Diabetes: A Worldwide Epidemic
Comprehensive Overview

Pamela Combs, Certified Nurse Practitioner
Endocrine Metabolic Institute
Cleveland Clinic
Objectives

• Discuss the revisions to the American Diabetes Association’s Standards of Care

• Overview the 10 facts regarding diabetes presented by the World Health Organization in the 2016 update

• Review specific preventions as treatment for type two diabetes
Objectives

• Overview the mechanisms of actions of modern classes of drugs available for the treatment of diabetes: incretins and Sodium Glucose Transporter inhibition (SGLT)

• Review basic principles of insulin pump use

• Discuss patient centered care in terms of treatment for type two diabetes and comorbidities
2017 ADA Summary of Revisions

Every Life Deserves World Class Care
American Diabetes Association 2017 Summary of Key Revisions

• Health Promotion
  – Recommendations were added to assess patients’ social context and resource utilization

• Classification
  – Proposed reclassification that focuses on beta-cell function

• Comprehensive medical evaluations
  – The addition of sleep quality and patterns as a part of the medical evaluation as evidence is emerging suggesting a relationship between sleep quality (Obstructive Sleep Apnea) and glycemic control

Standards of Medical Care in Diabetes-2017. Diabetes Care Volume 40, Supplement 1, S4-S5, January 2017
Lifestyle management

- The addition of fat and protein counting to carbohydrate counting to reflect evidence that these dietary factors influence glucose
- Prolonged sitting should be interrupted every 30 minutes with short bouts of activity

Prevention or Delay

- Begin formal assessment for pre-diabetes using an assessment tool
- Metformin approved for use in prevention of new onset diabetes
  - New evidence of an association between metformin and B12 deficiency (periodic measurement)

Obesity management

- Bariatric Surgery now referred to as Metabolic Surgery to reinforce its role in the treatment of Type Two Diabetes
Original Article

Bariatric Surgery versus Intensive Medical Therapy for Diabetes — 5-Year Outcomes

Bariatric Surgery versus Intensive Medical Therapy for Diabetes — 5-Year Outcomes

• Five-year outcome data showed that, among patients with type 2 diabetes and a BMI of 27 to 43, bariatric surgery plus intensive medical therapy was more effective than intensive medical therapy alone in decreasing, or in some cases resolving, hyperglycemia.

• N ENGL J MED 376;7 February 16, 2017
World Health Organization: Diabetes Facts

Every Life Deserves World Class Care
10 Facts Regarding Diabetes Worldwide

• #1 422 million people worldwide with diabetes

• #2 One of the leading causes of death worldwide

• #3 Two main types of diabetes
  – Type 1 – lack of endogenous insulin
  – Type 2 – ineffective use of endogenous insulin

• #4 Gestational diabetes
  – Both mother and infant at risk to develop full blown diabetes

• #5 Type two is 90% of all diabetes world-wide

http://www.who.int/features/factfiles/diabetes/en/
10 Facts Regarding Diabetes Worldwide

• #6 People with diabetes can lead long healthy lives

• #7 Early diagnosis and intervention are key

• #8 Low and middle income countries have more overall deaths related to diabetes

• #9 Diabetes is an important cause of blindness, kidney failure and amputation

http://www.who.int/features/factfiles/diabetes/en/
10 Facts Regarding Diabetes Worldwide

#10 TYPE TWO DIABETES CAN BE PREVENTED!
The mission of the WHO Diabetes Programme is to prevent diabetes whenever possible and, where not possible, to minimize complications and maximize quality of life.
Every Life Deserves World Class Care

Prevention as Treatment
Natural History of Type 2 Diabetes

Adapted from Kendall DM, Bergenstal RM © 2005 International Diabetes Center, Minneapolis, MN. All rights reserved.
Natural History of Type 2 Diabetes

Impaired glucose tolerance → Undiagnosed diabetes → Known diabetes

- Insulin resistance
- Insulin secretion
- Postprandial glucose
- Fasting glucose

Microvascular complications
Macrovascular complications

Adapted from Ramlo-Halsted BA, Edelman SV. Prim Care. 1999;26:771-789
Metabolic Syndrome
Associated Conditions

Pre-Diabetes

- Atherosclerosis
- Dyslipidemia
- Decreased fibrinolytic activity
- Endothelial dysfunction
- Hyperuricemia
- Hypertension
- Impaired glucose tolerance
- Obesity (central)
- Polycystic ovary disease

