



**UPMC**  
LIFECHANGINGMEDICINE

# Medication and Diabetes

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# Objectives

1. Outline key differences between Type 1 Diabetes and Type 2 Diabetes mellitus.
2. Identify the medication classes utilized to treat patients with Diabetes mellitus.
3. Describe the recommended treatment options for patients with Type 1 Diabetes mellitus (T1DM).
4. Describe the recommended treatment options for patients with Type 2 Diabetes mellitus (T2DM).

# Diabetes at a Glance...

- A disease caused by the body's inability to produce enough insulin or use it properly
  - Insulin is produced by the pancreas and controls how glucose is used by the body
- Diabetes prevents the body from properly using the energy from the food you eat
  - Glucose is the sugar that provides energy to the cells of the body
- Vast majority of cases fall into 2 types:
  - Type 1 Diabetes Mellitus
  - Type 2 Diabetes Mellitus



# The Difference Between Type 1 and Type 2 Diabetes:

## Definitions:

- **Type 1 Diabetes Mellitus (T1DM)**
  - Pancreas does not produce enough/any insulin
  - 5 – 10% of diabetic population
- **Type 2 Diabetes Mellitus (T2DM)**
  - The body cannot use the insulin that is produced and/or it is not producing enough insulin
  - ~90 – 95% of diabetic population

# How the body works after a meal:



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Amylin and GLP-1 work by: slowing down the stomach so sugar doesn't get into blood TOO FAST; Signals the brain to turn off appetite; Keeps the liver from making too much sugar

1

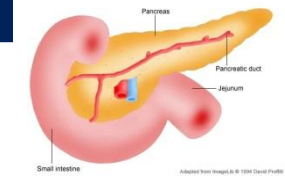
Carbohydrates digested in stomach and turned into sugar  
• Intestines release GLP-1



Carbohydrates: pasta, rice, bread, potatoes, sweets, milk, fruit

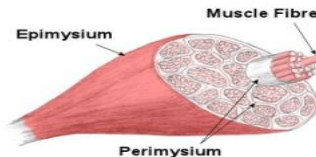
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Pancreas releases insulin and amylin when there is sugar in the blood



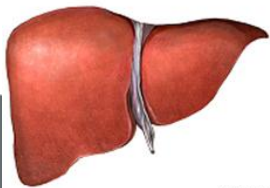
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Insulin helps take the sugar from the blood stream into the cells for energy



4

Extra amounts of insulin tell the liver to stop producing sugar



5

ADAM

# Diabetes changes how the body works:

Carbohydrates digested in stomach and turned into sugar  
• Intestines release GLP-1

Not enough GLP-1 produced in the intestines OR not enough Amylin produced in the pancreas

Amylin and GLP-1 work by: slowing down the stomach so sugar doesn't get into blood TOO FAST. Signals the brain to turn off appetite; Keeps the liver from making too much sugar

Pancreas releases insulin and amylin when there is sugar in the blood

Not enough insulin is produced by pancreas or the sugar cannot get into cells for energy → blood sugar rises

