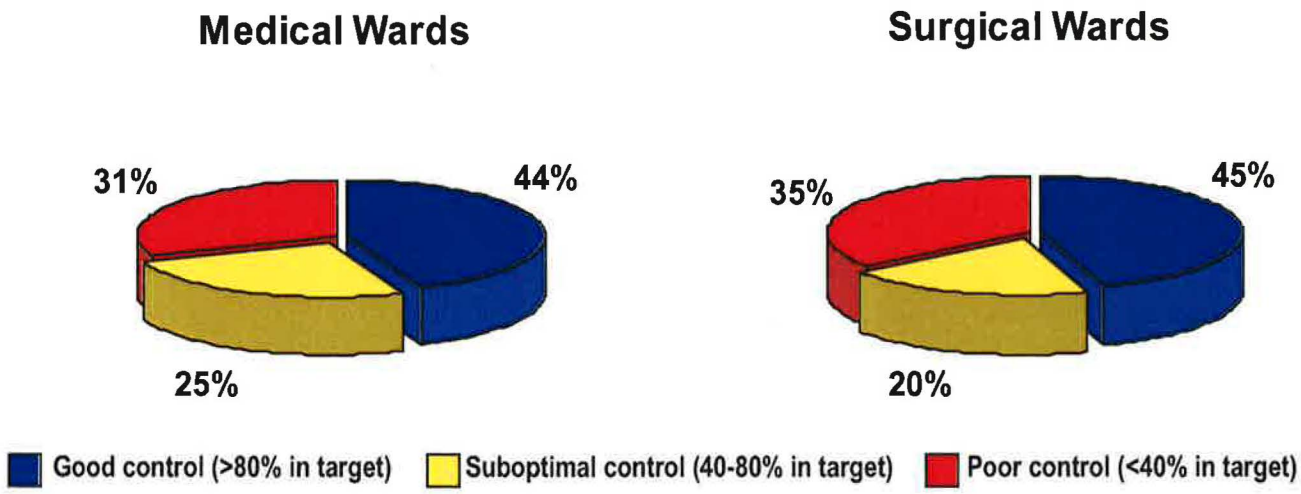
Management of Hyperglycemia and Diabetes in the Hospital

Diabetes Management in the Hospital



Philip Raskin, M.D.
Internal Medicine Grand Rounds
UT Southwestern Medical Center at Dallas

January 26, 2006

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Management of Hyperglycemia and Diabetes in the Hospital

Medical Grand Rounds

UT Southwestern Medical Center

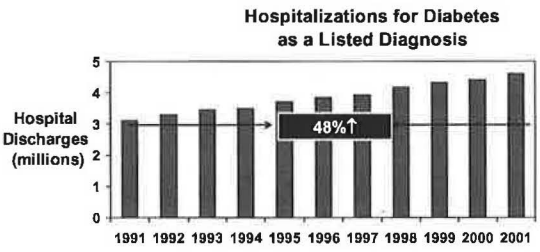
Philip Raskin, MD
Professor of Medicine

January 26, 2006

Diabetes in Hospitalized Patients

- More than 4 million people with diabetes are hospitalized annually
- Another 1.5 million people have hyperglycemia during hospitalization without a history of diabetes
- 90% of hospital admissions in diabetic patients are for reasons other than diabetes
- 75% of hospital admissions are for cardiovascular disease
- Diabetic patients with acute illnesses and hyperglycemia are at increased risk for acute complications

