Diabetes Meds for Type 2: Objectives

1. Describe the main action of the different categories of type 2 diabetes medications.
2. Discuss using the AACE and ADA 2015 Guidelines to determine best therapeutic approach.
3. Using the ADA Guidelines, describe strategies to initiate and adjust insulin therapy.
Path to Type 2 Diabetes

Patti Labelle "divabetic" -- that's a mix of diabetic and diva
Natural Progression of Type 2 Diabetes

<table>
<thead>
<tr>
<th>Years of Diabetes</th>
<th>Plasma Glucose</th>
<th>Postprandial glucose</th>
<th>Fasting glucose</th>
</tr>
</thead>
<tbody>
<tr>
<td>-20</td>
<td>126 mg/dL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior to diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>After diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Adapted from Bergenstal et al. 2000; International Diabetes Center.
Antihyperglycemic Therapy – 1st Step

- Lifestyle Changes
  - Weight control
  - Healthy eating
  - Activity

ADA-EASD Position Statement: Management of Hyperglycemia in T2DM
Diabetes Care 2012;35:1364–1379
Diabetologia 2012;55:1577–1596

Patient Centered Approach

“...providing care that is respectful of and responsive to individual patient preferences, needs, and values - ensuring that patient values guide all clinical decisions.”

- Gauge patient’s preferred level of involvement.
- Explore, where possible, therapeutic choices.
- Utilize decision aids.
- Shared decision making – final decisions re: lifestyle choices ultimately lie with the patient.

ADA-EASD Position Statement: Management of Hyperglycemia in T2DM
Diabetes Care 2012;35:1364–1379
Diabetologia 2012;55:1577–1596
Other Considerations

- Cost
- Hypoglycemia
- Age
- Weight
- Comorbidities
  - Kidney disease
  - Heart disease – CHF, CAD
  - Liver dysfunction

ADA-EASD Position Statement: Management of Hyperglycemia in T2DM

ADA Standards of Care 2015
Glycemic Targets - ADA

- **Adult non pregnant A1c goals**
  - **A1c < 7%** - a reasonable goal for adults.
  - **A1c < 6.5%** - may be appropriate for those without significant risk of hypoglycemia or other adverse effects of treatment.
  - **A1c < 8%** - may be appropriate for patients with history of hypoglycemia, limited life expectancy, or those with longstanding diabetes and vascular complications.

---

**Goals for Glycemic Control**

- **A1c ≤ 6.5%**
  - For healthy patients without concurrent illness and at low hypoglycemic risk
- **A1c > 6.5%**
  - Individualize goals for patients with concurrent illness and at risk for hypoglycemia
Multiple, Complex Pathophysiological Abnormalities in T2DM

Adapted from: Inzucchi SE, Sherwin RS in: Cecil Medicine 2011...

- incretin effect
- hepatic glucose production
- renal glucose excretion
- peripheral glucose uptake
- pancreatic insulin secretion
- pancreatic glucagon secretion

HYPERGLYCEMIA

Treating Hyperglycemia with Meds

- For all of the following case studies, we assume we are providing ongoing education on lifestyle – including referral to a RD and diabetes educator.
- In describing what meds match the patient best, I am speaking as an advocate for patients and a consultants to providers.
## Oral Diabetes Medications

