Diabetes: a “broad spectrum” treatment

Leanne Current, PharmD, BCPS
Objectives

• Review epidemiology and pathophysiology of DM
• Identify diagnostic criteria and goals of treatment for diabetes
• Discuss provider to patient education on monitoring, treatment, nutrition and wellness
• Understand treatment strategies and quality measures for patient care with diabetes
• Examine the new ICU guidelines for glucose management and treatment strategies for inpatient insulin use
• Outline hyperglycemic crisis treatment
Economic Burden

• Prevalence
  • 26 million Americans ≥ 20 years old
  • 79 million more at high risk of developing diabetes

• Cost:
  • 218 billion dollars in 2007
  • $700 for every US citizen

• Complications
  • Results in 65,000 lower extremity amputations
  • Leading cause of ESRD
  • Cardiovascular event is the leading cause of death

\textsuperscript{2} Dipiro J. Pharmacotherapy A pathophysiologic approach. 9th edition
The Diabetes Epidemic: Global Projections, 2010–2030

*World*

2011 = 366 million
2030 = 552 million
Increase = 51%

(Adapted with permission from: Ismail-Beigi et al. *Ann Intern Med* 2011;154:554)
Classification

• Metabolic disorder characterized by:
  • Hyperglycemia
  • Absolute insulin deficiency (type 1)
  • Insulin resistance with insufficient insulin secretion (type 2)\(^1\)
  • Abnormalities in carbohydrate, fat and protein metabolism
  • Microvascular, macrovascular, and neuropathic disorders

\(^1\) Dipiro J. Pharmacotherapy: A pathophysiologic approach. 9\(^{th}\) edition
Main Pathophysiological Defects in T2DM

- **HYPERGLYCEMIA**
  - Decreased incretin effect
  - Increased gut carbohydrate delivery & absorption
  - Decreased pancreatic insulin secretion
  - Increased glucagon secretion
  - Increased hepatic glucose production
  - Decreased peripheral glucose uptake

Adapted from: Inzucchi SE, Sherwin RS in: *Cecil Medicine* 2011
Who to screen

Type 1
Not recommended in asymptomatic

Type 2
BMI >25 plus one of the following
- Physical inactivity
- 1st degree relative
- HTN
- HLD
- Low HDL
- PCOD
- Cardiovascular disease

Dipiro J. Pharmacotherapy: A pathophysiologic approach. 9th edition
Benefits of Screening

- Sponsored events
- Prevention
- No PCP
- Rapport with MDs
- Learning for Interns
- Increase loyal customers
- Change of pace
- Higher level patient care
- Knowing your patients
## Diagnosis

### Criteria for: Diagnosis

<table>
<thead>
<tr>
<th>Test</th>
<th>Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1C</td>
<td>$\geq 6.5$ (NATIONAL)</td>
</tr>
<tr>
<td>Fasting glucose</td>
<td>$\geq 126$ md/dL (8hrs)</td>
</tr>
<tr>
<td>2 Hour tolerance test</td>
<td>$\geq 200$ mg/dL (75gm glucose)</td>
</tr>
<tr>
<td>Random plasma glucose</td>
<td>$\geq 200$ mg/dL (classic symptoms)</td>
</tr>
</tbody>
</table>

### Criteria for: Impaired Glucose Tolerance

<table>
<thead>
<tr>
<th>Test</th>
<th>Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1C</td>
<td>5.7-6.4% (NATIONAL)</td>
</tr>
<tr>
<td>Fasting glucose</td>
<td>100-125 md/dL (8hrs)</td>
</tr>
<tr>
<td>2 Hour tolerance test</td>
<td>140-199 mg/dL (75gm glucose)</td>
</tr>
<tr>
<td>Random plasma glucose</td>
<td>140-199 mg/dL <em>extrapolated</em></td>
</tr>
</tbody>
</table>

*Dipiro J. Pharmacotherapy: A pathophysiologic approach. 9th edition*
Clinical pharmacist

“I have taught diabetes in the classroom for 8 years. And yet I was surprised when I was diagnosed with diabetes. I found myself tired, thirsty, and obviously urinating all the time as a result of drinking juice in large amounts. When my doctor told me I had diabetes I laughed. I had come to him with the classic symptoms of a disease state I had taught for years and yet didn’t recognize it in myself.”
### Clinical Presentation

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Type 1 DM</th>
<th>Type 2 DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>&lt;30 years</td>
<td>&gt;30 years</td>
</tr>
<tr>
<td>Onset</td>
<td>Abrupt</td>
<td>Gradual</td>
</tr>
<tr>
<td>Body habitus</td>
<td>Lean</td>
<td>Obese or hx of obesity</td>
</tr>
<tr>
<td>Symptoms</td>
<td>Symptomatic</td>
<td>Often Asymptomatic</td>
</tr>
<tr>
<td>Insulin resistance</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Ketones</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Need for insulin</td>
<td>Immediate</td>
<td>Years after diagnosis</td>
</tr>
<tr>
<td>Acute complications</td>
<td>Diabetic Ketoacidosis</td>
<td>Hyperosmolar Hyperglycemic State</td>
</tr>
</tbody>
</table>

*Dipiro J. Pharmacotherapy A pathophysiologic approach. 9th edition*
Metabolic Syndrome

*Individuals with 3 or more components meet criteria for diagnosis of the metabolic syndrome

