Diabetes Treatment in a New Era: When to Begin Insulin and How to deliver it.
Objectives

1. Briefly review the evolution of insulin therapy.
2. Identify the types of insulin currently available for treatment of Type 2 DM.
3. Describe the action profiles of the different insulin therapies and relate these profiles to treatment regimens for patients with Type 2 DM.
4. Identify patients appropriate for insulin therapy in the treatment of Type 2 DM.
5. Recognize the barriers to the initiation of insulin therapy in patients with Type 2 DM and discuss strategies to overcome these barriers.
6. Review algorithms for the initiation of insulin therapy in patients with Type 2 DM.
7. Describe available insulin delivery systems.
8. Introduce new insulin therapies.

*Focus is Type 2 DM-adult nonpregnant patient
Questions to address:

- **What?**
  - Insulin
- **Why?**
  - Evolution of insulin therapy to become more physiologic
- **Who?**
  - Appropriate patients for insulin therapy
- **When?**
  - Appropriate time to initiate insulin therapy and appropriate insulin regimen
- **How?**
  - Appropriate insulin delivery systems
Types of Insulin

- **Rapid** acting (analogs)
  - Lispro (Humalog)
  - Aspart (Novolog)
  - Glulisine (Apidra)
- **Short** acting (human)
  - Regular (Humulin R, Novolin R)
- **Intermediate** acting (human)
  - NPH (Humulin NPH, Novolin NPH)
- **Long** acting (analogs)
  - Glargine (Lantus)
  - Detemir (Levemir)
<table>
<thead>
<tr>
<th>INSULIN</th>
<th>FDA APPROVAL DATE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rapid acting</strong></td>
<td></td>
</tr>
<tr>
<td>Lispro (Humalog)</td>
<td>June 1996</td>
</tr>
<tr>
<td>Aspart (Novolog)</td>
<td>November 2001</td>
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<tr>
<td>Glulisine (Apidra)</td>
<td>February 2004</td>
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<tr>
<td><strong>Short acting</strong></td>
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<tr>
<td>Regular (Humulin R 100U)</td>
<td>October 1982</td>
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<td>Regular (Novolin R)</td>
<td>June 1991</td>
</tr>
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<td><strong>Intermediate acting</strong></td>
<td></td>
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<tr>
<td>NPH (Humulin N)</td>
<td>October 1982</td>
</tr>
<tr>
<td>NPH (Novolin N)</td>
<td>July 1991</td>
</tr>
<tr>
<td><strong>Long acting</strong></td>
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<tr>
<td>Glargine (Lantus)</td>
<td>April 2000</td>
</tr>
<tr>
<td>Detemir (Levemir)</td>
<td>June 2005</td>
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<tr>
<td><strong>Mix insulin</strong></td>
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<td>70% NPH and 30% regular (Humulin 70/30)</td>
<td>April 1989</td>
</tr>
<tr>
<td>70% NPH and 30% regular (Novolin 70/30)</td>
<td>June 1991</td>
</tr>
<tr>
<td>50% insulin lispro protamine and 50% insulin lispro (Humalog 50/50)</td>
<td>June 1996</td>
</tr>
<tr>
<td>75% insulin lispro protamine and 25% insulin lispro (Humalog 75/25)</td>
<td>December 1999</td>
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<td>70% insulin aspart protamine and 30% insulin aspart (Novolog 70/30)</td>
<td>November 2001</td>
</tr>
<tr>
<td>INSULIN</td>
<td>Onset (hrs)</td>
</tr>
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<td>----------------------</td>
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<td><strong>Prandial/Bolus Insulin</strong></td>
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<tr>
<td><strong>Rapid acting</strong></td>
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</tr>
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<td>0.1-0.25</td>
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<tr>
<td>Aspart (Novolog)</td>
<td>0.1-0.25</td>
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<tr>
<td>Glulisine (Apidra)</td>
<td>0.1-0.25</td>
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<tr>
<td><strong>Short acting</strong></td>
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<tr>
<td>Regular</td>
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<td><strong>Basal</strong></td>
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<td>Glargine (Lantus)</td>
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<td>Detemir (Levemir)</td>
<td>2-4</td>
</tr>
</tbody>
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Barriers to insulin therapy

- Weight gain
- Time
- Cost
- Hypoglycemia
Barriers to Insulin Therapy

- Provider related
- Health system related
- Patient related

Barriers to Insulin Therapy

- **Provider related**
  - **Physician beliefs**
    - Pessimistic attitude toward disease
    - About the medication itself
    - Efficacy
    - Weight gain
    - Hypoglycemia
    - Side effects
  - **Physician concerns about patient dissatisfaction**
    - Insulin therapy is inconvenient and painful for patients
  - **Physician knowledge, treatment goals and experience**
  - **Time**

Barriers to Insulin Therapy

- **Health system related**
  - Cost
  - Diabetes education

Barriers to Insulin Therapy

• Patient related
  ▫ Fears
    • Weight gain
    • Needles/injections
    • Hypoglycemia
    • Diabetes complications
    • Failure
  ▫ Impact on life/job
  ▫ Cost and access
  ▫ Comorbid depression

Barriers to Insulin Therapy

- Patient related:
  - Needle/injection
  - Is it a real barrier?
    - American Association of Diabetes Educators survey conducted by Harris Interactive examined a group of 500 patients who require insulin and showed that:
      - 33% of patients identified that they have some level of dread associated with taking their daily injections
      - 14% felt that the insulin injections had a negative impact on their life
      - 29% felt that injecting insulin was the hardest aspect of their diabetes care

**BUT**

- 52% did not proactively communicate with their healthcare team about quality of life issues

And these patients are already taking insulin

- Which is worse fear of the unknown or known?