The Increasing Rate of Diabetes Among Hospitalized Patients



Available at: http://www.cdc.gov/diabetes/statistics/dmany

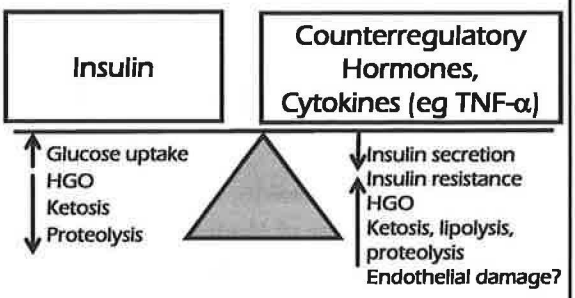
Cost of Inpatient Diabetes Care

- $40 Billion annually
- Annual Per Capita: $6300 vs. $1300 with out diabetes
- Increased Costs from:
  - increased length of stay
  - increased frequency of hospitalizations

Diabetes Care 26: 917-932, 2003

Stress Hyperglycemia

Metabolic Changes Associated with Stress



Hyperglycemia in Acutely Ill Patients

- Hyperglycemia is associated with adverse outcomes for hospitalized patients with and without diabetes
  - death
  - disability after CV events
  - infections
- Improvement in outcomes occurs with improved glycemic control

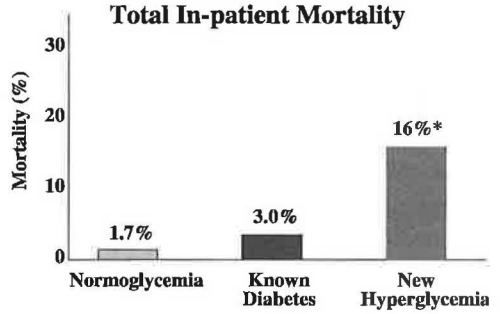
Montori, JAMA 288: 2167-2169, 2002

Hyperglycemia in Patients With Undiagnosed Diabetes

- Hyperglycemia occurred in 38% of patients admitted to the hospital
  - 26% had known history of diabetes
  - 12% had *no* history of diabetes
- Newly discovered hyperglycemia was associated with:
  - Higher in-hospital mortality rate (16%) compared with patients with a history of diabetes (3%) and patients with normoglycemia (1.7%; both $P < 0.01$)
  - Longer hospital stays; higher admission rates to intensive care units
  - Less chance to be discharged to home (required more transitional or nursing home care)

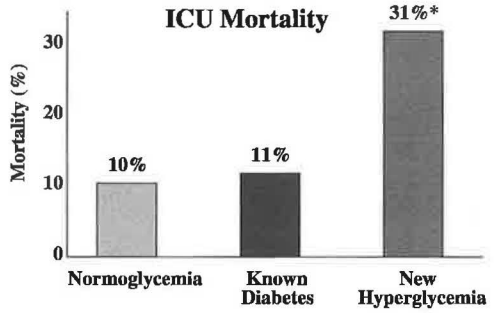
Umpierrez GE, et al. J Clin Endocrinol Metab 87:978, 2002

Hyperglycemia: An Independent Marker of In-Hospital Mortality



*P<0.01 Umpierrez et al. *J Clin Endocrinol Metab* 87:978, 2002

Hyperglycemia: An Independent Marker of In-Hospital Mortality



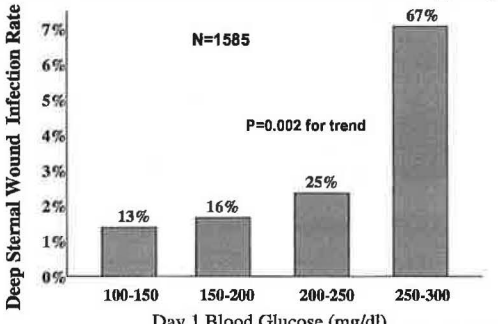
*P<0.01 Umpierrez et al. *J Clin Endocrinol Metab* 87:978, 2002

Stress Hyperglycemia Outcomes after Cardiac Surgery

- Prospective study in 1585 patients undergoing cardiac surgery
- Major outcome—deep-wound (leg and chest) infections, n=33 (2.1%)
- Part 1: Observational findings—elevated BG at 48 hours was significantly associated with increased risk of infection ($P<0.002$)
- Multivariate analysis: 48-hour BG >200 mg/dL predicted infection ($P<0.005$)

Zerr KJ, et al. *Ann Thorac Surg.* 1997;63:356-361.