- Abdominal Circumference:
  - Men >40 in
  - Women >35 in

- Triglycerides:
  - >150 mg/dL

- HDL:
  - Men <40 mg/dL
  - Women <50 mg/dL

- Blood Pressure:
  - ≥130/≥85

- Fasting Glucose:
  - ≥110 mg/dL
Goals

- Reduce microvascular disease
- Reduce macrovascular disease
- Ameliorate symptoms
- Reduce mortality
- Improve quality of life
- Prevent hyperglycemic crisis
- Reduce complications
  - Poor wound healing
  - Compromised WBC function

**A1C**
- <7% (ADA)
- ≤6.5% (ACE)

**Preprandial**
- 70-130 mg/dL (ADA)
- <110 mg/dL (ACE)

**Postprandial**
- <180 mg/dL (ADA)
- <140 mg/dL (ACE)
Monitoring for Complications

- **Dilated Eye Exams**: Yearly
- **Blood Pressure**: Each visit
- **Feet Exam**: Each Visit
- **Urine: Microalbumin**: Yearly
- **Lipid Test**: Yearly

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Approach to management of hyperglycemia:

- **Patient attitude and expected treatment efforts**
  - More stringent: highly motivated, adherent, excellent self-care capacities
  - Less stringent: less motivated, non-adherent, poor self-care capacities

- **Risks potentially associated with hypoglycemia, other adverse events**
  - Low
  - High

- **Disease duration**
  - Newly diagnosed
  - Long-standing

- **Life expectancy**
  - Long
  - Short

- **Important comorbidities**
  - Absent
  - Few/mild
  - Severe

- **Established vascular complications**
  - Absent
  - Few/mild
  - Severe

- **Resources, support system**
  - Readily available
  - Limited

(Adapted with permission from: Ismail-Beigi et al. Ann Intern Med 2011;154:554)
**Glycemic Control Algorithm For Type 2 Diabetes Mellitus In Adults**

**Glycemic Goals**

<table>
<thead>
<tr>
<th>Individualized goal based on patient risk factors</th>
<th>Initial Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>A1C ≤ 6% ≤ 7% ≤ 8%</td>
<td>1. Diabetes Self-Management Education and Support and/or 2. Self-monitored Blood Glucose and/or 3. Medical Nutrition Therapy, Weight Control, Exercise and/or 4. Monotherapy if A1C &lt; 9% above goal otherwise Dual Therapy (optimize therapy as tolerated)</td>
</tr>
</tbody>
</table>

If A1C < 9% above goal:
- If on monotherapy → add second agent (oral or GLP-1 receptor agonist)
- If on dual therapy → add third agent (oral or GLP-1 receptor agonist)

If A1C ≥ 9% above goal:
- If on monotherapy → add second agent +/− once-daily insulin
- OR add two non-insulin agents (oral or GLP-1 receptor agonist)
- If on dual therapy → add third agent (oral or GLP-1 receptor agonist)
- OR add insulin

**Goals Achieved**

- Continuous Therapy
- A1C every 3-6 months

**Goals not met after 3 months of optimized therapy**

- Add or intensify insulin
- Consider referral to an endocrinologist/diabetes specialist

**Recommendations for Dual Therapy**

- Metformin +TZD or DPP-4 + Su or GLP-1 or Meglitinide or co-enzyme

**Recommendations for Triple Therapy**

- Metformin +TZD or DPP-4 + GLP-1 or AGL or co-enzyme
- Metformin +TZD or DPP-4 + AGL or Su or co-enzyme
- + Insulin

**Abbreviations**

- A1C: Hemoglobin A1C
- AGI: Alpha-glucohydrolase inhibitors
- DPP-4: Dipeptidyl peptidase-4 inhibitor
- FPG: Fasting plasma glucose
- GLP-1: Glucagon-like peptide-1 agonist
- PP: Prandial
- Su: Sulfonylurea
- TZD: Thiazolidinedione

**Footnotes**


2. If initial A1C on presentation ≤ 10%, consider the use of insulin, with or without oral agents, as the initial intervention (see Insulin Algorithm). Other agents may be introduced in a glycemic control hierarchy. If ketonuria or recent rapid weight loss, consider Type 1 diabetes.

3. These interventions should be maintained lifelong (refer to Medical Nutrition, Weight Loss, and Exercise Algorithms).


5. If a SS is selected, use a daily glimepiride ER or glimepiride are recommended because they have a lower incidence of hypoglycemia than glyburide.

6. Refer to Insulin Algorithm for Type 2 Diabetes Mellitus in Children and Adults / Initial Insulin Therapy for Type 2 Diabetes Mellitus in Children and Adults: A Simplified Approach

**Texas diabetes council recommendation**
Key Points about treatment

• Glycemic targets and therapies much be individualized
• Diet exercise and education are foundation
• Metformin is first line therapy unless contraindicated
• After starting metformin there is little data to guide us.
  • Combo 1-2 oral or injectables are both reasonable
  • Aim to minimize side effects
• Patient centered approach focusing on their needs
• Think about cardiovascular risk reduction

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Choosing Healthier Foods

• Eat a variety of foods from different food groups
  • Eat plenty of fruits and veggies
• Low Fat diet
  • Avoid fried foods
  • Salad bar savvy (no to creamy dressing, bacon, croutons)
• Avoid high salt content
  • Processed foods (canned, boxed, frozen)
• Sugar in moderation
  • Moderation of sweets
  • Say no to regular soda
• Alcohol in moderation

www.choosemyplate.gov
Nutrition Education

http://www.lillydiabetes.com/Pages/carbohydrate-counter.aspx

• Proteins
  • Small effect on blood sugar

• Fats
  • Slow down absorption
  • Lower sugars after meals
  • High sugars longer after meals