Liver produces too much sugar

Extra amount of insulin tell the liver to stop producing sugar

Insulin help take the sugar from the blood stream into the cells for energy



# Risk Factors for Diabetes

## Type 1 Diabetes:

- Family history
- Illness that injures the pancreas

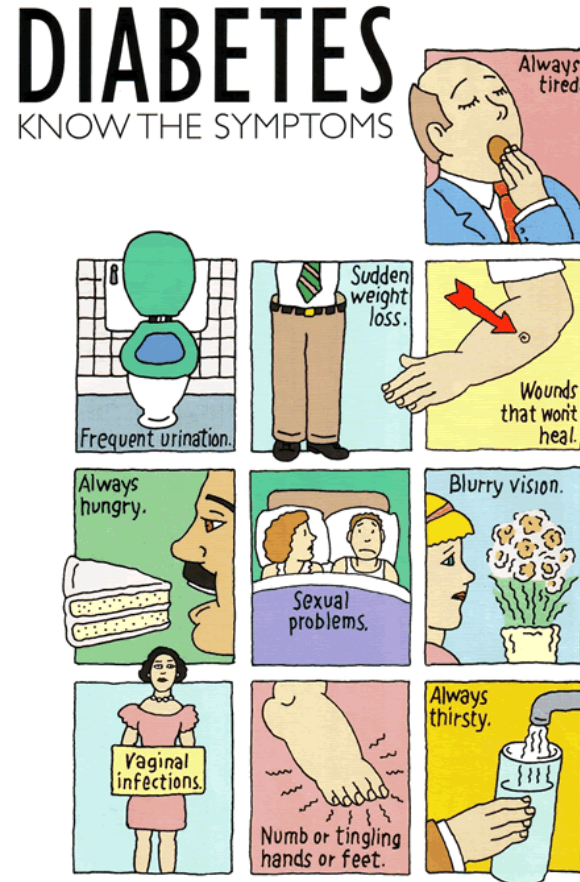


## Type 2 Diabetes:

- Family history
- Overweight
- Diabetes during pregnancy
- Giving birth to a baby weighing over 9lbs
- High blood pressure or high cholesterol

# Symptoms of Diabetes

- Increased thirst or dry mouth
- Increased urination
- Blurry vision
- Weight loss
- Fatigue
- Wounds that heal slowly; foot sores
- Numbness or tingling in the feet
- Nervousness
- Dry, itchy skin



If you have any of these symptoms, see your doctor. For more information about diabetes call Eli Lilly and Company at 1-800-545-5979 or Boehringer Mannheim Corporation at 1-800-858-8072.

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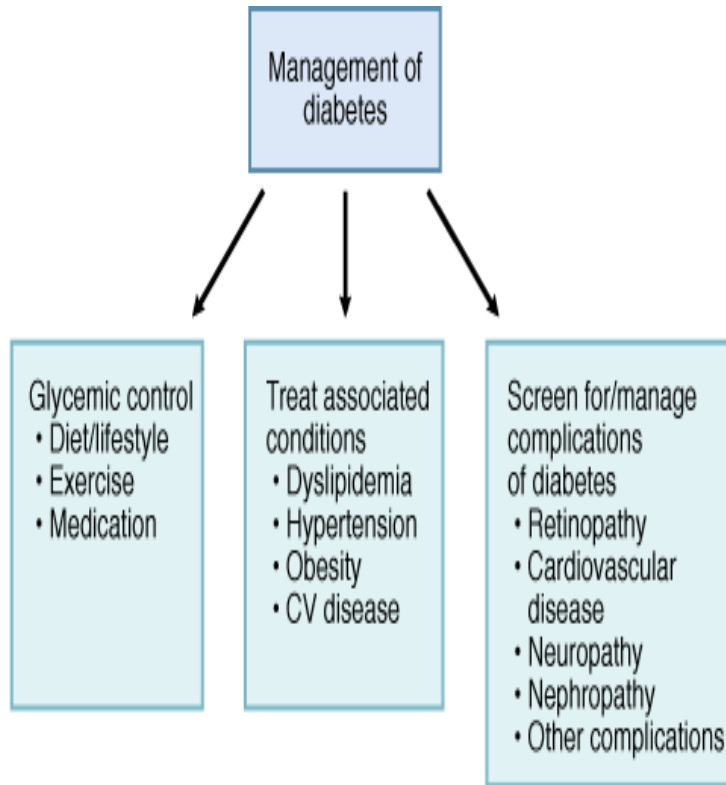
**Some patients may not have any symptoms!!!**

# Diagnosis of Diabetes

<b>TEST</b>	<b>ADA &amp; AACE</b>
<b>Fasting Blood Sugar</b>	<b>&gt;126 mg/dl</b>
<b>Casual plasma Glucose + Diabetes Symptoms</b>	<b>&gt;200 mg/dl</b>
<b>2-hour Post Glucose Test</b>	<b>&gt;200 mg/dl</b>
<b>Hemoglobin A1C</b>	<b>≥ 6.5%</b>

American Diabetes Association (ADA)  
American College of Endocrinology (AACE)

# Management of Diabetes



Source: Brunton LL, Chabner BA, Knollmann BC: *Goodman & Gilman's The Pharmacological Basis of Therapeutics, 12th Edition*: [www.accessmedicine.com](http://www.accessmedicine.com)  
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## A road map of diabetes: where to watch for problems

In diabetes, high blood glucose, high blood pressure, high cholesterol, and other factors can all combine to create problems down the road. Fixing just one thing can help you stay in good running condition, but it's even better if you work on all of them at once.

### stomach

Carrying extra fat around the middle (an "apple-shaped" body) can increase the risk of heart disease. Being very overweight can also make it hard for the cells to respond to insulin, and the body reacts by releasing more insulin.

### feet

High blood glucose can damage nerves, leading to pain, weakness, and numbness in hands and feet (peripheral neuropathy).