Insulin Resistance

Recent studies have identified certain ‘susceptibility genes’

‘Heredity loads the gun, **BUT** behaviour pulls the trigger!’
Prevention

• Lifestyle
  – Nutrition
  – Physical activity

• Pharmacologic Interventions

• Prevention of cardiovascular disease

• Diabetes Self – Management Education and Support
Nutrition: Mediterranean Diet (MedDiet)

The Traditional Mediterranean Diet

- High consumption of
  - Legumes
  - Vegetables
  - Grains
  - Fruits
  - Nuts
  - and Olive Oil

- Moderate consumption of
  - Fish and wine

- Low consumption of
  - Red and processed meat and whole-fat dairy products

Reduction in the Incidence of Type 2 Diabetes with the Mediterranean Diet

- Participants were randomly assigned to education on
  - A low-fat diet (control group) or
  - To one of two MedDiets:
    - Supplemented with either
      - Free virgin olive oil (1 liter/week) or
      - Nuts (30 g/day)

Reduction in the Incidence of Type 2 Diabetes with the Mediterranean diet

Median Follow Up at 4 years revealed

• When the two MedDiet groups were pooled and compared with the control group, diabetes incidence was reduced by 52%

• In all study arms, increased adherence to the MedDiet was inversely associated with diabetes incidence

• Diabetes risk reduction occurred in the absence of significant changes in body weight or physical activity

Physical Activity:
The Diabetes Prevention Program (DPP)

• This trial is the strongest evidence for diabetes prevention

• It demonstrated that an intensive lifestyle intervention could reduce the incidence of type 2 diabetes by 58% over 3 years

• Goals of the DPP
  – Achieve and maintain a minimum of 7% weight loss
    – **Caloric restriction**
  – 150 minutes of physical exercise per week
    – **Brisk walking**
Physical Activity: The Diabetes Prevention Program (DPP)

• Suggest
  
  – 150 minutes per week

  – Divide minimally over 3 days

  – 75 minutes of strength training could be applied towards the 150 minute goal
Prevention: Pharmacologic

• Metformin
  – Biguanide (Glucophage)
    – Improves insulin sensitivity

• Alpha-glucosidase inhibitors
  – Acarbose and Miglitol (Precose and Glyset)
    – Slow absorption of carbohydrates

• Orlistat
  – Xenical – lipase inhibitor
    – Inhibits absorption of dietary fat
Prevention: Pharmacologic

- Glucagon-like peptide 1 (GLP-1) receptor agonists
  - Liraglutide, Albiglutide, Dulaglutide, Lixisenatide
  - AKA Victoza, Tanzeum, Trulicity and Adlixin
  - Enhance insulin secretion and effect other hormones involved in glucose regulation

- Thiazoledinediones
  - Pioglitazone and Rosiglitazone
  - AKA Actos and Avandia
  - Increase insulin sensitivity and decrease glucose production
The phenomenon of ongoing beneficial effects on diabetic complications after a period of improved glycaemic control, even if followed by a return to usual (often poorer) metabolic control, has been described as representing “metabolic memory” by the DCCT/EDIC investigators and as a “legacy effect” by the UKPDS investigators.
Prevention: Cardiovascular Disease

• Those with pre-diabetes are at risk for cardiovascular disease

• Particularly, those with pre-diabetes who also have hypertension and hyperlipidemia

• The goal is to identify this and treat
Prevention: Self-Management Education and Support in those with Pre-diabetes

- Resources are scarce

- Pre-diabetes often not reimbursed by commercial insurances

- Rigorous life style changes are most cost – effective
Case Study

• Mickey, a 41 year old hispanic male presents to the clinic for his annual flu shot and to get blood work for a new job he just started. He is working 12 hour night shift

• When you ask if he has any concerns, he tells you he has gained weight, and needs some advice

• What are some important questions you might ask Mickey?
Case Study – Screening Tool

Are You at Risk for Type 2 Diabetes?

Diabetes Risk Test

1. How old are you?
   - Less than 40 years (0 points)
   - 40–49 years (1 point)
   - 50–59 years (2 points)
   - 60 years or older (3 points)

Write your score in the box.