<table>
<thead>
<tr>
<th>Class/Main Action</th>
<th>Name(s)</th>
<th>Daily Dose Range</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biguanides</td>
<td>metformin (Glucophage)</td>
<td>500 – 2500 mg (usually BID or TID)</td>
<td>Side effects: nausea, bloating, diarrhea. Use XR to minimize. Lactic acidosis precaution: avoid in pts with creat ≥ 1.4 mg/dL, 1.5 mg/dL during illness or surgery. Benefits: decreased cholesterol, no weight gain or hypoglycemia. lowers A1c: 1.0% – 2.0%.</td>
</tr>
<tr>
<td></td>
<td>Extended Release XR (Glucophage XR) (Glumetza) (Fortamet)</td>
<td>1x daily (or TID)</td>
<td>500 – 2000 mg 600 – 2500 mg 600 – 2500 mg</td>
</tr>
<tr>
<td>Sulfonylureas</td>
<td>glyburide (Micronase, Diabeta) (Olynae)</td>
<td>1.25 – 20 mg 0.75 – 12 mg</td>
<td>Can take once or twice daily before meals. Side effects include hypoglycemia and weight gain. Eliminated via kidney. Caution: Glyburide most likely to cause hypoglycemia. Lowers A1c: 1.0% – 2.0%.</td>
</tr>
<tr>
<td></td>
<td>glipizide (GlucoHex, Glucotrol XL)</td>
<td>2.5 – 40 mg 2.5 – 20 mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>glimepiride (Amaryl)</td>
<td>1.0 – 8 mg</td>
<td></td>
</tr>
<tr>
<td>DPP – 4 Inhibitors</td>
<td>sitagliptin (Januvia)</td>
<td>100 mg daily (eliminated via kidney)</td>
<td>If creatinine elevated, see pill insert for dosing info. No weight gain or hypoglycemia. Side effects include nasopharyngitis, headache and upper-respiratory tract infection. Report signs of pancreatitis (abdominal pain, nausea, vomiting). Lowers A1c: 0.6% – 0.8%.</td>
</tr>
<tr>
<td></td>
<td>saxagliptin (Onglyza)</td>
<td>Up to 5 mg daily (eliminated via kidney, feces)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>exubalogliptin (Tradjenta)</td>
<td>5 mg daily (eliminated via feces)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>alogliptin (Nesina)</td>
<td>25 mg once daily (eliminated via kidney)</td>
<td></td>
</tr>
</tbody>
</table>

More medications on back. Note: These meds are for people with Type 2 diabetes and should not be used during pregnancy. Content is for educational purposes only; please consult prescribing information for details.

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### SGLT2 Inhibitors
- Decrease glucose reabsorption in kidneys
- "Glucotoxic" action
- Canagliflozin (Invokana)
- Dapagliflozin (Farxiga)
- Empagliflozin (Jardiance)

### Thiazolidinediones
- "TZDs" increase insulin sensitivity
- Pioglitazone (Actos)
- Rosiglitazone (Avandia)

### Glucosidase Inhibitors
- Delay carb absorption
- Acarbose (Precose) miglitol (Glyset)

### Dopamine Receptor Agonists
- Reset circadian rhythm
- Bromocriptine mesylate—Quick Release "QR" (Cyprosyl)

### Meglitinides
- Stimulate rapid insulin burst
- repaglinide (Prandin)
- nateglinide (Starlix)
**Injectables That Lower Glucose**

<table>
<thead>
<tr>
<th>Class/Main Action</th>
<th>Name</th>
<th>Dose Range</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>GLP-1 Agonist</td>
<td>exenatide (Byetta)</td>
<td>5 or 10 mcg BID</td>
<td>Side effects for all: Nausea, vomiting, weight loss, injection site reaction. Report signs of acute pancreatitis (severe abdominal pain, vomiting), stop med.</td>
</tr>
<tr>
<td></td>
<td>exenatide XR (Bydureon)</td>
<td>2mg 1x a week (renal excretion)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>liraglutide (Victoza)</td>
<td>0.6 - 1.8 mg daily</td>
<td></td>
</tr>
<tr>
<td>Amylin Mimetic</td>
<td>degludec</td>
<td>26 units sc daily</td>
<td>For Type 1 or 2 on insulin. Black box warning: severe hypoglycemia risk, 3 hrs post injection. Prevent hypoglycemia, decrease insulin dose when starting pramlintide. Side effects: nausea, weight loss.</td>
</tr>
<tr>
<td></td>
<td>pramlintide (Symlin)</td>
<td>15 - 60 mg sc daily</td>
<td></td>
</tr>
</tbody>
</table>

The information listed here are general guidelines only, please consult prescribing information for details.