### brain

Insulin resistance (the cause of type 2 diabetes) is linked to an increased build-up of plaque in arteries, which can keep blood from flowing to the brain, causing stroke.

### eyes

High blood glucose and high blood pressure can damage tiny blood vessels in the eyes (retinopathy).

### heart

High blood pressure and insulin resistance together double the risk for heart disease.

### kidneys

High blood pressure (which damages small blood vessels), and high blood glucose make the kidneys work too hard, and they become too weak to clean waste from the blood. The kidney damage, in turn, can cause blood pressure to rise higher.

### veins

Too much "bad" cholesterol can clog blood vessels with plaque and insulin resistance can weaken them. Together, these can raise blood pressure to dangerous levels.

# Goals of Diabetes Care

- A1C: < 7%
- Blood Pressure: <130/80 mmHg
- Cholesterol
  - LDL < 100 mg/dL
  - HDL > 40 mg/dL in men and > 50 in women
  - Triglycerides < 150 mg/dL



# Goals for Glycemic Control in Diabetes Patients

	<b>Goals for Glycemic Control</b>	
<b>Biochemical Index</b>	<b>ADA</b>	<b>ACE</b>
A1C (Hemoglobin A1C)	< 7%	≤ 6.5%
Fasting/pre-prandial glucose	90 – 130 mg/dL	< 110 mg/dL
Peak post-prandial glucose	< 180 mg/dL	< 140 mg/dL

ADA = American Diabetes Association

ACE = American College of Endocrinology

# Diabetes Medication Options

## Type 1 Diabetes

- **Insulin** (Rapid- vs. Short-, vs. Long-acting, vs. Combination products)
- **Amylin replacement**

## Type 2 Diabetes

- Oral medications:
  - Metformin
  - Insulin Sensitizers
    - Thiazolidinediones
  - Insulin Secretagogues:
    - Glinides
    - Sulfonylureas
  - Starch blockers
    - Alpha-glucosidase inhibitors
  - Incretin-based therapy
    - Dipeptidyl peptidase-4 inhibitors
- Injectable medications:
  - Incretin based
  - Amylin analog therapy

# Treatment Strategies for Patients with Type 1 Diabetes



# Insulin Therapy

- Necessary for ALL patients with Type 1 Diabetes
- How it works:
  - Supplements the body's natural insulin hormone that is released from beta cells in the pancreas
  - Helps slow down the liver from producing more glucose
- Many types:
  - Rapid-acting
  - Short-acting
  - Long-acting
  - Combination products
- Many treatment regimens
- Patients will need both a basal and bolus insulin therapy
  - Basal insulin: background insulin to help the patient between meals and through the night
  - Bolus insulin: “meal-time” replacement. Helps to lower glucose after a patient eats a meal



# Amount of Insulin Depends on Many Factors

- Body weight
- Body build (fat & muscle)
- Level of physical activity
- Daily food intake
- Other medications
- Emotions (stress)
- General health
- Smoking

# Rapid-Acting Insulin

- Products:

- Humalog (lispro)
- Novolog (aspart)
- Apidra (glulisine)

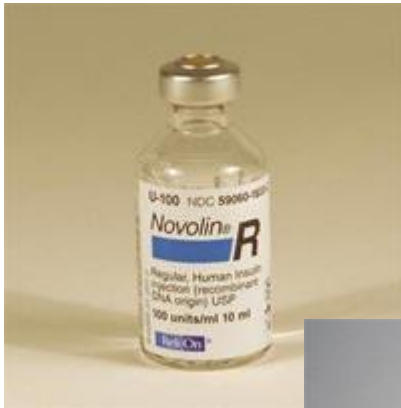


- Onset: 5 to 15 minutes
  - Inject within 15 minutes of a meal (three times per day)
- Peak effect: 1 hour
- Duration of effect: lasts 2 to 4 hours
- Because it is dosed before meals it is used as “bolus” insulin
- Type of insulin used for patients on a continuous subcutaneous insulin infusion (CSII) pump

# Regular Insulin

- Products:

- Humulin R
- Novolin R



- Onset: Begins to work in 30 minutes
  - Inject within 30 minutes of a meal (three times per day)
- Peak effect: 2 to 4 hours
- Duration of effect: lasts 5 to 8 hours
- Because it is dosed before meals it is used as “bolus” insulin

# Insulin NPH

- Products:

