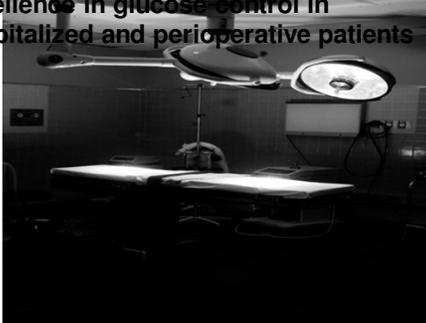
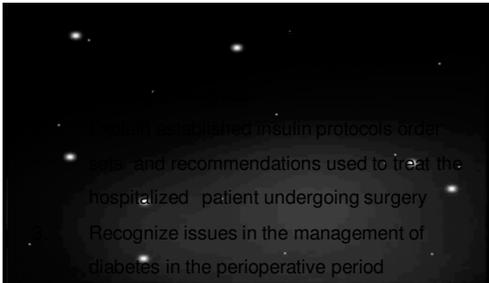


Let's not sugar coat it: Promoting excellence in glucose control in hospitalized and perioperative patients



WELCOME !



Rosie Pine, PhD, RN, BC, CDE

Diabetes: A Global Health Problem



- **Number of people with diabetes, 2011: 346 million**
- **Predicted number of people with diabetes, 2030: 552 million**
- **Top 3 countries with diabetes:**
 - India**
 - China**
 - United States**

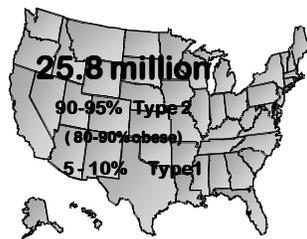
World Health Organization, 2011; International Diabetes Foundation, 2011

World Diabetes



- Every 10 seconds, a person dies from diabetes-related causes
- Every 10 seconds, two people develop diabetes

Diabetes : USA



Center for Disease Control, 2011

Diabetes in Texas



Prevalence



HOWDY

- Total : 1.8 million (9.7%)**
Harris County : ~326,679
- White, non-Hispanic: 8.5%
 - Black, non-Hispanic: 13.0%
 - Hispanic: 11.0%
 - Other: 7.5%

22.7% of adults ages 65+ years



**30% with 1°
or 2°
diagnosis of
diabetes**





Diabetes is a group of metabolic diseases characterized by high levels of blood glucose resulting from defects in insulin secretion, insulin action, or both.



Types of Diabetes

Type 1 Diabetes

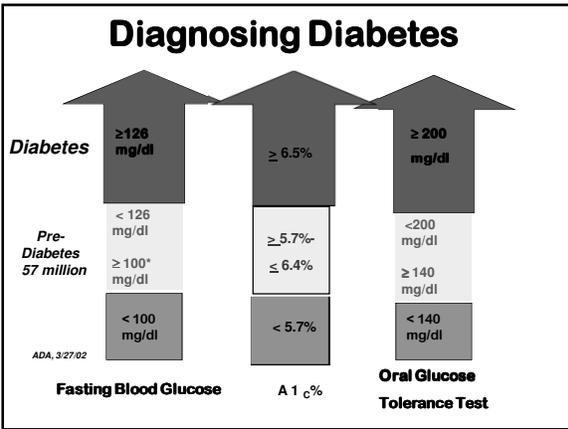
- Beta cell destruction leading to absolute insulin deficiency
- Profound hyperglycemia, ketosis prone

