

Medications for Diabetes

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Session summary

- **What you (should) already know**
 - Pathophysiology, general epidemiology, and diagnosis of Type 1 & Type 2 diabetes mellitus, diabetes complications
 - Function of insulin, glucagon, glucose, glycogen, and gluconeogenesis
(you can review this information in the supplemental slides provided)
- **What we will discuss today**
 - Effects of exercise on blood glucose levels
 - Different types of insulin and their pharmacokinetics
 - Different classes of medications for diabetes
 - Adverse effects (AE) of diabetes medications
 - Effects of diabetes medications on physical therapy
- **What you should be able to do**
 - Explain appropriate timing of insulin injections with physical therapy
 - Identify which diabetes medications are more likely to cause hypoglycemia
 - Identify major AE associated with classes of DM medications
 - Apply this information to your PT practice

Physical Therapy and Diabetes

- You can have a BIG impact on your patients with diabetes
 - Physical activity can prevent the progression of diabetes and diabetes complications
 - Physical activity can decrease the need for medications
- A patient's diabetes status and medications will change their PT therapy

Low-to-Moderate Intensity Exercise in Patients with Diabetes

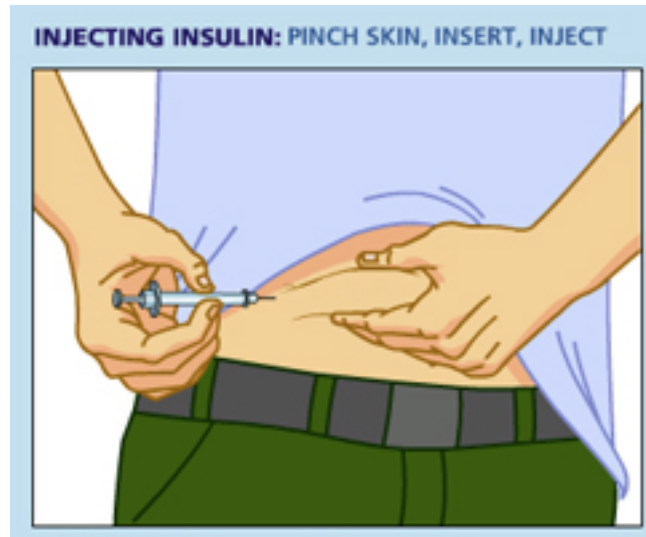
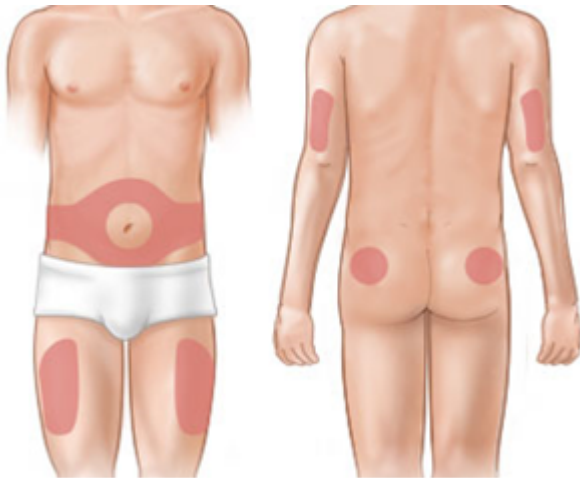
- **Response in non-diabetics**
 - Increased glucose utilization by tissues
 - ↓ insulin secretion
 - ↑ glucagon secretion
 - ↓ blood glucose
- **Response in diabetics**
 - No insulin (Type 1)
 - No effect from insulin
 - ↑ glucagon secretion
 - ↑ blood glucose
 - Too much insulin (recent DM therapy)
 - ↑ glucose into tissues
 - ↓↓ blood glucose

High Intensity Exercise in Patients with Diabetes

- **Response in non-diabetics**
 - ↑ catecholamines (increases BG)
 - ↑ insulin post-exercise (decreases BG)
 - ↔ blood glucose
- **Response in diabetic patients**
 - ↑ catecholamines
 - ↔ insulin
 - ↑ blood glucose

Insulin

- Replaces absent or deficient insulin
- Necessary for Type 1 DM
- May need to be used for Type 2 DM



