin to sc?

Transitioning insulin to sc

- Overlap IV administration and subcutaneous administration is necessary due to short half life of IV insulin and delay in start of subcutaneous insulin. Give Both long + short acting insulin
- Time of overlap depends on insulin being used:
 - Regular insulin begins working subcutaneously 30-45 min.
 - Intermediate acting insulin (NPH) begins working subcutaneously 2-3 hrs.
 - Long acting insulin (glargine/detemir) begins working subcutaneously 3-4 hrs.
- To transition:
 - 1) Calculate total daily dose (TDD).
 - When insulin rate is stable for 4-6 hrs when pt NPO. Then take hourly rate of insulin drip x 20 For Basal insulin only
 - 2) Weight based formula- Preferred Method.
 - 0.6U insulin/kg of body weight May need higher rates if patient still under increased stress (infection).

Transitioning IV insulin to SC

- Once the daily dose is determined must further divide dose.
- There are multiple strategies:
 - If pt is eating:
 - Basal bolus regimen with scheduled premeal + correction
 - If the patient is not eating:
 - Q 6 hour dose; consider 70/30 if on tube feedings

MHH – when PO

4	0 +	Add to Phase - Start: Now Duration: None	
-	7	Component Status	Details
霧山	sulin	Sub-Q Orders for Patients on Oral Nutrition MPP (Planned Pending)	
	/ledica	tions	
✓		MD to Nurse Order, Misc	Discontinue all previous insulin orders.
V	¥ 🗷	Point of Care Blood Glucose AC4	T;N, Routine, Before Meals & Bedtime
☑		Notify MD	Notify MD for blood glucose > 300mg/dl or < 60 mg/dl.
굣	_ 💆		Notify MD if patient becomes NPO or if parenteral/enteral nutrition is stopped (review insulin orders).
	B 🦠	***SCHEDULED BASAL INSULIN (Please select one)***	
		Recommended for Fasting Blood Glucose greater than 180 mg/dl. Start	with 0.2 units/kg (MAX 30 to 40 units) Sub-Q daily dose.
		If pre-meal glucose is persistently above target, consider Increasing Bas	al dose by 20%
		insulin glargine	unit, Route: SUB-Q, Daily
_	_		Check with prescriber prior to holding the dose.
	Z	insulin isophane (insulin isophane-NPH)	unit, Route: SUB-Q, Q12H
_	e Care		Check with prescriber prior to holding the dose.
		insulin detemir	unit, Route: SUB-Q, Daily
1	52 / 8.	**CCLIEDLU ED DDE MEAL TAICLUTAI***	Check with prescriber prior to holding the dose.
	B 🦠	**SCHEDULED PRE MEAL INSULIN***	
	_2	Start with 0.05 units/kg (MAX 10 units) before meals	un't Deuter CUD O TID Defens Mark
		insulin aspart	unit, Route: SUB-Q, TID-Before Meals Before Breakfast, Lunch and Dinner ONLY. If pre-lunch and bedtime glucose is persistently above target
	[7	Insulin regular	unit. Route: SUB-Q. TID-Before Meals
	كا	Insulin regular	Before Breakfast, Lunch and Dinner ONLY
	i 😘	***INSULIN CORRECTION DOSES***	belove breakingly, carrell and brillier offer
, sa	∞ ×	Please select a Starting, Medium or High Correction Dose regimen and	consider a bedtime Correction Dose regimen in addition
	- Š	Aspart (Novolog) Starting Correction Doses MPP	
	4		
		Aspart (Novolog) High Correction Doses MPP	
	- Ģ.	Aspart (Novolog) Bedtime Correction Doses MPP	
	<u> </u>	Do NOT order Regular Insulin Correction dose along with Aspart pre-m	ieal or Aspart correction doses
	Ģ,	Regular Insulin Starting Correction Doses MPP	·
	9.	Regular Insulin Medium Correction Doses MPP	
	9	Regular Insulin High Correction Doses MPP	
	9	Regular Insulin Bedtime Correction Doses MPP	
	Æ	<u>.</u>	