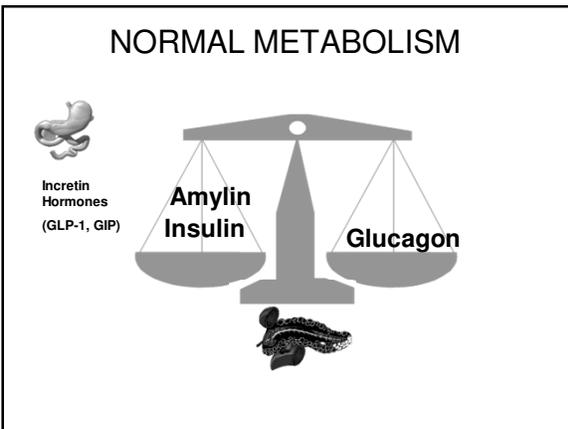


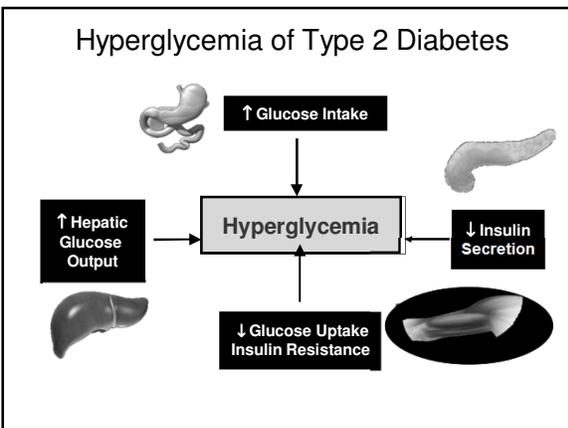
Type 2 Diabetes

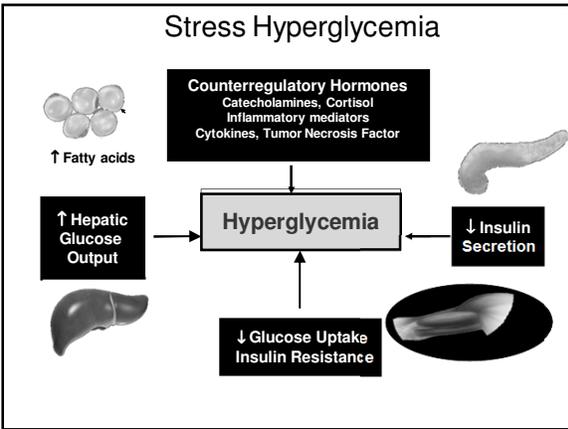
Basic defect is **Insulin Resistance** and usually have relative rather than absolute insulin deficiency











Physiologic Mechanisms

- Elevated FFA associated with arrhythmias, increased sympathetic overactivity, elevated BP
- Prolonged fasting, volume contraction contribute to metabolic decompensation
- ↑ BG inhibits leukocyte function which increases rate of infections
- ↑ BG reduces collagen synthesis, resulting in poor wound healing

Regulates metabolism of glucose, protein and fat

- Lowers blood glucose
- Increases synthesis of liver and muscle glycogen
- Inhibits lipolysis, ketogenesis
- Inhibits protein breakdown
- Facilitates amino acid uptake into cells

Beta cell

Effects of Insulin



Other Metabolic Effects of Insulin

Cardioprotective Neuroprotective

- **Anti-Inflammatory**
Suppresses levels of inflammatory mediators - TNF alpha, interleukins, C-Reactive Proteins
- **Antithrombotic**
Reduces PAI-1 (Plasminogen activator inhibitor)
- **Vasodilation and platelet inhibition**
↑ nitric oxide release
- **Antioxidant**
Reduces reactive oxygen species
- **Effect on lipid metabolism**
Reduces TG, FFA - prevent arrhythmias
- **Enhances cellular potassium uptake**

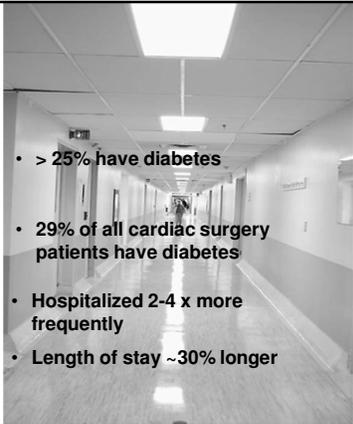


Hyperglycemia in Hospitalized Patients

Causes:

1. Known diabetes
2. Prediabetes
3. Unrecognized diabetes
4. Hospital-associated diabetes (iatrogenic or stress-related)





Fast Facts on Hospitalized Patients With Diabetes

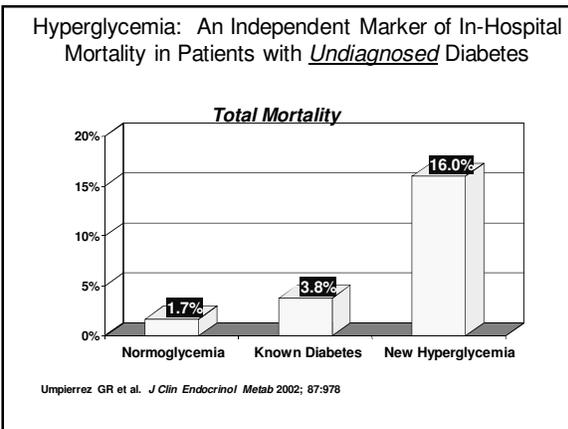
- > 25% have diabetes
- 29% of all cardiac surgery patients have diabetes
- Hospitalized 2-4 x more frequently
- Length of stay ~30% longer

Fast Facts on Hospitalized Patients Without Diabetes

New-onset hyperglycemia associated with highest mortality rates compared with known diabetics

2x length of stay

3x likely to be admitted to ICU



Hyperglycemia Predicts Morbidity and Mortality

Several studies and data from the National Surgery Data Base have reported an increased operative and postoperative mortality among patients with diabetes.



Landmark Study in Surgical ICU

N = 1548 (13% DM)
 Conventional Rx : BG 180-200
 (IV insulin only if BG > 215)
 Intensive Rx: 80-110
 (IV insulin if >110)

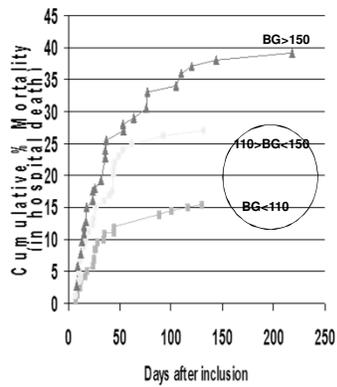
Results : Intensive therapy reduced

- In-hospital mortality by **34%**
- Sepsis by **46%**
- Acute renal failure by **41%**
- Blood transfusions by **50%**
- Polyneuropathy by **44%**

Van Der Berghe, G. et al. 2001. Intensive therapy in critically ill patients. N Eng J Med. 345,1359-1367

Surgical ICU Mortality

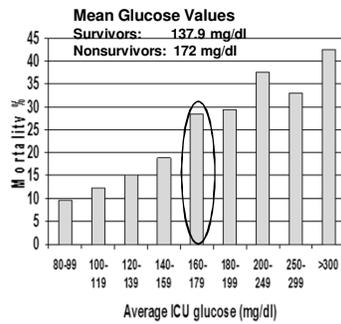
Effect of Average BG



Van den Berghe et al (Crit Care Med 2003; 31:359-366)

Hyperglycemia and Hospital Mortality

1826 consecutive ICU patients
 10/99 thru 4/02,
 Stamford CT



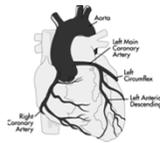
Krinsley JS: Mayo Clin Proc 78: 1471-1478, 2003

Outcome Studies: Perioperative Blood Glucose Control



Golden SH, et al Diabetes Care 1999
 Study of 411 patients who had CABG to assess relationship of perioperative glycemic control to subsequent risk of infections and complications. BG postop levels divided into 4 groups:

- 1) 121-206 mg/dl
- 2) 207-229 mg/dl
- 3) 230-252 mg/dl
- 4) 253-352 mg/dl

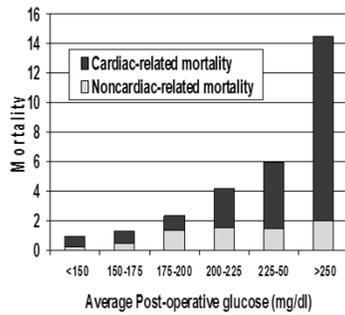


Results:

Those in groups 2,3, and 4 were at progressively higher risk for infections. In patients with diabetes who undergo CABG, postoperative hyperglycemia is an independent predictor of short-term infectious complications.

Bottom line: Consider BG target of <200 mg/dl to reduce risk of infections.