2. Are you a man or a woman?
   - Man (1 point)
   - Woman (0 points)

3. If you are a woman, have you ever been diagnosed with gestational diabetes?
   - Yes (1 point)
   - No (0 points)

4. Do you have a mother, father, sister, or brother with diabetes?
   - Yes (1 point)
   - No (0 points)

5. Have you ever been diagnosed with high blood pressure?
   - Yes (1 point)
   - No (0 points)

6. Are you physically active?
   - Yes (3 points)
   - No (1 point)

7. What is your weight status?
   - (See chart at right)

If you scored 5 or higher:
You are at increased risk for having type 2 diabetes. However, only your doctor can tell for sure if you do have type 2 diabetes or prediabetes (a condition that precedes type 2 diabetes in which blood glucose levels are higher than normal). Talk to your doctor to see if additional testing is needed.

Type 2 diabetes is more common in African Americans, Hispanics/Latinos, American Indians, and Asian Americans and Pacific Islanders.

Higher body weights increase diabetes risk for everyone. Asian Americans are at increased diabetes risk at lower body weights than the rest of the general public (about 15 pounds lower).

For more information, visit us at diabetes.org or call 1-800-DIABETES (1-800-342-2383)

Lower Your Risk
The good news is that you can manage your risk for type 2 diabetes. Small steps make a big difference and can help you live a longer, healthier life.

If you are at high risk, your first step is to see your doctor to see if additional testing is needed.

Visit diabetes.org or call 1-800-DIABETES (1-800-342-2383) for information, tips on getting started, and lower your risk.

Adapted from Bang et al., Am Intern Med 141:275-282, 2004
Original algorithm was validated without gestational diabetes as part of the model.

Classification and Diagnosis of Diabetes Supplement 1 S15

Standards of Medical Care in Diabetes-2017. Diabetes Care Volume 40, Supplement 1, S15, January 2017
According to this BMI chart... I am too short.
• You find out he has a family history of both diabetes and heart disease

• You also do a 24 hour diet history with him and find that he eats one large meal daily around 4 pm, and that is usually fast or frozen food. Otherwise he just drinks soda throughout the day

• He states he is too busy to get any exercise, he sleeps all day and works all night

• Your counseling will consist of what advice re: diet, exercise, weight loss and sleep patterns?
Case Study

• Diet?

• Exercise?

• Weight loss?

• Sleep patterns?
Progress?

Survival advantage?

www.diabetes-education.net/pdf/annual_conference/2014/metabolic_memory.pptm
How to become an effective lifestyle counselor

You Live It !!
Available Medications

Timeline of Anti-diabetic Approvals

1920
Banting/Best
Insulin isolated from dogs

1940
SU

1950
Biguanide

1970
UGDP

1980
Rec Human insulin

1990
Inhaled Insulin

1990-2000
Metformin
Alpha-glucosidase inhibitors
Thiazolidinediones
Glinides

1990-2000
SGLT-2 inhibitors

2000-present
GLP analogues
Amylin analogues
DPPIV-inhibitors
Bromocriptine
colesevelam