MHH – when NPO/TFs

4 ∫ S	+ Add to Phase - Start: Now Duration: None									
8	Component Status	Details								
潔 Ins	Insulin Sub-Q Orders for Patients on Parenteral/Enteral Nutrition or NPO MPP (Planned Pending)									
⊿ Me	Medications									
	Do NOT use for patients being converted from Insulin drips									
<u> </u>	MD to Nurse Order, Misc	Discontinue all previous insulin orders.								
区		T;N, Routine, Q6H								
$\overline{\mathbf{v}}$	Notify MD Notify MD	Notify MD for blood glucose > 300mg/dl or < 60 mg/dl.								
<u> </u>		Notify MD if patient becomes NPO or if Parenteral/Enteral nutrition stopped (review insulin orders).								
寥	· · · · · · · · · · · · · · · · · · ·									
	Daily Basal Insulin recommended for patients with HA1c greater than	8% or average blood glucose > 200 mg/dL								
	Start with 0.2 units/kg/day (MAX 30 to 40 units)									
_	If glucose is persistently above target, consider Increasing Basal dose									
	insulin detemir	unit, Route: SUB-Q, Daily								
_	6	Do not hold insulin without contacting the prescriber.								
	📝 insulin glargine	unit, Route: SUB-Q, Daily								
	(and in the second seco	Do not hold insulin without contacting the prescriber.								
	insulin isophane (insulin isophane-NPH)	unit, Route: SUB-Q, Q8H Do not hold insulin without contacting the prescriber.								
家	***INSULIN CORRECTION DOSES***	bo not note installing without contacting the prescriber.								
1328 	Aspart (Novolog) for Parenteral/Enteral or NPO Startin									
	Aspart (Novolog) for Parenteral/Enteral or NPO Mediu									
	Aspart (Novolog) for Parenteral/Enteral or NPO High									
	Regular Insulin for Parenteral/Enteral or NPO Starting									
	Regular Insulin for Parenteral/Enteral or NPO Medium									
	Regular Insulin for Parenteral/Enteral or NPO High Cor									
	- K									

MHH – hypoglycemic protocol

- A		
- 🈘		
	MD to Nurse Order, Misc	Hypoglycemia Orders (BG < or = 60 mg/dL): See Order Comments Review medications for management of BG < or = 60 mg/dL. For BG 40-60 mg/dL and patient AWAKE
Ż	Dextrose 50% in Water IV (Dextrose 50% Syringe)	25 mL, Route: IVP, PRN, PRN Blood Glucose Results For patients that are Unconscious or Unable to Swallow or NPO, if Blood Glucose 40-60 mg/dL
	Dextrose 50% in Water IV (Dextrose 50% Syringe)	50 mL, Route: IVP, PRN, PRN Blood Glucose Results if Blood Glucose < 40 mg/dL
3 💆	glucagon	1 mg, Route: IM, PRN, PRN Blood Glucose Results For BG < 60 mg/dL if no IV access and patient is either Unconscious, unable to swallow or npo
atient	Care (MD to Nurse)	
	Patient Education AC4	Daily, Instructions: Allow/instruct patient to self administer insulin.
₹	Point of Care Blood Glucose AC4	q10-15min Until Blood Glucose is > 100 mg/dL
	Notify MD	
onsult	ts	
3	Nutrition Consult/Dietitian Consult (Consult Nutrition/Dietitian)	
	atient	glucagon atient Care (MD to Nurse) Patient Education AC4 Point of Care Blood Glucose AC4 Notify MD Consults Nutrition Consult/Dietitian Consult (Consult