Mortality of DM Patients Undergoing CABG



Furnary et al J Thorac Cardiovasc Surg 2003;123:1007-21

Hyperglycemia, Mortality and Morbidity in CABG



- Hyperglycemic patients undergoing cardiac surgery have greater mortality, increased deep-wound infections and more overall infection.
- Hyperglycemia, on the ***first and second postoperative days***, was the single most important predictor of serious infectious complications.
- Length of hospital stay was reduced by 1 day for each 50 mg/dl lowering of the average 3-day postop blood glucose.

Furnary et al J Thorac Cardiovasc Surg 2003;123:1007-21
 Furnary et al J Circulation 2000;102, #18 II-556.

NICE SUGAR STUDY!



NICE – SUGAR Study
 N = 6,104 pts in critical care units (20% with DM)
 Randomized, unblinded, international, multi-site

Intensive BG target = 81-108 mg/dl
 Control BG target = 144 – 180 mg/dl

Outcome Measures:

Primary : Mortality at 90 days
 Other : 28 day mortality, Vent days, Hospital / ICU LOS
 Dialysis, + blood culture, RBC transfusion

Normoglycemia in Intensive Care Evaluation – Survival Using Glucose Algorithm Evaluation
 NEJM 2009 :360.1283-1297.
 March 24, 2009

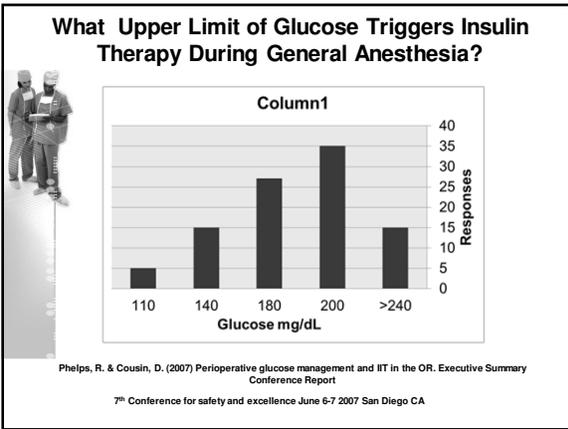
NICE-SUGAR STUDY RESULTS



	Control (Mean: 145)	Intensive (Mean:118)
90 day mortality	24.9%	27.5% RR= 1.14
28 day mortality	20.8%	22.3%
Severe hypo (< 40)	0.5%	6.8%

No difference in hospital/ICU LOS, vent days, need for dialysis or transfusions.

Normoglycemia in Intensive Care Evaluation – Survival Using Glucose Algorithm Evaluation
 NEJM 2009 :360.1283-1297.



- ### Challenges in Perioperative Management
1. Lack of definitive data that IIT and TGC during surgery improves perioperative outcomes
 2. Uncertainty of the ideal target in the OR
 3. The danger of iatrogenic hypoglycemia

Does Tight Glucose Control Improve Long Term Patient Outcomes?

Mayo Clinic study (2007) received IIT without significant difference in outcomes

Portland study (2006) found that tight control was a predictor of mortality, deep wound infection and LOS

Brief duration of OR care is insufficient to affect patient outcomes (Van den Berghe, 2007)

What is the optimal Glucose Level for Patients in the OR?



Portland study (2006) found that tight control was a predictor of mortality, deep wound infection and LOS

Brief duration of OR care is insufficient to affect patient outcomes (Van den Berghe, 2007)

These results have not been reconfirmed.

What is the Danger of Hypoglycemia for Patients under General Anesthesia?



- Autonomic and neurological signs of hypoglycemia are masked or absent during GA (anesthetics and Beta blockers can blunt physiologic response)
- Little is known about the frequency, severity and consequences of intraoperative hypoglycemia.
- Variables such as brain temperature may impact neurological outcomes

Goals of Perioperative Management

- Prevent hypoglycemia
- Prevent hyperglycemia
- Prevent lipolysis, protein catabolism, electrolyte disturbances
- Preserve cardiovascular function



Glycemic Targets

Critically ill : surgical
 Target : 110 mg/dl
 Generally < 140 mg/dl

80 - 110 mg/dl (AACE)*

Critically ill: nonsurgical
 110-140 mg/dl

Non-critically ill:
 No clear evidence for specific
 BG goals but suggest
 <126 mg/dl fasting
 <180-200 mg/dl random