Inhaled Insulin
Anti-diabetic Agents: Major Sites of Action

**Insulin secretion**
- ↑ Sulfonyureas
- ↑ Meglitinides
- ↑ Incretins

**Glucagon secretion**
- ↓ Incretins
- ↓ Amylin

**GI**
- Incretins
- α glucosidase inhibitors
- Amylin
- Bile acid sequestrant

**Hepatic glucose output**
- ↓ Metformin
- ↓ Thiazolidinediones

**Lipotoxicity**
- Thiazolidinediones
- Salicylates

**Appetite control**
- Incretins
- Amylin

**CNS**
- Dopamine

**Glucose reabsorption**
- ↓ SGLT2 inhibitors

**Glucose uptake and utilization**
- ↑ Thiazolidinediones
- ↑ Metformin

**Hyperglycemia**
<table>
<thead>
<tr>
<th>Oral 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 (?other)</td>
<td>• Extensive experience</td>
<td>• Gastrointestinal</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>• ↓ Hepatic glucose production</td>
<td>• No hypoglycemia</td>
<td>• Lactic acidosis (rare)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Weight neutral</td>
<td>• B-12 deficiency</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• ? ↓ CVD</td>
<td>• Contraindications</td>
<td></td>
</tr>
<tr>
<td>Sulfonylureas</td>
<td>• Closes KATP channels</td>
<td>• Extensive experience</td>
<td>• Hypoglycemia</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>• ↑ Insulin secretion</td>
<td>• ↓ Microvascular risk</td>
<td>• ↑ Weight</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>• ? Blunts ischemic preconditioning</td>
<td></td>
</tr>
<tr>
<td>Meglitinides</td>
<td>• Closes KATP channels</td>
<td>• ↓ Postprandial glucose</td>
<td>• Hypoglycemia</td>
<td>Mod</td>
</tr>
<tr>
<td></td>
<td>• ↑ Insulin secretion</td>
<td>• Dosing flexibility</td>
<td>• ↑ Weight</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• ? Blunts ischemic preconditioning</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Dosing frequency</td>
<td></td>
</tr>
<tr>
<td>TZDs</td>
<td>• PPAR-g activator</td>
<td>• No hypoglycemia</td>
<td>• ↑ Weight</td>
<td>Low</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 (pio)</td>
<td>• Bone fractures</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• ↑ HDL-C</td>
<td>• ↑ LDL-C (rosi)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• ? ↓ CVD events (pio)</td>
<td>• ↑ MI (rosi)</td>
<td></td>
</tr>
</tbody>
</table>

Diabetes Care 2015;38:140-149; Diabetologia 2015;58:429-442
<table>
<thead>
<tr>
<th>Oral Class</th>
<th>Mechanism</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Cost</th>
</tr>
</thead>
</table>
| α-Glucosidase inhibitors  | • Inhibits α-glucosidase  
• Slows carbohydrate digestion / absorption | • No hypoglycemia  
• Nonsystemic  
• ↓ Postprandial glucose  
• ? ↓ CVD events | • Gastrointestinal  
• Dosing frequency  
• Modest ↓ A1c | Mod.    |
| DPP-4 inhibitors          | • Inhibits DPP-4  
• Increases incretin (GLP-1, GIP) levels | • No hypoglycemia  
• Well tolerated | • Angioedema / urticaria  
• ? Pancreatitis  
• ? ↑ Heart failure | High   |
| Bile acid sequestrants    | • Bind bile acids  
• ? ↓ Hepatic glucose production | • No hypoglycemia  
• ↓ LDL-C | • Gastrointestinal  
• Modest ↓ A1c  
• Dosing frequency | High   |
| Dopamine-2 agonists       | • Activates DA receptor  
• Alters hypothalamic control of metabolism  
• ↑ insulin sensitivity | • No hypoglycemia  
• ? ↓ CVD events | • Modest ↓ A1c  
• Dizziness, fatigue  
• Nausea  
• Rhinitis | High   |
| SGLT2 inhibitors          | • Inhibits SGLT2 in proximal nephron  
• Increases glucosuria | • ↓ Weight  
• No hypoglycemia  
• ↓ BP  
• Effective at all stages | • GU infections  
• Polyuria  
• Volume depletion  
• ↑ LDL-C  
• ↑Cr (transient) | High   |

Diabetes Care 2015;38:140-149; Diabetologia 2015;58:429-442
<table>
<thead>
<tr>
<th>Injectable Class</th>
<th>Mechanism</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Cost</th>
</tr>
</thead>
</table>
| **Amylin mimetics** | • Activates amylin receptor  
• ↓ glucagon  
• ↓ gastric emptying  
• ↑ satiety | • ↓ Weight  
• ↓ Postprandial glucose | • Gastrointestinal  
• Modest ↓ A1c  
• Injectable  
• Hypo if insulin dose not reduced  
• Dosing frequency  
• Training requirements | High |
| **GLP-1 receptor agonists** | • Activates GLP-1 R  
• ↑ Insulin, ↓ glucagon  
• ↓ gastric emptying  
• ↑ satiety | • ↓ Weight  
• No hypoglycemia  
• ↓ Postprandial glucose  
• ↓ Some CV risk factors | • Gastrointestinal  
• ? Pancreatitis  
• ↑ Heart rate  
• Medullary Ca (rodents)  
• Injectable  
• Training requirements | High |
| **Insulin** | • Activates insulin receptor  
• Myriad | • Universally effective  
• Unlimited efficacy  
• ↓ Microvascular risk | • Hypoglycemia  
• Weight gain  
• ? Mitogenicity  
• Injectable  
• Patient reluctance  
• Training requirements | Variable |
Glycemic Management in Type 2 Diabetes

Modern Antihyperglycemic Therapies
The Incretin Effect
Glycemic Management in Type 2 Diabetes: Modern Antihyperglycemic Therapies

DPP-4 INHIBITORS
DPP-4 Inhibitors

FDA-Approved Agents

• Alogliptin
  —Nesina*

• Linagliptin
  —Tradgenta*

• Saxagliptin
  —Onglyza*

• Sitagliptin
  —Januvia*

Key Features

• Oral administration

• Increase endogenous GLP-1 and GIP levels

• Increase glucose-dependent insulin secretion

• Suppress glucagon production

*Trade names

DPP-4, dipeptidyl peptidase 4; GIP, glucose-dependent insulino tropic polypeptide; GLP-1, glucagon-like peptide 1.

