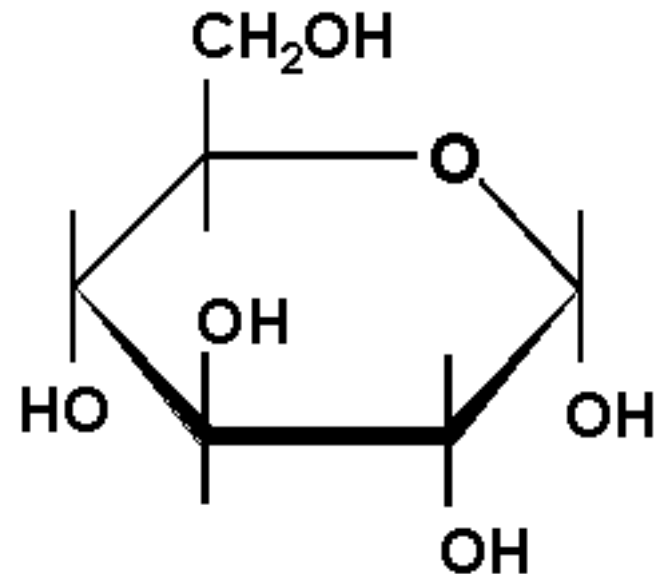
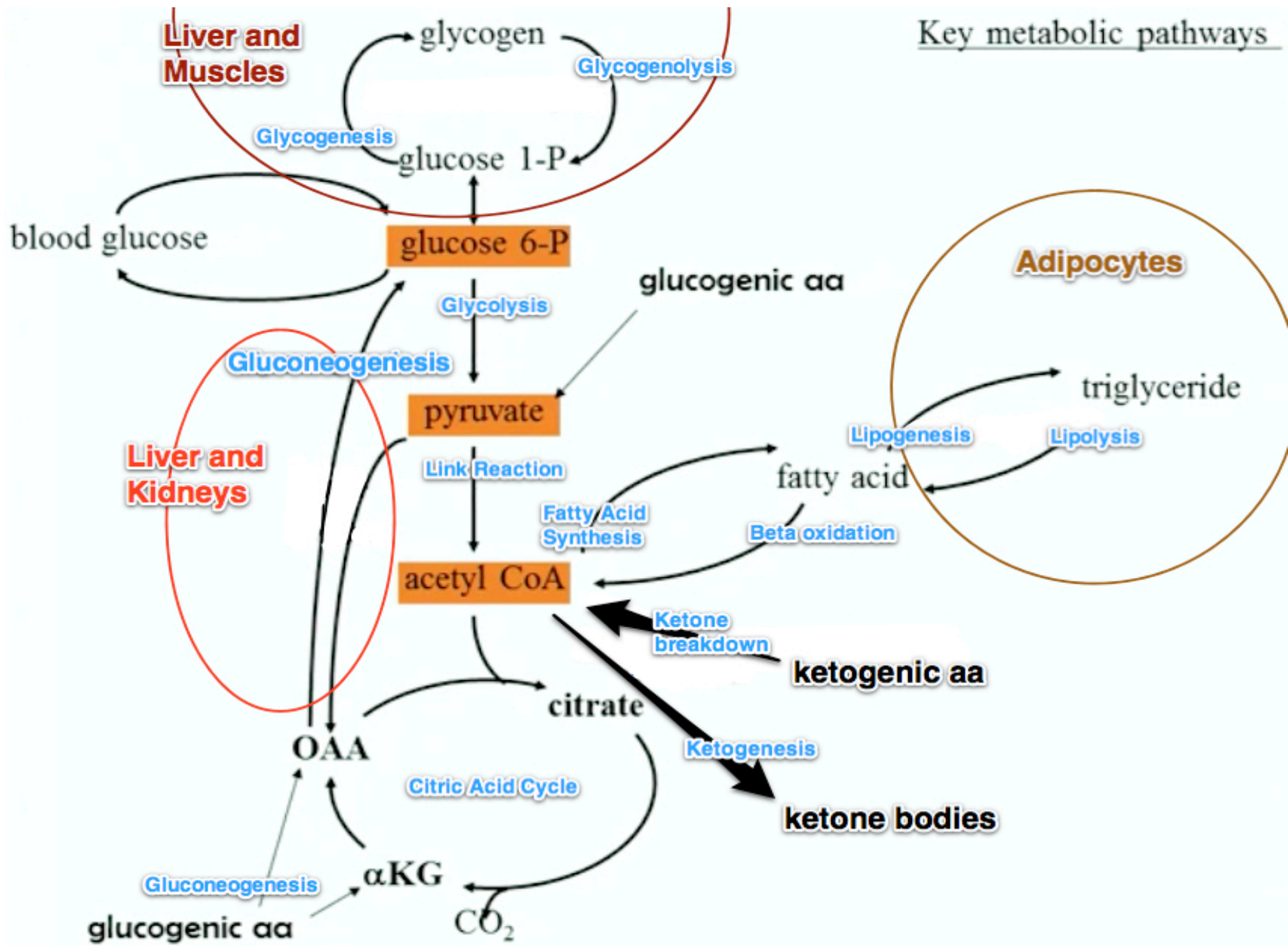