AACE and ADA Consensus Statement on Inpatient Glycemic Control
 Endocrine Practice 15(4) May/June 2009

Consequences of Hypoglycemia

BS below 45 mg/dL
 Altered mentation, leading to
 seizures, unconsciousness
 and coma

Below 36 mg/dL
 EEG changes persist even after
 restoration of plasma sugar

Below 18 mg/dL
 Neuronal necrosis likely



Jackson, AM, Musen, G, Ryan, CM et al(2007) Long term effects of diabetes and its treatment on cognitive function. NEJM. 356: 1842-52.

Glycemic Control in the Hospital: An Elusive Goal

- "Stress Hyperglycemia"
- Decreased physical activity
- Discontinuation of outpatient regimens
- IV dextrose/TPN
- Sliding scales
- Medication/insulin errors
- Fear of hypoglycemia

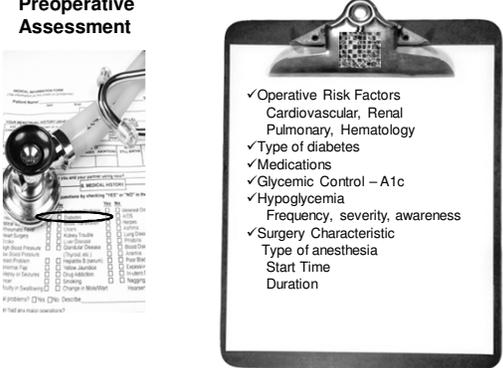
Hyperglycemic Influences

- Decreased caloric intake, meal interruptions
- Medication / insulin errors
- Sliding scales
- Overly aggressive therapy
- Altered cognitive status

Hypoglycemic Influences

Metchick, LN, et al. Am.J.Med.2002;113:317

Preoperative Assessment



- ✓ Operative Risk Factors
Cardiovascular, Renal
Pulmonary, Hematology
- ✓ Type of diabetes
- ✓ Medications
- ✓ Glycemic Control – A1c
- ✓ Hypoglycemia
Frequency, severity, awareness
- ✓ Surgery Characteristic
Type of anesthesia
Start Time
Duration

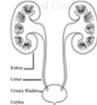
Diabetes Complications

Preoperative Assessment

Microvascular

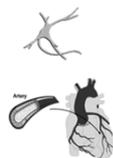


Retinopathy



Nephropathy

Neuropathy
Autonomic, "silent MI"



Macrovascular
CAD, PVD

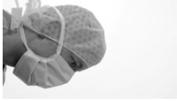
Perioperative Management

General Rules



- First case, early AM if possible
- BGs should be checked every 1-2 hours before, during, and after procedure
- IV insulin preferred for patients with major surgery pre-op, intra-op, post-op for as long as patient requires intensive care
- Source of glucose should be present while patient is receiving IV insulin

Society of Hospital Medicine



Perioperative Management

- Type 1 patients need insulin at all times even if NPO. Can become ketotic within 12-24 hours if insulin held even if BG is < 250 mg/dl

General Rules

Minor Surgery:

Type 1 and Type 2 on insulin

- Can use subcutaneous insulin
- Glargine – can continue usual dose on day of surgery. Some recommend reducing dose by ~20%
- NPH – on day of surgery, can reduce morning dose by ½
- Glargine/aspart regimen – can continue usual dose of glargine, premeal doses of aspart should be held until meals are tolerated

Emergency Surgery

- Pre-op Assessment
 - Metabolic status: stat plasma glucose, pH, BUN/Cr, lytes
 - Volume Status : check for orthostasis, elevated BUN/Cr
 - Cardiac Status: ECG
- Rule out DKA. Delay surgery if possible to stabilize metabolic status.