Glycemic Management in Type 2 Diabetes: Modern Antihyperglycemic Therapies

GLP-1 RECEPTOR AGONISTS
GLP-1 Receptor Agonists

FDA-Approved Agents

- Albiglutide
  - Tanzeum*

- Dulaglutide
  - Trulicity*

- Exenatide
  - Byetta*

- Exenatide ER
  - Bydureon*

- Liraglutide
  - Victoza*

- Lixisenatide
  - Lyxumia – Adlixin*

Key Features

- Injectable administration
- Mimic action of native GLP-1
- Increase glucose-dependent insulin secretion
- Suppress glucagon production
- Slow gastric emptying

*Trade names

Glycemic Management in Type 2 Diabetes: Modern Antihyperglycemic Therapies

SGLT2 INHIBITORS
Glucose reabsorption by the proximal convoluted tubule

SGLT2 Inhibitors

FDA-Approved Agents

• Canagliflozin
• Dapagliflozin
• Empagliflozin

Key Features

• Oral administration
• Inhibit reabsorption of glucose into the bloodstream from renal fluid

SGLT2, sodium-glucose cotransporter 2.
Glycemic Management in Type 2 Diabetes: Efficacy and Safety of Modern Antihyperglycemic Therapies

INHALED INSULIN
Inhaled Insulin

• Inhaled administration

• Rapid-acting insulin
  – Peak levels achieved in ~15 minutes

Inhaled Insulin: AFREZZA

AFREZZA is an inhaled human insulin powder.

AFREZZA offers fast absorption into the body through the lungs.

AFREZZA reaches maximum (peak) level in 12 to 15 minutes.

https://www.afrezza.com/afrezza-mealtimel
Inhaled Insulin: AFREZZA

AFREZZA reaches maximum level, or peak, in 12 to 15 minutes

By 3 hours blood sugar levels return to baseline

https://www.afrezza.com/afrezza-mealtime/
### Safety Considerations with Inhaled Insulin

<table>
<thead>
<tr>
<th>Condition</th>
<th>Considerations</th>
</tr>
</thead>
</table>
| **Lung disease**| • Contraindicated in asthma, COPD, and other chronic lung diseases  
• Perform spirometry to assess lung function before initiating inhaled insulin, after 6 months of therapy, and annually thereafter, even in the absence of pulmonary symptoms  
• Do not use in patients with active lung cancer and use with caution in patients with a history of lung cancer or those at risk for lung cancer |
| **Heart failure**| • Observe for signs and symptoms of fluid retention or heart failure, especially when used with TZDs |
| **Hypoglycemia**| • Increase frequency of glucose monitoring |

Afrezza (insulin human) inhalation powder prescribing information. Danbury, CT: MannKind Corporation; 2014.
2012 ADA/EASD Position Statement

Insulin Pumps: Fundamentals
Continuous Subcutaneous Insulin Infusion - CSII

Every Life Deserves World Class Care
History of Pumps
Insulin pumps
Components of Pump Therapy

Change reservoir and infusion set every 2 to 3 days

= Pump therapy
Insulin Infusion

Optional automatic insertion device can make set placement virtually painless.

Low-profile site uses a flexible cannula for insulin infusion. Tubing comes in a choice of lengths.