Week 4-Glucose Metabolism and Pharmacology



Key metabolic pathways



When the system goes awry...

- Type-1 diabetes (juvenile onset)
 - Autoimmune reaction against the insulin-producing beta cells of the pancreas
 - No insulin can be produced
- Type-2 diabetes (adult onset)
 - Increased resistance to insulin in the muscles, liver, and adipose tissue in addition to decreased insulin production from pancreatic beta cells

Classes of Anti-Diabetic Drugs

- Insulin
- Sensitizers (decrease insulin resistance)
- Sulfonylureas (directly increase insulin output from the pancreas)
- Alpha-Glucosidase Inhibitors (slows starch digestion in the small intestine)
- Peptide Analogs (indirectly increase insulin output from the pancreas)

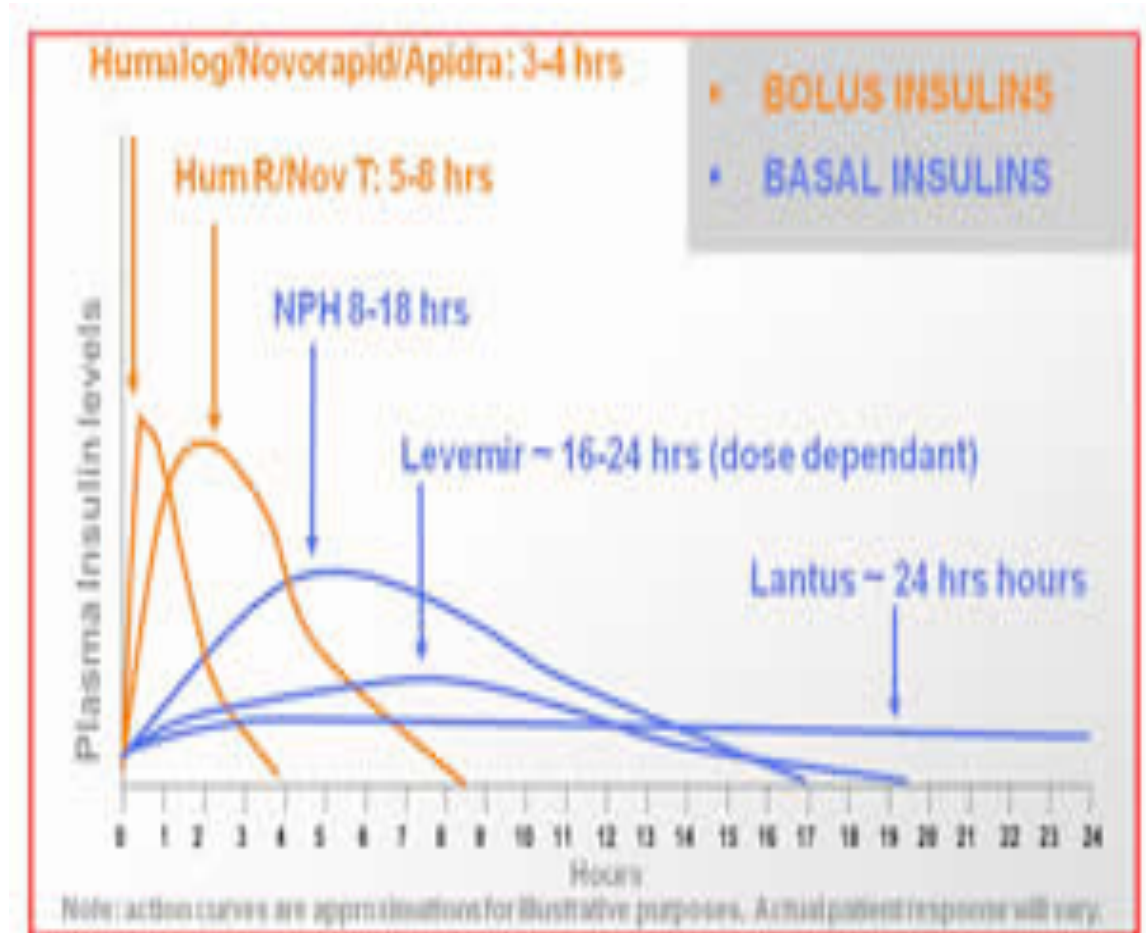
Insulins

- Fast-acting (e.g. Humalog, Novalog)
- Intermediate-acting (e.g. Humulin, Novolin)
- Slow-acting (e.g. Lantus, Levemir)
 - This class of insulin analogs is created as insulin microcrystals, which will slowly release insulin and mimic the pancreas' basal production of insulin

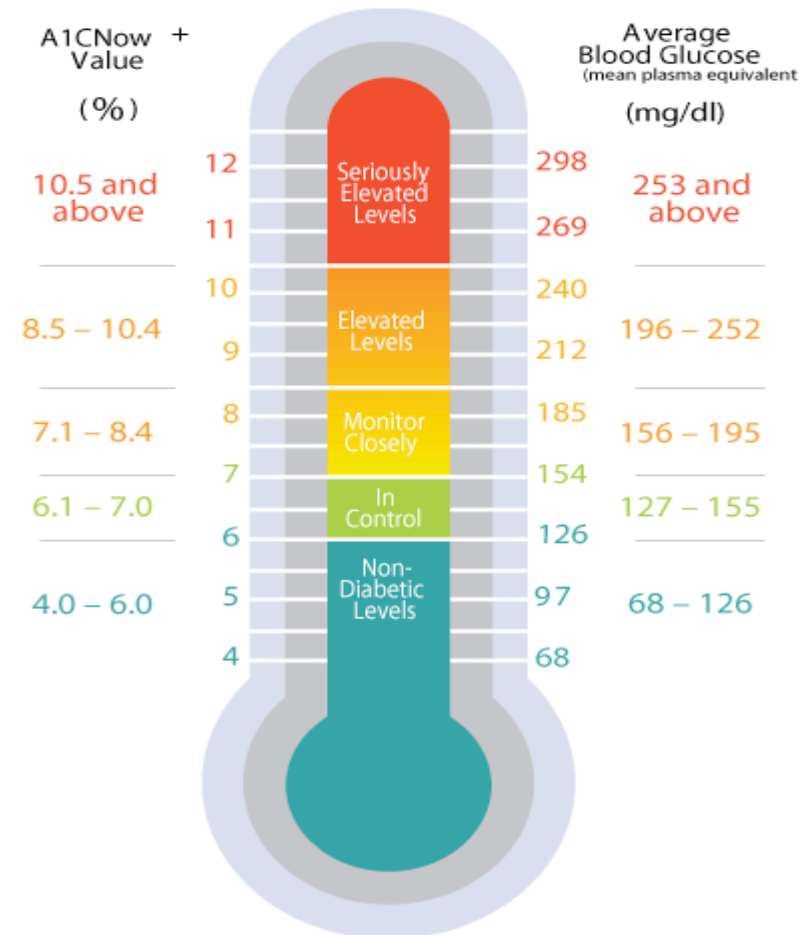
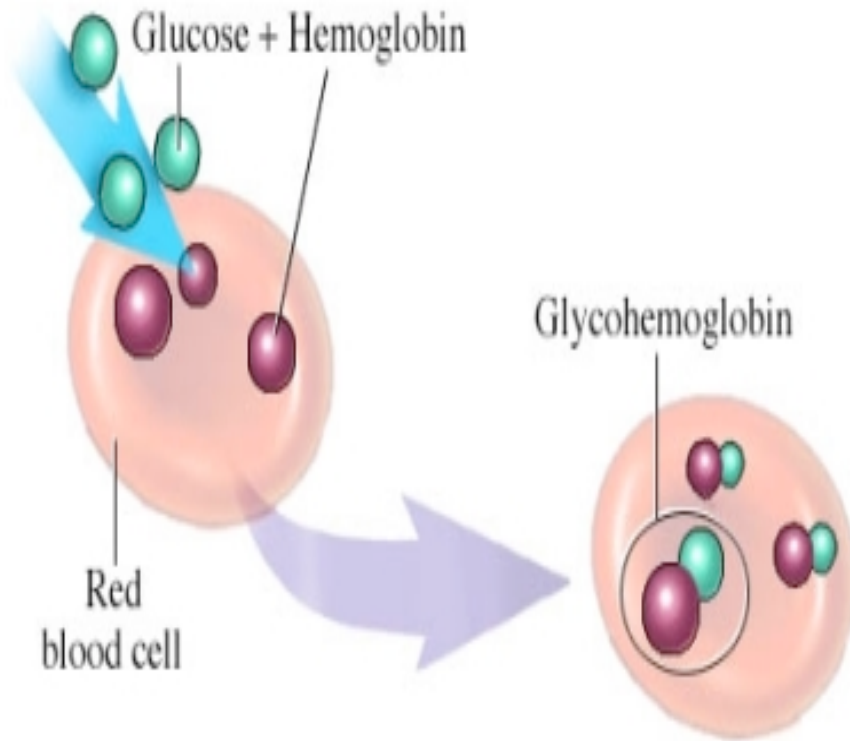
Basal vs. Bolus Insulins