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**Multiple, Complex Pathophysiological Abnormalities in T2DM**

Adapted from: Inzucchi SE, Sherwin RS in: Cecil Medicine 2011

[Diagram showing various mechanisms and medications related to blood glucose regulation.]
Life Study

- 61 year old overweight woman with type 2 diabetes 3 months. Has been trying to control diabetes with diet and exercise. GFR in 90s. Worried about weight gain.
- Most recent A1c 6.9%
  - ADA
  - AACE
  - Cash pay

ADA Step Wise Approach to Hyperglycemia 2015

- Start with lifestyle coaching
- When lifestyle alone is not achieving A1c goal – Metformin should be added at, or soon after diagnosis (unless contraindicated).
- Metformin has a long standing evidence base for efficacy and safety, is cheap and may reduce CV risk.
When goal is to avoid weight gain

- These meds are weight neutral
  - Metformin
  - DPP-IV Inhibitors: Januvia, Onglyza, Tradjenta, Nesina
  - Acarbose

- These meds associated with wt loss
  - GLP-1 agonists (Byetta, Bydureon, Victoza, Tanzeum, Trulicity)
  - SGLT-2 Inhibitors (Canagliflozin, Dapagliflozin, Empagliflozin)
  - Symlin (Pramlintide)
When goal is to minimize cost

- Go generic.

- Oral Meds - Metformin and Sulfonylureas
  - Walmart offers 3 mo supply of following meds for ~ $10
  - Metformin and Metformin XR
  - Glipizide, Gliburide, Glimepiride

- Insulins – Oldies but Goodies
  - NPH, Regular, 70/30 mix
  - $25 a vial at Walmart – ReliOn
  - Vials and needles cheaper

---

**Glycemic Control Algorithm**

**Lifestyle Modification** (including Medically Assisted Weight Loss)

- **ENTRY A1c < 7.5%**
  - Monotherapy*
    - Metformin
    - GLP-1 RA
    - DPP-4
    - SGLT-2
    - TZD
    - GL/N

- If A1c > 8.5% in 3 months add second drug (Dual Therapy)

- **ENTRY A1c > 9.0%**
  - Insulin + other agent
    - ADD OR INTENSIFY INSULIN

- **ENTRY A1c > 7.5%**
  - Dual Therapy
    - GLP-1 RA
    - DPP-4
    - SGLT-2

- **ENTRY A1c > 9.0%**
  - Triple Therapy
    - Metformin
    - GLP-1 RA
    - DPP-4
    - SGLT-2

**Progression of Disease**

* Order of medications listed are a suggested hierarchy of usage

** Based upon phase 3 clinical trial data

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Diabetes Education Services© 1998-2015
Life Study

- 61 year old overweight woman with type 2 diabetes 3 months. Has been trying to control diabetes with diet and exercise. GFR in 90s. Worried about weight gain.
- Most recent A1c 6.9%
  - ADA
  - AACE
  - Cash pay
- Solutions?
  - Start no meds and monitor (ADA)
  - Start Metformin 500 mg 1-2 x a day

Life Study

- 54 year old smoker, creatinine 1.2, BMI 27. Not checking BG, even though he has glucose meter. On Metformin 500mg BID for past 4 months. Had bad experience with hypoglycemia on glyburide.
- Most recent A1c 7.9%
  - ADA
  - AACE
When goal is to avoid Hypoglycemia

- Avoid sulfonylureas
- Careful insulin dosing
- May need to up adjust glucose goals
- Monitor kidney function
- Reinforce for patients on insulin to “TIE”
  - Test
  - Inject
  - Eat
Life Study

- 54 year old smoker, creatinine 1.2, BMI 27. Not checking BG, even though he has glucose meter. On Metformin 500mg BID for past 4 months. Had bad experience with hypoglycemia on glyburide.
- Most recent A1c 7.9%
- Solution:
  - Change to Metformin XR and double dose
  - Add SGLT-2 or
  - Add GLP-1
  - If cash pay consider adding SU or insulin
Life Study

- 71 year old woman with type 2 diabetes for past year. BMI 24. Has been trying to control diabetes by limiting carbs and exercise. Creat 1.6. Good social support.
- Most recent A1c 8.6%
  - She has great insurance or
  - She is cash pay or
  - She hates needles