LBJ – insulin subq

Medications - Please select an IV solution to reduce the risk of hypoglycemia should the tube feeding or TPN be interrupted Please select an IV solution to reduce the risk of hypoglycemia if the patient is made NPO after receiving basal insulin Physician should evaluate need to discontinue previous basal insulin orders. This can be done in the Medications Activity. Insulin glargine (Lantus) or 70/30 should only be used in patients taking insulin at home Suggested basal insulin for naive patients: o 0.2 units per kg per day for diabetes in 2 divided doses o units per kg per day if not previously diagnosed or ESRD in 2 divided doses insulin NPH (NovoLIN N) 100 unit/mL injection BREAKFAST Subcutaneous, DAILY WITH BREAKFAST For 30 Days, Routine insulin NPH (NovoLIN N) 100 unit/mL injection BEDTIME Subcutaneous, AT BEDTIME Starting today at 9:00 PM For 30 Days, Routine insulin glargine (LANTUS) 100 unit/mL injection Subcutaneous, Routine insulin 70-30 (NOVOLIN) NPH and regular 100 unit/mL injection BREAKFAST Subcutaneous, EVERY MORNING BEFORE BREAKFAST For 30 Days, Routine insulin 70-30 (NOVOLIN) NPH and regular 100 unit/mL injection SUPPER Subcutaneous, EVERY EVENING BEFORE DINNER For 30 Days, Routine If patient made NPO after receiving morning Basal insulin, start D5W @ 100 ml/hr Intravenous, at 100 mL/hr, AS DIRECTED For 30 Days, Routine If patient made NPO after receiving morning Basal insulin, start D5W + 0.45 % NaCl @ 100 ml/hr at 100 mL/hr, Intravenous, AS DIRECTED For 30 Days, Routine Pre-meal Insulin Orders Provider should evaluate need to discontinue previous pre-meal insulin orders. This can be done in the Medications Activity. insulin regular (HUMULIN R) 100 unit/mL injection Subcutaneous, Routine insulin lispro (HumaLOG) 100 unit/mL injection Subcutaneous Routine Fixed Interval Insulin For patients on Enteral or Parenteral Feedings Provider should evaluate need to discontinue previous fixed interval insulin orders. This can be done in the Medications Activity. Please select only one order insulin NPH HUMAN (NOVOLIN N) 100 unit/mL injection Subcutaneous, EVERY 12 HOURS For 30 Days, Routine insulin regular human (NOVOLIN R) 100 unit/mL injection (suggest every 6 hours) Subcutaneous, Routine Give D10%W infusion @ 100 ml/hr if feeding or TPN interrupted Intravenous, at 100 mL/hr, AS DIRECTED For 30 Days, Routine Give D10 %, + NaCl infusion @ 100 ml/hr if feeding or TPN interrupted (must select NaCl concentration) at 100 mL/hr. Intravenous. AS DIRECTED. Routine Correction (Supplemental) Insulin Orders to cover blood glucose (NOT for bedtime use) Provider should evaluate need to discontinue previous insulin correction orders. This can be done in the Medications Activity. When selecting a medication, please indicate if insulin should be administered as pre-meal PRN (NOT for bedtime) or at a specified interval PRN. If pre-meal insulin ordered, consider using same insulin type for correction. Notify physician team before giving if patient is NPO insulin regular human (NOVOLIN R) 100 unit/mL injection Subcutaneous, Routine insulin lispro (HumaLOG) 100 unit/mL injection (requires FCC Approval) Subcutaneous, Routine Correction (Supplemental) Insulin Orders BEDTIME ONLY Provider should evaluate need to discontinue previous insulin correction orders. This can be done in the Medications Activity. If pre-meal insulin ordered, consider using same insulin type for correction. Includes orders for both prn and bedtime correction · Notify physician team before giving if patient is NPO insulin regular human (NOVOLIN R) 100 unit/mL injection Subcutaneous, BEDTIME PRN For 30 Days, Other, See Administration Instruction, Routine insulin lispro (HumaLOG) 100 unit/mL injection (requires FCC Approval) Subcutaneous, BEDTIME PRN For 30 Days, Other, See Administration Instruction, Routine Hypoglycemia Medication Orders Hypoglycemia Management Protocol http://hhintranet02/departments/pharmacydept/epic/smartsets/guidance/Hypoglycemia Management.pdf dextrose (INSTA-GLUCOSE) 40 % oral jel Oral, PRN For 30 Days, Other, Administer per Standing Orders for Hypoglycemia Management, Routine glucagon (human recombinant) (GLUCAGEN) injection 1 mg, Intramuscular, PRN For 30 Days, Administer per Standing Orders for Hypoglycemia Management, Routine V IV Push, PRN For 30 Days, Administer per Standing Orders for Hypoglycemia Management, Routine dextrose 50 % injection

