Dilemmas in Inpatient Glucose Management

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What is the next best step?

55 yo man with history of HTN w/o DM is admitted after STEMI with stent
On admit has an elevated BS of 220 mg/dL

1) Start on Metformin alone and follow FS qid
2) Start sliding scale insulin alone
3) Start Metformin with sliding scale insulin
4) Start basal-bolus insulin regimen

Hyperglycemia and morbidity/ mortality

- Hypo and hyperglycemia increase mortality in STEMI
- Increased mortality and morbidity in stroke
- Increased mortality in cardiac surgery
- Non-diabetics with hyperglycemia have a 5.3 times higher in hospital mortality risk than diabetics

Umpierrez GE, Clin Endocrinol Metab 2002; 87: 978– 982.
Pinto DS J Am Coll Cardiol. 2005 Jul 5;46(1):178-80.
Doenst T Thorac Cardiovasc Surg. 2005 Oct;130(4):1144.
Capes SE Stroke. 2001;32:2426 –2432.

What is the enemy?

1. Hyperglycemia in the non-diabetic
2. Hypoglycemia in the diabetic
3. Hypoglycemia in the non-diabetic
4. Hyperglycemia in the diabetic

Choosing your weapon






Despite the valiant efforts of the research group, the insulin suppository still had one major drawback.

Oral Agents

Oral anti-hyperglycemics

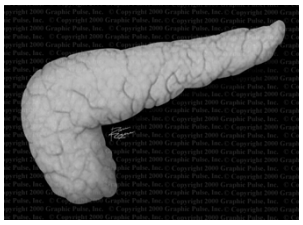
Class/Drugs	Side effects to watch out for
Biguanide / metformin	Contrast associated nephropathy Lactic acidosis
Thiazalidinediones / Rosiglitizone, pioglitazone	Fluid Retention Hepatitis Associated with Myocardial Infarction
Sulfonylureas / glipizide, glyburide, glimepride, chlorpropamide	Hypoglycemia if NPO Most are renally excreted particularly glyburide
Meglitinides / nateglinide	Hypoglycemia Renal and hepatic metabolism

Newer Medications to know about

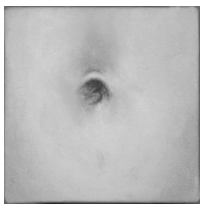
Class/Drug	Side Effects to watch out for
α-glucosidase inhibitors/ acarbose	Abdominal pain and hypoglycemia
Incretins/ exenatide	Elevates your INR
DPP IV inhibitor/ sitagliptin	Careful in renal and hepatic impairment

If you can't beat the endocrine pancreas…

BE THE ENDOCRINE PANCREAS



Ins and Outs of Insulins

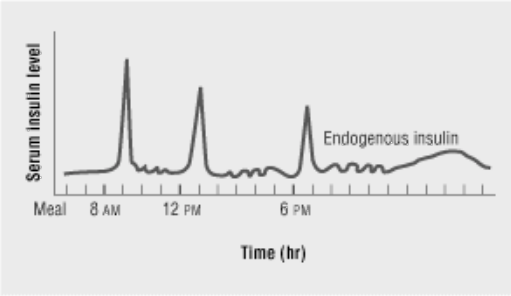


Insulin Preparations

Rapid-acting	Onset	Peak	Duration
Insulin aspart injection (NovoLog)	5-15 min	30-90 min	<5 h
Insulin lispro injection (Humalog)	5-15 min	30-90 min	<5 h
Insulin glulisine injection (Apidra)	5-15 min	30-90 min	<5 h
Insulin human (rDNA origin) Inhalation Powder (Exubera) (2)	5-15 min	30-90 min	5-8 h
Short-acting			
Regular	30-60 min	2-3 h	5-8 h
Intermediate, basal			
NPH	2-4 h	4-10 h	10-16 h
Long-acting, basal			
Insulin glargine injection (Lantus)[ab]	2-4 h[c]	No peak	20-24 h
Insulin detemir injection (Levemir)[ab] (3)	3-8 h	No peak	5.7-23.2 h

AACE Diabetes Mellitus Guidelines, Endocr Pract. 2007;13(Suppl 1) 2007

Normal Insulin Secretion



Categories of Insulin

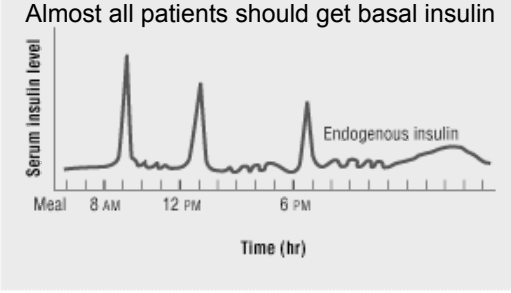
1. Basal
   Options are subQ insulin pump, IV insulin continuous infusion, glargine, NPH