Basal Insulins are designed to work slower over a long period of time.

Bolus Insulins are designed to work faster over a small period of time (typically post-meal).



Hemoglobin A1C Test



<http://guardianlv.com/2013/10/blood-sugar-levels-may-affect-hippocampus-and-memory-says-study/>

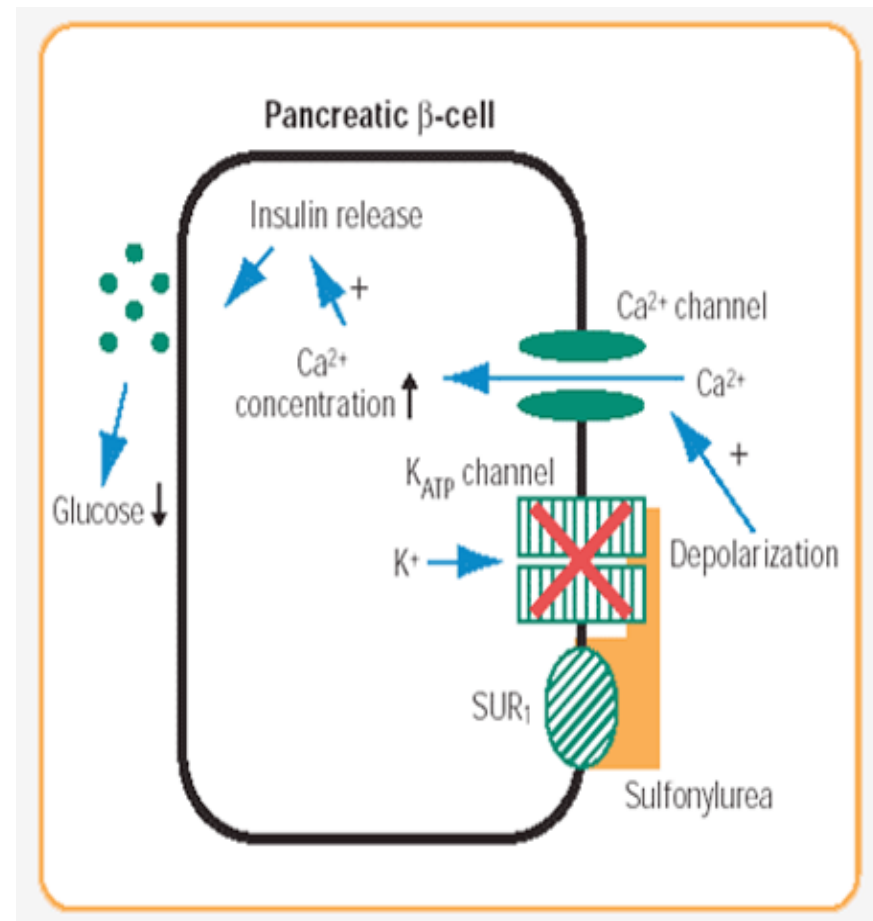
<http://drugline.org/medic/term/a1c/>

Sensitizers

- Biguanides (e.g. Metformin)
 - Complete mechanism not understood, but decreases hepatic gluconeogenesis and peripheral insulin resistance by increasing AMPK signaling
 - Typical A1C decrease from 1.5-2%
- Thiazolidinediones (e.g. Pioglitazone)
 - Agonists for PPARs, which are regulatory proteins for genes involved in glucose metabolism, resulting in more efficient glucose usage
 - Typical A1C decrease from 1.5-2%

