Glycemic Control:
*Is Blood Glucose the 6th vital sign?*

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**Agenda**

- Prevalence of Diabetes
- Types of Diabetes
- Complications
- Treatment of Diabetes
- Glycemic Control Inpatient Management
  - Why to manage?
  - How to manage?
  - Case studies
Classification of Diabetes Mellitus by Etiology (ADA 2011)

Type 1 diabetes (β-cell destruction -> absolute insulin deficiency)
- Immune mediated
- Idiopathic

Type 2 diabetes (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly secretory defect with insulin resistance)

Other specific types
- Genetic defects of β-cell function
- Genetic defects in insulin action
- Diseases of the exocrine pancreas, other endocrinopathies
- Drug or chemical induced (e.g. steroids)
- Infections
- Uncommon forms of immune-mediated diabetes, other genetic syndromes

Gestational diabetes mellitus

Late-Onset Type 1 Diabetes - LADA

- About half of patients with type 1 diabetes are diagnosed after age 18. Autoimmune process may differ and is slower
- Often mistaken for type 2 diabetes—may make up 10%–30%
- More likely to have antibodies (anti Islet cell and anti-GAD)
- Oral agents are usually ineffective—insulin therapy is eventually required
- Certain features age of onset <50 years, acute symptoms, BMI <25 kg/m2, and personal or family history of autoimmune disease can help predict.
- The presence of 2+ criteria above had a 90 percent sensitivity and 71 percent specificity for identifying patients positive for anti-GAD antibodies.

Pre-diabetes

Blood glucose levels that are higher than normal but not high enough to be classified as diabetes.
- Elevated HgA1c, elevated fasting plasma glucose levels & elevated OGTT
- Precursor to DM Type 2 (11%/year)
- 1.5% increased risk of CV disease
- Responds well to lifestyle changes

Natural History of Type 2 Diabetes
**Insulin Deficiency**

- **Insulin level**
- **Glucose level**

**Diagnosis of Diabetes**

<table>
<thead>
<tr>
<th>Diagnosis of Diabetes</th>
<th>Normal</th>
<th>Pre-diabetes</th>
<th>Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting Blood Glucose (FBG)</td>
<td>&lt; 100</td>
<td>100-125</td>
<td>≥ 126</td>
</tr>
<tr>
<td>Blood Glucose 2 hours after a</td>
<td>&lt; 140</td>
<td>140-199</td>
<td>≥ 200</td>
</tr>
<tr>
<td>75 gram glucose tolerance test</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Random Blood Glucose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A1C</td>
<td>&lt; 5.7</td>
<td>5.7-6.4</td>
<td>≥ 6.5</td>
</tr>
</tbody>
</table>

**Screening for Diabetes**

**Risk factors for type 2 diabetes**

- Pre-diabetes
- Older age
- Overweight or obese
- Physical inactivity
- Family history of diabetes
- Ethnic populations that are at higher risk: African Americans, Hispanics, Indian, Native Alaskan, Asian or Pan-Asian
- Gestational diabetes or had a baby that weighed more than 9 lb
- History of heart disease
- High blood pressure
- HDL cholesterol less than or equal to 35
- Triglyceride level greater than or equal to 250
- Polycystic ovarian syndrome

**Diabetes Prevention Program Outcomes Study 2009**

10 year follow-up of diabetes incidence and weight-loss in the diabetes prevention program outcomes study.

The Lancet. DOI: 10.1016/S0140-6736(09)61631-7
Hemoglobin A1c level

Complications of Diabetes

- Microvascular
  - Nephropathy
  - Neuropathy
  - Retinopathy

- Macrovascular
  - Coronary Artery Disease
  - Peripheral Artery Disease
  - Stroke
Complications of Diabetes

- 2 times the risk of death
- Dx at age 40 loose 11-14 years of life, and 18-22 years of QALY life years
- 2-4 times the risk of developing heart disease
- 2-4 times the risk of having a stroke
- Leading cause of blindness (12,000-24,000 per year)
- Leading cause of kidney failure (46,000 new dialysis pts per year)
- Leading cause of lower limb amputation (71,000 per year)
- 60-70% of all people with diabetes have some form of mild to severe nerve disease
- 2-3 times more likely to report they are unable to walk a quarter mile, climb stairs, do housework or use a mobility aid if 60 years or older
- 1 in 5 US health care dollars

Inpatient Hyperglycemia Morbidity and Mortality

- New hyperglycemia 16% ↑ chance of death
- 6 X ↑ life threatening infections
- 4 X ↑ risk death with acute MI, CHF
- 60% ↑ in post-op infections in surgery patients BG >200
- Direct link of perioperative hyperglycemia in CABG patients:
  - Normal BG < 2%, Known DM 3%,
    - Mediastinitis (DSWI), morbidity, mortality, LOS, and cost
  - 2 X ↑ risk death with stroke