At-site disconnect
Insulin Pumps
Dosage instructions are entered into the pump's small computer and the appropriate amount of insulin is then injected into the body in a calculated, controlled manner.
Insulin Pump Benefits

• More flexible lifestyle for patients

• Gives insulin sensitive patients a level of precision not available with routine injection therapy

• Patients may also decrease the basal rate in preparation for or while participating in intense exercise

• Patient can disconnect the pump temporarily in order to participate in water or contact sports
Insulin Pump Benefits

• Single injection every three days
• Use only one type of insulin
• Much more predictable rate of absorption
• Mimic the normal glycemic response in both fasting and postprandial states
• Hypoglycemic unawareness is reduced/restored
• Incidence of hypoglycemia is significantly reduced
CSII Improves Control
Hypoglycemia is reduced on switching from MDI to CSII

Linkeschova R, Raoul M, Bott U, Berger M & Spraul M. Less severe hypoglycaemia, better metabolic control, and improved quality of life in Type 1 diabetes mellitus with continuous subcutaneous insulin infusion (CSII) therapy; an observational study of 100 consecutive patients followed for a mean of 2 years. Diabetic Medicine 2002;19:746-751.
A few words about hypoglycemia ...........
Counter regulatory hormone response

- 82 mg/dl: Inhibition of endogenous insulin secretion
- 70 mg/dl: Counterregulatory hormone release (GLUCAGON, CATECHOLAMINES)
- 50-60 mg/dl: Onset of autonomic and neuroglycopenic symptoms
- < 50 mg/dl: Cognitive dysfunction
- < 30 mg/dl: Coma, convulsions

Hypoglycemia Unawareness Is a Dangerous Complication of Diabetes

• Each episode of hypoglycemia reduces counter-regulatory response to low glucose even after one episode

• Reduction in catecholamine response decreases awareness/symptoms even after a single episode

• Nocturnal hypoglycemia is most pathogenic and unrecognized

• Hypoglycemic awareness decreases significantly in the elderly
Complications and Sequelae of Hypoglycemia

- **Increased risk of cardiac arrhythmia**
  - Abnormal prolonged cardiac repolarization—↑ in QTc and QTd—associated with ↑ levels of epinephrine and hypokalemia
  - Cardiac death

- **Neuroglycopenia**
  - Reduced attention span
  - Inability to focus
  - Personality change
  - Confusion
  - Seizure
  - Coma
  - Brain death

---

CV Consequences of Hypoglycemia

• Prolonged QT - intervals
  – Can be of prolonged duration
• Greater with higher catecholamine levels
• Associated with angina / ischemic EKG changes
• Associated with arrhythmias
• Associated with sudden death
• Increased glycemic variability = adverse ICU outcomes / increased vascular inflammation
Mechanisms by which hypoglycemia may affect cardiovascular events

Souza CV. Hypoglycemia, Diabetes, and Cardiovascular Events DIABETES CARE, VOLUME 33, NUMBER 6, JUNE 2010
A healthy pancreas releases insulin automatically, on average, every 10-to 14-minutes\(^1\), in amounts appropriate for your varying blood glucose levels.


**Normal Insulin Production: The Pancreas**

- **Bolus dose**
- **Basal dose**

Normal Insulin Secretion

---

Conventional Therapy: *NPH and Short-Acting Insulin*

- Normal Insulin Secretion
- Short-acting Insulin
- NPH

Schematic representation only
Intensive Therapy: **MDI With Lantus® and Rapid-Acting Insulin**

- Long-acting basal insulin plus rapid-acting insulin before meals

- Requires 4 – 5 injections / day

Schematic representation only. Lantus is a registered trademark of Aventis Pharmaceuticals.
How can we achieve a more physiologic insulin/glucose pattern with an insulin pump?
The Insulin Pump: More Like a Healthy Pancreas

- Delivery that's customizable, flexible, adjustable
- Can more closely match the natural delivery patterns of the pancreas

![Insulin Delivery Graph](image)

- **Normal Insulin Secretion**
- **Pump Delivery**

*Schematic representation only*
The only insulins used in an insulin pump are SHORT acting insulins

- Humalog - lispro
- Novolog – aspart
- Apidra – glulisine
- ***R regular insulin - rarely
3 Components Any Insulin Program

• **Basal Insulin**
  – Scheduled

• **Bolus: nutritional insulin**
  – Scheduled

• **Correction insulin**
  – Algorithmic
The Basal Component

• This is the continuous rate at which the insulin pump is delivering insulin over a 24 hour period

• It could vary from hour to hour based on patient’s needs and can be given in increments of units

• If the patient is going to transition off of the pump, Lantus is used and given in the total amount of basal insulin the pump is delivering
The Basal Component

• Example Patient is receiving basal rate as such:
  – 0.5 units/hr from 12mn to 7 am ( 7 x 0.5  =  3.5 units)
  – 0.7 units/hr from 7am to 5pm    (10 x 0.7  =  7 units)
  – 1.0 units/hr from 5pm to 12mn  ( 7 x 1.0  =  7 units)