2. Correction (sliding scale, supplement)
   Options are regular, humalog, aspart, glulisine

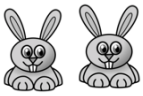
3. Prandial (nutritional, bolus)
   Use same type of insulin as used for correction

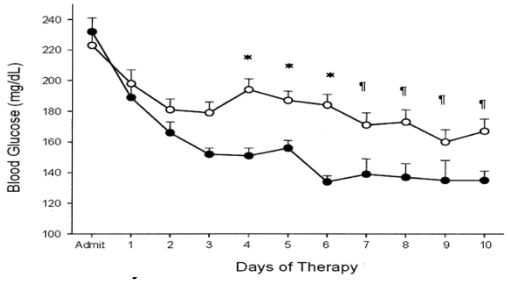
Four times a day insulin dosing

Almost all patients should get basal insulin



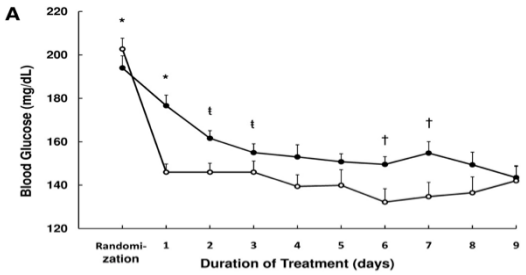
RABBIT 2 Trial





Umpierrez (RABBIT 2 trial). Diabetes Care. 2007 Sep;30(9):2181-6. Epub 2007 May 18.

RABBIT 2 Surgery Trial



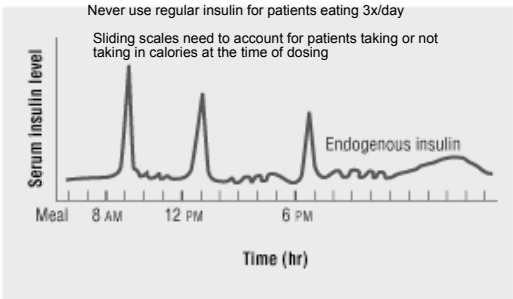
Umpierrez GE (RABBIT 2 surgery).Diabetes Care. 2011 Feb;34(2):256-61. Epub 2011 Jan 12.

Four times a day insulin dosing

Consistent carbohydrate meals should be ordered
-Standard is 1800 calories 70g carbohydrate

Never use regular insulin for patients eating 3x/day

Sliding scales need to account for patients taking or not taking in calories at the time of dosing



Example Lispro Sliding Scale

Blood Glucose mg / dL	**Sensitive** Type 1 DM Stress Hyperglycemia Normal body weight		**Resistant** Type 2 DM Steroids Overweight / Obese		**Extra Resistant** Blood Glucose uncontrolled by "Resistant"table		**Customized**	
≤ 70	Implement Hypoglycemia orders		Implement Hypoglycemia orders		Implement Hypoglycemia orders		Implement Hypoglycemia orders	
	Receiving Calories	**No Calories**	**Receiving Calories**	**No Calories**	**Receiving Calories**	**No Calories**	**Receiving Calories**	**No Calories**
71-124	3 units	No Insulin	6 units	No Insulin	10 units	No Insulin	___units	___units
125-149	3 units	No Insulin	7 units	1 unit	11 units	1 unit	___units	___units
150-199	4 units	1 unit	8 units	2 units	12 units	2 units	___units	___units
200-249	5 units	2 units	10 units	4 units	14 units	4 units	___units	___units
250-299	6 units	3 units	12 units	6 units	16 units	6 units	___units	___units
300-349	7 units	4 units	14 units	8 units	18 units	8 units	___units	___units
≥ 350	Call MD		Call MD		Call MD		Call MD	

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On admit has an elevated BS of 220 mg/dL

1) Start on Metformin alone and follow FS qid
2) Start sliding scale insulin alone
3) Start Metformin with sliding scale insulin
4) Start basal-bolus insulin regimen

What do you order for insulin dose to bring the blood glucose to an appropriate level?

55 yo man is 3 days into a floor admission for STEMI w/stent and hyperglycemia
On his insulin regimen he required 80 units of insulin in the last 24 hours
Nurse calls with a FS of 400 pre-lunch

1) Give 10 units of rapid acting insulin subQ
2) Give 13 units of rapid acting insulin subQ
3) Give 16 units of rapid acting insulin subQ
4) Start an insulin drip with goal FS 80-110mg/dL

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What to correct to?

