Measures have been taken, by the Utah Department of Health, Bureau of Health Promotions, to ensure no conflict of interest in this activity.

CNE/CPE/CEU’s are available for this live webinar. You must take the pre and post tests. 80% is required on the post test to receive CNE/CPE/CEU’s.

Certificates will be emailed out to you.
You will receive the post test link in your email after a hour after the webinar.

Diane Bezzant Ogborn, PharmD

Diane Bezzant Ogborn, PharmD, is a pharmacist with Smith's Food and Drug. She is a staff pharmacist, clinical team member, and primary residency preceptor. She earned her pharmacy doctor degree at the University of Utah College of Pharmacy. Diane completed a PGY1 Community Practice Residency with University of Utah HealthCare where she provided diabetes education and medication management through collaborative practice. Diane provides diabetes coaching for Kroger employees at Smith's. Diane is a trained faculty presenter in the "The Pharmacist and Patient-Centered Diabetes Care".

When not at work, Diane likes to read, fish, laugh, and hang out with family members. And ride her "moto". In November 2015, Diane was blessed to be part of a two-week medical mission providing health care for some amazing people in Haiti.

Medications for Treating Type 2 Diabetes

Diane Bezzant Ogborn, PharmD
February 17, 2016

Objectives

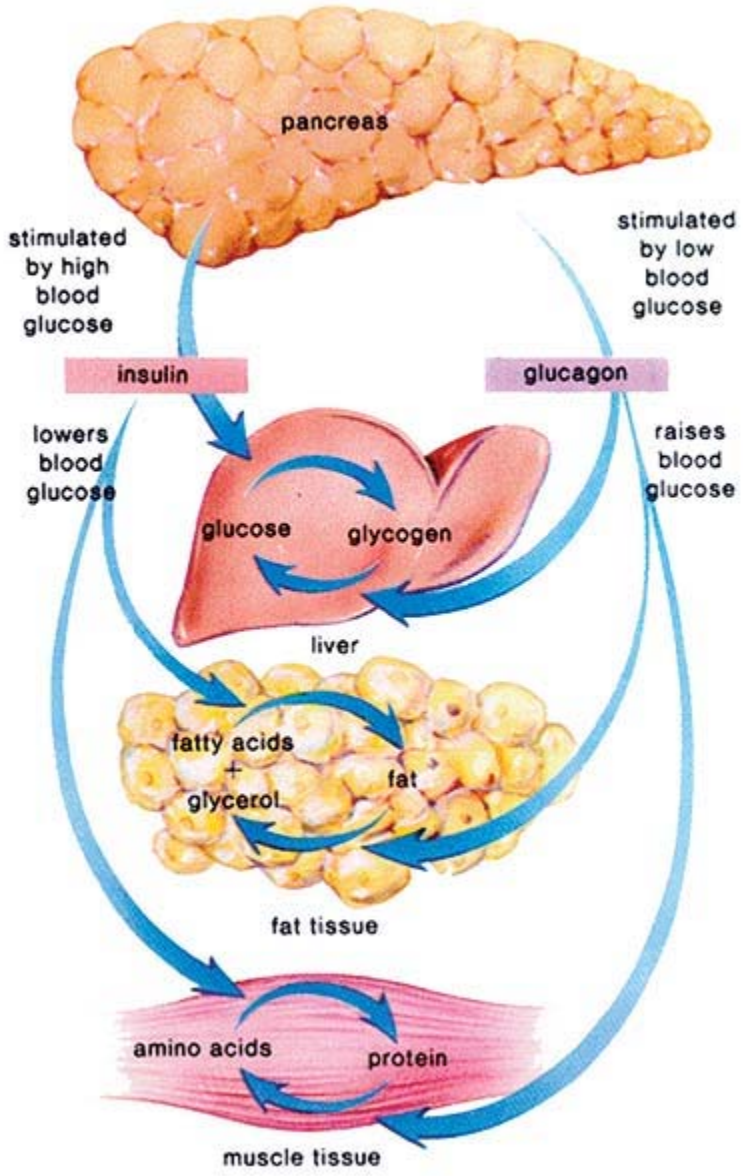
1. Explain the basic pathogenesis of Type 2 Diabetes Mellitus (T2DM)
2. List the classes of medications used to treat T2DM
3. State the main points of the American Diabetes Association (ADA) medication treatment recommendations for T2DM

Objectives

4. For each class of medication:
   - On a single drawing, identify the main target organ(s) affected or mechanism of action
   - Place diabetes medications into the appropriate medication class by generic name
   - State significant side-effects of each medication class
   - Give a rough estimate of the cash price for one month of medication in the class

Blood Glucose Balance

Insulin and glucagon work to balance glucose levels in the blood stream



http://healthwise-everythinghealth.blogspot.com/2012_03_01_archive.html

Pathogenesis of Type 2 Diabetes Mellitus

+**Insulin Resistance** in the body tissues

+Relative impairment of **Insulin Secretion**

+Pancreas **β-cell Function Decline**

+Higher levels of blood glucose (**Hyperglycemia**)

=Type 2 Diabetes Mellitus

Stumvoll M, Goldstein BJ, van Haeften TW. Type 2 diabetes: principles of pathogenesis and therapy. Lancet. 2005 Apr 9-15;365(9467):1333-46. Review. PubMed PMID: 15823385.

Pathogenesis of Type 2 Diabetes Mellitus

Associated with:

- older age
- obesity
- race
- ethnicity
- family history of diabetes
- impaired glucose metabolism
- physical inactivity

http://www.gpha.org/assets/CELESSONS/treatment%20of%20hyperglycemia%20in%20type%202%20diabetes.pdf

Medication Classes
Type 2 Diabetes Mellitus

- Biguanides
- Sulfonylureas
  - First-Generation
  - Second-Generation
- Incretin-based Drugs
  - Glucagon Like Peptide-1 (GLP-1) Agonists
  - Dipeptidyl Peptidase-4 (DPP4) Inhibitors

Medication Classes
Type 2 Diabetes Mellitus

Sodium Glucose Cotransporter-2 (SGL2) Inhibitors

Thiazolidinediones (TZDs)

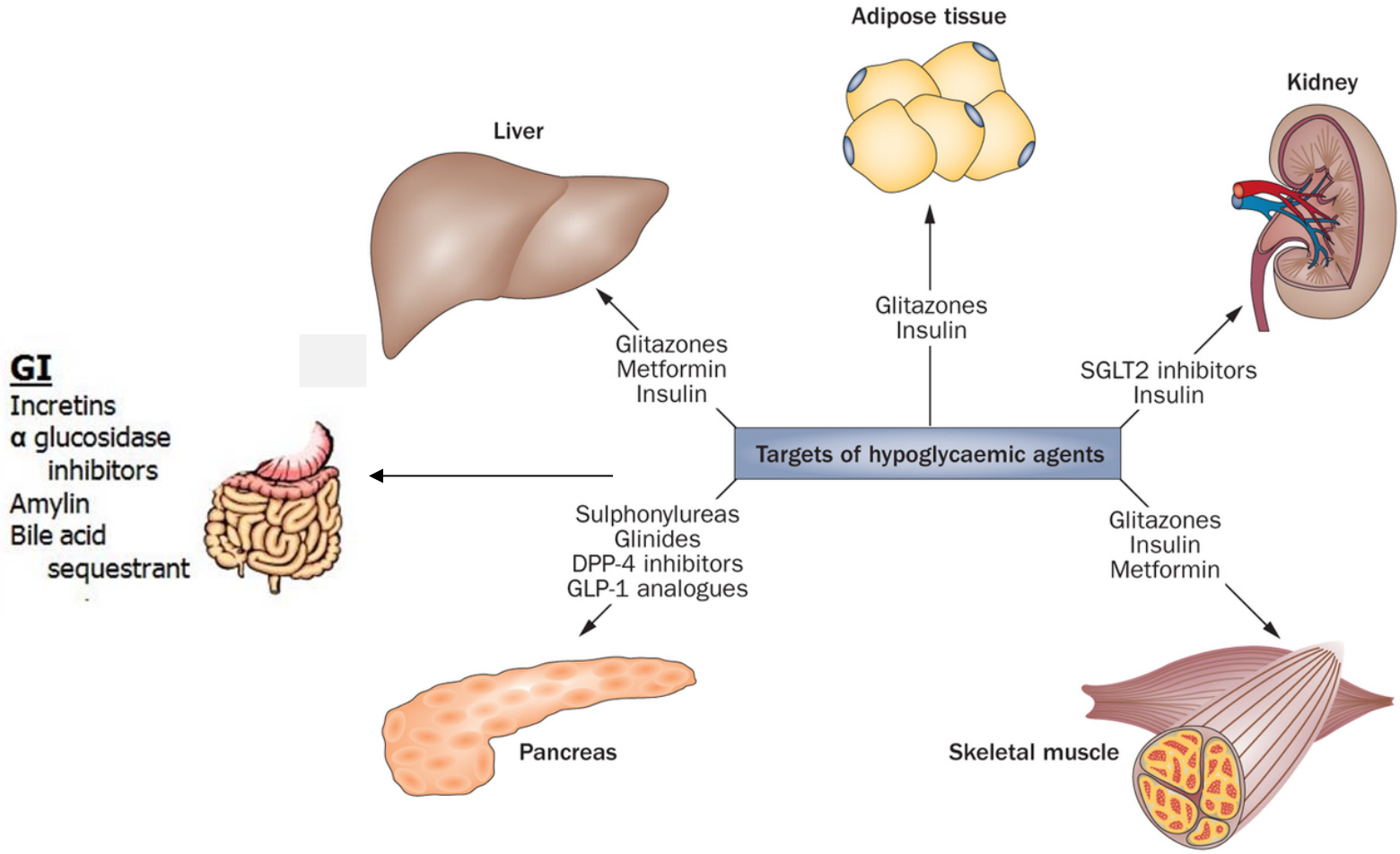
Meglitinides

α-Glucosidase Inhibitors

Insulins

- Long-acting
- Short and rapid-acting

Diabetes Medications Target Organs



Jenssen T, Hartmann A. Emerging treatments for post-transplantation diabetes mellitus; Nature Reviews Nephrology 11, Pages:465–477 Year published: (2015) doi:10.1038/nrneph.2015.59