Older Adults - Considerations

- Reduced life expectancy
- Higher CVD burden
- Reduced GFR
- At risk for adverse events from polypharmacy
- More likely to be compromised from hypoglycemia

✓ Less ambitious targets
✓ A1c <7.5–8.0%
✓ Focus on drug safety
Life Study

- 71 year old woman with type 2 diabetes for past year. BMI 24. Has been trying to control diabetes by limiting carbs and exercise. Creat 1.6. Good social support.
- Most recent A1c 8.6%
  - She has great insurance or
  - She is cash pay or
  - She hates needles
Life Study

- 71 year old woman type 2 diabetes.
  - BMI 24. Has been trying to control diabetes by limiting carbs and exercise.
  - Creat 1.6. GFR low 30s. Good social support.
- Most recent A1c 8.6%
- Solutions
  - Great insurance – DPP-IV Inhibitor + Basal insulin
  - She is cash pay or – Sulfonylurea, NPH or 70/30
  - She hates needles – Sulfonylurea, DPP-IV Inhibitor - if doesn’t work, see if she will reconsider insulin
What next?

- 69 year old male, BMI 31, on Metformin 2000mg a day and Glipizide 40mg a day.
- A1c 9.1%. Creat 1.2
- Pt is obese, 11 yr history of diabetes
  - What next?
  - Insurance
  - No insurance
What next?

- 69 year old male, BMI 31, on Metformin 2000mg a day and Glipizide 40mg a day. Wt 100kg
- A1c 9.1%. Creat 1.2
- Pt is obese, 11 yr diabetes
- Solutions
  - Insurance – Add SGLT-2, GLP-1
  - No insurance – Stop Glipizide, keep metformin
  - Add 70/30 insulin 1-2 times a day. 100kg x 0.5 = 50 units daily (30 units am/ 20 units dinner)

Case Study

- 70 yr old, weighs 100kg
- History of CABG, tobacco
- A1c – 11.3%, BG 400-500 for past weeks
- Insulin – 100+ units Lantus at hs (solostar)
- Oral Meds: Metformin, Invokana
- Pt can’t afford Lantus insulin pen or Invokana – what other option?
### Insulin PocketCard™

<table>
<thead>
<tr>
<th>Action</th>
<th>Insulin Name</th>
<th>Onset</th>
<th>Peak</th>
<th>Effective Duration</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bolus</strong></td>
<td>Rapid Acting Analogs</td>
<td>5 - 15 min</td>
<td>30 - 90 min</td>
<td>&lt; 5 hrs</td>
<td>Bolus insulin lowers after-meal glucose. Efficacy reflected in post-meal BG.</td>
</tr>
<tr>
<td></td>
<td>Aspart (Novolog)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lispro (Humalog)</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Glulisine (Apidra)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Short Acting</td>
<td>30 - 60 min</td>
<td>2 - 3 hrs</td>
<td>5 - 8 hrs</td>
<td></td>
</tr>
<tr>
<td><strong>Basal</strong></td>
<td>Intermediate</td>
<td>2 - 4 hrs</td>
<td>4 - 10 hrs</td>
<td>10 - 16 hrs</td>
<td>Basal insulin controls BG between meals and HS. Efficacy reflected in fasting BG.</td>
</tr>
<tr>
<td></td>
<td>NPH</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Long Acting</td>
<td>3 - 8 hrs</td>
<td>No peak</td>
<td>6 - 24 hrs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Detemir (Levemir)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Glargine (Lantus)</td>
<td>2 - 4 hrs</td>
<td>No peak</td>
<td>20 - 24 hrs</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Bolus +</strong></td>
<td>Intermediate + rapid</td>
<td>5 - 15 min</td>
<td>Dual peaks</td>
<td>10 - 16 hrs</td>
<td>Side effects: hypoglycemia, weight gain. Typical dosing range: 0.5-1.0 units/kg body wt/day. Discard opened insulin vials after 28 days.</td>
</tr>
<tr>
<td></td>
<td>Novolog® Mix 70/30</td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>70/30 = 70% NPH + 30% aspart</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Humalog® Mix 75/25 = 75% NPL + 25% lispro</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>50/50 = 50% NPL + 50% lispro</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Bolus +</strong></td>
<td>Intermediate + short</td>
<td>30 - 60 min</td>
<td>Dual peaks</td>
<td>10 - 16 hrs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Combo of NPH + Reg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>70/30 = 70% NPH + 30% Reg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>50/50 = 50% NPH + 50% Reg</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Adapted from American Association of Clinical Endocrinologists Guidelines 2007. Because insulin action times can vary with each injection, time periods listed here are general guidelines only; please consult prescribing information for details.