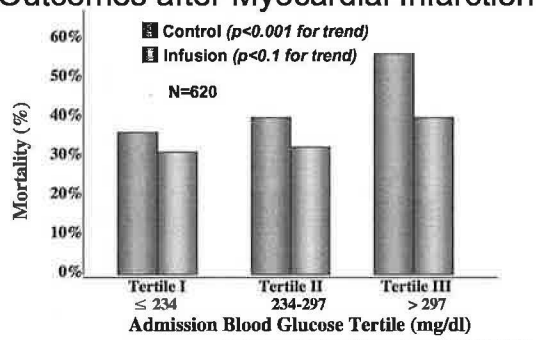
Stress Hyperglycemia & Outcomes after Cardiac Surgery



Zerr KJ et al. Ann Thorac Surg 63:356, 1997

Stress Hyperglycemia

Outcomes after Myocardial Infarction

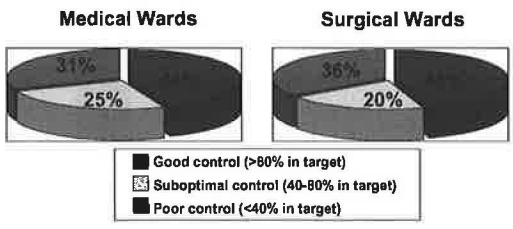


Malmberg K et al. *Circulation* 99:2626, 1999

Causes of Hyperglycemia in Hospitalized Diabetic Patients

- Disruption in normal routine and activities
- Disruption in meal timing
- Erratic absorption of subcutaneous insulin due to fluid shifts and hemodynamic changes
- Disruption in usual insulin timing
- Stress, drug effects (i.e. steroids)
- Nutrient and drug absorption altered by changes in gut motility, fasting state, & other nutritional issues (appetite, dietary prescription, food palatability & preferences)

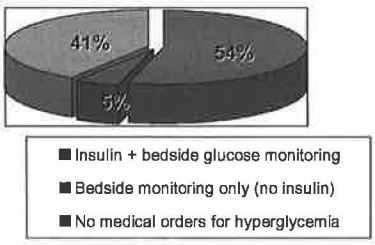
Frequency of Poor Diabetes Management in the Hospital



Target = pre-prandial BG 72-162 mg/dl

Bhattacharyya A et al. Diabetic Med 19:412, 2002

Monitoring & Management Of "Newly Hyperglycemic*" Patients



* No h/o DM; BG >200 mg/dl (mean peak 299 (202-503)

Levetan CS et al. Diabetes Care 21:246, 1998

Reasons for Good Diabetes Control in Hospitalized Patients

The Data

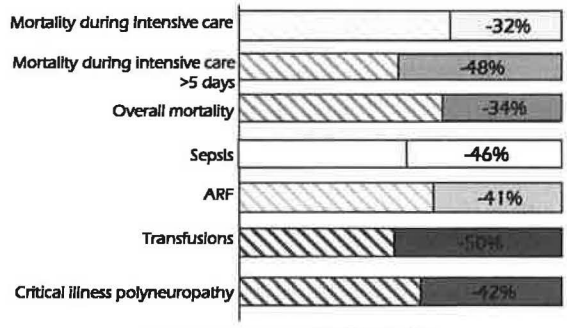
Intensive Insulin Treatment in ICU Patients

Study Design

- Prospective study in 1548 ICU patients, (13% DM), randomized to intensive insulin treatment (infusion started if BG>110 mg/dl, glucose goal 80-110 mg/dl) or conventional treatment.
- Conventional treatment mandated starting insulin infusion only if BG>215 mg/dl, (glucose goal 180-225mg/dl).
- Average BG levels - 103 mg/dl vs 153 mg/dl