Target Sites of Action for Drugs Used to Treat T2DM

Organ	Major Effect	Minor Effect
Pancreas	Insulin	Sulfonylureas Meglitinide Analogues GLP-1 Agonists
Liver	Metformin	TZDs
Muscle	TZDs	Metformin
Adipose	TZDs	Metformin

Diabetes Care. 1999; 22(Supp 3)C1—3.

Target Sites of Action for Drugs Used to Treat T2DM

Organ	Major Effect	Minor Effect
Gastro-intestinal Tract		GLP-1 Agonists DPP-IV Inhibitors α-Glucosidase Inhibitors
Brain (Satiety Center)		GLP-1 Agonists
Kidney		SGLT-2 Inhibitors

Diabetes Care. 1999; 22(Supp 3)C1—3.

ADA Guidance

- There are several drug classes for treating Type 2 Diabetes Mellitus.
- The American Diabetes Association (ADA) has established clinical practice recommendations regarding medication therapy for treating Type 2 Diabetes Mellitus

Diabetes Care, 2015, Volume 38, Supplement 1: pp S41-S48.

The ADA recommends a patient-centered approach regarding the choice of pharmacological agents.

- Efficacy
- Cost
- Weight
- Comorbidities
- Potential side effects
- Hypoglycemia risk
- Patient preferences

Diabetes Care, 2015, Volume 38, Supplement 1: pp S41-S48

Biguanides: Metformin

Major Target: Liver

Minor Targets: Skeletal Muscle, Adipose Tissue

Biguanides:
Pharmacology

Description: Insulin sensitizer

Helps insulin action by lowering blood glucose

Does not increase insulin secretion

Major Target Organ: LIVER

Clinical Effect:

Reduces fasting blood glucose by 60 mg/dL

Lowers A1C by 1.5%

http://www.gpha.org/assets/CELESSONS/treatment%20of%20hyperglycemia%20in%20type%202%20diabetes.pdf

Metformin:
Pharmacology

Mechanism of Action:

Liver: reduces glucose production in the liver

reduces fatty liver

Muscle: increases rate of stored glucose

Adipose: increases lipolysis

Polycystic Ovary Syndrome: restores ovarian function

http://www.gpha.org/assets/CELESSONS/treatment%20of%20hyperglycemia%20in%20type%202%20diabetes.pdf;
http://diabetes.diabetesjournals.org/content/51/7/2074.short

Metformin:
FDA Approved Indications

Type 2 Diabetes Mellitus

Most widely used first-line drug

Polycyclic Ovary Syndrome (PCOS):

- Ovaries develop small collections of fluids and may fail to release eggs.
- Frequent or prolonged menstrual periods or
- excess male hormone (androgen) levels.

http://www.gpha.org/assets/CELESSONS/treatment%20of%20hyperglycemia%20in%20type%202%20diabetes.pdf; http://www.mayoclinic.org/diseases-conditions/pcos/multimedia/polycystic-ovary-syndrome/img-20007768

Metformin:
Benefits

Solid evidence of safety and efficacy

Often leads to weight reduction or weight stabilization

May reduce cardiovascular events

Modest effect on reducing dyslipidemia

Does not cause hypoglycemia

Inexpensive drug

http://www.gpha.org/assets/CELESSONS/treatment%20of%20hyperglycemia%20in%20type%202%20diabetes.pdf

Metformin:
Side Effects

Gastrointestinal (20%)

- Lack of appetite
- Nausea
- Abdominal cramping
- Diarrhea

The effects can be minimized by gradually increasing dose based on gastrointestinal symptoms

Extended Release tablets may reduce GI side effects

Am J Health-Syst Pharm, April 15, 1997; 54: 893-903

Local Utah Prices January 2016: Metformin

Generic Drug	*Quantity*	*Cheapest Cash Price*
Metformin 500 mg	120 tablets	$8
Metformin 1000 mg	60 tablets	$4
Metformin ER 500 mg	120 tablets	$8
Metformin ER 1000 mg	60 tablets	$1,473

Smith's, Costco, Walmart

Metformin: Contraindications

Renal disease

Hepatic disease

Alcoholism

Conditions associated with hypoxia:

(eg. cardiac and pulmonary disease, surgery)

Can cause lactic acidosis (build up of lactate in blood) but this is a RARE occurrence

http://www.medsafe.govt.nz/profs/PUarticles/5.htm

Metformin:
When to Withhold:

Temporarily hold metformin with the potential of affecting renal function:

- IV administration of iodinated contrast media
- Severe infection
- Shock

http://www.australianprescriber.com/magazine/37/1/2/5

Sulfonylureas (SU)

Target: Pancreas

Sulfonylureas
Pharmacology

History: Oldest class of oral hypoglycemic drugs

Target Organ: PANCREAS

Clinical Effect:

Decreases fasting blood glucose by 50 to 60 mg/dL

A1C reduction: 1% to 2%

http://www.gpha.org/assets/CELESSONS/treatment%20of%20hyperglycemia%20in%20type%202%20diabetes.pdf

Sulfonylurea: Indications

FDA approved indications:

Type 2 Diabetes Mellitus

Neonatal Diabetes (permanent)

(usually the second-generation Sulfonylurea are used for therapy)

Sulfonylurea Pharmacology

Mechanism of action: stimulates the beta (β) cells of the pancreas to release insulin.

- Depends on the presence of functioning β cells
- 5 % to 20% of patients will experience failure within 1 to 2 years due to β-cell failure

http://www.gpha.org/assets/CELESSONS/treatment%20of%20hyperglycemia%20in%20type%202%20diabetes.pdf;

Sulfonylurea Pharmacology

Two generations of sulfonylurea

Main difference between these generations is in the way they are eliminated from the body.

First Generation: usually eliminated through kidneys

Second-Generation:

- Preferred when there is poor function of the kidneys
- More commonly prescribed

Both equally efficacious when dosed correctly

http://www.medicinenet.com/script/main/art.asp?articlekey=18045

Local Utah Pricing January 2016
Sulfonylureas: First Generation

Generic Drug	*Quantity*	*January 2016 Cheapest Price*
Chlorpropamide		
100 mg	60	$8
250 mg	60	$132
Tolazamide 250 mg	60	$140
Tolbutamide 500 mg	60	$71

Smith's, Costco, Walmart

Local Utah Pricing January 2016
Sulfonylureas: Second Generation

Generic Drug	*Quantity*	*Cheapest Cash Price*
Glyburide 2.5, 3, 5, or 6 mg	60 120 240	$8 $13 $27
Glimepiride 4 mg 2 mg 1 mg	30 60 120	$4 $8 $13
Glipizide 5 mg or 10 mg XL 5 mg or 10 mg	30 60 60	$4 $8 $17-$20

Smith's, Costco, Walmart

Sulfonylurea:
Side Effects

Hypoglycemia!