- 5X ↑ risk of post-op renal transplant rejection and 100% serious infections
- DM2 pts undergoing cancer surgery >50% ↑ risk mortality
- >70% ↑ risk death with PNA and >50% hospital complication rate
- Decrease survival in leukemia (ALL) from 7 to 2 ½ years
  - Increase leukemia sepsis from 8% to 16%
- Pre-TPN and 24 hr TPN hyperglycemia predicts mortality and morbidity
  - >180 3X ↑ PNA, 2X ↑ ARF
  - 2X ↑ risk hospital death
First Large Randomized Controlled Trial:
Effect of Intensive Glycemic Control in Critically Ill Patients--Surgical ICU

**The New England Journal of Medicine**

1548 patients
AM glucose (mg/dL): 103 versus 153 intensive vs standard
Mortality decreased from 8.0% to 4.6% (only in patients with >5 d ICU stay)
Intervention resulted in decreased multiple-organ failure, sepsis, dialysis, transfusion, and neuropathy
Severe hypoglycemia (≤ 40 mg/dL): 7.0% vs 1.1% intensive vs standard

AACE Inpatient Glycemic Control Resource Center

Hypoglycemia Morbidity & Mortality

- ICU Inpatient Hypoglycemia Predicts Mortality
  Landmark Study
  - NEJM March 26th, 2009 NICE SUGAR Trial
  - International multicenter trial MICU Study > 6000 patients
  - Tight glycemic control BG 81 – 108 vs. 144 - 180
  - 7% severe hypoglycemia vs. 0.5%
  - Increased Mortality!
  - Hypoglycemia also increases costs, LOS
  - Placed Rates of Hypoglycemia on TJC Radar

AACE-ADA Consensus Statement on Inpatient Glycemic Control

**AACE/ADA Consensus Statement**

AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS
AND AMERICAN DIABETES ASSOCIATION
CONSENSUS STATEMENT ON INPATIENT GLYCEMIC CONTROL


ACP Clinical Practice Guidelines
Feb 2011

Use of Intensive Insulin Therapy for the Management of Glycemic Control in Hospitalized Patients: A Clinical Practice Guideline From the American College of Physicians
Amir Qaseem, MD, PhD, MHA; Linda L. Humphrey, MD, MPH; Roger Chou, MD; Vincenza Snow, MD; and Paul Shekelle, MD, PhD, for the Clinical Guidelines Committee of the American College of Physicians
General Ward Inpatient Hypoglycemia Predicts Mortality

Hypoglycemia and Clinical Outcomes in Patients with Diabetes Hospitalized in the General Ward (Diabetes Care, July 2009)

- Each day of BG < 50 -> inc odds death 85%
- If survived hospitalization 1 year mortality inc 66%
- Each 10 mg/dl decrease BG -> 3x chance death
- Each day BG < 50 inc LOS 2.5 days
- Possible Never Events

Hypoglycemia

- Hypoglycemia can be life-threatening
- Common causes of hypoglycemia in the hospital include:
  - Too much insulin or insulin given out of sync with meals
  - Inadequate food intake, vomiting
  - Oral hypoglycemic agents, with or without insulin, continued with changes in eating status (e.g. NPO)
  - Unexpected transport off unit after insulin given

Normal Insulin Physiology

Action Profiles of Insulin

<table>
<thead>
<tr>
<th>Type of Insulin</th>
<th>Action Profile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid Acting</td>
<td>Humalog (lispro), Apidra (glulisine), or NovoLog (aspart) 4-6 hours</td>
</tr>
<tr>
<td>Short Acting</td>
<td>Regular 6-8 hours</td>
</tr>
<tr>
<td>Intermediate</td>
<td>NPH 12-20 hours</td>
</tr>
<tr>
<td>Long Acting</td>
<td>Lantus (glargine) or Levermir (determir) 18-24 hours</td>
</tr>
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</table>
**Normal Daily Insulin Profile**

**Normal Daily Glucose Profile**

- **Insulin level**
- **Glucose level**

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**Physiologic Insulin Treatment**

- **Basal Insulin** (intermediate or long acting)
- **Mealtime Insulin** (rapid acting or short acting)

**Time of day**

- B = breakfast; L = lunch; D = dinner

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**Glycemic Variability leads to:**

- Vasoconstriction
- Inflammation
- Thrombosis
- Immune system dysfunction
**Sliding Scale Insulin**

- Reactive
- Goal is hyperglycemia; no endpoints
- “One size fits all”
- No critical thinking
- Rarely re-evaluated
- No basal insulin coverage

**No Sliding Scale**

**Use of oral anti-diabetic agents in the inpatient setting**

- Slow to titrate
- Last a long time
- Many contraindications for inpatients

Highest risk:
- sulfonylureas (glipizide, glyburide, glimepiride)
- metiglitinides
- metformin

**Sulfonylurea Mechanism of Action**

Binds to receptor on beta cell

Insulin is secreted into blood

Blood vessel

Islets of Langerhans containing beta cells

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http://www.pre-diabetes.com/download/medical/islets-of-langerhans.png

• = sulfonylurea
• = insulin
Metformin

Contraindicated if patient:

- Hypotensive
- Volume depleted
- Has acute kidney injury or CKD
- Will receive IV contrast
AACE/ADA Consensus Statement 2009

• “In the hospital setting, insulin therapy is the preferred method of glycemic control in the majority of clinical situations... Oral agents have a limited role in the in-patient setting,” and “scheduled subcutaneous insulin with basal, nutritional and correction components is the preferred method for achieving and maintaining glucose control in non-critically ill patients.”