Van Den Berghe, *NEJM* 345:1359,2001

Intensive Insulin Treatment in Critically Ill Patients



van den Berghe, et al. NEJM 345:1359, 2001

DIGAMI Study

(Diabetes Mellitus, Insulin Glucose Infusion in Acute Myocardial Infarction)

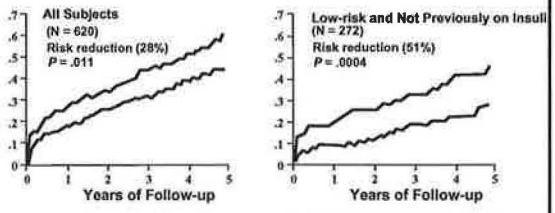
STUDY DESIGN

- Randomized prospective study in 19 Swedish hospitals
- 620 diabetic patients (BG>11mM [198 mg/dl])
- Acute myocardial infarction within 24 hrs
- Treatment with insulin-glucose infusion for at least 24 hrs followed by 4 daily insulin injections for at least 3 months or standard therapy
- Follow-up for 3.4 yrs (1.6-5.6 yrs)

Malmberg,et al BMJ 214:1512,1997

CVD Mortality After MI (DIGAMI Study)

— Standard treatment
— IV insulin 48 hours, then 4 injections daily



BMJ 314: 1512-1515, 1997

DIGAMI 2

Study Design

- 1253 individuals with type 2 diabetes or an admission blood glucose value > 11 mmol/L
- Acute myocardial infarction in the previous 24 hours
- Random assignment to one of three groups
- Multi-centered prospective trial

Malmberg, et al European Heart Journal 26:650, 2005

DIGAMI-2

Study Design

3000 AMI patients with T2DM

Group 1
Intensive Inpatient/Outpatient
- IV insulin-glucose x 24h (target: 126-180 mg/dl)
- Multi-dose insulin x 3 years (target: FPG 90-126 mg/dl)

Group 2
Intensive Inpatient Only
- IV insulin-glucose x 24h (target: 126-180 mg/dl
- Routine outpatient DM care

Group 3
Conventional
- Routine inpatient DM care
- Routine outpatient DM care

Malmberg, et al European Heart Journal 26:650, 2005

DIGAMI 2

Results

- Steering Committee stopped study after 1274 patients
  - Poor recruitment; mean follow-up 1.9 years
  - Unanticipated minor differences in glucose control
- Mean glucose 164 (Groups 1,2) vs. 180 mg/dl Group 3 @ 24 hours; otherwise equivalent
- Mean HbA1c slightly better @ 3 months in Groups 1,2 but overall equivalent (~7% in all 3 groups)
- Overall mortality rate only 21.3% (predicted ~30%)
  - Extensive use of β-blockers, ACEIs, ASA

Malmberg, et al European Heart Journal 26: 659, 2005

DIGAMI 2

Results

	CV Mortality
Group 1 (Intensive In-Outpatient)	18.4%*
Group 2 (Intensive Inpatient Only)	19.7%
Group 3 (Conventional DM Care)	17.3%

*HR=1.09 (0.77-1.54); P=0.62

Malmberg, et al European Heart Journal 26: 659, 2005

Mortality Among Post-CT Surgery Patients

Glycemic Control Comparing SQ or Continuous Insulin Infusion

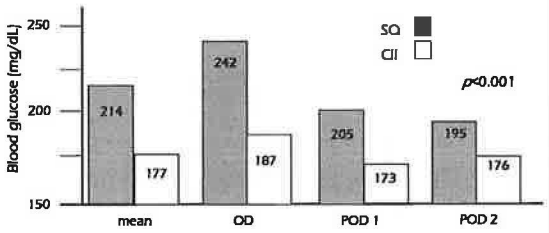
Study Design

- "Prospective" study in 3554 patients with diabetes undergoing CABG
- Treated with either subcutaneous (SQ) insulin (1987-1991) or continuous insulin infusion (CII) (1992-2001)
- Goal in SQ group - BG <200 mg/dl
- Goals in CII group
  - BG 150-200 mg/dl (91-98)
  - BG 125-175 mg/dl (99-01)
  - BG 100-150 mg/dl (2001)