- Humulin N
- Novolin N



- Onset: begins to work in 2 to 4 hours
  - Usually injected once or twice daily
- Peak effect: 6 to 10 hours
- Duration of effect: 10 to 16 hours
- Can be used as a basal insulin

# Long-Acting Insulin

- Products:

- Lantus (glargine)
- Levemir (detemir)



- Onset: begins to work in 1 to 2 hours
  - Inject once or twice daily
- Peak effect:
  - Lantus: has no peak effect
  - Levemir: 3 to 9 hours
- Duration of effect: 12 to 24 hours
- Can be used as a basal insulin

# Combination Insulins

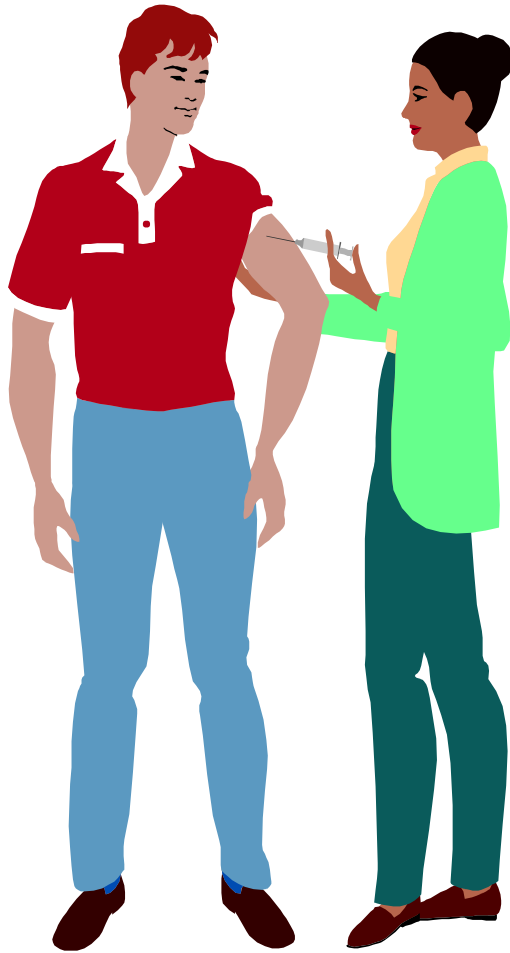
- Rapid-acting + intermediate-acting
  - Humalog Mix 75/25
  - Novolog Mix 70/30
- Short-acting + intermediate-acting
  - Humulin 70/30
  - Novolin 70/30
  - Humulin 50/50
- Inject twice daily 15 minutes before a meal
- Combines bolus and basal insulin into one injection
- Less intense dosing for patients

# Insulin Routines

- Typically start with two injections of insulin per day of two different insulin types and generally will progress to three to four injections per day of different types of insulin
- The types of insulin products used, depend on blood glucose levels
- Studies have shown that more intensive insulin routines (i.e. three to four injections per day) give better glucose control and can prevent or delay the eye, kidney and nerve damage caused by diabetes
- Another insulin routine is the use of an insulin pump (CSII)
  - Delivers insulin 24 hours a day to a patient through a catheter placed under the skin (MOST INTENSE REGIMEN)



# Insulin Injection Sites



- Fastest absorption from the abdomen
  - Slower absorption from the arms and legs
  - Slowest absorption from the buttocks
- Important to rotate injection sites!!!
- Use a new needle with each injection

# Special Considerations

- Storage and Handling:
  - Keep unopened vials and pens in refrigerator
  - Do NOT freeze
  - When opened, can keep at room temperature or in refrigerator
    - Be cautious of specific expiration dates
- Traveling with Insulin:
  - Take more than enough
  - Protect from extreme temperatures
  - Keep in carry-on luggage

# Symlin (Pramlintide acetate)

- Can be used in patients with Type 1 and Type 2 Diabetes in combination with insulin, metformin and sulfonylurea
- How it works:
  - Amylin analog – slows down motility of stomach, turns off appetite, and stops liver production of glucose
- Administer as a subcutaneous injection with meals
  - Do NOT mix in same syringe as insulin
- Side effects: nausea/vomiting, hypoglycemia, weight loss



# Treatment Strategies for Patients with Type 2 Diabetes

# Controlling Type 2 Diabetes

Step 1: Get diabetes education, monitor blood glucose, **make lifestyle changes**

Step 2: Add a medicine, Metformin or blood glucose normalizing medicine

Step 3: Add a second medicine, Insulin or another non-insulin medicine

Step 4: Add a third medicine, Insulin (basal or intensified therapy) or another non-insulin medicine

Step 5: Insulin (intensified therapy) with/without selected medicines



"Jim was diagnosed with diabetes, and his doctor says he needs to keep active, so I hide his TV remote three times a week."