Complications

Cerebral edema:

- With excessively rapid correction of Na and osmolarity, cerebral edema can occur. Exact etiology not known.
- More common in pediatric patients, but can occur in adults.
- Presents as headache, deterioration in consciousness or LOC, seizures.
- Treat with mannitol (1-2 gm/kg to load), steroids, loop diuretics.
- These patients tend not to survive.
- ARDS
- Embolism
 - DKA is hypercoaguable state.
- Acute gastric dilation (from excess prostaglandins)
 - Treat with reglan.

Sick Day Management DM Type 1

- Continue background insulin
- Monitor ketones if Glucose > 250 mg/dl
- Maintain hydration
- **Continue caloric intake with rapid insulin
- Treatment of underlying stressor/infection
- Treatment of nausea
- Close contact with health care provider

Alcoholic Ketoacidosis

- Nausea/vomiting + abdominal pain
- EtOH level undetectable
- 75% pancreatitis
- Glucose usually < 150 mg/dl, 15% < 50 mg/dl
- Acidosis with increased anion gap, predominantly ß-OH butyrate
- Treatment: IV dextrose, thiamine ± insulin

Common Errors in Treatment of DKA

- Slow recognition (especially if glucose < 400)
- Inadequate or intermittent initial therapy
- Inadequate K+ replacement
- Inappropriate Phosp replacement
- Early decrease or termination of insulin
- Poor transition to SQ insulin

- What are current recommendations for glucose targets in non-DKA patients?
- Are they different among surgical and medical patients, if so- how do they differ?

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INTENSIVE INSULIN THERAPY IN CRITICALLY ILL PATIENTS

GREET VAN DEN BERGHE, M.D., PH.D., PIETER WOUTERS, M.Sc., FRANK WEEKERS, M.D., CHARLES VERWAEST, M.D., FRANS BRUYNINCKX, M.D., MIET SCHETZ, M.D., PH.D., DIRK VLASSELAERS, M.D., PATRICK FERDINANDE, M.D., PH.D., PETER LAUWERS, M.D., AND ROGER BOUILLON, M.D., PH.D.

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Intensive Insulin Therapy in the Medical ICU

Greet Van den Berghe, M.D., Ph.D., Alexander Wilmer, M.D., Ph.D., Greet Hermans, M.D., Wouter Meersseman, M.D., Pieter J. Wouters, M.Sc., Ilse Milants, R.N., Eric Van Wijngaerden, M.D., Ph.D., Herman Bobbaers, M.D., Ph.D., and Roger Bouillon, M.D., Ph.D.

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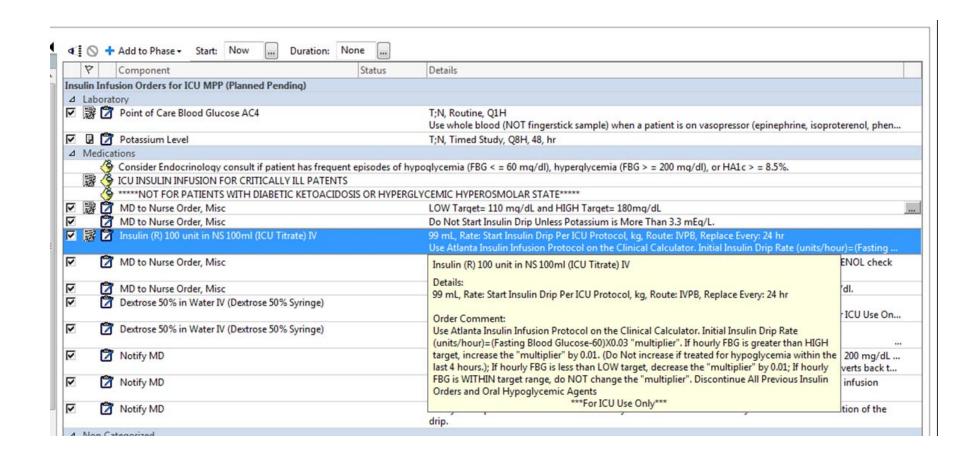
MARCH 26, 2009