Management of Diabetes and Hospital Hyperglycemia

- Oral Agents**

Generally not recommended for acutely ill hospital patients.
Not appropriate for rapid titration to treat hyperglycemia.
May be restarted in hospital as part of discharge planning process unless contraindicated
- IV Insulin**

Drug of choice in critically ill patients
Allows for rapid titration
- Subcutaneous Insulin**

Drug of choice for controlling hyperglycemia in majority of non-critically ill patients



Oral Agents



- **Sulfonylureas** (*Glucotrol, Micronase, Diabeta, Amaryl*)

Routinely continued day before surgery and withheld on day of procedure
Higher risk of hypoglycemia in hospital patients due to poor oral intake and long half-life



- **Meglitinides** (*Starlix, Prandin*)

Routinely continued day before surgery and withheld on day of procedure
Drug works to lower postprandial BG and risk of hypoglycemia is increased when:
- patient has very poor intake
- meal contains less than 240 calories
- meal delivery is delayed



Oral Agents



- **Metformin** (*Glucophage, Glucophage XR*)

• Regular metformin can be held on day of procedure
• Sustained-release metformin should be held on the evening before procedure
• Potential serious side effect is *lactic acidosis* which can be precipitated by infections, hypoxia, renal insufficiency and iodinated contrast studies
• May worsen nausea and diarrhea
• Can be resumed 48 hrs post-op after renal function is normal.



- **TZD's** (*Avandia, Actos*)

• Discontinue on day of surgery
• Can cause fluid retention, increase risk of CHF, watch for abnormal liver function tests



Intravenous Insulin



IV insulin infusion is standard therapy for the preoperative management of diabetes in type 1 patients and type 2s undergoing major procedures.

Insulin protocols and algorithms can facilitate communication among medical staff, provide a method to determine insulin infusion rate required to achieve target blood glucose range.

Insulin

Subcutaneous

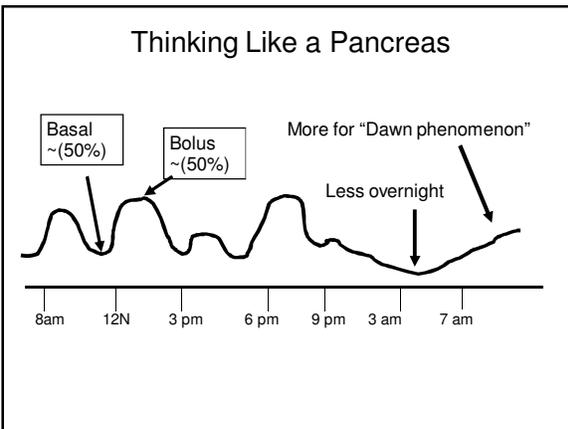
Transitioning from IV to SQ Insulin
 When patients are medically stable and tolerating meals, the insulin regimen should be physiologic i.e., it should meet both basal and prandial needs

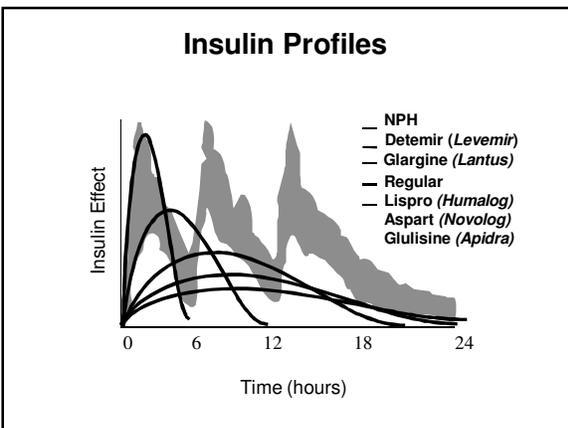
Components of Physiologic Insulin Regimen

1. Basal
2. Bolus/Prandial/Nutritional
3. Correction/Supplemental
aka "sliding scale"

- Do not discontinue IV insulin until SQ insulin has been initiated.. May be discontinued 1 hour after administration of Reg or aspart and 2 hours after NPH or glargine/detemir.