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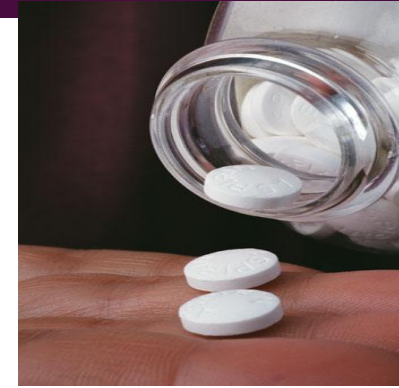
AACE/ACE recommends a treatment algorithm that defines treatment according to A1C levels

# How your Doctor chooses your medication:

- Determine stage of diabetes
- Determine when blood glucose levels are highest
- Cost of medication(s)
- Other medications taken

# Oral Medication Options

- Glucophage (Metformin)
  - Reduce glucose production from liver
- Dipeptidyl peptidase-4 Inhibitors
  - Incretin based pills that help decrease glucose levels
- Thiazolidinediones (glitazones) aka sensitizers
  - Enhance sugar removal from bloodstream
- Insulin releasing pills (secretagogues)
  - Increase insulin release from the pancreas
- Starch blockers
  - Slow starch (sugar) absorption from the gut



# Biguanides



**Metformin is the most commonly prescribed medication for Type 2 Diabetes worldwide**

# Glucophage (Metformin)

- Products:

- \*Glucophage
- \*Glucophage XR
- \*Glumetza
- \*Fortamet

## Combination products

- \*Glucovance
- \*JanuMet
- \*AvandaMet
- \*PrandiMet
- \*Actoplus Met
- \*Metaglip

- How it works:

- Helps to decrease the production of glucose by the liver
- Improves the use of glucose in the tissues

- When to take:

- Regular release: twice a day with meals
- Extended release: once a day with evening meal

- Side effects: metallic taste in mouth, upset stomach, and diarrhea (take with food)

Caution in renal disease!!!

# Insulin Sensitizers



PHOTO: JB REED/BLOOMBERG VIA GETTY IMAGES



## Thiazolidinediones (glitazones/TZD)

# Glitazones

- Avandia  
(Rosiglitazone)
- Actos (Pioglitazone)
- Both products should NOT be used in patients with severe heart failure
- Patients should have liver function monitored
- **New WARNING for Avandia:** patients must enroll into a risk evaluation and mitigation strategy program in order to take this medication
- How they work:
  - Help insulin work better in the muscle and fat
  - Also reduces glucose production in the liver
- When to take:
  - Once daily with or without food
- Side effects: weight gain, heart failure, fluid retention

# Secretagogues



**Sulfonylureas (SU)**  
**Meglitinides (Glinides)**

# Sulfonylureas

- Amaryl (Glimepiride)
- Glucotrol (Glipizide)
- Micronase (Glyburide)
- How they work:
  - Stimulate beta cells of the pancreas to release more insulin
- When to take: 1 to 2 times a day with meals
  - Extended release product: once daily 30 minutes before meal
- Side effects: weight gain, upset stomach, hypoglycemia, skin rash (sulfa allergy)

Caution in renal disease (Amaryl and Micronase)

# Glinides

- Prandin (Repaglinide)
- Starlix (Nateglinide)
- How they work:
  - Stimulate beta cells of the pancreas to release more insulin
- When to take: 1 to 30 minutes before each meal
- Side effects: weight gain, hypoglycemia, headache

# Starch Blockers



**Alpha glucosidase inhibitors**

# Alpha glucosidase Inhibitors

- Precose (Acarbose)
- Glyset (Miglitol)
- How they work:
  - Block the breakdown of starch in the intestines
  - Slows the rise of blood glucose levels after meals
- When to take:
  - Three times a day with first bite of meals
- Side effects: **gas**, abdominal pain and diarrhea

# Incretin Based Therapies



**Dipeptidyl Peptidase-4 (DPP-4) Inhibitors**  
**GLP-1 Analogs**

# DPP-4 Inhibitors

- Onglyza (Saxagliptin)
- Januvia (Sitagliptin)
- How they work:
  - Inhibits the breakdown of hormones (GLP-1) which in turn increases insulin secretion and decreases glucose production
- When to take: once a day with or without food
  - Smaller dose in renal disease
- Side effects: (very minimal) sore throat, runny nose, respiratory infection, pancreatitis