• Carbohydrate
  • Biggest impact on blood sugars
  • Count your carbs
  • Check total carbohydrate
  • Read sugar free labels carefully
  • Pay attention to serving size
Staying Active

• Look for an activity you enjoy
• Make sure the activity matches your level of fitness
  • Start slowly
• Effect on glucose
  • Have snacks handy that contain sugar
  • Wear an medical ID bracelet
• Check blood sugar before and after you exercise
  • Avoid exercise if blood sugar is <70mg/dL or >250mg/dL
  • Especially if you take insulin, a sulfonylurea, or a meglitinide
• Wear comfy shoes
• Drink plenty of water

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Benefits to activity

- Aerobic activity improves insulin sensitivity
- Reduces cardiovascular risk factors
- Contributes to weight loss
- Goal: 150min/wk moderate activity
- Check with MD about appropriate level of activity for you
Sick Day Education

• Caloric intake declines
  • Goal of 120-150g of carbohydrates per day
• Insulin sensitivity decreases
  • May take greater amounts of insulin to control glucose
  • Usual insulin regimen with supplemental rapid acting insulin
• Ketone testing in insulin dependent diabetics
• Choose sugar free drinks to stay hydrated
• Identification of DKA or HHS
Patient Education

• Education on diabetes is lifelong
  • Every pt encounter could be an education opportunity
• Lifestyle change requires coaching and motivation
• Recognition of hyper and hypo glycemia
• Healthy eating
• Patient care visits
• Management of risk factors for CVD
• Become a CDE?
Prevention of Diabetes

• No medication FDA approved for the prevention of diabetes
• Metformin??
  • In conjunction with lifestyle changes
• DREAM trial
• ACT now trial

• THE ONLY PREVENTITIVE MEASURE IS WEIGHT LOSS AND LIFESTYLE MODIFICATION!!! EDUCATE!!!!
Hypoglycemia management

• Ask about symptomatic and asymptomatic hypoglycemia at each encounter
• Glucose 15-20gm for conscious individuals
  • recheck in 15min of treatment
  • redose if necessary
• Hypoglycemia unawareness or severe hypoglycemic episode should trigger treatment re-evaluation
• Raise glycemic targets to avoid hypoglycemia if necessary
Vaccination Recommendations

• Annual flu vaccine
• Pneumococcal polysaccharide
  • All diabetics ≥ 2 years of age
  • One time revaccination >65
• Hepatitis B vaccination
# Properties of anti-hyperglycemic agents

<table>
<thead>
<tr>
<th>Class</th>
<th>Mechanism</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biguanides</td>
<td>• Activates AMP-kinase</td>
<td>• Extensive experience</td>
<td>• Gastrointestinal</td>
<td>Low</td>
</tr>
<tr>
<td>(Metformin)</td>
<td>• ↓ Hepatic glucose production</td>
<td>• No hypoglycemia</td>
<td>• Lactic acidosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Weight neutral</td>
<td>• ? ↓ CVD events</td>
<td>• B-12 deficiency</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Contraindications</td>
<td></td>
</tr>
<tr>
<td>SUs /</td>
<td>• Closes KATP channels</td>
<td>• Extensive experience</td>
<td>• Hypoglycemia</td>
<td>Low</td>
</tr>
<tr>
<td>Meglitinides</td>
<td>• ↑ Insulin secretion</td>
<td>• ↓ Microvascular risk</td>
<td>• Weight gain</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Low durability</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• ? ↓ Ischemic preconditioning</td>
<td></td>
</tr>
<tr>
<td>TZDs</td>
<td>• Activates PPAR-g</td>
<td>• No hypoglycemia</td>
<td>• Weight gain</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td>• ↑ Insulin sensitivity</td>
<td>• Durability</td>
<td>• Edema / heart failure</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• ↓ TGs, ↑ HDL-C</td>
<td>• Bone fractures</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• ? ↓ CVD events (pio)</td>
<td>• ? ↑ MI (rosi)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• ? Bladder ca (pio)</td>
<td></td>
</tr>
<tr>
<td>a-GIs</td>
<td>• Inhibits a-glucosidase</td>
<td>• No hypoglycemia</td>
<td>• Gastrointestinal</td>
<td>Mod.</td>
</tr>
<tr>
<td></td>
<td>• Slows carbohydrate absorption</td>
<td>• Nonsystemic</td>
<td>• Dosing frequency</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• ↓ Post-prandial glucose</td>
<td>• Modest ↓ A1c</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• ? ↓ CVD events</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Diabetes Care* 2012;35:1364–1379  
*Diabetologia* 2012;55:1577–1596
<table>
<thead>
<tr>
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<th>Mechanism</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Cost</th>
</tr>
</thead>
</table>
| DPP-4 inhibitors      | • Inhibits DPP-4  
• Increases GLP-1, GIP                                            | • No hypoglycemia  
• Well tolerated                             | • Modest ↓ A1c  
• ? Pancreatitis  
• Urticaria  
• GI                                                | High   |
| GLP-1 receptor agonists | • Activates GLP-1 receptor  
• ↑ Insulin, ↓ glucagon  
• ↓ gastric emptying  
• ↑ satiety                                      | • Weight loss  
• No hypoglycemia  
• ? ↑ Beta cell mass  
• ? CV protection                                 | • GI  
• ? Pancreatitis  
• Medullary ca  
• Injectable                                     | High   |
| Amylin mimetics       | • Activates amylin receptor  
• ↓ glucagon  
• ↓ gastric emptying  
• ↑ satiety                                       | • Weight loss  
• ↓ Post-prandial glucose                         | • GI  
• Modest ↓ A1c  
• Injectable  
• Hypo w/ insulin  
• Dosing frequency                                | High   |
| Bile acid sequestrants | • Binds bile acids  
• ↓ Hepatic glucose production                                     | • No hypoglycemia  
• Nonsystemic  
• ↓ LDL-C                                         | • GI  
• Modest ↓ A1c  
• ↑ TGs  
• Dosing frequency                                | High   |
| Dopamine-2 agonists   | • Activates DA receptor  
• Modulates hypothalamic control of metabolism  
• ↑ Insulin sensitivity                            | • No hypoglycemia  
• ? ↓ CVD events                                    | • Modest ↓ A1c  
• Dizziness/syncope  
• Nausea  
• Fatigue                                        | High   |