• *** thus over a 24 hour period the patient is getting 17.5 units of BASAL insulin****

• If pump came off for any reason would give 17-18 units of Lantus in transition
The Bolus or Prandial Component

• This is usually given based on the amount of carbohydrate (CHO) the patient is eating

• The patient will know their insulin to carbohydrate ratio

• It could be one unit of insulin for every 5 grams of CHO, or for every 15 grams or every 7 grams

• It could vary from meal to meal
The Bolus or Prandial Component

• For example, it is lunch time, the patient calculates that there are 60 grams of CHO in the meal, and he plans to eat it all. His insulin to carbohydrate ratio is 1 unit of insulin for every 15 grams CHO

• The patient will take how many units of insulin?
The Correction or Supplemental Component

• The insulin pump patient will correct based on a predetermined correction factor

• Usually the patient will have a goal glucose of 100-120, and for every so many points over that goal, they will take extra insulin
The Correction or Supplemental Component

- For example, the same patient in the previous example will take 4 units of insulin for the 60 grams of CHO, however his pre-lunch glucose is 200.

- The patient corrects by taking one unit for every 50 over his goal glucose of 100 mg/dl.

- How much correction insulin will he take?

- How much total insulin will he take?
Clinical caveats in pump management

1. The pump site should be assessed every 24 hours for signs and symptoms of infection

2. The pump set should be changed every 48-72 hours

If the patient is experiencing a low blood sugar remind them to suspend the pump until glucose levels recover
Further Clinical Caveats in Pump Management

1. YOU and the Patient should have a sense of urgency if

   – The pump malfunctions
   – Remember there is only short acting insulin in the pump, they need some Lantus or other long acting 24 hour insulin right away

   – If 2 to 3 consecutive glucose readings are above 200
   – Patient should know to begin to trouble shoot
     – Change the set, and assess site
     – Check every two hours, rebolus if indicated, until glucose controlled
     – If glucose still elevated, go to subcutaneous injected insulin with a syringe
Patient Centered Care: Special Populations

Every Life Deserves World Class Care
Patient Centered:

Defined as care that is respectful of and responsive to individual patient preferences, needs and values and ensuring that patient values guide all clinical decisions.
Which TARGET for WHOM?
Factors Deciding the Target HbA1c

• Several factors can be taken into consideration when tailoring treatment including
  – Duration of diabetes
  – Stage of disease
  – Life expectancy
  – Risk of hypoglycemia
  – Risk factors for CV disease (CVD)
## Patient Centered Approach to HgA1c

### Approach to the Management of Hyperglycemia

<table>
<thead>
<tr>
<th>Patient / Disease Features</th>
<th>More stringent</th>
<th>A1C 7%</th>
<th>Less stringent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risks potentially associated with hypoglycemia and other drug adverse effects</td>
<td>low</td>
<td></td>
<td>high</td>
</tr>
<tr>
<td>Disease duration</td>
<td>newly diagnosed</td>
<td></td>
<td>long-standing</td>
</tr>
<tr>
<td>Life expectancy</td>
<td>long</td>
<td></td>
<td>short</td>
</tr>
<tr>
<td>Relevant comorbidities</td>
<td>absent</td>
<td></td>
<td>few / mild</td>
</tr>
<tr>
<td>Established vascular complications</td>
<td>absent</td>
<td></td>
<td>severe</td>
</tr>
<tr>
<td>Patient attitude and expected treatment efforts</td>
<td>highly motivated, adherent, excellent self-care capabilities</td>
<td></td>
<td>less motivated, nonadherent, poor self-care capabilities</td>
</tr>
<tr>
<td>Resources and support system</td>
<td>readily available</td>
<td></td>
<td>limited</td>
</tr>
</tbody>
</table>

Standards of Medical Care in Diabetes-2016. *Diabetes Care* Supplement, January 2016
### Table 11.1—Framework for considering treatment goals for glycemia, blood pressure, and dyslipidemia in older adults with diabetes