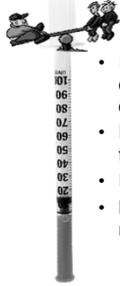




Insulin "Sliding Scale"

Advantages

- Easy



Disadvantages

- Ignores the amount and effect of corresponding doses on previous days
- Does not anticipate needs over the next 6-8 hours
- Pattern of too little then too much
- No insulin ordered if patient has normal BG

Subcutaneous Supplemental Schedule (Aspart/Lispro)

Glucose (mg/dl)	Low Dose Regimen	Medium Dose Regimen	High Dose Regimen
Less than 70	Give ½ ampule of D50 or 4 ounces of juice if patient tolerates oral intake.	Give ½ ampule of D50 or 4 ounces of juice if patient tolerates oral intake.	Give 1 ampule of D50 or 4 ounces of juice if patient tolerates oral intake.
70-120	0 units	0 units	0 units
121-150	2 units	4 units	5 units
151-200	4 units	6 units	10 units
201-250	6 units	8 units	14 units
251-300	8 units	10 units	17 units
301-350	10 units	16 units	20 units
351-399	12 units	18 units	24 units
Greater than 399	14 units and call MD	20 units and call MD	26 units and call MD

Hospital Hypoglycemia



- Reported incidence of hospital hypoglycemia ranges from 1.2% - 20%
- Mortality rates have been reported 22 - 27%
- Associated with poor outcomes and co-morbidities
- Analyses of reports disclose patterns of predisposing conditions and triggering events .
- Hospital hypoglycemia is predictable and preventable.
- Use of hospital-wide protocols for hypoglycemia beneficial

American Diabetes Association Workgroup
On Hypoglycemia, Diabetes Care :2005

Risk Factors for Hospital Hypoglycemia



Predisposing Conditions

- Diabetes
- Chronic renal, hepatic failure
- Malnutrition
- Sepsis/shock/mechanical ventilation
- CHF, CVA
- Advanced age
- Hypoglycemic unawareness

*American Diabetes Association Workgroup
On Hypoglycemia, Diabetes Care :2005*

Hospital Hypoglycemia: Triggering Events



- Sudden reduction of corticosteroid dose
- Discontinuing TPN, enteral feeding, IV dextrose
- Altered patient ability to self-report symptoms
- New NPO status / reduction in oral intake
- Insulin given at the wrong time relative to meal delivery
- Use of sulfonylureas in patients with renal impairment
- Unexpected transport from nursing unit after administration of rapid acting insulin
- Medication errors
- Protocol violations
- Infrequent or missed monitoring

*American Diabetes Association Workgroup
On Hypoglycemia, Diabetes Care :2005*

Barriers to Good Control



- Reliance on sliding scale insulin regimens
- Fear of hypoglycemia
- Inadequate knowledge and understanding of diabetes, hyperglycemia and its management among health care providers
- Lack of integrated information systems for tracking and trending of glycemic control and hypoglycemia
- Poor communication during patient hand-offs
Lack of ownership for hyperglycemia

Inpatient Diabetes and Glycemic Control: A Call to Action Conference. Position Statement, May, 2006.

Diabetes Care in the Hospital

Recommendations:

All patients with diabetes admitted to the hospital should :

- Be identified in the medical record as having diabetes
- Have an order for BG monitoring with results available to all members of the health care team
- Have insulin doses given in relation to meals and adjusted according to point of care BG levels. Traditional sliding scale insulin regimens are ineffective and NOT recommended.



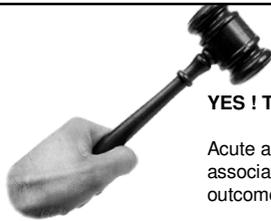
Diabetes Care in the Hospital

Recommendations:

All patients with diabetes admitted to the hospital should :

- Have a plan established for treating hypoglycemia. Episodes of hypoglycemia should be tracked
- Have an A1c obtained for discharge planning
- Have a diabetes education plan ("survival skills education") and follow-up should be developed





Conclusions

YES ! There is evidence....

Acute and chronic hyperglycemia is associated with adverse inpatient outcomes.

Hypoglycemia risk is still a concern and septic patients exhibit a high risk of hypoglycemia with difficult control.

Reversal of hyperglycemia linked to better clinical outcomes in medical and surgical patients, especially in AMI, cardiac surgery, infection and critically ill patients



Conclusions

Joint Statement from ADA and AACE

Until more info available, reasonable to use less intensive yet good BG control targets (140-180).

Thank You !