- This is why you may need to give glucagon
- Higher with long-acting sulfonylureas
  - i.e., chlorpropamide and glyburide
- When a patient is fasting, sick, or doesn't eat

Decreased effectiveness over time

Gastrointestinal upset

Weight gain

Photosensitivity

Sulfa allergy? Generally not an issue

http://www.gpha.org/assets/CELESSONS/treatment%20of%20hyperglycemia%20in%20type%202%20diabetes.pdf

Sulfonylurea: Contraindications

- Pregnancy/Breast feeding
- Type 1 Diabetes Mellitus
- Elderly and Liver disease
- Liver and kidney disease
- Person debilitated
- Person malnourished
- Presence of adrenal or pituitary insufficiency

The “Incretin Effect”

Incretins

Target: Gastrointestinal Tract, Satiety Center in Brain

Incretin-Based Drugs

- GLP-1 Agonists
- DPP-4 (Enzyme) Inhibitors

The “Incretin Effect”

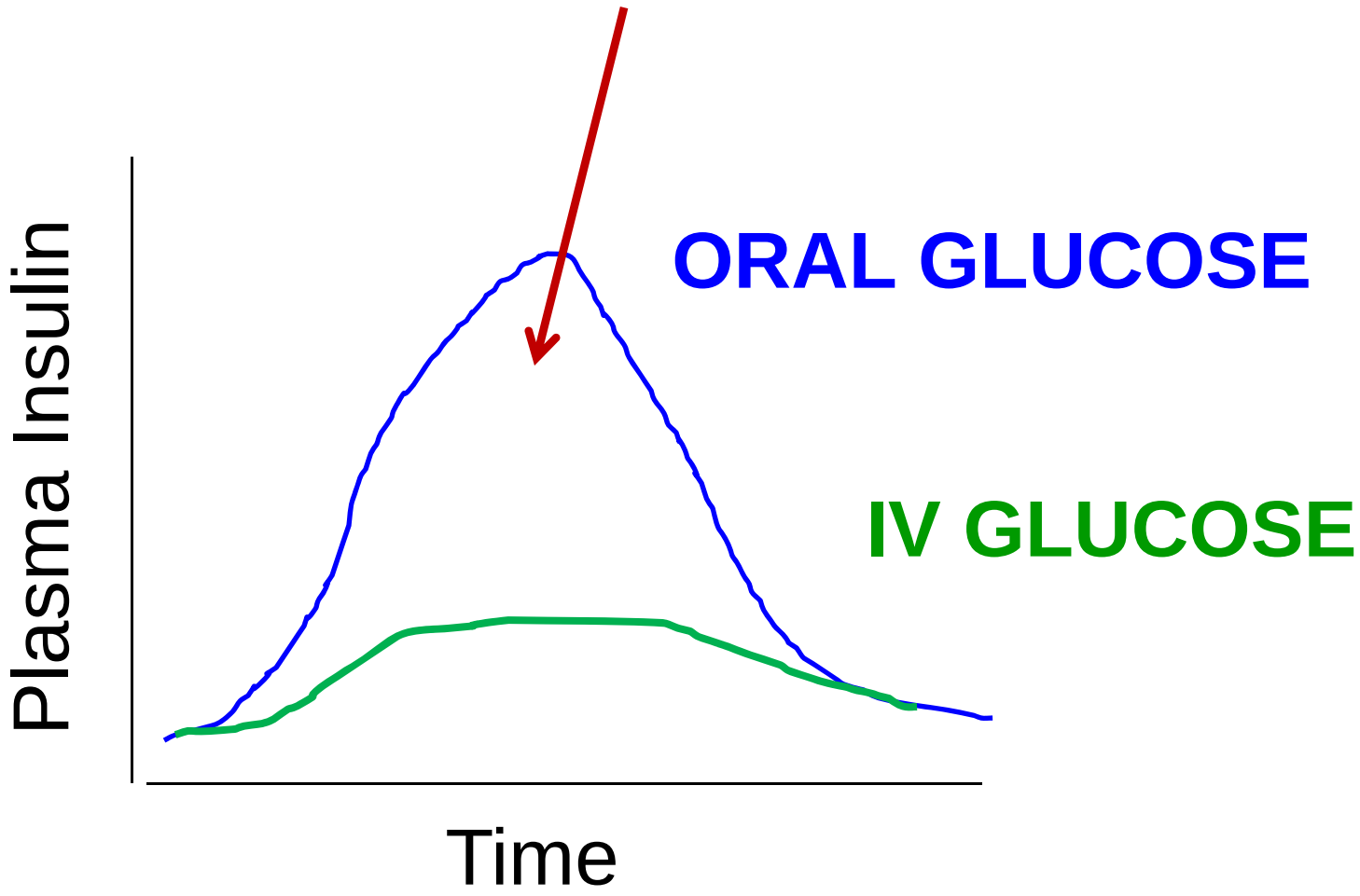
Explanation of the Incretin Effect:

Oral glucose stimulates insulin secretion to a greater extent than Intravenous (IV) glucose

Next slide: illustrates Incretin Effect in persons with persons without diabetes:

Current Diabetes Reviews, 2013; 9: 161-193;
Diabetes Care, 2010; 33(7): 1691-1692.

The Incretin Effect in Persons without Diabetes



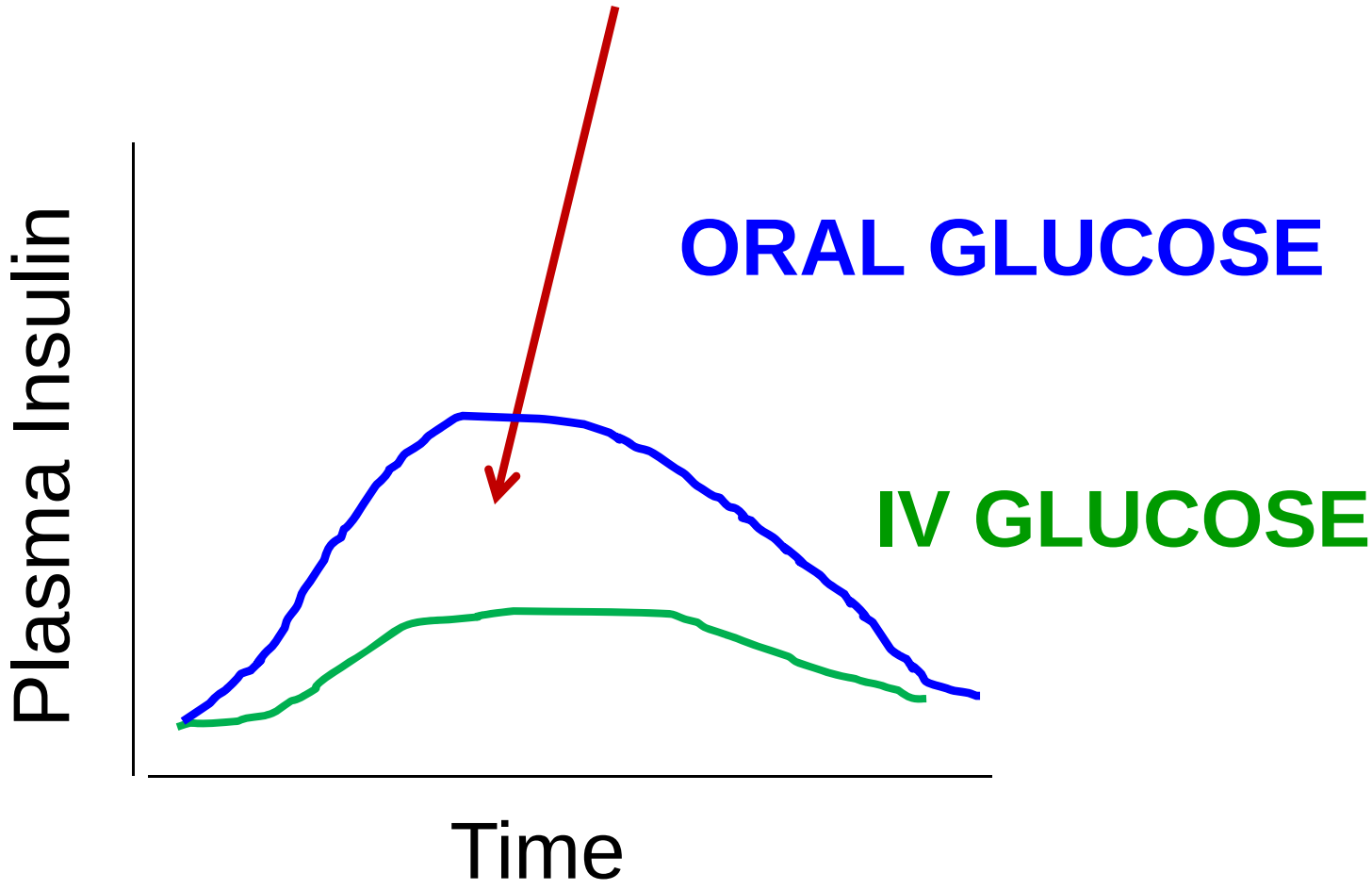
The "Incretin Effect"

In Type 2 DM: Incretin Effect is markedly decreased (approximately ½) that observed compared to persons with normal glucose tolerance.

Next slide: illustrates Incretin Effect in persons with Type 2 Diabetes Mellitus:

Current Diabetes Reviews, 2013; 9: 161-193;
Diabetes Care, 2010; 33(7): 1691-1692.

Decreased Incretin Effect in Persons with Type 2 Diabetes



The “Incretin Effect” and Incretins

What is going on?

Oral glucose causes the release of two incretins, (gut hormones):

- Glucose-Dependent Insulinotropic Polypeptide (GIP)
- Glucagon-Like Peptide-1 (GLP-1)

Current Diabetes Reviews, 2013; 9: 161-193;
Diabetes Care, 2010; 33(7): 1691-1692.