---

### Cost Per Vial in Northern CA

<table>
<thead>
<tr>
<th>Per vial cost</th>
<th>Walmart</th>
<th>Walgreens</th>
<th>Costco</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regular Insulin</td>
<td>$25*</td>
<td>$92</td>
<td>$99</td>
</tr>
<tr>
<td>NPH</td>
<td>$25*</td>
<td>$92</td>
<td>$99</td>
</tr>
<tr>
<td>70/30</td>
<td>$25*</td>
<td>$92</td>
<td>$101</td>
</tr>
<tr>
<td>Humalog</td>
<td>$200</td>
<td>$220</td>
<td>$178</td>
</tr>
<tr>
<td>Novolog</td>
<td>$197</td>
<td>$217</td>
<td>$178</td>
</tr>
<tr>
<td>Apidra</td>
<td>$180</td>
<td>$246</td>
<td>$178</td>
</tr>
<tr>
<td>Levemir</td>
<td>$300</td>
<td>$300</td>
<td>$300</td>
</tr>
<tr>
<td>Lantus</td>
<td>$226</td>
<td>$221</td>
<td>$206</td>
</tr>
</tbody>
</table>
Case Study

- 70 yr old, weighs 100kg
- History of CABG
- A1c – 11.3%, BG 400-500 for past weeks
- Insulin – 100+ units Lantus at hs (solostar).
- Metformin 1000mg BID
- What is max basal insulin should he be on?

When is it Too much basal insulin?

Basal Insulin
(usually with metformin or other non-insulin agent)

- Start 1U/d or 1.4-2 U/kg/day
- Adjust: 10-15% or 2-4 U once twice weekly to reach FBO target.
- For hypoglycemic treat first and address causes.

ulins injections gest meal C premixed i
Case Study

- 70 yr old, weighs 100kg
- History of CABG
- A1c – 11.3%, BG 400-500 for past weeks
- Insulin – 100+ units Lantus at hs (solostar)
- Metformin 1000mg BID
- What is max basal insulin should he be on?
  - 100kg x 0.5 = 50 units a day
- What can we do next to improve BG?
Case Study

What is max basal insulin should he be on?
- 100kg x 0.5 = 50 units a day
- What can we do next to improve BG?
  - Add GLP-1 (Exenatide, Victoza, Trulicity, Tanzeum)
  - Add bolus insulin to largest meal
  - Switch him to 70/30 insulin ac breakfast and dinner
    - Total previous basal dose – 100 units
    - 2/3 in am – 65 units am (43 NPH and 22 regular)
    - 1/3 pre dinner – 35 units pm (23 NPH and 12 regular)

Case Study

- 70 yr old, weighs 100kg
- History of CABG, tobacco
- A1c – 11.3%, BG 400-500 for past weeks
- What will inform you of how to proceed?
  - Insurance coverage
  - His willingness to stick to a complex regimen
  - His ability to self-monitor
  - His social support and connection to his medical team
Critical Points

- Individualize Glycemic targets & BG-lowering
- Diet, exercise, & education: foundation T2DM therapy
- Metformin = optimal 1st-line drug.
- After metformin, data limited. Combo therapy reasonable
- Ultimately, many T2 patients will require insulin therapy
- All treatment decisions should be made in conjunction with the patient (focus on preferences, needs & values.)

- CV risk reduction - a major focus of therapy.

ADA-EASD Position Statement: Management of Hyperglycemia in T2DM

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Diabetologia 2012;55:1577–1596

Thank You

- Thanks for joining us!
- Please let us know if we can be of more service to you.
- www.DiabetesEd.net