Inpatient Basal insulin dosing

Recommended for:

• DM Type 1 (and not on insulin drip or pump)
• HgA1c ≥ 10%
• DM 2 on home insulin
• DM 2 uncontrolled on oral agents
• Uncontrolled BGs (> 180 mg/dL)
• Most patients transitioning off insulin drip

To be given even if NPO (as hepatic gluconeogenesis serves as a continuous source of blood glucose).

Inpatient Nutritional insulin dosing

Recommended for:

• DM 1 not on insulin pump or infusion
• HgA1c ≥ 10% on basal insulin
• Patients receiving nutrition who are requiring high doses correction insulin

Rapid-acting insulins should be given within 15 minutes of meal, or directly after meal.

Not given if patient NPO or is poorly eating.

Inpatient Nutritional insulin dosing

• Dose is given even when patient’s blood glucose is in the normal range.

• Rapid-acting insulins should be given within 15 minutes of meal, or directly after meal.

• Not given if patient NPO or is poorly eating.
Correction insulin dosing

- If patient requiring any significant dose of correction insulin (i.e. > 10 units/day), consider adding or increasing basal and/or nutritional dosing.

F-U 48 y.o. with TB infxn.

Hypoglycemia and oral anti-diabetic agents
# CV Surgery Insulin Mgmt

- Insulin drips post-op for elevated BG
- Insulin drip + nutritional insulin if still in ICU on POD #1, and tolerating diet
- Transition to sub Q regimen when ready to leave ICU
- Daily evaluation and titration of insulin regimen until discharge

# Nurse’s Role in Glycemic Control

- Appropriate timing of BG check and insulin administration
- Knowing when to hold insulin (or not!)
- Appropriate patient hand-off
- Avoidance of hypoglycemia
- Appropriate treatment of hypoglycemia
- Notifying physician if BGs out of control
- Coordination of patient activities to meals and meds
- Patient education

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# Inpatient Glycemic Control Data

**Measuring the efficacy and safety of glycemic control.**

**Efficacy** – What % of patients are within goal target range (70-180 mg/dL)?

**Safety** – How often are there episodes of hypoglycemia (< 70 mg/dL) and severe hyperglycemia (> 300 mg/dL)?

# How do we improve safety and efficacy with inpatients?

- Physiologic Insulin Dosing

- BE THE PANCREAS!!!!
Insulin - Definitions

- **Basal** – background, long-acting insulin steadily released throughout the day to meet basic metabolic needs
- **Nutritional** – rapid-acting insulin given to cover the glycemic spike that occurs due to carbohydrate intake. Also refers to scheduled insulin given to cover the carbohydrate load from tube feedings and TPN
- **Correction** – rapid-acting insulin that is given in addition to regularly scheduled insulin as a response to pre-existing high BG levels.

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**Pharmacokinetics of Insulin Products**

![Graph showing the pharmacokinetics of different types of insulin products, including rapid (lispro, aspart, glulisine), short (regular), intermediate (NPH), and long (glargine, detemir).]


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**Maintaining Physiologic Insulin Delivery in the Hospital**

![Graph showing the delivery of basal, supplemental or “stress” mealtime insulin.]

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So what can YOU do??

- Multidisciplinary approach is key
- Physician buy-in is essential
- Start small and build up
- Find champions!!!
Evaluate what you have

- Order sets
- Hypoglycemia protocols
- Documentation tools
- Insulin types used in-house
- Use of oral medications
- Data collection

“2 Over 200” Campaign

- 588 people signed on to the campaign
  - > 400 nurses
  - 78 physicians
  - 32 pharmacists
Glucose meters and pumps
Insulin Pumps

Medtronic Minimed
Animas Ping
Omnipod

Infusion sets

Utilize Resources

- American Association of Clinical Endocrinologists
  [http://resources.aace.com](http://resources.aace.com)
- Society for Hospital Medicine
  [www.hospitalmedicine.org](http://www.hospitalmedicine.org) (resource rooms)
- American Diabetes Association
  [www.diabetes.org](http://www.diabetes.org)
- Contact us!
  laneI1@sutterhealth.org
  gearys@sutterhealth.org
Conclusion

• Diabetes is becoming a world-wide epidemic
• Diabetes leads to significant health consequences
• Inpatient glycemic control is critical to reducing morbidity and mortality
• Nurses play a key role in helping manage glycemic control