Glucose-Dependent Insulinotropic Polypeptide (GIP)

GIP:

- GIP is produced in the gastrointestinal tract in response to oral glucose and enhanced by fat
- Actions of GIP:
  - acts on beta cells to increase insulin secretion, and
  - promotes triglyceride storage into fat cells.

Note: There are no drugs for GIP on US market

Diabetes Care, 2010; 33(7): 1691-1692

Glucagon-Like Peptide-1 (GLP-1)

GLP-1 is produced in the gastrointestinal tract in response to oral glucose.

GLP-1 has three actions:

Intestinal tract: slows gastric emptying

Hypothalmus: acts centrally to regulate appetite

Pancreas:

- Release insulin
- Suppress glucagon release

Prog Mol Biol Transl Sci. 2014; 121:23-65;
Diabetes Care, 2010; 33(7): 1691-1692

Dipeptidyl-Pepitase-4 (DPP-4)

Description

DPP-4 is an ENZYME

Location:

found throughout the body

Mechanism of Action:

In the gastrointestinal tract, the DPP-4 degrades both GLP-1 and GIP

Diabetologia, 2014 Sept; 57(9): 1876-1883 Diabetes Care, 2010; 33(7): 1691-1692; http://www.gpha.org/assets/CELESSONS/treatment%20of%20hyperglycemia%20in%20type%202%20diabetes.pdf

GLP-1 and DPP-4: Mechanism of Action

Persons without diabetes:

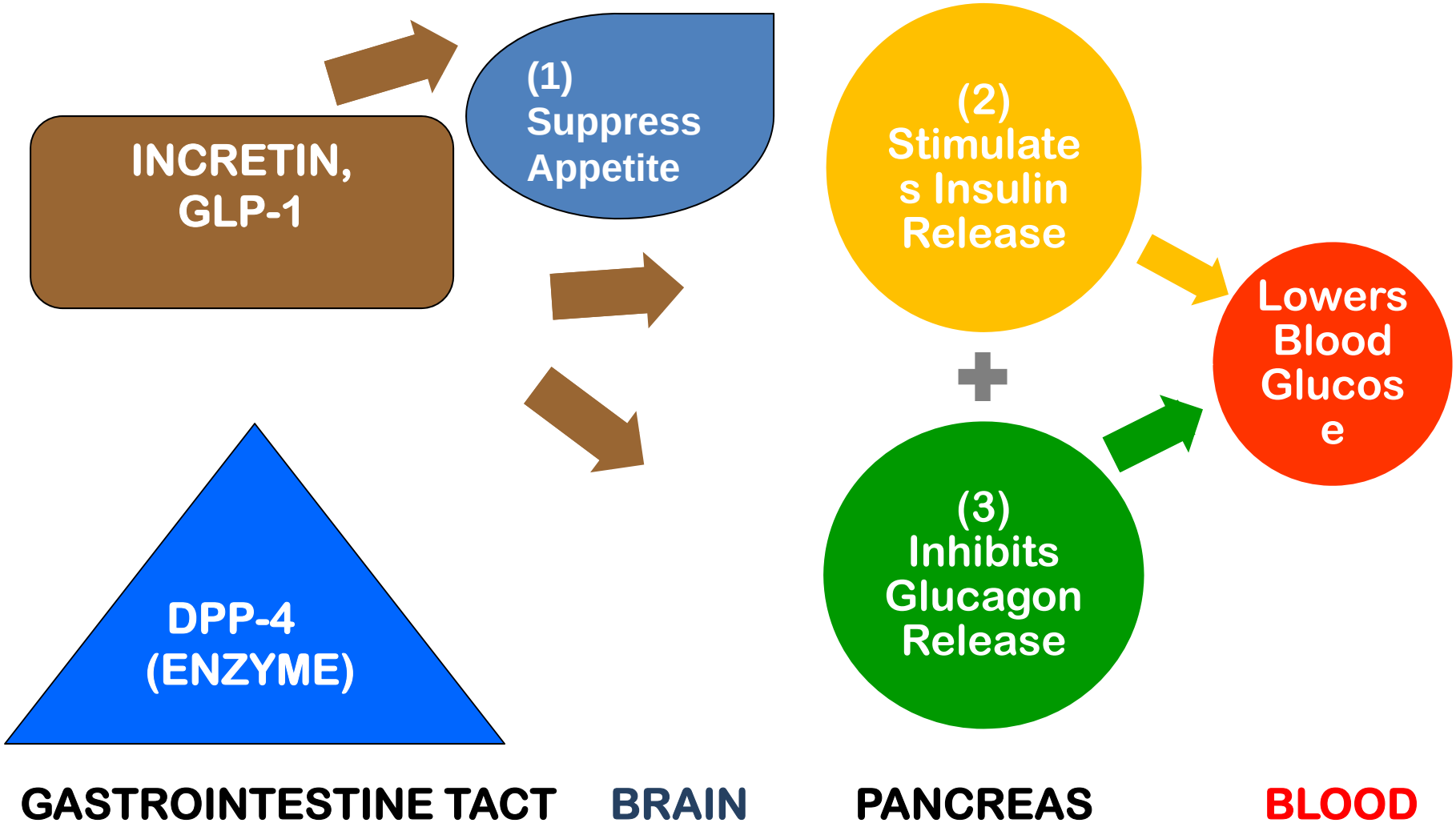
Glucagon Like Peptide -1 (GLP-1) lowers blood glucose

Dipeptidyl Peptidase-4 Enzyme eventually degrades GLP-1

Prog Mol Biol Transl Sci. 2014; 121:23-65;
Diabetes Care, 2010; 33(7): 1691-1692

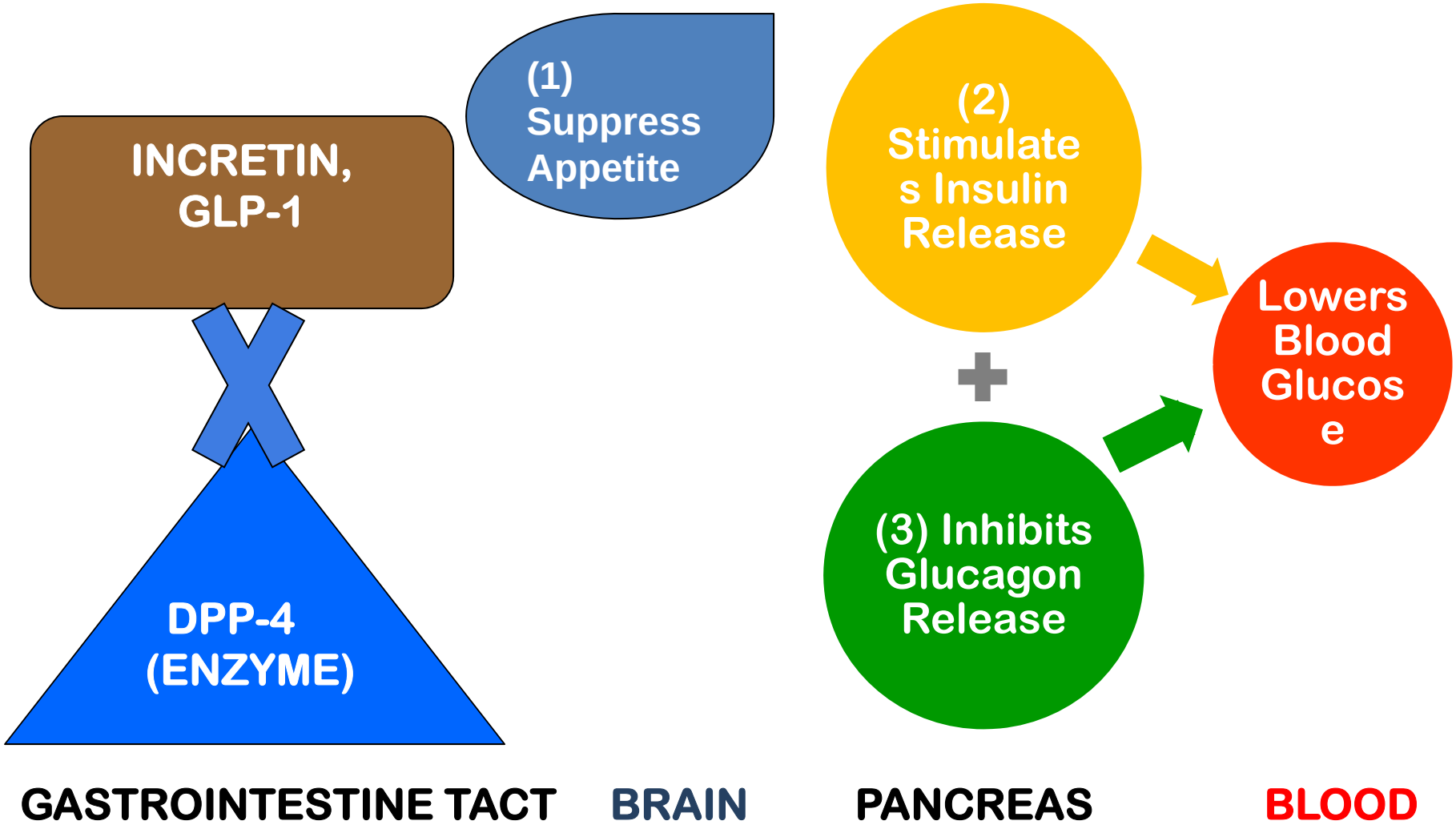
WITHOUT DIABETES:

3 Effects of Incretin & Glucagon-Like Peptide-1



WITHOUT DIABETES:

Dipeptidyl Peptidase-4 Enzyme degrades GLP-1



Persons with Type 2 DM

In persons with Type 2 Diabetes Mellitus :

- Dipeptidyl Peptidase-4 enzyme (DPP-4) activity is increased
- Some studies have reported that Glucagon-Like Peptide -1 (GLP-1) is reduced

Diabetologia, 2014 Sept; 57(9): 1876-1883 Diabetes Care, 2010; 33(7): 1691-1692; http://www.gpha.org/assets/CELESSONS/treatment%20of%20hyperglycemia%20in%20type%202%20diabetes.pdf

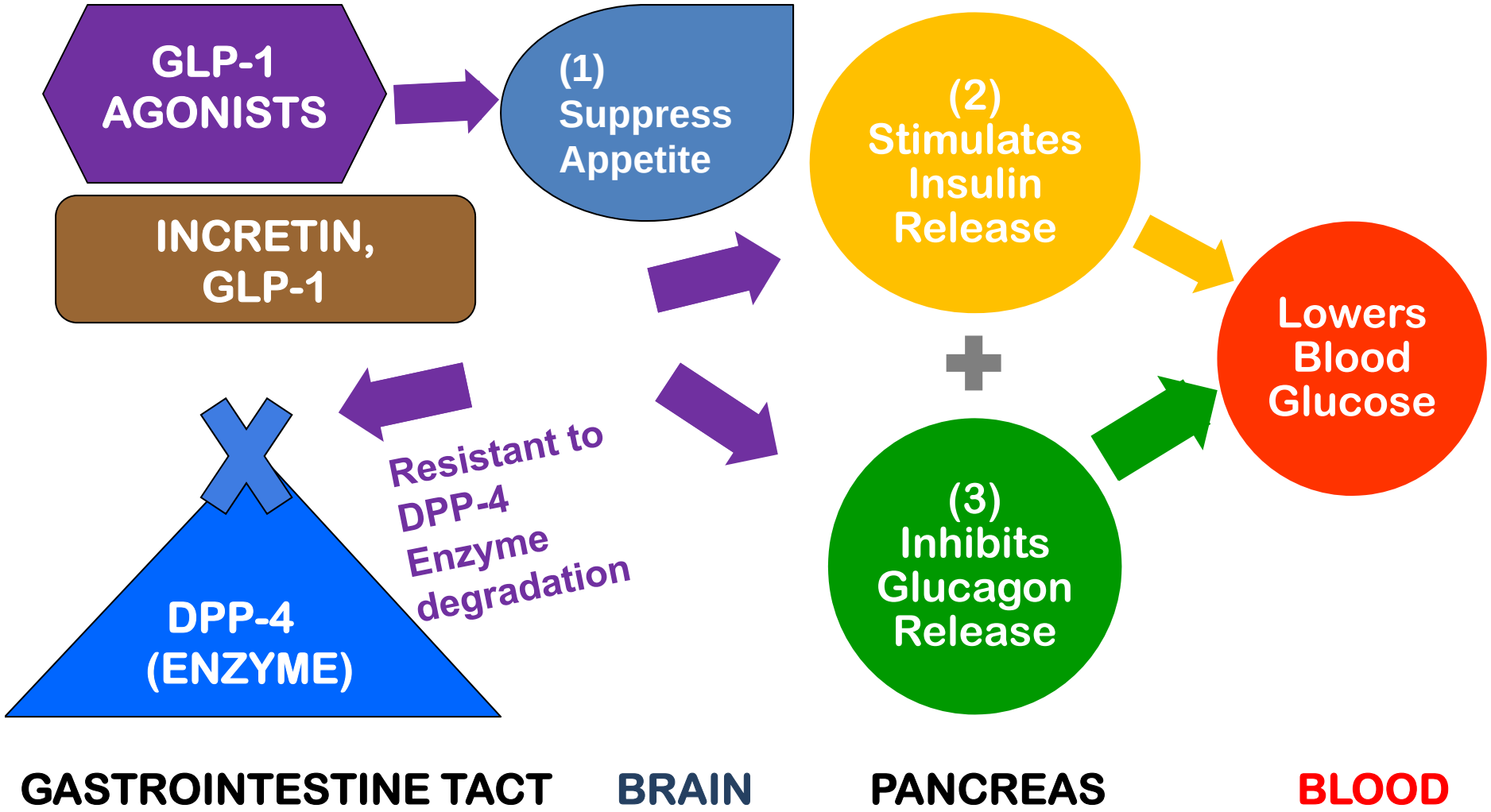
GLP-1 Agonists:
Mechanism of Action

Persons with Type 2 Diabetes:

GLP-1 Agonists (or Analogues)

- Work the same way as GLP-1
- GLP-1 Agonists are resistant to DPP-4 enzyme degradation

WITH DIABETES: Effect of Glucagon-Like Peptide-1 Agonists



DPP-4 Inhibitors: Mechanism of Action

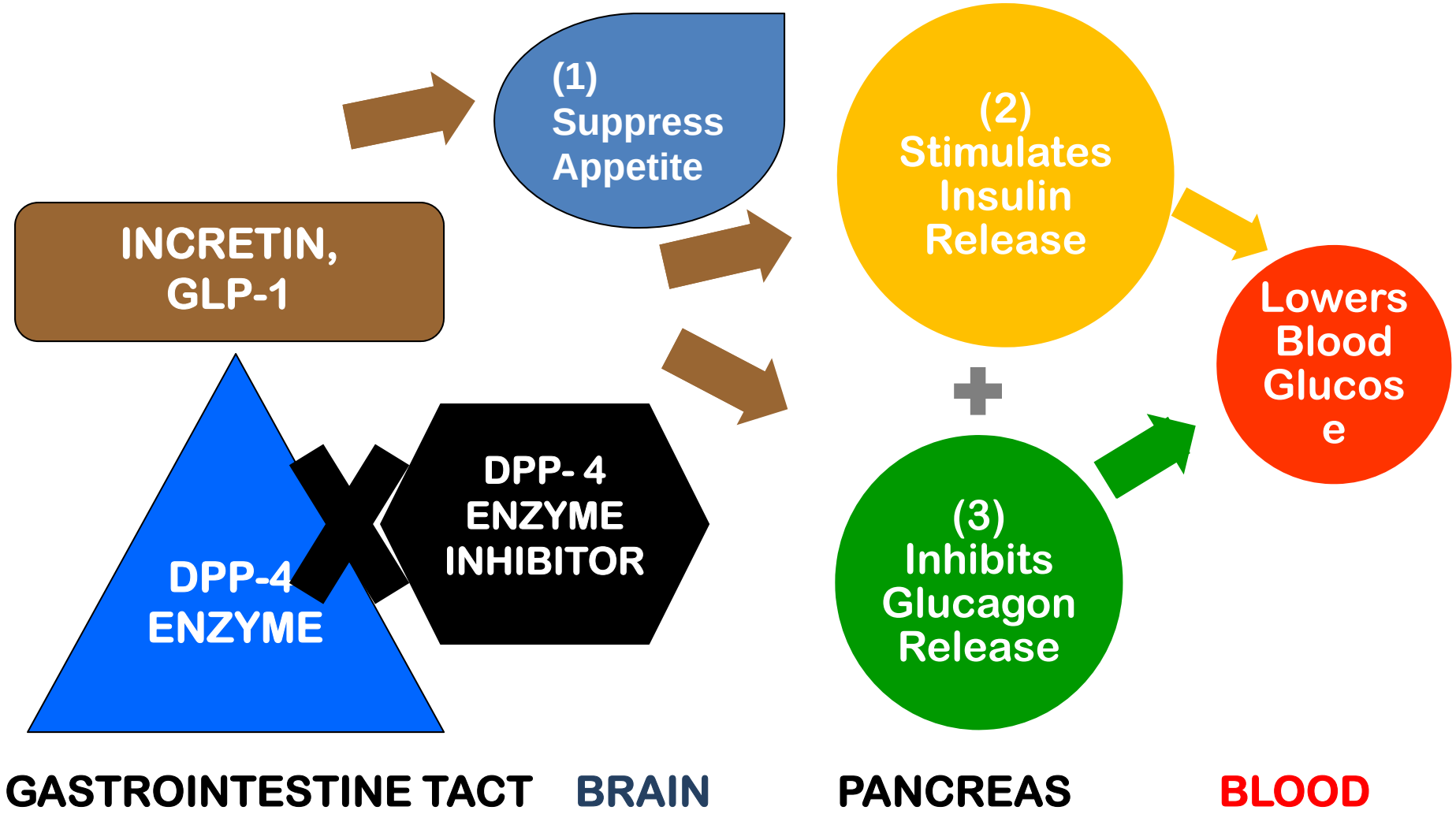
Persons with Type 2 Diabetes:

DPP-4 Enzyme Inhibitors

- Block the reaction by inhibiting the DDP-4 enzyme in the gastrointestinal tract

WITH DIABETES:

Dipeptidyl Peptidase-4 Enzyme Inhibitors Block DPP-4 Enzyme



Glucagon-Like Peptide-1 Agonists
Drugs on the US Market

Glucagon-Like Peptide-1 Agonists

Other names:

Incretin Mimetics

GLP-1 Analogues

Drug treatment for persons with type 2 diabetes

Designed to restore insulin response to glucose

Administered subcutaneously

Currently: five drugs available in US

http://www.gpha.org/assets/CELESSONS/treatment%20of%20hyperglycemia%20in%20type%202%20diabetes.pdf

GLP-1 Receptor Agonists:
US Market

Exenatide

Synthetic version (analogue) of the protein derived from the saliva of the Gila monster

Mechanism of Action:

Prolongs the Incretin Effect by:

Mimicking endogenous GLP-1 activity

Being resistant to DPP-4 deactivation

www.medscapecom/viewarticle/751632

GLP-1 Receptor Agonists: US Market

Exenatide ER

- Extended release formulation of Exenatide
- Some concern for tumor formation

Other GLP-1 Receptor Agonists:

- Synthetic drugs
- Have an effect similar to Exenatide

http://www.gpha.org/assets/CELESSONS/treatment%20of%20hyperglycemia%20in%20type%202%20diabetes.pdf

GLP-1 Receptor Agonists: Local Utah Prices

Generic Name (Trade Name)	Number of Doses	Cash Price per Month
Exenatide Byetta®	60	$722
Exenatide ER Bydureon® vials Bydureon® pens	 4 4	 $685
Liraglutide Victoza® 2 pack Victoza® 3 pack	 30 30	 $576 $864

Smith's, Costco, Walmart.

GLP-1 Receptor Agonists: US Market

Generic Name (Trade Name)	Number of Doses	Cash Price per Month
Dulaglutide Trulicity®	4	$717
Albiglutide Tanzeum®	4	$548

Smith's, Costco, Walmart

GLP-1 Receptor Agonists: Prescribing

Clinical Effects:

- Decrease in A1C: 0.5-1.5%
- Improvement in glucose control
- Weight loss

Adverse effects:

- Nausea (mild to moderate)
  - decreased by dose titration
  - less with Exenatide ER

http://www.gpha.org/assets/CELESSONS/treatment%20of%20hyperglycemia%20in%20type%202%20diabetes.pdf; Clinical Diabetes 2013; 3194): 148-157

GLP-1 Receptor Agonists: Safety Information

Exenatide ER, Liraglutide, Dulaglutide, Albiglutide

BLACK BOXED WARNING:
RISK OF THYROID C-CELL TUMORS

Not recommended with a personal or family history of medullary thyroid cancer.

Other serious associated conditions: .

pancreatitis

renal insufficiency

http://www.gpha.org/assets/CELESSONS/treatment%20of%20hyperglycemia%20in%20type%202%20diabetes.pdf

All GLP-1 Receptor Agonists: Prescribing Concerns

Caution in prescribing if person has:

- Gastroparesis (delayed gastric emptying)
- Persistent abdominal pain
- Pancreatitis

Lack of long-term studies to assess safety

Expensive drugs

ADA suggests using these drugs as first-line treatment when weight loss is needed.

http://www.gpha.org/assets/CELESSONS/treatment%20of%20hyperglycemia%20in%20type%202%20diabetes.pdf

DPP-4 Inhibitors: Pharmacology

Descriptive Terms:

- "DPP-4 (enzyme) inhibitors"
- Also called "Gliptins"
- Incretin Enhancers

Target Organ: Gastrointestinal Tract

http://www.hopkinsguides.com/hopkins/ub/view/Johns_Hopkins_Diabetes_Guide/547042/all/DPP_IV_Inhibitors; www.globalrph.com/DPP-4-inhibitors.htm#

DPP-4 Inhibitors: Pharmacology

Mechanism of Action: Prolong the "Incretin Effect"

Clinical Effect:

- Decrease A1C from 0.73 to 1.2%
- Literature suggests beneficial effects of DPP4-Inhibitors on all diabetes-related microvascular complications

Dosage Forms:

Oral medications administered once daily

http://www.hopkinsguides.com/hopkins/ub/view/Johns_Hopkins_Diabetes_Guide/547042/all/DPP_IV_Inhibitors; www.globalrph.com/DPP-4-inhibitors.htm#
Diabetes Care, October 2014; 37(10): 2884-2894.

DPP-4 Enzyme Inhibitors: Safety Profile

FDA warns: may cause severe joint pain

Other concerns:

- Risk for pancreatitis: insufficient evidence
- Pancreatic cancer: does not seem to be an increased risk
- Looks like a neutral effect for cardiovascular events

http://www.fda.gov/Drugs/DrugSafety/ucm459579.htm;
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4110853/; .

DPP-4 Enzyme Inhibitors: Safety Profile

Monitor all patients for:

- Hypersensitivity reactions
- Skin disorders

Monitor:

- Renal function if taking Sitagliptin

http://www.fda.gov/Drugs/DrugSafety/ucm459579.htm;
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4110853/; .

DPP-4 (Enzyme) Inhibitors: Local Utah Prices

Generic Name	Number of Doses	Cash Price per Month
Sitagliptin Januvia®	30	$477
Saxagliptin Onglyza®	30	$453
Linagliptin Trajenta®	30	$445
Alogliptin Nesina®	30	$427

Smith's, Costco, Walmart

Drug Prescribing Choice

	GLP-1 Agonists	DPP-4 Enzyme Inhibitors
Administration route	Injection	Oral
↑ GLP-1	Sustained	Meal-related
Effect on A1C	↓	↓
Effects on body weight	↓	← →
Side effects	Nausea, Rare: pancreatitis	(Well tolerated) Nasopharyngitis, skin rashes, Stevens-Johnson syndrome
β-cell function	↑	↑

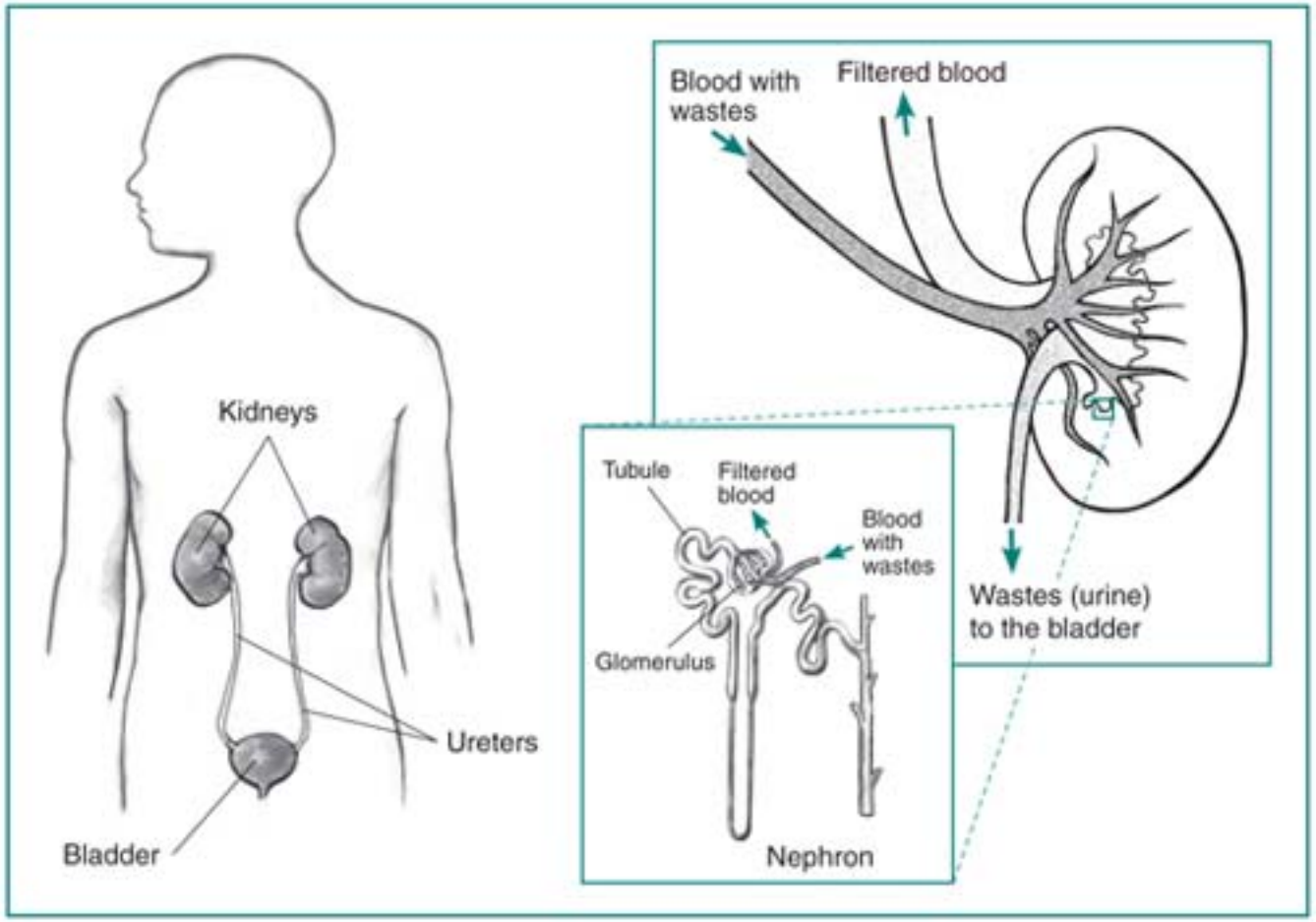
Lipids online: http://www.lipidsonline.org/