Furnary, et al J Thor Cardiovasc Surg, 125:1007, 2003

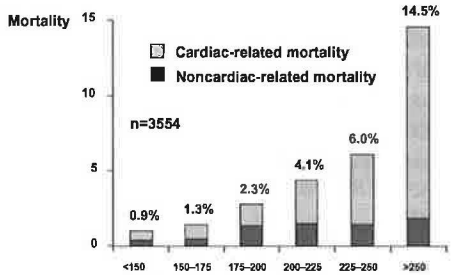
Mortality Among Post-CT Surgery Patients

Glycemic Control Comparing SQ or Continuous Insulin Infusion



Furnary, *et al. J Thor Cardiovasc Surg* 125:1007, 2003

Mortality Among Post-CT Surgery Patients



Furnary AP, et al. J Thoracic Cardiovasc Surg. 125:1007, 2003

Hyperglycemia and Infections

Hyperglycemia and Infections

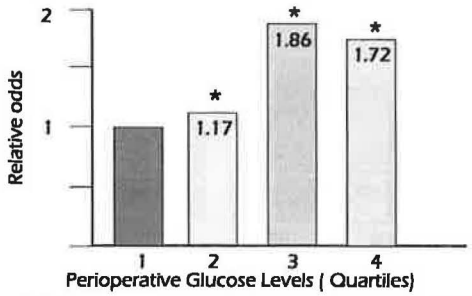
- Impairment in host defenses
  - Neutrophils
  - Complement proteins
- Increase in postoperative infections
- Impaired wound healing
- Increased incidence of sepsis and multi-organ failure

Perioperative Glycemic Control and Risk of Infections

- 411 patients undergoing coronary artery surgery (chart review)
- Major outcomes: leg and chest wound infections, pneumonia, UTI
- Mean postoperative blood glucose levels (6 tests during 36-h postoperative) divided into quartiles:
  - 1: 121-206 mg/dl 2: 207-229 mg/dl
  - 3: 230-252 mg/dl 4: 253-352 mg/dl

Golden, et al *Diabetes Care 22:1408,* 1999

Perioperative Glycemic Control and Risk of Infections



* p=.05 vs Quartile 1

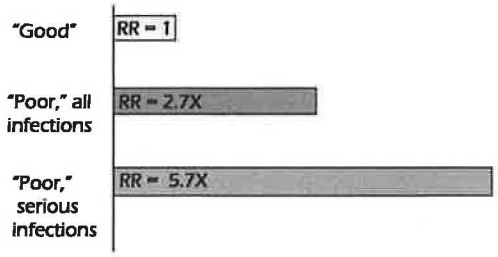
Golden, et al *Diabetes Care 22:1408,* 1999

Perioperative Glucose Control and Risk of Infections

- 100 patients with DM2, prospective, observational
- Cardiac or abdominal surgery
- Two groups (regimens not specified):
  - —"Good" control: all BG ≤220 mg/dL
  - —"Poor" control: ≥1 BG >220 mg/dL
- Found increased infection rates with POD 1 glucose >220 mg/dL

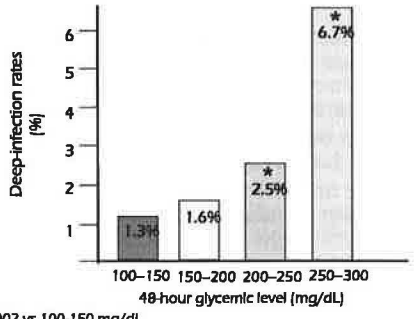
Pomposelli JJ, et al. J Parenter Enteral Nutr. 1998;22:77-81.