VOL. 360 NO. 13

Intensive versus Conventional Glucose Control in Critically Ill Patients

The NICF-SUGAR Study Investigators*

MHH – Atlanta protocol



Atlanta Protocol

- Glucose 60 X Conversion Factor (0.03)
- If glucose not at target, increase conversion factor by 0.01. If glucose below target, reduce conversion factor by 0.01

• Example;

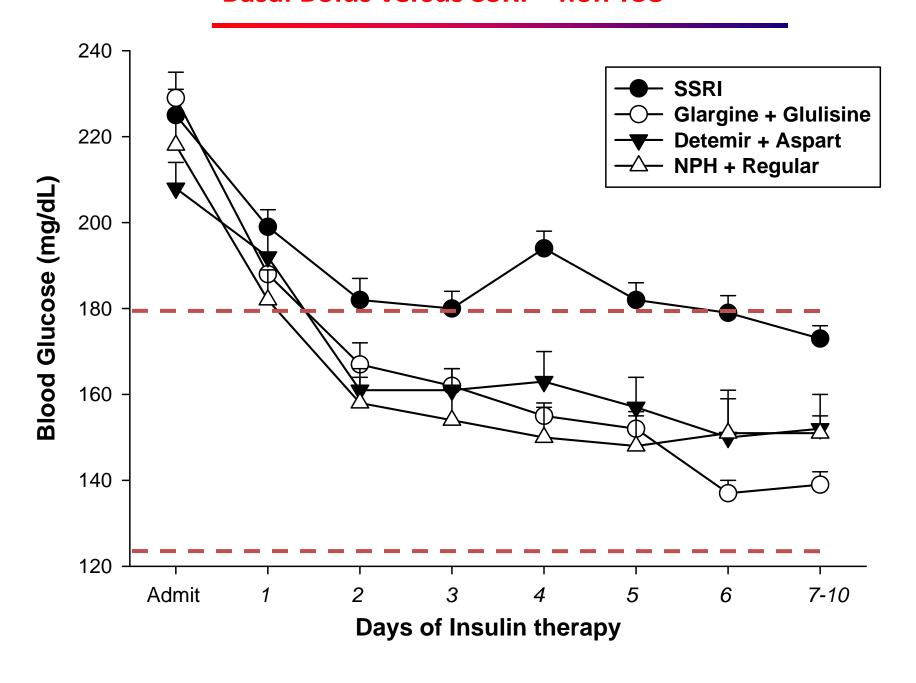
```
Glucose 260 - 60 \times 0.03 = 6 \text{ units/hour}
```

Glucose 300 – 60 X 0.05 = 12 units/hour

Atlanta Protocol

- Not for patients that are eating would transition to SQ insulin regimen
- Not for patients with Type 1 diabetes