- Severe hypoglycemia defined as <40
- Hypoglycemia defined as FS<70
- Diabetes is fasting FS ≥ 126 mg/dL
- Significant hyperglycemia is FS ≥140 mg/dL
- Glycosuria starts at approximately 160-190mg/dL

Standards of Medical Care in Diabetes—2011. *Diabetes Care*. January 2011 34:S11-S61.

Randomized controlled trials for non-critically ill patients

ADA/AACE Recommendations

	Non-critically ill	
	Preprandial	**Postprandial**
Initiate treatment	<140	<180 mg/dL
Target glucose	140-180 mg/dL	140-180 mg/dL

Moghissi ES Endocr Pract. 2009 May-Jun;15(4):353-69.
Standards of Medical Care in Diabetes—2011. *Diabetes Care*. January 2011 34:S11-S61.

How much correction do I give?

- Insulin Sensitivity Factor (ISF)
- Approximated by dividing 1600 by the paitent's 24 hour insulin requirement
  - eg if a patient requires an average of 40 units of glargine at night and 40 units throughout the day of Lispro, then his/her ISF is 20 (1600÷80 = 20)

Insulin Sensitivity

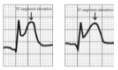
Decreased Insulin Sensitivity	Increased Insulin Sensitivity
High glucose "glucose toxicity"	Exercise
Increased body fat percentage	Decreased PO intake
Glucocorticoids	Decreased GFR
Pregnancy in 2nd and 3rd trimester	Pregnancy during 1st trimester
IV Hydration with lactated Ringers solution	Liver disease
Uremia	Adrenal insufficiency

DIGAMI 1 Trial

- 620 patients admitted to the CCU with a diagnosis of diabetes and probable MI
- Insulin drip with goal 126-180mg/dL vs standard subcutaneous insulin protocol
- In hospital mortality of 9.1% vs 11.1%
- Mortality at one year of 18.6% vs 26.1%
- Particularly bad for patients never on insulin

Malmberg K. J Am Coll Cardiol. 1995 Jul;26(1):57-65.

DIGAMI 2 Trial



- 1253 patient admitted with suspected acute myocardial infarction and type 2 diabetes
- Three treatment strategies
  - Insulin drip on admit followed by SC insulin on discharge
  - Insulin drip on admit followed by normal care on discharge
  - Routine care of hyperglycemia on admit and discharge
- No difference in mortality up to 3 years out
- No difference in Hg A1C up to 3 years out

Malmberg K, Eur Heart J 2005;26:650-61 .

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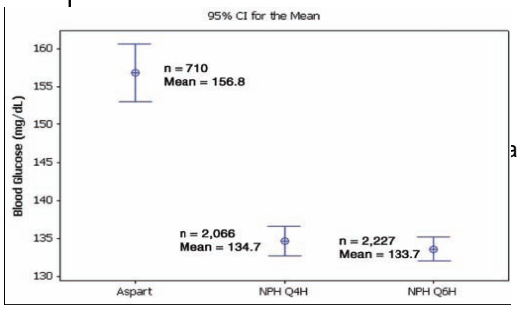
How do you manage insulin with continuous tube feeds?

55 yo man admitted for STEMI and hyperglycemia suffers in hospital CVA
Due to dysphagia, tube feeds are started

1) Continue his basal with rapid acting insulin regimen
2) Just give basal insulin to match basal carb intake
3) Give basal insulin with the addition of regular insulin sliding scale qid
4) Start an insulin drip with goal FS 80-110mg/dL

Continuous carbohydrate load



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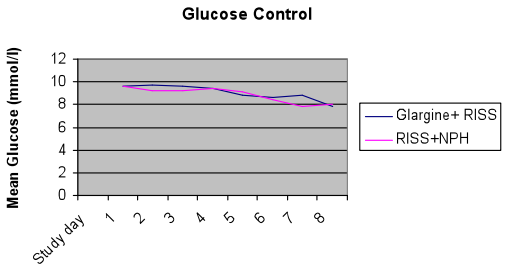
What to use for basal



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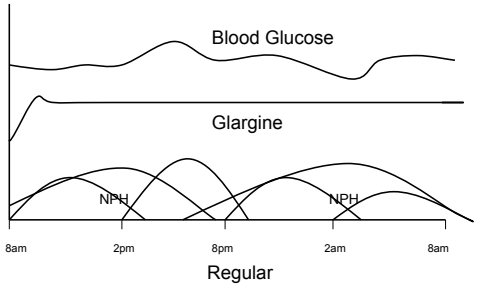
TPN and Continuous Tube Feeds



Continuous Tube Feeds and TPN

Regular Insulin Sliding Scale **+** NPH or Detemir or Glargine **=** Control of hyperglycemia

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What is the hyperglycemia management in the ICU?