Perioperative Glucose Control and Risk of Infections



Pomposelli JJ, et al. J Parenter Enteral Nutr. 1998;22:77-81.

Perioperative Glycemic Control and Risk of Infection in Diabetes



*P=0.002 vs 100-150 mg/dl

Zerr KJ, et al. Ann Thorac Surg. 1997;63:356-361.

In-Patient Diabetes Management

How To Do It!

In-Patient Diabetes Management

- Hyperglycemia in the hospital is common
- Majority treated with subcutaneous insulin
- Current prescribing practices and philosophies vary greatly and commonly do not enable targeted glucose control
- Insulin is one of five "high alert meds" with significant risk for causing medication error injuries

Healthcare Risk Management 22:19-20, 2000

Maintaining Glycemic Control with Insulin in Hospitalized Diabetic Patients

- **Patients with type 1 and those with insulin-deficient type 2 diabetes will need insulin administration to control glycemia during illness**
- **In a well-controlled patient the insulin regimen followed at home can be used**
- **An intravenous insulin infusion will provide basal insulin needs whether IV glucose, enteral feeding, or food is the source of substrate**

Maintaining Glycemic Control in Hospitalized Diabetic Patients

Basic Issues to Consider

- **Does the patient have Type 1 or Type 2 diabetes?**
- **What is the patient's usual diabetic treatment?**
- **What is the HbA1c?**
- **What is the potential effect of the patient's acute illness on glycemic control?**
- **Is the patient eating, receiving parental nutrition?**
- **What is the potential impact of the patient's treatment's) (e.g. surgery, pharmacotherapy, fluids) on glycemic control?**

Maintaining Glycemic Control with Insulin In Hospitalized Diabetic Patients

- **When patients begin to eat, short acting insulin should be given before meals relative to blood glucose levels and the amount of carbohydrate to be consumed**
- **Intermediate or long acting insulin should be given for basal needs**
- **The goal for any insulin deficient patient is to maintain insulin replacement as close to physiologic as is possible**
- **There should be a plan for treating hypoglycemia**

Hypoglycemia Protocol

University Diabetes Treatment Center

- If patient has signs or symptoms of hypoglycemia, or if suspected to be hypoglycemic, check the blood glucose level
- If blood glucose level is <65 mg/dl and
  - patient is able to swallow without danger of aspirating
    - Blood glucose level is 50-65 mg/dl, give 4 oz. juice or regular soda;
    - Blood glucose level is <50 mg/dl, give 8 oz. juice or regular soda.
  - patient is not able to swallow safely or is NPO:
    - If IV access present, give 25 cc (1/2 amp) D50 IV push;
    - If no IV access present, give ½ cc (0.5 mg) Glucagon IM.
- Recheck blood glucose level in 15-20 minutes
- If blood glucose level is still <65 mg/dl, repeat above steps until blood glucose level is >65 mg/dl

Possible In-Hospital Insulin Delivery Methods

- Usual Home SQ Dose
- Intermittent SQ Administration
- Intermittent IV Administration
- Continuous IV Administration
- Insulin Glargine

Possible In-Hospital Insulin Delivery Methods

Usual Home SQ Dose

- Easiest choice
- Use when patient is eating and no interruption in daily activity planned
- May need reduction in total daily dose

Case Study

55 year old lady with a ten year history of Type 2 diabetes, admitted to hospital with E coli urosepsis. She was doing well with respect to her diabetes prior to her illness. She was taking two daily injections of NovoMix® 30 insulin, 40 units before breakfast and 20 units before supper. On this regimen a recent HbA1c was 7.3%

After admission to hospital she was treated with intravenous antibiotics. She was eating and generally doing well.

You are asked to see this lady to help manage her diabetes in the hospital.

What insulin orders should you write?