<table>
<thead>
<tr>
<th>Patient characteristics/health status</th>
<th>Rationale</th>
<th>Reasonable A1C goal†</th>
<th>Fasting or preprandial glucose</th>
<th>Bedtime glucose</th>
<th>Blood pressure</th>
<th>Lipids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy (few coexisting chronic illnesses, intact cognitive and functional status)</td>
<td>Longer remaining life expectancy</td>
<td>&lt;7.5% (58 mmol/mol)</td>
<td>90–130 mg/dL (5.0–7.2 mmol/L)</td>
<td>90–150 mg/dL (5.0–8.3 mmol/L)</td>
<td>&lt;140/90 mmHg</td>
<td>Statin unless contraindicated or not tolerated</td>
</tr>
<tr>
<td>Complex/intermediate (multiple coexisting chronic illnesses* or 2+ instrumental ADL impairments or mild-to-moderate cognitive impairment)</td>
<td>Intermediate remaining life expectancy, high treatment burden, hypoglycemia vulnerability, fall risk</td>
<td>&lt;8.0% (64 mmol/mol)</td>
<td>90–150 mg/dL (5.0–8.3 mmol/L)</td>
<td>100–180 mg/dL (5.6–10.0 mmol/L)</td>
<td>&lt;140/90 mmHg</td>
<td>Statin unless contraindicated or not tolerated</td>
</tr>
<tr>
<td>Very complex/poor health (LTC or end-stage chronic illnesses** or moderate-to-severe cognitive impairment or 2+ ADL dependencies)</td>
<td>Limited remaining life expectancy makes benefit uncertain</td>
<td>&lt;8.5%‡ (69 mmol/mol)</td>
<td>100–180 mg/dL (5.6–10.0 mmol/L)</td>
<td>110–200 mg/dL (6.1–11.1 mmol/L)</td>
<td>&lt;150/90 mmHg</td>
<td>Consider likelihood of benefit with statin (secondary prevention more so than primary)</td>
</tr>
</tbody>
</table>

This represents a consensus framework for considering treatment goals for glycemia, blood pressure, and dyslipidemia in older adults with diabetes. The patient characteristic categories are general concepts. Not every patient will clearly fall into a particular category. Consideration of patient and caregiver preferences is an important aspect of treatment individualization. Additionally, a patient’s health status and preferences may change over time. ADL, activities of daily living. †A lower A1C goal may be set for an individual if achievable without recurrent or severe hypoglycemia or undue treatment burden. *Coexisting chronic illnesses are conditions serious enough to require medications or lifestyle management and may include arthritis, cancer, congestive heart failure, depression, emphysema, falls, hypertension, incontinence, stage 3 or worse chronic kidney disease, myocardial infarction, and stroke. By “multiple,” we mean at least three, but many patients may have five or more (40). **The presence of a single end-stage chronic illness, such as stage 3–4 congestive heart failure or oxygen-dependent lung disease, chronic kidney disease requiring dialysis, or uncontrolled metastatic cancer, may cause significant symptoms or impairment of functional status and significantly reduce life expectancy. ‡A1C of 8.5% (69 mmol/mol) equates to an estimated average glucose of ~200 mg/dL (11.1 mmol/L). Looser A1C targets above 8.5% (69 mmol/mol) are not recommended as they may expose patients to more frequent higher glucose values and the acute risks from glycosuria, dehydration, hyperglycemic hyperosmolar syndrome, and poor wound healing.
## Special Population: Children

### Table 12.1—Blood glucose and A1C goals for children and adolescents with type 1 diabetes

<table>
<thead>
<tr>
<th>Blood glucose goal range</th>
<th>Bedtime/overnight</th>
<th>A1C</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before meals</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>90–130 mg/dL (5.0–7.2 mmol/L)</td>
<td>90–150 mg/dL (5.0–8.3 mmol/L)</td>
<td>&lt;7.5%</td>
<td>A lower goal (&lt;7.0% [53 mmol/mol]) is reasonable if it can be achieved without excessive hypoglycemia</td>
</tr>
</tbody>
</table>

### Key concepts in setting glycemic goals:

- Goals should be *individualized*, and lower goals may be reasonable based on a benefit-risk assessment.
- Blood glucose goals should be modified in children with frequent hypoglycemia or hypoglycemia unawareness.
- Postprandial blood glucose values should be measured when there is a discrepancy between preprandial blood glucose values and A1C levels and to assess preprandial insulin doses in those on basal-bolus or pump regimens.
Special Populations

• Food Insecure
  – Avoid drugs that lead to hypoglycemia

• Impoverished
  – Consider cheapest options first

• Homeless
  – Research community resources
THANK YOU!!
Every life deserves world class care.