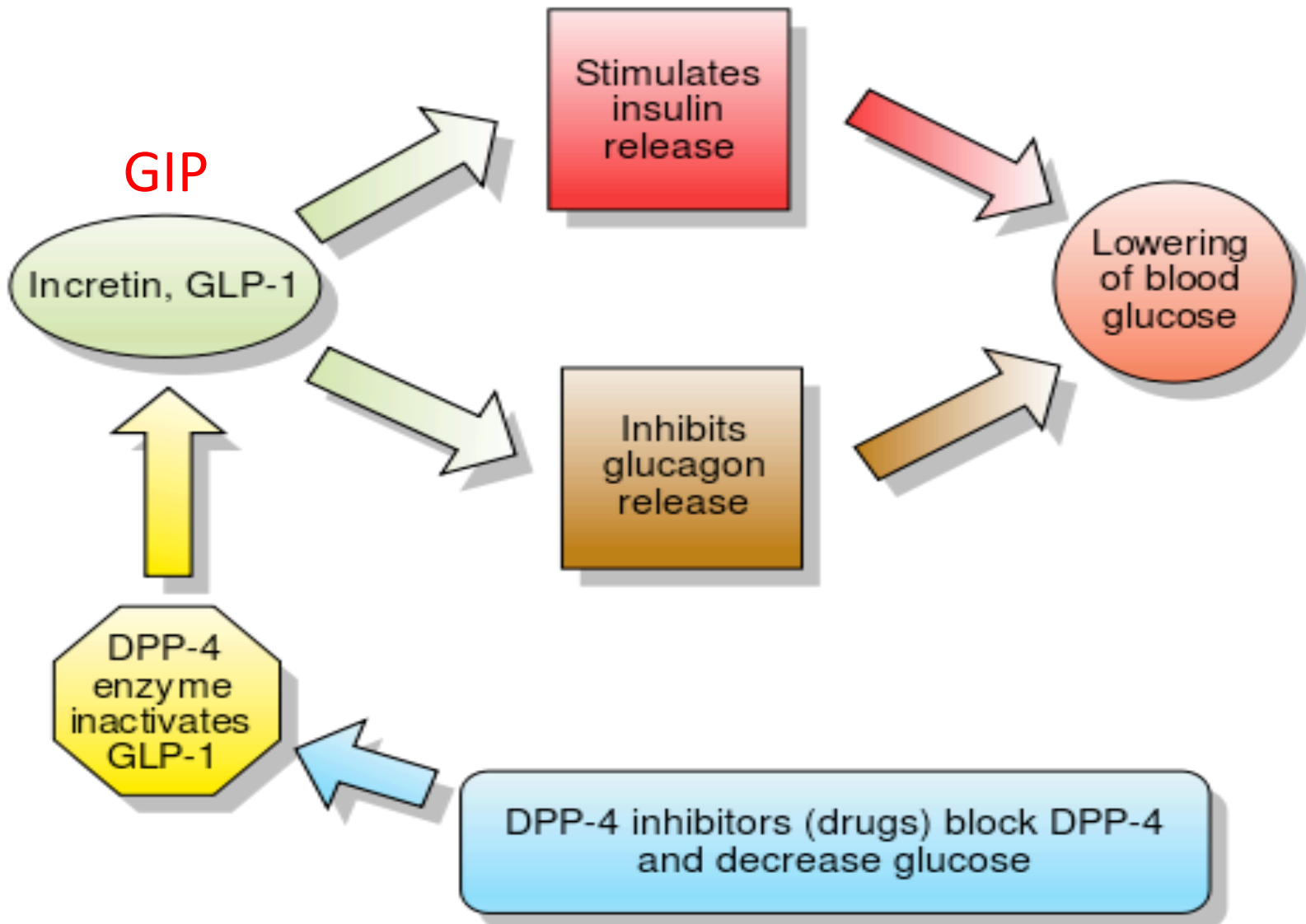
Sulfonylureas (e.g. Glimepiride, Glyburide)

- Block K-ATP channels on beta cells
- Prevents hyperpolarization and activates Ca²⁺ channels
- Stimulates insulin vesicle exocytosis
- Typical A1C decrease from 1-2%



Alpha-Glucosidase Inhibitors

- Ex. Acarbose, Miglitol, etc.
- Saccharides that act as competitive inhibitors of the enzyme located on the brush border of the small intestine
- Slows the digestion and metabolism of carbohydrates
- Typical A1C decrease from 0.5-1%



https://en.wikipedia.org/wiki/File:Incretins_and_DPP_4_inhibitors.jpg

Peptide Analogs

- GLP Agonists (e.g. Byetta, Victoza)
- GIP Agonists (in trial phases)
- DPP-4 Inhibitors (e.g. Januvia, Onglyza)
- Typical A1C decrease from 0.5-1%