Diabetes Care 2012;35:1364–1379
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<th>Advantages</th>
<th>Disadvantages</th>
<th>Cost</th>
</tr>
</thead>
</table>
| Insulin | • Activates insulin receptor  
            • ↑ Glucose disposal  
            • ↓ Hepatic glucose production | • Universally effective  
            • Unlimited efficacy  
            • ↓ Microvascular risk | • Hypoglycemia  
            • Weight gain  
            • ? Mitogenicity  
            • Injectable  
            • Training requirements  
            • “Stigma” | Variable |

### Type Onset Peak Duration Max Duration

<table>
<thead>
<tr>
<th>Type</th>
<th>Onset</th>
<th>Peak</th>
<th>Duration</th>
<th>Max Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid</td>
<td>Aspart/Lispro 15-30 min</td>
<td>1-2 hours</td>
<td>3-5 hours</td>
<td>5-6 hours</td>
</tr>
<tr>
<td>Short</td>
<td>Regular 30-60 min</td>
<td>2-3 hours</td>
<td>3-6 hours</td>
<td>6-8 hours</td>
</tr>
<tr>
<td></td>
<td>Intermediate NPH 2-4 hours</td>
<td>4-6 hours</td>
<td>8-12 hours</td>
<td>14-18 hours</td>
</tr>
<tr>
<td>Long</td>
<td>Glargine 4-5 hours</td>
<td>n/a</td>
<td>18-20 hours</td>
<td>24 hours</td>
</tr>
<tr>
<td></td>
<td>Detemir 2 hours</td>
<td>6-8 hours</td>
<td>14-24 hours</td>
<td>24 hours</td>
</tr>
</tbody>
</table>
Insulin overview

• All lower A1C
• Weight gain and hypoglycemia
• Larger doses and aggressive titration= higher risk of adverse effects
• Long acting reduces overnight hypoglycema
• Rapid acting reduce postprandial glucose excursions
• Generally no clinical significance in lowering A1C between “fancy insulin” and human insulin (NPH, Regular)

Dipiro J. Pharmacotherapy A pathophysiologic approach. 9th edition
Diabetes Care 2012;35:1364–1379
Diabetologia 2012;55:1577–1596
Sequential insulin strategies in type 2 diabetes

Inzucchi S E et al. Dia Care 2012;35:1364-1379
Copyright © 2011 American Diabetes Association, Inc.
Insulin Release

- Basal Insulin
  - Normally supplied by the pancreas continuously
- Bolus Insulin
  - Extra amounts of insulin the pancreas makes in response to glucose
- Modifications in the hospital???
Insulin Therapy in the Hospital

• Goal:
  • Mimic the body’s release of insulin (Basal/Bolus)
  • Maintain glucose control 80-180mg/dL (NICE-SUGAR)
    • ICU guidelines discuss 100-150mg/dL
  • Prevent hypoglycemia caused by therapy
  • Regimen that is manageable
Changes in insulin requirements inpatient

• Change in diet
  • NPO
  • Reduced appetite/ healthier eating
  • Tube feedings
  • TPN

• Medications
  • Steroids
  • Dextrose containing IVPB
  • Dextrose containing gtts
  • Discontinuation of oral diabetic agents (metformin)

• Change in patient condition
  • Stress induced hyperglycemia (sepsis, CV event, etc)
  • Edema
  • Perfusion (pressors)
Insulin Dosing

- Long acting to cover basal
- Short acting for correction and carbohydrate coverage
- Total daily insulin requirements should be divided to be:
  - If eating full diet (same as at home) on TF or TPN
    - 70-80% long acting insulin
    - 20-30% short acting insulin
  - If not eating full diet
    - 50% long acting insulin
    - 50% short acting insulin
- Why???
Approaches to insulin therapy inpatient

• Calculation protocols utilizing TDD (total daily dosing), ISF (Insulin sensitivity factor), and carb ratio
  • Advanced education
  • Best with glucose calculator program
    • In these programs you type in the ratios and the patient's glucose and they calculate the insulin dose
  • Can modify each component separately
  • Diet changes dose
  • Physician driven, nurse implemented, order dependent
  • Proactive approach vs reactive
  • Benefits to patients on diet