Renal Tubular Physiology

Sodium Glucose
Cotransporter-2 Inhibitors
(SGLT2 Inhibitors, Glifozins)

Target: Kidney

Kidney and Nephron: Anatomy



http://www.niddk.nih.gov/health-information/health-topics/kidney-disease/high-blood-pressure-and-kidney-disease/Pages/facts.aspx

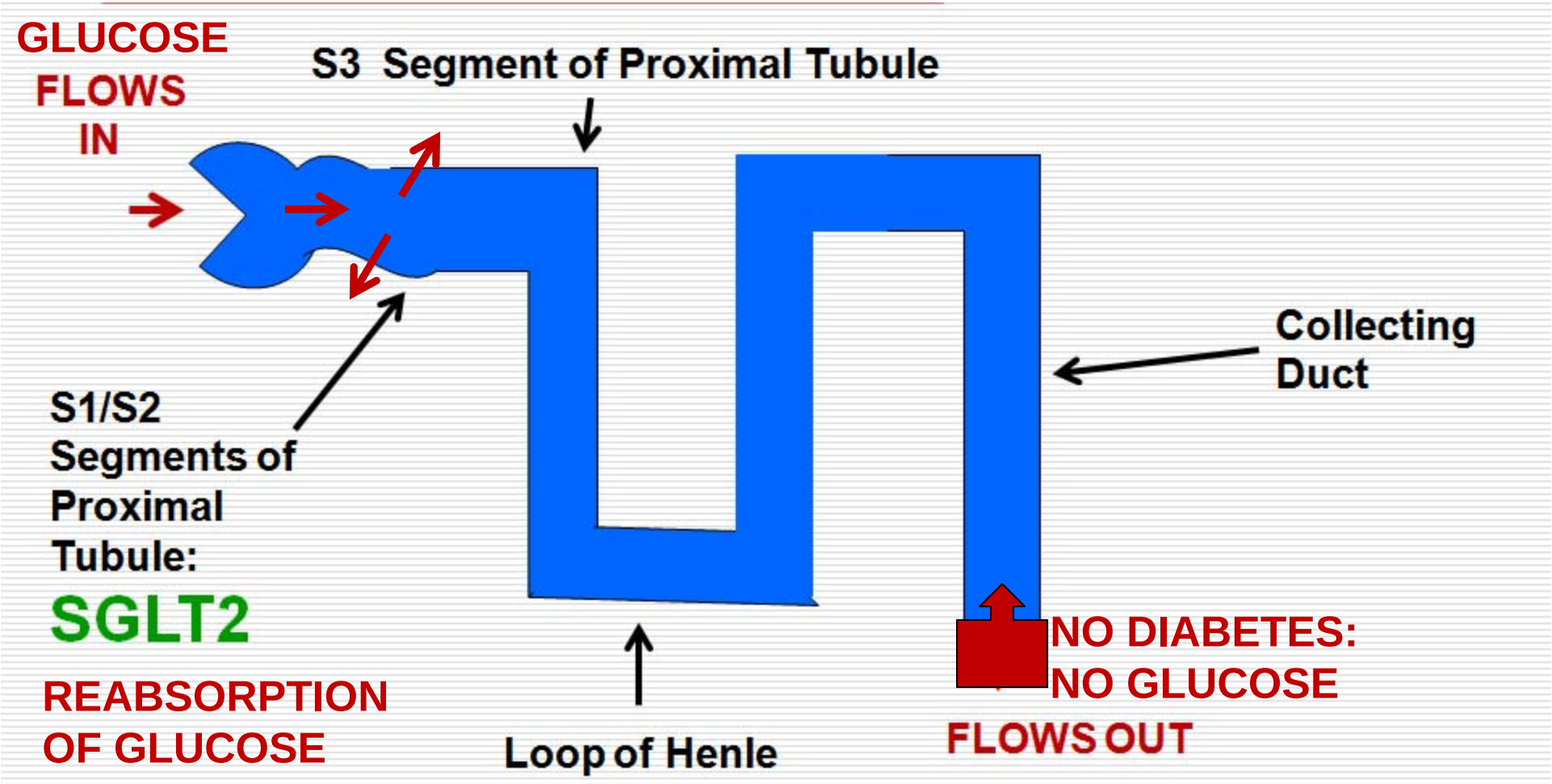
Nephron:
Physiology

Kidneys plays a major role in glucose homeostasis (balance) primarily by reabsorption of glucose from the nephron to the blood stream

Sodium-glucose co-transporters, SGLT1 and GLTP2 are located inside the renal proximal tubule of the nephron and are involved in the reabsorption of glucose

Clinical Diabetes, 2012; 30(4): 151-155

Nephron:
Physiology



Renal Tubular Physiology: Renal Threshold

Glucose in kidneys of persons without diabetes:

Approximately 180 grams of glucose filtered per day

Almost complete absorption of glucose

Glucose in kidneys of persons with diabetes:

hyperglycemia leads to glucose excreted in the urine

Clinical Diabetes, 2012; 30(4): 151-155

Sodium Glucose Co-Transporter 2 Inhibitors: Pharmacology

Two Descriptive Terms:

- SGLT2 Inhibitors
- Gliflozins

Target Organ: Segments 1 and 2 of the proximal tubule of the nephron

Clinical Effect:

- Decrease blood glucose by allowing approximately 100 grams of glucose to be excreted per day

Selective SGLT2 Inhibitors: Pharmacology

Mechanism of Action:

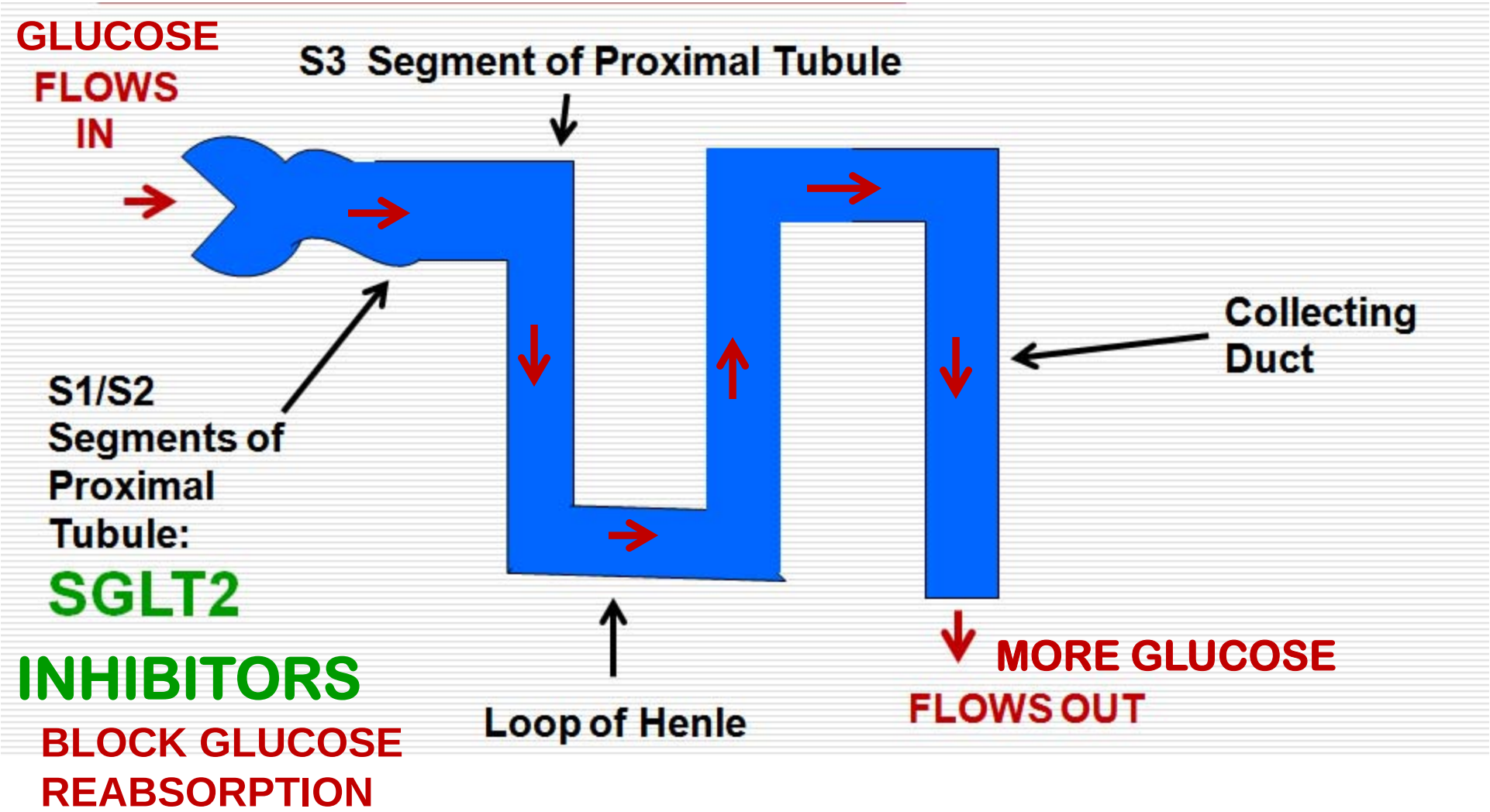
These drugs are selective for Sodium Glucose Transporter 2