55 yo man s/p STEMI w/stent and hyperglycemia
He is transferred to the ICU for hypotension
Blood glucose is poorly controlled at 190-350mg/dL

1) Continue on his floor basal bolus insulin regimen
2) Allow permissive hyperglycemia in hypotension
3) Start an insulin drip with goal FS 144-180mg/dL
4) Start an insulin drip with goal FS 80-110mg/dL

Blood Glucose Target

Cardiac surgery patients

- 2467 diabetic patients undergoing open heart surgery
  - Insulin drip to goal blood glucose <200 mg/dL vs subcutaneous insulin and standard care
  - decreased sternal wound infections from 2.0% to 0.8%
- 141 diabetic patients undergoing CABG
  - Insulin drip to goal blood glucose 125-200 mg/dL vs subcutaneous insulin to goal <250mg/dL
  - 1 insulin infusion patient died vs 6 controls at 2 years and this persisted for 5 years

Furnary AP. Thorac Surg 67:352-360, 1999.
Lazar HL,. Circulation 2004,109:1497-1502.

Van den Berghe SICU trial

- 1548 patients with hyperglycemia admitted to a surgical ICU on mechanical ventilation
- Insulin drip to goal blood glucose 80-110 mg/dL vs. goal 180-200mg/dL
- In hospital mortality rate of 7.2% vs 10.9%
- Hypoglycemia (FS<40mg/dL) in 5.1% vs. 0.8%
- Longer ICU stay was associated with greater benefit from intensive insulin therapy (IIT)

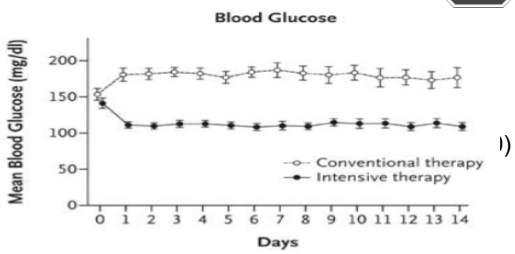
Van den Berghe G. N Engl J Med. 2001 Nov 8;345(19):1359-67.

Van den Berghe MICU trial

- 1200 patients admitted to a medical ICU expected to stay >3 days (eating)
- Insulin drip to goal blood glucose 80-110 mg/dL vs. goal 180-200mg/dL
- In hospital mortality rate of 37.3% vs 40.0%
- Hypoglycemia (FS<40mg/dL) in 18.7% vs. 3.1%
- Increased mortality of IIT for patients <3 days in the ICU but could not be predicted

Van den Berghe G. N Engl J Med. 2006 Feb 2;354(5):449-61.

VISEP Trial



Brunkhorst FM . N Engl J Med. 2008 Jan 10;358(2):125-39.

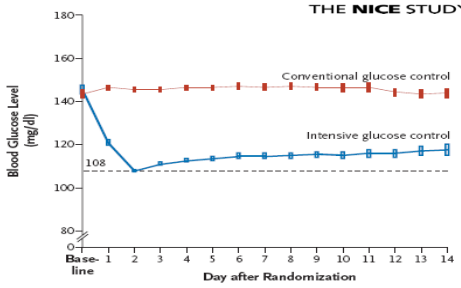
GLUCONTROL Trial

- 1,101 patients admitted to medico-surgical ICU's with hyperglycemia
- Insulin drip with glucose goal 80-110 vs 140-180
- 8.7% vs 2.7% rates of hypoglycemia (FS<40)
- No difference in 28 day mortality

Preiser JC. Intensive Care Med. 2009 Oct;35(10):1738-48. Epub 2009 Jul 28.

NICE SUGAR

THE NICE STUDY



Finfer S. N Engl J Med. 2009 Mar 26;360(13):1283-97. Epub 2009 Mar 24.

ADA/AACE Recommendations

		Non-critically ill	
	Critically ill	**Preprandial**	**Postprandial**
Initiate treatment	<180 mg/dL	<140	<180 mg/dL
Target glucose	140-180 mg/dL	100-180 mg/dL	100-180 mg/dL

Moghissi ES Endocr Pract. 2009 May-Jun;15(4):353-69.

Standards of Medical Care in Diabetes—2011. *Diabetes Care*. January 2011 34:S11-S61.

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Take home points

- Basal-bolus insulin on the floor controls FS better with no increase in hypoglycemia
- Target BG on the floors is <180 and estimate needs for acute dosing of rapid acting insulin using the 1600 rule
- Use a regular insulin sliding scale with basal insulin for continuous tube feeds or TPN
- Use an insulin drip for critically ill hyperglycemic patients and target a blood glucose 140-180

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