<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
<th>Physician Orders</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td><strong>GlucoStabilizer – Adult SubQ Insulin</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>The person initiating entry should write clearly, date the form (using Mo / Day / Yr), enter time, sign, and indicate their title.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Until signed, these are for general information and reference only. They should not be relied upon as a substitute for the independent professional judgment of the physician.</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Medications</strong> – Insulin lispro (Humalog) (rapid acting)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Initial Insulin Sensitivity Factor (ISF) and insulin to carbohydrate ratio settings are for insulin lispro (Humalog) only.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Insulin lispro (Humalog) SubQ, to be dosed per the Subcutaneous GlucoStabilizer Program</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Initial Insulin Sensitivity Factor (ISF) and carbohydrate ratio</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Use automated ISF and carbohydrate ratio settings (see below), use default settings if no other settings are specified</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Weight for calculation equal to or greater than 68 kg (150 lbs). (ISF=30 carbohydrate ratio = 10)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Weight for calculation less than 68 kg (150 lbs). (ISF = 60 carbohydrate ratio = 10)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>If completed do not use above default settings.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Use if you do not want carbohydrate coverage:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- No Carbohydrate ratio = 999 (nurse enter 999 to disable carbohydrate coverage)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(if completed do not use above default settings).</td>
</tr>
</tbody>
</table>

**Note to physician: Determining ISF and carbohydrate ratio:**

If converting from IV insulin use option #0 recommendations from the IV GlucoStabilizer Program. If patient already on insulin use their TDD (total daily dose): ISF = 1800/TDD |

Carbohydrate ratio = ISF/3 |

If patient insulin naive use weight based default settings above: |

Tip: Keep ISF - 3 times greater than the Carbohydrate ratio |

These recommendations are designed to assist the clinician in insulin adjustment. They are not intended to replace clinical judgment. |

**Blood Glucose default target settings with SubQ GlucoStabilizer Program:**

- For patient's who are eating 100-150 mg/dl, daytime and 200-250 mg/dl, at night unless specified otherwise (below) |

**Blood Glucose target settings with SubQ GlucoStabilizer Program:**

If eating: |

- Day: _________ mg/dl (if completed do not use above default targets) |
- Night: _________ mg/dl (if completed do not use above default targets) |

If NPO: |

- Day and Night: _________ mg/dl (if completed do not use above default targets) |

Blood glucose is corrected down to the mid point of the target for insulin lispro (Humalog) correction dose.
Insulin Calculations- a closer look

• Total Daily Dose (TDD)
  • Total daily insulin both long and short acting in 24 hours
    - Lantus: 90 units qhs
    - Correction (ISF): + 15 units/24hrs
    - Carb coverage: + 15 units/24hrs
    - TDD: 120 Units

• Remember the ratios
  • If eating full diet (same as at home) on TF or TPN
    - 70-80% long acting insulin
    - 20-30% short acting insulin
  • If not eating full diet
    - 50% long acting insulin
    - 50% short acting
Calculations- a closer look

• **Insulin Sensitivity Factor (ISF)**
  - Definition= 1 unit of insulin will drop my blood glucose by ___
  - The lower the ISF...the less sensitive someone is to insulin
    - Result more insulin needed if lower ratio
  - \(1800 \div \text{TDD (insulin rapid)}, \ 1500 \div \text{TDD (insulin regular)}\)

• **Carb Ratio**
  - Definition= I need 1 unit of insulin for ___ carbs
  - The lower the Carb ratio the less carbs it takes to require insulin
    - Result more insulin needed if lower ratio
  - ISF\(\div 3\)
Insulin Sensitivity Factor

• Would a type 1 diabetic have a higher or lower ISF than a type 2 diabetic??
  • Remember the lower the number the less sensitive you are to insulin
  • Ex: An ISF of 8 means that for 1 unit of insulin by BG will only drop by 8mg/dL. Whereas if I have an ISF of 20, 1 unit of insulin will drop my BG by 20 mg/dL

• What would steroids or a normal state of stress do to my ISF??
Patient Case

• AB is a 65yoM in the ICU for sepsis. Currently on TF at 65ml/hr. Currently tolerating TF and will remain on same formula and rate until extubated. Was place on SSI alone for management of blood glucose. PMH for DM2 (home insulin regimen unknown)
  0400: DFS 226 (9 units)
  0800: DFS 256 (12 units)
  1200: DFS 202 (9 units)
  1600: DFS 180 (6 units)
  2000: DFS 230 (9 units)
  2400: DFS 301 (15 units)

• What is the TDD and ISF??
  • 1800 (rapid)/ TDD or 1500 (regular)/TDD

• How much long acting should we start them on?

• What is their carbohydrate ratio based on this?
Approaches to insulin therapy inpatient

- Basal bolus ordersets
  - Separate orders for basal, correction, and carb ratio
  - Correction based on predetermined scales instead of modification of ISF
  - Simplified education
  - No need for advanced technology or calculators
  - Orderset driven, Physician orders, nurse protocol for titration
  - Physician must
  - Proactive vs reactive
  - Benefits to patients on diet

<table>
<thead>
<tr>
<th>If Preprandial BG is:</th>
<th>Low dose (TDD &lt;40)</th>
<th>Medium dose (TDD 40-60)</th>
<th>High dose (TDD &gt;60)</th>
</tr>
</thead>
<tbody>
<tr>
<td>70-150</td>
<td>No change</td>
<td>No change</td>
<td>No change</td>
</tr>
<tr>
<td>151-200 then ADD</td>
<td>1 unit</td>
<td>2 units</td>
<td>3 units</td>
</tr>
<tr>
<td>201-250 then ADD</td>
<td>2 units</td>
<td>4 units</td>
<td>6 units</td>
</tr>
<tr>
<td>251-300 then ADD</td>
<td>3 units</td>
<td>6 units</td>
<td>9 units</td>
</tr>
<tr>
<td>301-350 then ADD</td>
<td>4 units</td>
<td>8 units</td>
<td>12 units</td>
</tr>
</tbody>
</table>
# Basal Bolus Orderset