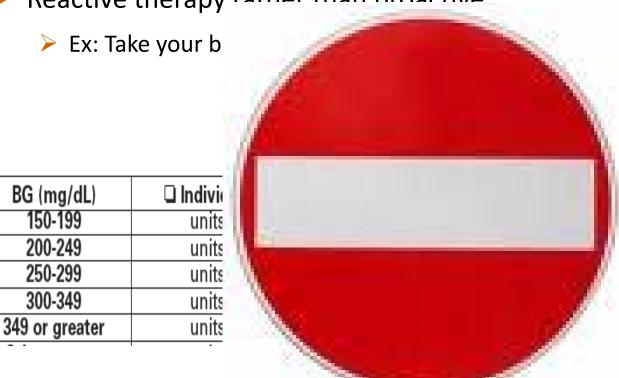
Basal Bolus versus SSRI - non-ICU



Insulin sliding scale:

> Patient receives short-acting insulin only if their glucose is elevated

> Reactive therapy rather than proactive



l High Dose	☐ Bed Time Dose
3 units	NONE
6 units	1 unit
9 units	2 units
12 units	3 units
15 units	4 units

4. SCHEDULED PREMEAL INSULIN				
4 SCHEDULED PREMEAL INSULIN	4	COLIEDIUE		INICIIIIN
	4	SCHEDULE	I) PREIVIEAL	IIVISUI IIV

Insulin, aspart (Novolog) administered immediately prior to meals

Before Breakfast	Before Lunch	Before Dinner			
units Sub-Q	units Sub-Q	units Sub-Q			

- **CORRECTION DOSES:** Given PRN Glucose Results in addition to scheduled basal and premeal insuln if applicable
 - Insulin, aspart (Novolog) Immediately prior to meals OR
 - Insulin, regular (Novolin R. Humulin R) 15-30 minutes prior to meals

BG (mg/dL)	☐ Individual	☐ Starting Dose	☐ Medium Dose	☐ High Dose
150-199	units	1 unit	2 units	3 units
200-249	units	2 units	4 units	6 units
250-299	units	3 units	6 units	9 units
300-349	units	4 units	8 units	12 units
349 or greater	units	5 units	10 units	15 units
Other	units			



Note: LBJ scale is different

HYPOGLYCEMIA (BG < 60 mg/dL)

PG (mg/dl)	AWAKE/ALERT	UNCONSCIOUS			
BG (mg/dL)	and able to swallow	or unable to swallow			
40-60	Give 6 oz. OJ, non-fat milk, or regular soda	Give 50 ml of D50W IV push STAT and notify MD			
Less than 40	Give 25 ml of D50W IV push STAT and notify MD	Give 30 iiii of B3000 iv push GiAi and nothly MB			

Check fingerstick glucose q 10-15 minutes and follow hospital hypoglycemia protocol until BG is greater than 100 mg/dL Notify MD if hypoglycemia persists beyond 30 minutes

- CONSULT: Diabetes nurse educator & Nutritionist
- **NURSING EDUCATION:** Allow/instruct patient to self administer insulin

Nurse's Signature

Basal Bolus Insulin Regimen: Summary

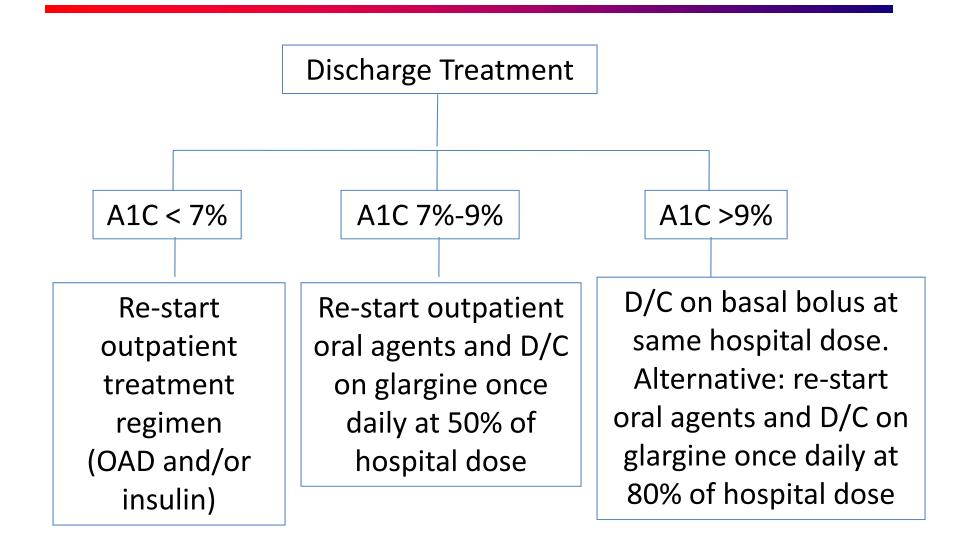
- > D/C oral antidiabetic drugs on admission
- Starting total daily dose (TDD):
 - 0.3 U/kg/d in elderly and renal failure (lean?)
 - 0.4 U/kg/d x BG between 140-200 mg/dL
 - 0.5 U/kg/d x BG between 201-400 mg/dL
- Half of TDD as insulin glargine and half as rapidacting insulin (lispro, aspart, glulisine)
- Decrease outpatient insulin dose by 20-25%