<http://www.uofmhealth.org/health-library/aa128295>

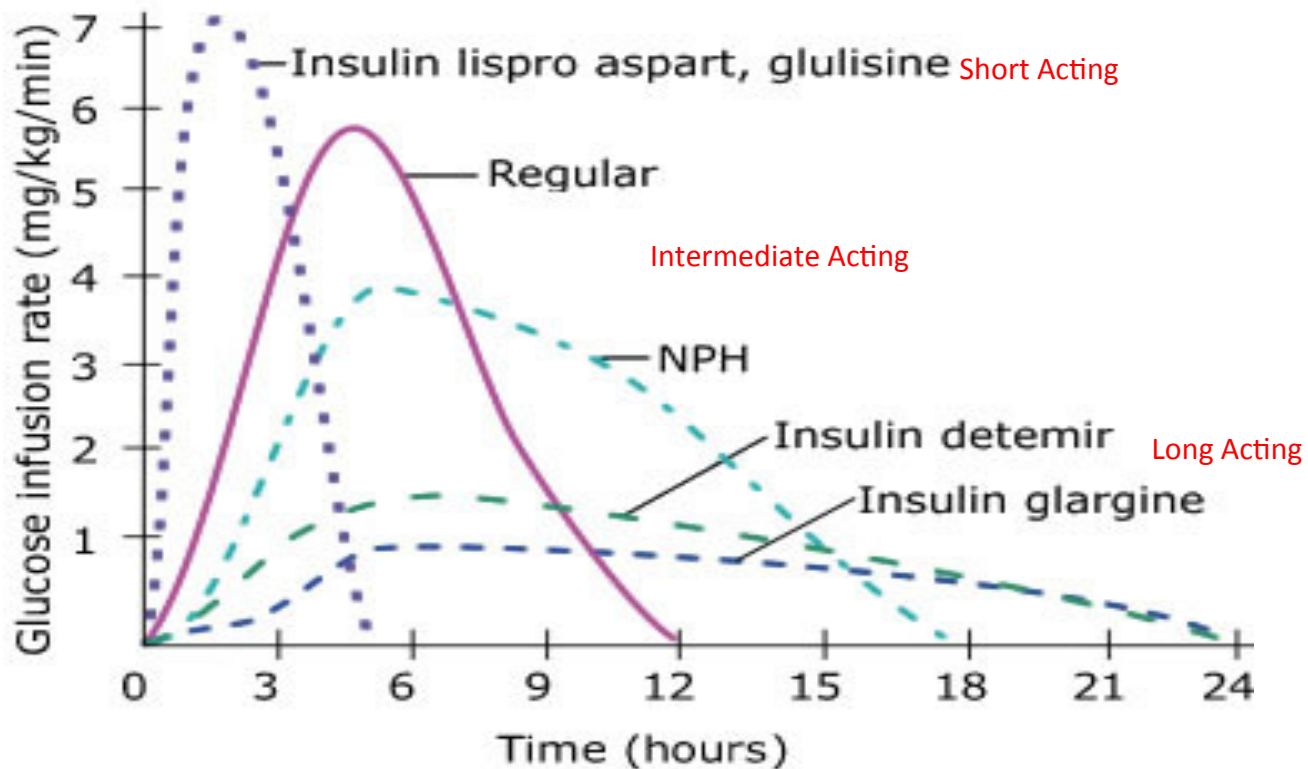
<http://www.bd.com/ca/diabetes/english/page.aspx?cat=14501&id=14757>

<http://www.dupont.com/products-and-services/plastics-polymers-resins/thermoplastics/case-studies/injector-pen-materials.html>

Insulin:

Pharmacokinetics

Activity Profiles of Different Types of Insulin



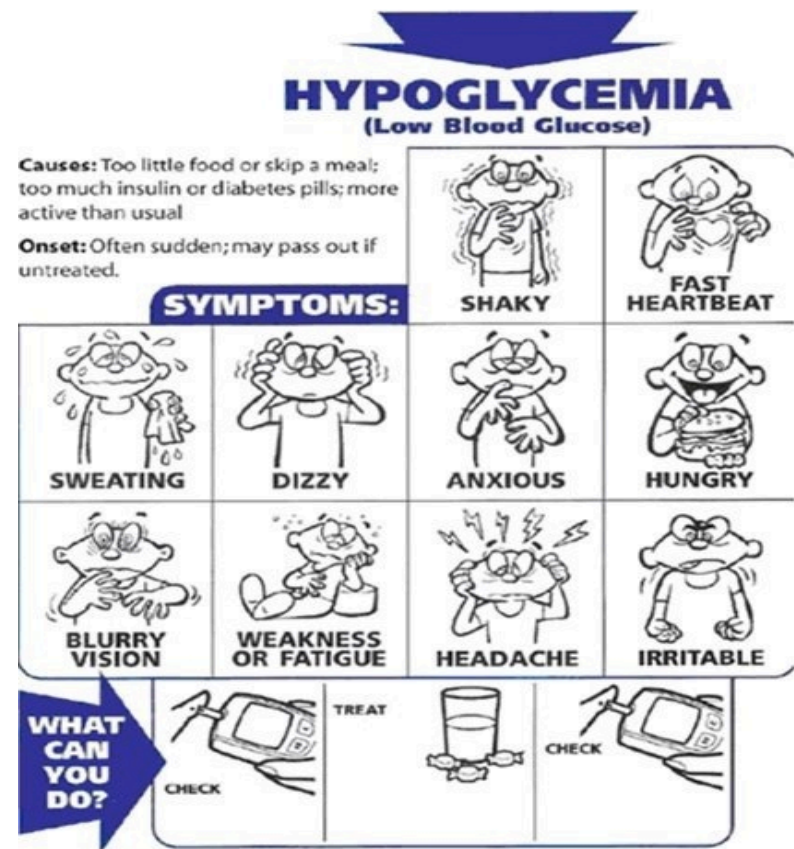
Insulin:

Available Forms

Class	Type	Onset	Peak	Duration
Rapid-acting	regular (human)	30-60 min	2-4 hr	6-8 hr
	glulisine (Apidra®) aspart (Novolog®) lispro (Humalog®)	5-15 min	1-2 hr	3-5 hr
Intermediate	NPH	1-2 hr	6-10 hr	12+ hr
Long-acting	detemir (Levemir®)	1 hr	None (flat)	12-24 hr
	glargine (Lantus®)	1.5 hr	None (flat)	24 hr

Hypoglycemia

- Low blood glucose
- BG < 70 mg/dL
- Symptoms
- **Life-threatening**
- **15-15-15 rule**
 - Take **15g** of sugar
 - Wait **15** minutes
 - Re-test BG
 - If still low, take **15g**
- Glucagon Injection



Diabetic Ketoacidosis (DKA)

- Very **high** blood glucose
- BG > 250 mg/dL and + ketones (bad for the brain!)
- **Life-threatening**
- Causes
 - Non-adherence to diabetes meds
 - Infection/illness
 - Medications
- Symptoms
 - Altered mental status (confusion-> coma)
 - Polydipsia, polyuria
 - Nausea, vomiting
 - Fruity breath
 - Shortness of breath
- **Send them to the ED**



Insulin:

Clinical Relevance in Physical Therapy

- Patients who have **low** levels of insulin may have worsening **hyperglycemia** during low-to-moderate intensity exercise
- Patients who have **high** levels of insulin may experience **hypoglycemia** during low-to-moderate intensity exercise
- High intensity exercise can lead to **hyperglycemia**
- Best to **avoid insulin injections** right before physical therapy sessions
- Each patient can have a different response!

Biguanide Antidiabetic

metformin (Glucophage®)

- **Mechanism**

- ↓ hepatic glucose output
- ↑ insulin sensitivity in peripheral tissues/
muscles

- **Adverse effects**

- GI symptoms (diarrhea, abdominal cramping)
- Lactic acidosis (rare but serious)

Sulfonylureas (SFUs)

glipizide, glyburide, glimepiride

- The gli(y)-ides
- **Mechanism**
 - ↑ *insulin secretion*
 - ↓ hepatic glucose output
- **Adverse effects**
 - *Hypoglycemia*
 - Weight gain

Non-Sulfonylurea Insulin Secretagogues

nateglinide, repaglinide

- The -glinides
- Mechanism
 - ↑ *insulin secretion*
 - Only active in the presence of glucose
 - Very short acting
- Adverse effects
 - Hypoglycemia
 - Weight gain

Thiazolidinediones (TZDs) *pioglitazone (Actos[®]), rosiglitazone*

- The –glitazones
- **Mechanism**
 - ↑ peripheral insulin sensitivity
 - ↓ hepatic glucose output
- **Adverse effects**
 - Fluid retention (be careful in heart failure!)
 - Weight gain
 - ↑ risk of **bone loss & fractures**

α -Glucosidase Inhibitor *acarbose*

- **Mechanism**

- Delays CHO digestion
- Slows glucose absorption in small intestine

- **Adverse effects**

- GI symptoms



Glucagon-like Peptide-1 (GLP-1) Analogs

exenatide (Byetta[®], Byureon[®])

- **Mechanism**
 - ↑ insulin secretion post-prandial
 - ↓ glucagon post-prandial
- **Adverse effects**
 - GI symptoms
 - Hypoglycemia (worse in combo with SFU)
 - Pancreatitis (*rare*)
 - Increased heart rate
- **Weight loss**
- **Injected subcutaneously before meals**