Insulin Orders

	B	S
NPH insulin	30	20
Regular insulin	10	10

Insulin Orders

	B	L	S	HS
NPH insulin	40	0	20	0
Regular insulin				
<200	10	0	10	0
201-250	12	2	12	0
251-300	13	3	13	2
>300	14	4	14	3

Possible In-Hospital Insulin Delivery Methods

Intermittent SQ Insulin

- In ill patients, not the best choice
- If "sliding scale" regular insulin is used, long acting insulin (NPH, glargine) should be used for overnight coverage

Possible In-Hospital Insulin Delivery Methods

Intermittent IV Insulin

- **Bad Idea**
- **Half life of IV insulin very short**
- **Duration of action dependent on dose**
- **50 to 100 units of regular insulin must be given each hour to maintain adequate insulin action**

Possible In-Hospital Insulin Delivery Methods

Continuous IV Administration

- Safe and effective
- Looks complicated but it is easy
- Independent adjustment of both insulin and glucose infusions based on hourly blood glucose levels
- Use for perioperative, critical illness and any NPO situation
- Continue until after SQ insulin, restarted

Intravenous Insulin Therapy

Indications

- Diabetic ketoacidosis
- Non-ketotic hyperosmolar state
- Critical care illness
- Myocardial infarction or cardiogenic shock
- Post-operative period following heart surgery
- NPO status in type 1 diabetes
- Perioperative care
- Labor and delivery
- Organ Transplantation
- Severe hyperglycemia during steroid therapy
- "Dose-finding" strategy

Selection or Design of Protocol for Intravenous Insulin Infusion

Successful Protocol

- Accommodates the variability of insulin requirements among patients
- Can be executed by the nursing staff in response to a single physician order
- Facilitates communication between all services involved in patient care
- Corrects hyperglycemia over several hours and maintains normoglycemia, long term

Selection or Design of Protocols for Intravenous Insulin Infusion

Successful Protocol

- Maintains blood glucose within a defined target range
- Includes an algorithm for making temporary corrective increments or decrements of insulin and/or glucose infusion rates
- Allows for adjustment of the maintenance rate as patients' insulin sensitivity changes
- Provides specific guidelines for the transition to subcutaneous insulin

Insulin - Glucose Infusion

University Diabetes Treatment Center

Blood Glucose (mg/dl)	Insulin Infusion (1.0 U/cc)		D5%W
	U/hr	cc/hr	cc/hr
<70	0.5	0.5	150
70-100	1.0	1.0	125
101-150	2.0	2.0	100
151-200	3.0	3.0	50
201-250	4.0	4.0	0
251-300	6.0	6.0	0
>300	10.0	10.0	0

Insulin - Glucose Infusion

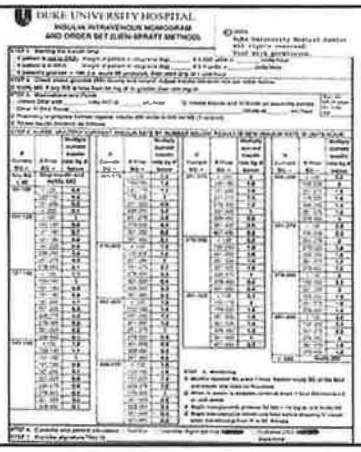
University Diabetes Treatment Center

Blood Glucose (mg/dl)	Insulin Infusion (1.0 U/cc)		D10%W
	U/hr	cc/hr	cc/hr
<70	0.5	0.5	75
70-100	1.0	1.0	65
101-150	2.0	2.0	50
151-200	3.0	3.0	25
201-250	4.0	4.0	0
251-300	6.0	6.0	0
>300	10.0	10.0	0