Umpierrez et al, Diabetes Care 2007; JCEM 2009; Diabetes Care 2011

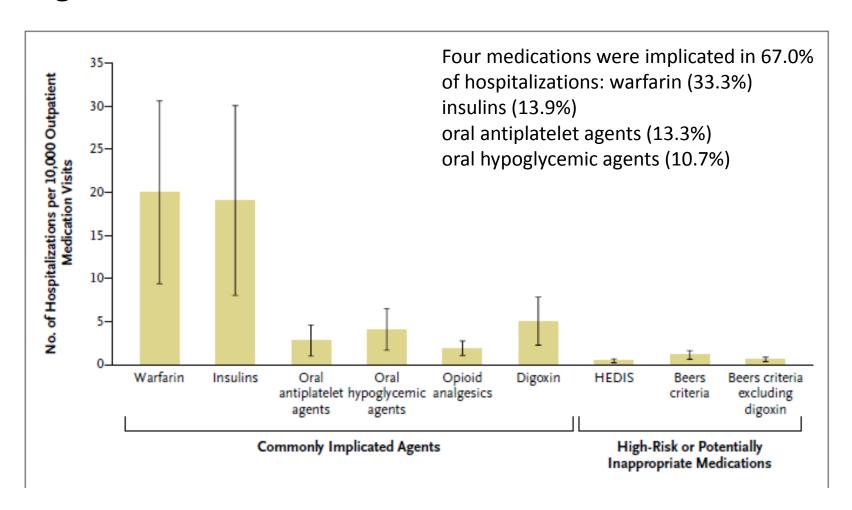
Basal Bolus: Insulin Dose Adjustment

Blood glucose levels	Change in Daily Insulin Dose*			
Fasting and pre-meal BG between 100-140 mg/dl in the absence of hypoglycemia	no change			
Fasting and pre-meal BG between 141-180 mg/dl in the absence of hypoglycemia	Increase by 10%			
Fasting and pre-meal BG between >181 mg/dl in the absence of hypoglycemia	Increase by 20%			
Fasting and pre-meal BG between 70-99 mg/dl in the absence of hypoglycemia	Decrease by 10%			
Fasting and pre-meal BG between <70 mg/dl	Decrease by 20%			

Emory Discharge insulin Algorithm



Estimated Rates of Emergency Hospitalizations for Adverse Drug Events in Older U.S. Adults, 2007–2009



Discharge Medications

- Supplies:
 - Meter, strips, lancets
 - Pens + Pen needles [300 units/pen]
 - Vials + Syringes [1000 units/vial]
- There is a significant difference in cost in insulins. Check with patient/insurance.