Caution:

- Waiting too long to initiate insulin therapy
- Conversations about insulin as a threat or punishment
- Waiting too long to intensify regimen
- Not matching the regimen to the patient
- Clinical inertia
- Utilization of multiple noninsulin hyperglycemic agents at maximal doses without consideration of insulin therapy
Goals of Insulin Therapy

- Achieve optimal glycemic control but avoid:
  - Hypoglycemia
  - Weight gain
  - Negative impact on patient’s lifestyle
- Understand the appropriate glycemic target for the individual patient
Algorithms for management of Type 2 DM

- American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology (ACE) Comprehensive Diabetes Management Algorithm

- Position Statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

Provide guidance regarding timing of insulin initiation
Definitions

- Basal/Background
- Bolus/Prandial
- MDI
Definitions

- Augmentation
- Replacement
- Carbohydrate ratio
- Correction factor (sensitivity factor)

How to add insulin therapy

- Weight based calculation
- Fixed starting dose with patient self titration
Starting insulin

• Varying strategies
  ▫ What can the patient do?
  ▫ How is your office equipped?
  ▫ How many injections daily and with which type of insulin?
Algorithms for insulin initiation and titration

- American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology (ACE) Comprehensive Diabetes Management Algorithm

- Position Statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) and update
Starting insulin

- Either weight based or fixed dose addition of basal insulin
- Caution with escalation of basal insulin without consideration of addition of prandial insulin
- Remember the physiology
- Consider addition of prandial insulin when basal insulin dose advanced to 0.5 units/kg
Effective insulin therapy

Initiation

Provider
Recommend/prescribe insulin

Patient
Must fill prescriptions and begin taking insulin

Adherence

Provider
Formulate an insulin regimen that patient can implement

Patient
Must adhere to regimen

Persistence

Provider
Must renew prescriptions

Patient
Must continue to refill and use prescriptions

Intensification

Provider
Intensify when appropriate

Patient
Must accept and implement

Effective Insulin Regimen

• Tailor to the patient
  ▫ Lifestyle needs
  ▫ Physical and mental health and capabilities
  ▫ Individual physiologic requirements
    • Weight
    • Insulin resistance
    • Comorbid conditions
Insulin Delivery

- Vial and syringe
- Insulin pens
- Insulin pumps
Challenges to insulin therapy

- Adherence to insulin therapy is lower than adherence to oral antihyperglycemic agents\(^1\)
- The challenges of therapy maintenance parallel barriers to initiation
  - Hypoglycemia
  - Weight gain
  - Regimen
- \(\frac{1}{3}\) of patients take insulin as prescribed\(^2\)

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• 6/27/2014 (updated 6/30/2014)
  • FDA approves Afrezza to treat diabetes
    • The U.S. Food and Drug Administration today approved Afrezza (insulin human) Inhalation Powder, a rapid-acting inhaled insulin to improve glycemic control in adults with diabetes mellitus. Afrezza is a rapid-acting inhaled insulin that is administered at the beginning of each meal.

From the FDA

www.fda.gov accessed July 2014
Afrezza

- **Ultra rapid acting mealtime insulin**
  - First in class
  - Peak insulin levels 12 to 15 minutes after inhalation
  - Cleared in 2-3 hours
- **Administration**
  - Dose (powder form contained in a cartridge)
  - Cartridge place in whistle sized inhaler

Afrezza

- **Side effects (in clinical trials)**
  - Hypoglycemia
  - Cough
  - Throat pain or irritation
- **Black box warning**
  - Acute bronchospasm
- **Do NOT use:**
  - Smokers
  - COPD
  - Asthma
  - DKA

From the FDA

2/25/2015

- FDA approval of Toujeo (U-300 insulin glargine)
  - 300 units per mL of insulin glargine

New Insulins in the Pipeline

- New generation basal insulin analogs
  - Degludec
    - What is it?
      - Insulin analog with a fatty acid side chain
      - Very long duration of action
    - Potential therapeutic advantages
      - Less fluctuation in glycemic control
      - Do not need to take at exact same time of day—greater flexibility of dosing
      - Less hypoglycemia
    - Concerns
      - Cardiovascular safety


NOT FDA APPROVED FOR USE
New Insulins in the Pipeline

• New generation basal insulin analogs
  ▫ PEGylated Lispro
  ▫ What is it?
    • Insulin Lispro + polyethylene glycol chain
    • Long half-life (2-3) days
    • Hepatopreferential effect (like endogenous insulin)
      • Potential therapeutic advantage
        ▫ Less weight gain
    • Safety concerns?

NOT FDA APPROVED FOR USE

Don’t Forget

- Conversation
  - Early
- Education
Additional References