Dipeptidyl Peptidase IV (DPP-IV) Inhibitors

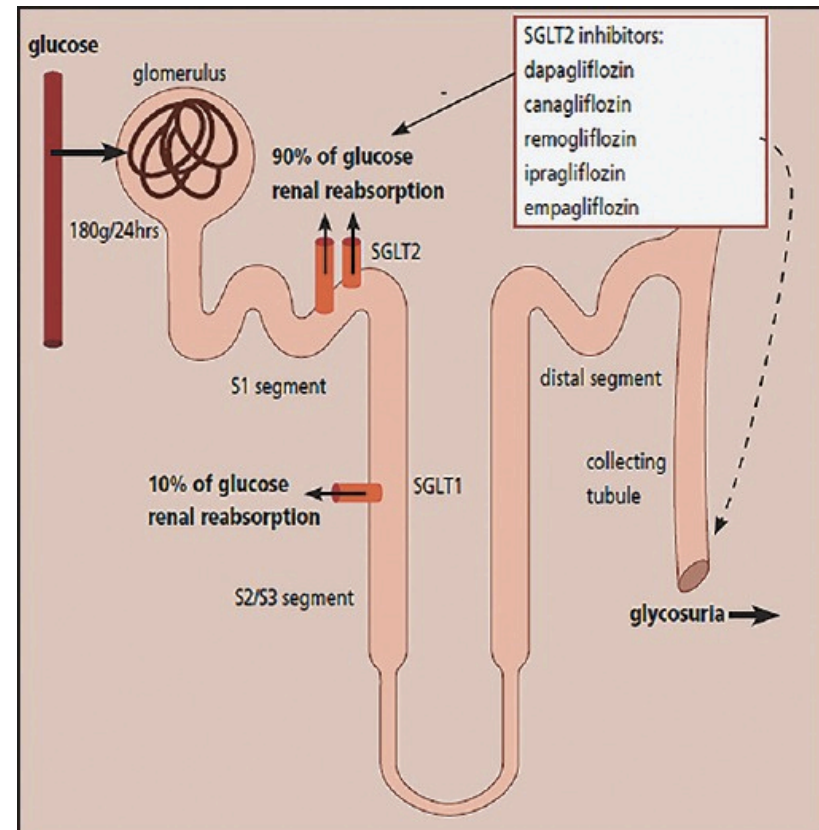
sitagliptin (Januvia[®]), saxagliptin, etc.

- The -gliptins
- Mechanism
 - Delays breakdown of GLP-1
- Adverse effects
 - Weight neutral
 - Nausea/diarrhea/constipation (minimal)
 - Hypoglycemia (minimal)
 - Pancreatitis (*rare*)