<table>
<thead>
<tr>
<th>LABS</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ HbA1c in AM (order if not available in last 60 days and no recent transfusion)</td>
</tr>
</tbody>
</table>

## PROVIDER TO RN:
- □ Do not hold insulin without communicating with physician
- □ RN may not advance dose of correction insulin. Only provider may advance dose.
- □ Notify physician if oral intake changes or enteral feedings are stopped
- □ Give Lispro Insulin within 15 minutes of meal (tray should be at bedside).
- □ If uncertain how much patient will eat, wait and give the Nutritional + Correction Insulin after patient eats at least 50% of carbohydrate in meal. If the patient doesn’t eat 50% of meal, then just give the Correction Insulin at that time.

## SCHEDULED INSULIN: ALL DOSES ADMINISTERED SUBCUTANEOUSLY

Total Daily Dose (TDD) _____ units (see page 3 for dosing recommendations)

### EATING

**Step 1:** Basal Insulin (long acting) 50% of TDD
- □ Glargine (Lantus) OR
- □ NPH (Humulin N)

<table>
<thead>
<tr>
<th>Insulin</th>
<th>Dose</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glargine (Lantus)</td>
<td>_____ units</td>
<td>0730, 2100, 0730 and 1700</td>
</tr>
<tr>
<td>NPH (Humulin N)</td>
<td>_____ units</td>
<td>Give with meals</td>
</tr>
</tbody>
</table>

**Step 2:** Nutritional/Prandial Insulin 50% of TDD divided by 3 if eating
- □ Lispro (Humalog)

<table>
<thead>
<tr>
<th>Dose</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>_____ units</td>
<td></td>
</tr>
</tbody>
</table>

**Step 3:** Select level for correction scale (Lispro Insulin)
- □ Low dose: TDD less than 40 units/day
- □ Bedtime correction scale
- □ Medium dose: TDD 40-80 units/day
- □ Bedtime correction scale
- □ High dose: TDD greater than 80 units/day

### NPO

**Step 1:** Basal Insulin (long acting) 50% of TDD
- □ Glargine (Lantus) OR
- □ NPH (Humulin N) *Consider reducing dosage by 1:3 to 1:2

<table>
<thead>
<tr>
<th>Dose</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>_____ units</td>
<td>0730, 2100, 0600 and 1800</td>
</tr>
</tbody>
</table>

**Step 2:** Select level for correction scale given every 6 hours (Regular Insulin)
- □ Low dose: TDD less than 40 units/day
- □ Medium dose: TDD 40-80 units/day
- □ High dose: TDD greater than 80 units/day
Approaches to insulin therapy inpatient

• Basal plus SSI protocol
  • Does not allow for separation of carb coverage and correction
  • Preset scale algorithms
  • Simple to follow
  • Higher incidence of hypoglycemia
  • Physician orders require no true calculations
  • Reactive insulin management
  • Not ideal for a patient on a diet
  • Ok in Tube feeds and TPN continuous feeds
Tube Feeds/TPN

- Continuous source of glucose
  - Doesn’t fit the physiological picture for basal/bolus insulin
- Complications??
Initiation of Insulin on TF

• If non diabetic
  • Watch and wait
  • If hyperglycemia occurs consider initiating SSI
  • Based on severity of hyperglycemia and insulin requirements may consider NPH
    • NPH vs Lantus

• If diabetic
  • Evaluate and consider starting home regimen
  • Expect increase in insulin requirements
Basal regimens and Tube feeds

- Mixed insulins are not appropriate...why?
- Considerations when using lantus?
- Consider taking the total basal and dividing by 3 for q8H dosing instead of by 2 for q12H dosing (remember peak is 4-6 hours, duration is 8-12H)
Insulin and TPN

• Goals
  • Prevent hyper/hypo glycemia
  • Simplicity for patient
  • Prevent wasting TPN

• Tx approaches
  • TPN Cycling?
  • Consider TDD/ISF/Carb Ratio
  • Underlying DM
  • Discussion with prescriber/ pharmacist/ dietitian
Insulin and TPN

• Insulin in TPN
  • Upside:
    • Simplicity in outpt setting
    • Cycled TPNs
    • Insulin source stopped if TPN stopped
  • Downside:
    • TPN wastage if too much insulin
    • Inflexible dosing...TPN hanging for 24H
      • Steroids stopped
      • No longer in stressed state
• Finding a balance
  • Pt still requiring 20-30% Short acting insulin
  • Plan with long acting insulin
  • Eclypsis charting ideas
Tube feed & TPN Complications

• Hyperglycemia can occur even in a non-diabetic because:
  •
• Hypoglycemia can occur when TF/TPN are stopped because of:
  •
• How do we prevent Hypoglycemia if TF/TPN need to be held??
Patient Case

Blood glucose
mg/dL

<table>
<thead>
<tr>
<th>Time</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>0:00</td>
<td>8u ssi</td>
</tr>
<tr>
<td>4:00</td>
<td>10u ssi</td>
</tr>
<tr>
<td>6:00</td>
<td>15u ssi + 15u NPH</td>
</tr>
<tr>
<td>8:00</td>
<td>6u ssi</td>
</tr>
<tr>
<td>11:00</td>
<td>8u ssi</td>
</tr>
<tr>
<td>16:00</td>
<td>D50</td>
</tr>
<tr>
<td>17:30</td>
<td>Glucose tab PRN</td>
</tr>
<tr>
<td>18:00</td>
<td>Glucagon</td>
</tr>
<tr>
<td>19:00</td>
<td>D10W infusion</td>
</tr>
<tr>
<td>20:00</td>
<td></td>
</tr>
<tr>
<td>22:00</td>
<td></td>
</tr>
<tr>
<td>22:30</td>
<td></td>
</tr>
<tr>
<td>0:00</td>
<td></td>
</tr>
<tr>
<td>4:00</td>
<td></td>
</tr>
</tbody>
</table>

Blood glucose levels and related interventions are shown in the graph.
How do you prevent hypoglycemia if continuous feeds need to be held?