Insulin - Glucose Infusion

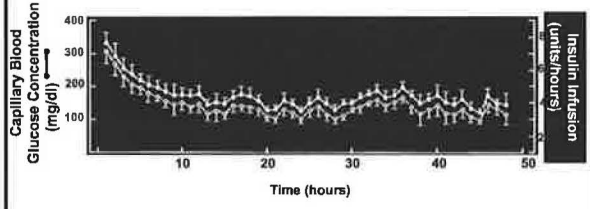
University Diabetes Treatment Center

Blood Glucose (mg/dl)	Insulin Infusion (1.0 U/cc)		D50%W
	U/hr	cc/hr	cc/hr
<70	0.5	0.5	25
70-100	1.0	1.0	20
101-150	2.0	2.0	15
151-200	3.0	3.0	10
201-250	4.0	4.0	0
251-300	6.0	6.0	0
>300	10.0	10.0	0


DUKE UNIVERSITY HOSPITAL

INSULIN INTRAVENOUS NOMOGRAM AND ORDER SET (LEIN-SPRATT METHOD)

Effects Of An Insulin - Glucose Infusion On The Management Of Diabetes In The Hospital



University Diabetes Treatment Center

Use of an Insulin-Glucose Infusion in Diabetic Ketoacidosis

The Parkland Experience 2001

- 176 episodes in 138 individuals
- All treated with University Diabetes Treatment Center protocols
- Total time on infusion protocols 36.3 ± 18 hours
- Urine ketones cleared in 31.7 ± 11.1 hours
- Fluids (NaCl, RL) administered 9.5 ± 3.5 liters
- Hypoglycemia (BG< 70 mg/dl) in 4 patients none clinically significant
- No deaths or episodes of cerebral edema

Newton and Raskin Arch Inter Med 164 1925, 2004

In-Hospital Glycemic Targets

- Intensive Care Unit <110 mg/dl
- Non-Critical Care Units
  - Pre prandial <110 mg/dl
  - Maximum <180 mg/dl
- Pre Labor
  - Pre prandial 100 mg/dl
  - 1-hr post prandial 120 mg/dl
- Labor and Delivery 100 mg/dl

ACE Position Statement on Inpatient Diabetes and Metabolic Control Endocr. Pract 10:2, 2004

Transition From IV To SQ Insulin

- Continue IV insulin until patient is able to tolerate solid food
- Continue IV insulin at least 2 hours after the first SQ insulin injection
- Don't use only basal insulin in patients with a HbA1c greater than 8.5% on 2 or more oral agents
- Don't switch to only oral agents from IV insulin in type 2 patients unless very low insulin infusion rates needed
- Arrange for follow up of patients placed on insulin in the hospital

INITIATE
HbA1c % Reduction

	BIAsp 30	Glargine	*p*-value
All Subjects	-2.79 ± 0.11	-2.36 ± 0.11	0.0057
Subjects with:			
HbA1c ≥8.5%	-3.13 ± 1.63	-2.60 ± 1.50	0.0026
HbA1c <8.5%	-1.40 ± 0.55	-1.42 ± 0.59	>0.05

Raskin, et al Diabetes Care 28: 260, 2005

Intravenous Insulin Infusion Protocol

SETTING ONE UP IN YOUR HOSPITAL

Intravenous Insulin Infusion Protocol

- All relevant hospital services (nursing, pharmacy, medicine and surgery) need to be involved
- A written protocol or protocols must be adopted
  - Bedside blood glucose monitoring
  - Meter standardization and calibration
- Nurse staffing (including aides) should be adequate on units where infusions are used
- One should define:
  - Thresholds for initiating the infusion
  - Target blood glucose range
- There needs to be a strategy for conversion to subcutaneous insulin treatment
- Experts in insulin treatment should be in charge

Insulin Treatment in Hospitalized Patients
Conclusions

- Glycemic control in hospitalized diabetic individuals is important
- Choice of insulin delivery dependent on clinical circumstances
- If possible, use home SQ insulin regimen
- Intermittent SQ short acting insulin ("sliding scale") a bad idea without long acting (basal) insulin
- Continuous IV insulin infusion best for critically ill, perioperative or NPO circumstances especially in Type 1 and insulin requiring Type 2 diabetes

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