# GLP-1 Analogs

- Byetta (Exenatide)
- Victoza (Liraglutide)
- How they work:
  - Increases insulin secretion (in the presence of glucose) by mimicking the body's natural hormones
  - Slows down motility of stomach, turns off appetite
- When to take:
  - Byetta: twice a day, 1 hour prior to meal
  - Victoza: once a day no specific time
- Side effects: nausea/vomiting, weight loss, hypoglycemia, and Byetta –caution with renal disease)

# Symlin (Pramlintide acetate)

- Can be used in patients with Type 1 and Type 2 Diabetes in combination with insulin, metformin and sulfonylurea
- How it works:
  - Amylin analog – slows down motility of stomach, turns off appetite, and stops liver production of glucose
- Administer as a subcutaneous injection with meals
  - Do NOT mix in same syringe as insulin
- Side effects: nausea/vomiting, hypoglycemia, weight loss



# Insulin Therapy for Type 2 Diabetes

- Most patients may need one injection per day without any diabetes pills
- Some patients may need one injection in the evening in combination with diabetes pills
- Occasionally, diabetes pills quit working, and patients will start to need two injections a day of 2 different types of insulin
  - Patients may progress similarly to patients with Type 1 Diabetes, at this point



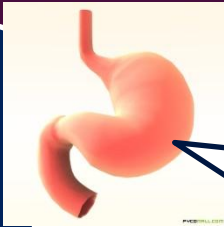
# Review: How Diabetes Pills Work in the Body

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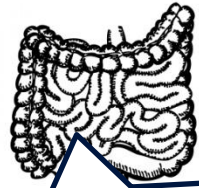


Decreases your appetite: **Byetta, Symlin**

Carbohydrates digested in stomach and turned into sugar  
 • Intestines release GLP-1



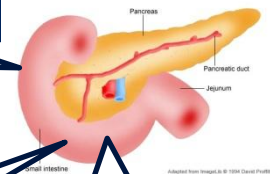
Slow absorption of sugar into the blood stream: **Precose, Glyset, Byetta, Symlin,**



Supplement GLP-1: **Byetta OR** increase GLP-1: **Januvia, Onglyza**

Amylin and GLP-1 work by: slowing down the stomach so sugar doesn't get into blood TOO FAST; Signals the brain to turn off appetite; Keeps the liver from making too much sugar

Pancreas releases insulin and amylin when there is sugar in the blood

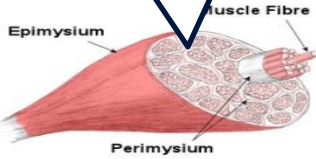


Supplement Insulin: **All insulin products**

Supplement Amylin: **Symlin**

Increase insulin production: **Glucotrol, Amaryl, Glynase, Glipizide, Glyburide, Micronase Prandin, Starlix**

Increase the use of blood sugar by your muscles: **Actos, Avandia, Glucophage**

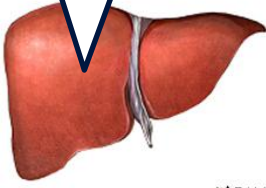


Extra amounts of insulin tell the liver to stop producing sugar

Insulin helps take the sugar from the blood stream into the cells for energy

Decrease sugar production from liver: **Glucophage, Byetta, Symlin, Januvia, Onglyza**

4



# Medication Safety

- Check your blood sugar and keep a log
- Take your drugs exactly as prescribed
- Listen to your body
- Don't use other people's medications
- Tell your doctor about everything you are taking
  - Including OTC, herbs, supplements, and vitamins
- If you take alternative therapies, **NEVER** stop your regular diabetes medicines prescribed by your doctor



# Summary

- Type 1 Diabetes – pancreas does not produce enough insulin
- Type 2 Diabetes - the body cannot use the insulin that is produced and/or it is not producing enough insulin
- There are different treatment options for patients with Type 1 and Type 2 Diabetes
  - Insulin therapy = necessity for ALL patients with Type 1 Diabetes
  - Medication selection for patients with Type 2 Diabetes is dependent upon: disease severity, blood glucose levels, other medicines taken
- Oral diabetes medicines include:
  - Metformin, Insulin sensitizers, Secretagogues, Incretin-based therapy, Starch blocking agents
- Check blood sugar levels frequently
- Take medicines exactly as prescribed!!!

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