• Add continuous dextrose source!

• Who needs it?
  • Those that have had a dose of Long acting insulin
  • Those with tight glucose control or low DFS checks while on TF

• Who should I order it on?
  • Consider ordering it in the PRN section for everyone with TF or TPN...because you can’t anticipate their sugars 10 days from now
ICU glucose infusion guidelines basic overview

• BG ≤ 150mg/dL triggers initiation of insulin therapy for ICU patients
• Titrate to keep BG values absolutely < 180 mg/dL
• Minimal BG excursions <100mg/dL
• BG ≤ 70mg/dL associated with increase in mortality
• BG monitored q1H on insulin gtt
• Hypoglycemia tx by stopping infusion, and administering 15-20gm dextrose (50%), repeat BG testing q15min until >70mg/dL achieved
• Basal and bolus insulin should be based on IV insulin infusion rate and carbohydrate intake
• GC protocols should address unplanned DC of any form of carbohydrate infusion
Glucostabilizer and drips

• Glucostabilizer or other programs can also be used on insulin gtts utilizing a multiplier

• How does it work?
  • Increases by ___ (usually 0.01) whenever the BG is above range
  • Decreases by ___ (usually 0.01) whenever the BG is below range
  • Multiplier = drip rate/ (BG-60)

• Example
  Current multiplier 0.04
  Current target range 100-150
  Current Blood glucose is 185
  Multiplier now becomes 0.05
DKA and HHS

- Precipitation factors:
  - Inadequate insulin therapy, Infection, Pancreatitis, CVA, MI, Drugs

<table>
<thead>
<tr>
<th>Consensus Statement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table 1—Diagnostic criteria for DKA and HHS</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Mild (plasma glucose &gt;250 mg/dL)</th>
<th>Moderate (plasma glucose &gt;250 mg/dL)</th>
<th>Severe (plasma glucose &gt;250 mg/dL)</th>
<th>HHS (plasma glucose &gt;600 mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial pH</td>
<td>7.25–7.30</td>
<td>7.00 to &lt;7.24</td>
<td>&lt;7.00</td>
<td>&gt;7.30</td>
</tr>
<tr>
<td>Serum bicarbonate (mEq/L)</td>
<td>15–18</td>
<td>10 to &lt;15</td>
<td>&lt;10</td>
<td>&gt;18</td>
</tr>
<tr>
<td>Urine ketone*</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
<td>Small</td>
</tr>
<tr>
<td>Serum ketone*</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
<td>Small</td>
</tr>
<tr>
<td>Effective serum osmolality†</td>
<td>Variable</td>
<td>Variable</td>
<td>Variable</td>
<td>&gt;320 mOsm/kg</td>
</tr>
<tr>
<td>Anion gap‡</td>
<td>&gt;10</td>
<td>&gt;12</td>
<td>&gt;12</td>
<td>Variable</td>
</tr>
<tr>
<td>Mental status</td>
<td>Alert</td>
<td>Alert/drowsy</td>
<td>Stupor/coma</td>
<td>Stupor/coma</td>
</tr>
</tbody>
</table>

* Nitropuside reaction method. † Effective serum osmolality: \( \frac{\text{measured Na}^+ (\text{mEq/L})}{2} + \text{glucose (mg/dL)} \) \* 18. § Anion gap: \( (\text{Na}^+) - [(\text{Cl}^-) + \text{HCO}_3^- (\text{mEq/L})] \).
(Data adapted from ref. 13.)
Figure 3. Pathogenesis of DKA and HHS
Stress, Infection and/or Insufficient Insulin

- Absolute Insulin Deficiency
  - Lipolysis
  - FFA to liver
  - Ketogenesis
  - Alkal reserve
  - Ketoacidosis
  - Triacylglycerol
  - Hyperlipidemia

- Counterregulatory Hormones
  - Protein synthesis
  - Proteolysis
  - Gluconeogenic substrates
  - Glucose utilization
  - Gluconeogenesis
  - Glycogenolysis
  - Hyperglycemia

- Relative Insulin Deficiency
  - Absent or minimal ketogenesis

Adapted from ref 1.

Hyperglycemic Crisis in Adult patients with Diabetes
Diabetes Care Volume 32, Number 7, 2009
Complete initial evaluation. Check capillary glucose and serum/urine ketones to confirm hyperglycemia and ketonemia/ketonuria. Obtain blood for metabolic profile. Start IV fluids: 1.0 L of 0.9% NaCl per hour.†

**IV Fluids**
- Determine hydration status
  - Severe hypovolemia
  - Mild dehydration
  - Cardiogenic shock
  - Administer 0.9% NaCl (1.0 L/hr)
  - Hemodynamic monitoring/pressors

**Bicarbonate**
- pH ≥ 6.9
- pH < 0.9
- No HCO$_3^-$
- 100mEq in 400ml H$_2$O + 20mEq KCl, infuse for 2 hours
- Repeat every 2 hours until pH ≥ 7
- Monitor serum K$^+$ every 2 hrs.