Insulins

- Short acting
 - Regular (\$25/vial)
 - Aspart (Fiasp*)
 - Lispro
 - Glulisine
 - Inhaled insulin
- Combinations
 - 70/30 (\$25/vial), 75/25

- Intermediate/Long
 - NPH (\$25 vial)
 - Detemir
 - Glargine (100/300)
 - Degludec (100/200)
 - U500 Regular
- Combinations
 - GLP-1 + Insulin

Diabetes Medications Type 2

- Insulin Secretogogues
 - Sulfonylureas
 - Non-sulfonylureas
- Incretins
 - GLP-1 agonists
 - Exenetide
 - Liraglutide
 - Extended release Exenetide
 - Dulaglutide
 - Albiglutide
 - Sitagliptin
 - Saxogliptin
 - Vildagliptin
 - Aloglipton
 - Linaglipton

- Metformin
- TZD's
 - Rosiglitazone*
 - Pioglitazone
- Alpha glucosidase inhibitors
 - Acarbose
 - Miglitol
- Colesevelam
- Bromocryptine QR
- Pramlinitide
- Sodium-glucose cotransporter 2 (SGLT2) inhibitors (gliflozins)*
 - Canagloflozin
 - Dapagloflozin
 - Emplagloflozin

Profiles of Antidiabetic Medications





	MET	GLP-1 RA	SGLT-2i	DPP-4i	AGi	TZD (moderate dose)	SU GLN	COLSVL	BCR-QR	INSULIN	PRAML
НҮРО	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Moderate/ Severe Mild	Neutral	Neutral	Moderate to Severe	Neutral
WEIGHT	Slight Loss	Loss	Loss	Neutral	Neutral	Gain	Gain	Neutral	Neutral	Gain	Loss
RENAL / GU	Contra- indicated if eGFR < 30 mL/min/ 1.73 m ²	Exenatide Not Indicated CrCl < 30 Possible Benefit of Liraglutide	Not Indicated for eGFR < 45 mL/min/1.73 m² Genital Mycotic Infections Possible Benefit of Empagliflozin	Dose Adjustment Necessary (Except Linagliptin) Effective in Reducing Albuminuria	Neutral	Neutral	More Hypo Risk	Neutral	Neutral	More Hypo Risk	Neutral
GI Sx	Moderate	Moderate	Neutral	Neutral	Moderate	Neutral	Neutral	Mild	Moderate	Neutral	Moderate
CHF CARDIAC ASCVD	Neutral	See #1	See #2	See #3	Neutral	Moderate May Reduce Stroke Risk	Neutral Possible ASCVD Risk	Neutral Benefit	Neutral Safe	CHF Risk Neutral	Neutral
BONE	Neutral	Neutral	Mild Fracture Risk	Neutral	Neutral	Moderate Fracture Risk	Neutral	Neutral	Neutral	Neutral	Neutral
KETOACIDOSIS	Neutral	Neutral	DKA Can Occur in Various Stress Settings	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral



Use with caution

^{1.} Liraglutide—FDA approved for prevention of MACE events.

^{2.} Empagliflozin—FDA approved to reduce CV mortality. Canagliflozin shown to reduce MACE events.

^{3.} Possible increased hospitalizations for heart failure with alogliptin and saxagliptin.

Insulin Pumps

This is a fully functioning hybrid pump



SmartGuard[™] features:

AUTO MODE¹

- Automatically adjusts your basal (background) insulin every five minutes based on your CGM readings.**
- Helps keep your sugar levels in your target range for fewer lows and highs — day and night.***.

See how Auto Mode works

SUSPEND BEFORE LOW

- Stops insulin up to 30 minutes before reaching your preset low limits.
- Automatically restarts insulin when your levels recover without bothersome alerts.*
- Helps you avoid lows and rebound highs.¹

This is not



Sharing CGMS data



The AACE/ACE Comprehensive Type 2 Diabetes Management Algorithm can by found by using the QR code below:



Prevention

- Use MPP's in EMR includes hypoglycemic protocol
- DM Nurse Educator/Nutritionist
- DKA Case Managers & Virtual f/u (@ MHH)
 - Laura McKinney/Cynthia Lew
 - Arrange for f/u and education
 - Myhealth Advocate
- Endocrinology consult (All insulin pumps)