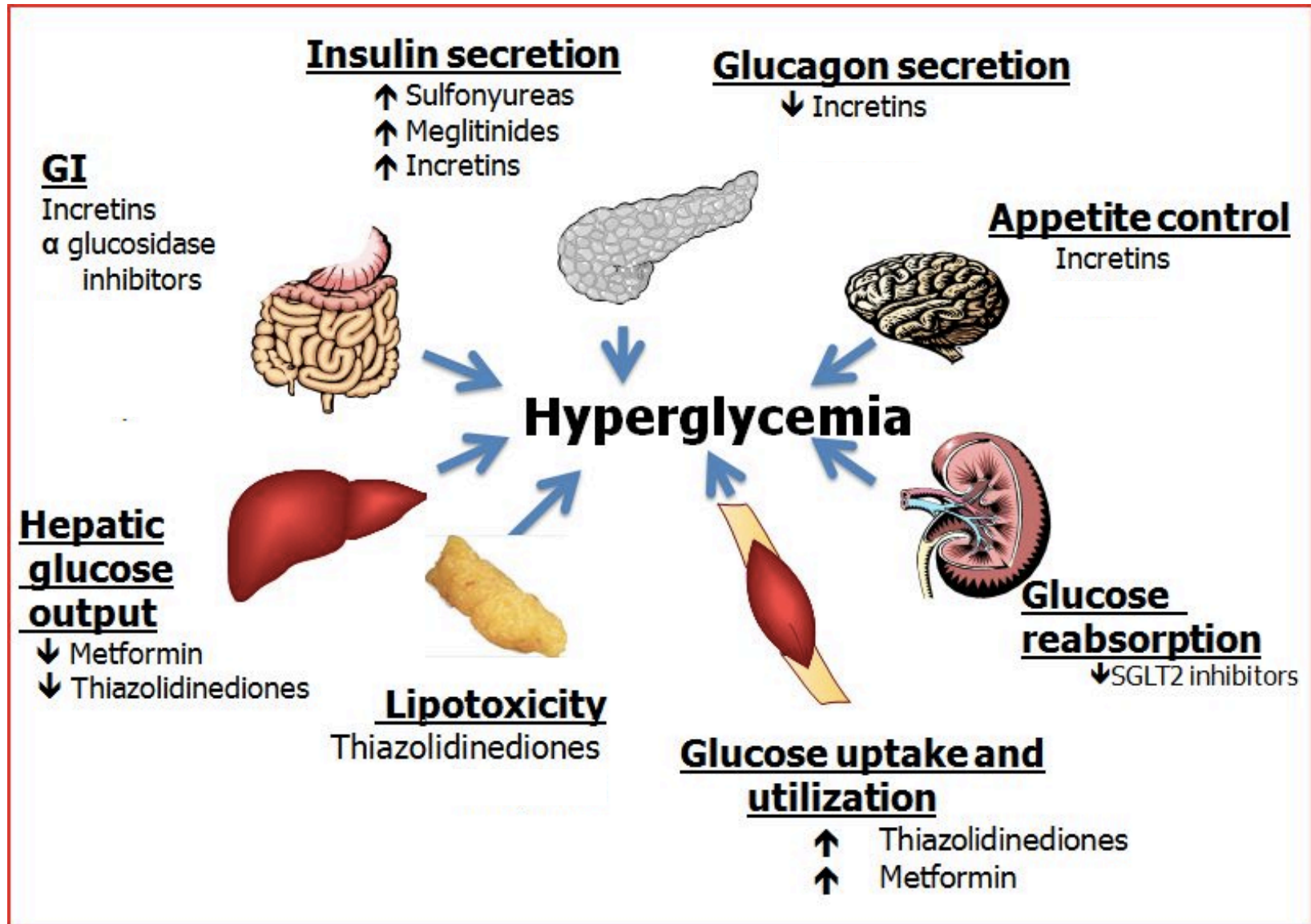
Sodium-Glucose Cotransporter 2 (SGLT-2) Inhibitors

canagliflozin(Invokana[®]), dapagliflozin, empagliflozin

- The –glifozins
- **Mechanism**
 - Inhibits reabsorption of glucose in kidney
 - Promotes excretion of glucose in urine
- **Adverse effects**
 - Hypotension
 - Hyperkalemia
 - Genitourinary infections
 - Polyuria

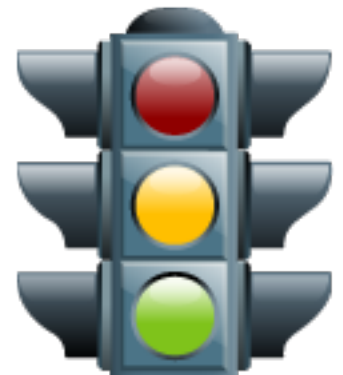


Overview of Treatments



Overview of Treatments

- **High** risk of hypoglycemia
 - Insulins
 - Sulfonylureas (gli(y)-ides)
 - Non-SFU insulin secretagogues (-glinides)
- **Medium-Low** risk of hypoglycemia
 - GLP-1 analogs (exenatide) ***unless in combo w/SFU***
 - DPPIV inhibitors (-gliptins)
- **Low-No** risk of hypoglycemia
 - Metformin
 - Thiazolidinediones (-glitazones)
 - Acarbose
 - SGLT-2 Inhibitors (-glifozins)



Diabetes Medications:

Clinical Relevance in Physical Therapy

- Exercise and PT can prevent and/or treat complications of DM (peripheral neuropathy, retinopathy, stroke, etc.)
- Patients with long-standing DM should have lower target heart rates
- Certain diabetes medications can put patients **at higher risk for hypoglycemia**
- Medications should be **timed appropriately** with PT treatments to **minimize the risk of hypoglycemia**

Diabetes Medications:

Clinical Relevance in Physical Therapy

- Hypoglycemia can be acutely **life-threatening** and all healthcare professionals should be aware of how to treat a hypoglycemic episode
- Poor glycemic control can result in blunted ANS warning symptoms (unusually rapid heartbeat, chest pain, etc.)
- Neuropathy due to diabetes can lead to a decreased pain sensitivity, leading to a higher risk of injury during exercise
- Patients with diabetic neuropathy may have foot injuries (ulcers, etc.) they are not aware of, feet should be checked before exercise
- Adverse effects of these medications could affect PT treatments

Questions?



References

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