**Insulin: Regular**
- IV Route (DKA and HHS)
  - 0.1 U/kg B.Wt. as IV bolus
  - 0.1 U/kg/hr IV continuous insulin infusion
  - If serum glucose does not fall by at least 10% in first hour, give 0.14 U/kg as IV bolus, then continue previous Rx

**DKA**
- When glucose reaches 200 mg/dl, reduce regular insulin infusion to 0.02 - 0.05 U/kg/hr IV, or give rapid-acting insulin at 0.1 U/kg SC every 2 hrs.
- Keep serum glucose between 150 and 200 mg/dl until resolution of DKA.

**HHS**
- When serum glucose reaches 300 mg/dl, reduce regular insulin infusion to 0.02 - 0.05 U/kg/hr IV. Keep serum glucose between 200 and 300 mg/dl until patient is mentally alert.

**Potassium**
- Establish adequate renal function (urine output ≥ 50 ml/hr)
  - K$^+$ < 3.3 mEq/L
    - Hold insulin and give 20 - 30 mEq/hr
    - Until K$^+$ > 3.3 mEq/L
  - K$^+$ > 5.2 mEq/L
    - Do not give K$^+$, but check serum K$^+$ every 2 hrs.

When serum glucose reaches 200 mg/dl (DKA) or 300 mg/dl (HHS), change to 5% dextrose with 0.45% NaCl at 150-250 ml/hr.

Check electrolytes, BUN, venous pH, creatinine and glucose every 2 - 4 hrs until stable. After resolution of DKA or HHS and when patient is able to eat, initiate SC multidos insulin regimen. To transfer from IV to SC, continue IV insulin infusion for 1 - 2 hr after SC insulin begun to ensure adequate plasma insulin levels. In insulin naïve patients, start at 0.5 U/kg to 0.8 U/kg body weight per day and adjust insulin as needed. Look for precipitating cause(s).
Example protocol for DKA or HHS

- Phase 1: ED
  - Basic BMP
  - Fluid resuscitation
  - Potassium check
  - Insulin drip start
  - q1H checks
Example protocol for DKA or HHS

- **Phase 2: Admittance to ICU**
  - IVF choice 1/2NS vs NS
  - Corrected sodium calculation
    - Add 1.6mg/dL to measured serum sodium for each 100mg/dL of glucose above 100mg/dL
- Addition of K
- Addition of dextrose when blood glucose is less than 200mg/dL (Gap is closed typically at this time)
DKA and HHS treatment overview

- Correction of dehydration
- Correction of hyperglycemia
- Identification of electrolyte imbalances
- Appropriate transition to Subcutaneous insulin
  - Long acting insulin in type 1 diabetics! (treating acidosis more than hyperglycemia)
Determinate Fasting Lipid Profile (FLP) yearly

Abnormal fasting lipids:
- Initial therapy with TLC & intensive glucose control (with AIC goal < 6%)
- Evaluate and treat secondary causes of dyslipidemia: alcohol, estrogen, anabolic steroids, corticosteroids, hypothyroidism, hepatic disease, nephrotic syndrome, chronic renal failure
- LDL-C is the primary target of therapy unless TG > 400 mg/dL, at which point TG then becomes the primary treatment target.

High LDL-C

- Elevated LDL-C
  - LDL-C at goal with at least one additional CV risk factor present

  - Start statin, titrate to goal, reinforce TLC
    - Goal: LDL-C < 100 mg/dL
      - (≤70 if history of CVD, CHD, or PVD)

- If LDL-C remains above goal and/or patient does not tolerate statin, then add bile acid resin, ezetimibe, niacin or orlistat

Optimize TLC with diet, exercise, weight loss

Isolated low HDL-C (with LDL-C & TG at target)

Optimize TLC, smoking cessation, fibrates, niacin, fish oil or statins

Elevated TG

- 150–199
  - Optimize TLC

- 200–399
  - Optimize TLC, smoking cessation, start fibrate, niacin and/or fish oil

- ≥ 400
  - Optimize TLC, smoking cessation, start fibrate, niacin and/or fish oil
    - When TG < 400, reassess LDL-C

LDL-C not at goal, follow elevated LDL-C guideline

Refer to Lipid Specialist

Footnotes:
1. If a fibrate is combined with a statin, then fenofibrate is preferred rather than gemfibrozil due to risk of myositis and rhabdomyolysis.

Definitions:
TLC = Therapeutic Lifestyle Change (refer to TDC Medical Nutrition, Weight Loss, and Exercise Algorithms)
Statins = HMG-Co-A Reductase inhibitor
TG = Triglyceride
CVD = Cardiovascular disease
CVA = Cerebrovascular accident
PVD = Peripheral vascular disease

Texas diabetes council recommendation
Session in review

- DM is a high economic burden
- Treatment approaches for type 2 begin with metformin and are very patient specific
- Education is important for all diabetics
- Insulin therapy inpatient can be complex and requires multiple considerations
- Basal bolus or calculations are best in patient receiving a diet
- Continuous feedings require a unique approach to treatment
- ICU guidelines recently released and address goals for insulin gtt
- DKA and HHS management is a stepwise approach that addresses dehydration, glucose, electrolytes and prevention of reoccurrence of acidosis