Binds to these transporters

- Inhibits re-absorption of glucose at S1/S2 segment of the proximal tubule of nephron →
- Increased excretion of glucose in urine →
- Lower blood glucose → ↓ A1C

Nutrition & Diabetes, 2014; 4: el43; coi:10.1038/nutd.2014.40

Nephron Physiology:
SGLT2 Inhibitors



Selective SGLT2 Inhibitors: Potential Advantages

- Lowers A1C (0.7 – 0.8%)
- May help with weight loss
- May lower blood pressure
- Low risk of hypoglycemia since drugs do not impair normal endogenous glucose production
- Can be combined with other drugs used to improve glycemic control

Clinical Diabetes 2012, 30(4): 151-155;
http://www.diabetesincontrol.com/articles/82-test-your-knowledge-answers/16605

Selective SGLT2 Inhibitors: Adverse Events

Higher incidence reported:

- Intestine: constipation, diarrhea, nausea
- Urinary and genitourinary infections (approximately 5%)

Low incidence reported:

- Orthostatic hypotension
- Dizziness

http://www.medscape.com/viewarticle/780901; Drug Design, Development and Therapy 2013: 13(7): 1399-1408

Selective SGLT2 Inhibitors: On US Market

Generic (Trade)	Number of Doses	Cash Price per Month
Canagliflozin Invokana®	30	$453
Dapagliflozin Farxiga®	30	$453
Empagliflozin Jardiance®	30	$453

Smith's, Costco, Walmart

Thiazolidinediones
TZDs, Glitazones

Targets: Adipose, Muscle, Liver

Thiazolidinediones: Pharmacology

Descriptive Terms:

"Insulin Sensitizers"

"Insulin Enhancers"

Glitazones

TZDs (Thiazolidinediones)

PPARγ agonists: Peroxisome proliferator-activated receptor agonists

NEJM, Sep 9, 2004; 35: 1106-1118

Thiazolidinediones: Pharmacology

Target Organs:

ADIPOSE TISSUE (FAT),

MUSCLE

LIVER

Clinical Effect:

- increasing insulin sensitizing effect
- decreases fasting blood glucose by 30 mg/dL or more
- lowers A1C by 0.5 to 1.4%

http://www.gpha.org/assets/CELESSONS/treatment%20of%20hyperglycemia%20in%20type%202%20diabetes.pdf; Diabetes Care 2005; 28(2): 488-493

Thiazolidinediones: Pharmacology

Mechanism of Action: acts on adipose tissue, muscle, and liver to:

- increase glucose utilization
- decrease glucose production

http://www.gpha.org/assets/CELESSONS/treatment%20of%20hyperglycemia%20in%20type%202%20diabetes.pdf

Local Utah Pricing January 2016
Thiazolidinediones

Generic Name	*Quantity*	*Cheapest Cash Price*
Rosiglitazone (Avandia) 2 mg 4 mg	 60 30	 $249 $369
pioglitazone	30	$90
rosiglitazone + metformin 2 mg/1000 mg 4 mg/1000 mg	 60 60	 $173 $291

Smith's, Walmart, Costco

Thiazolidinediones: Adverse Effects

Weight gain

- (No increase in visceral fat)

Fluid retention

- Contraindicated in persons with New York Heart Association Class III or IV heart failure

http://www.gpha.org/assets/CELESSONS/treatment%20of%20hyperglycemia%20in%20type%202%20diabetes.pdf.

Thiazolidinediones: Adverse Effects

Other suggested adverse risks:

- Evidence strongly suggests decrease in bone density and increase risk of fractures, particularly in women.
- Rosiglitazone had FDA restrictions for risk of myocardial infarctions (2010) but FDA removed these risks (2013).
- Pioglitazone may increase risk of bladder cancer.

http://www.gpha.org/assets/CELESSONS/treatment%20of%20hyperglycemia%20in%20type%202%20diabetes.pdf.

Thiazolidinediones: Other Concerns

May increase risk of pregnancy in persons taking oral contraceptives

May result in ovulation in:

- premenopausal anovulatory women
- menopausal women

http://pharmacy.oregonstate.edu/drug_policy/pages/dur_board/reviews/articles/TZD_ClassReview.pdf

Thiazolidinediones:
Black Box Warning

WARNING:

CONGESTIVE HEART FAILURE

http://general.takedapharm.com/content/file.aspx?filetypecode=actospi&cacheRandomizer=db944be5-261b-4c41-a660-e8271322067d; https://www.gsksource.com/pharma/content/dam/GlaxoSmithKline/US/en/Prescribing_Information/Avandia/pdf/AVANDIA-PI-MG.PDF.

Meglitinide Analogues (Glinides)

Target: Pancreas

Meglitinide Analogues: Pharmacology

Descriptive Terms:

- Rapid Insulin Releasers
- "Rapid-Acting" Oral Meds

Target Organ: PANCREAS

Clinical Effect:

- Lowers post-prandial blood glucose by 60 mg/dL
- Lowers A1C by 0.5% to 2.0%

www.diabetesnet.com/diabetestreatments/prandin_starlix.php,
Core Concepts Review Course, AADE, November 2004

Meglitinide Analogues: Clinical Effect

Mechanism of Action: stimulates beta cells of pancreas using the same mechanism as Sulfonylurea (SU)

These drugs bind to SU receptor on the beta cell at a different site than SU

Can be used with:

other oral agents or

basal insulin

Meglitinide Analogues: Local Utah Prices

Generic Drug	*Number of Tablets*	*Cash Price per Month*
Repaglinide 2 mg	180	$520
Nateglinide 120 mg	90	$134

Smith's, Costco, Walmart

Meglitinide Analogues: Adverse Effects

Hypoglycemia

- Less than sulfonylureas

Weight gain

- Less than sulfonylureas

Contraindicated in severe liver disease

Decrease dose in severe renal dysfunction

α-Glucosidase Inhibitors

Target: Small Intestine

α-Glucosidase Inhibitors: Pharmacology

Description term: "Starch Blockers"

Target Organ: SMALL INTESTINE

Clinical Effect: decreases post-prandial blood glucose (after meals)

By 50 mg/dL

Lowers A1C by 0.7% to 1.0%

http://www.diabetesnet.com/diabetestreatments/precose_glyset.php

α-Glucosidase Inhibitors: Pharmacology

Mechanism of Action:

Drug inhibits enzymes in the gastrointestinal tract that breakdown carbohydrates into monosaccharides

Results:

delays intestinal carbohydrate absorption

delays glucose entry into systemic circulation

http://www.diabetesnet.com/diabetestreatments/precose_glyset.php
http://biology.kenyon.edu/HHMI/Biol113/small%20intestine.htm

α-Glucosidase Inhibitors: Local Utah Prices

Generic Drug	*Number of Tablets*	*Cash Price per Month*
Acarbose	90	$81
Miglitol	90	$248

Smith's, Coscto, Walmart

α-Glucosidase Inhibitors: Adverse Effects

Gastrointestinal

- Bloating
- Nausea
- Diarrhea
- Excess gas

Note: side effects limit patient adherence

www.diabetesnet.com/diabetes_treatments/precose_glycet.php

α-Glucosidase Inhibitors: Contraindications

- Bowel Disorder/Disease
  - Intestinal obstruction
  - Irritable Bowel Syndrome
  - Crohn's Disease
  - Other GI conditions
- Severe Liver Dysfunction
  - Cirrhosis of liver
- Renal impairment

www.diabetesnet.com/diabetestreatments/precose/glyset.php

Core Concepts Review Course, AADE, November 2004

Recap

- ❑ Explain the basic pathogenesis of T2DM
- ❑ State the main points of the American Diabetes Association (ADA) medication treatment recommendations for T2DM

Recap

On the following chart:

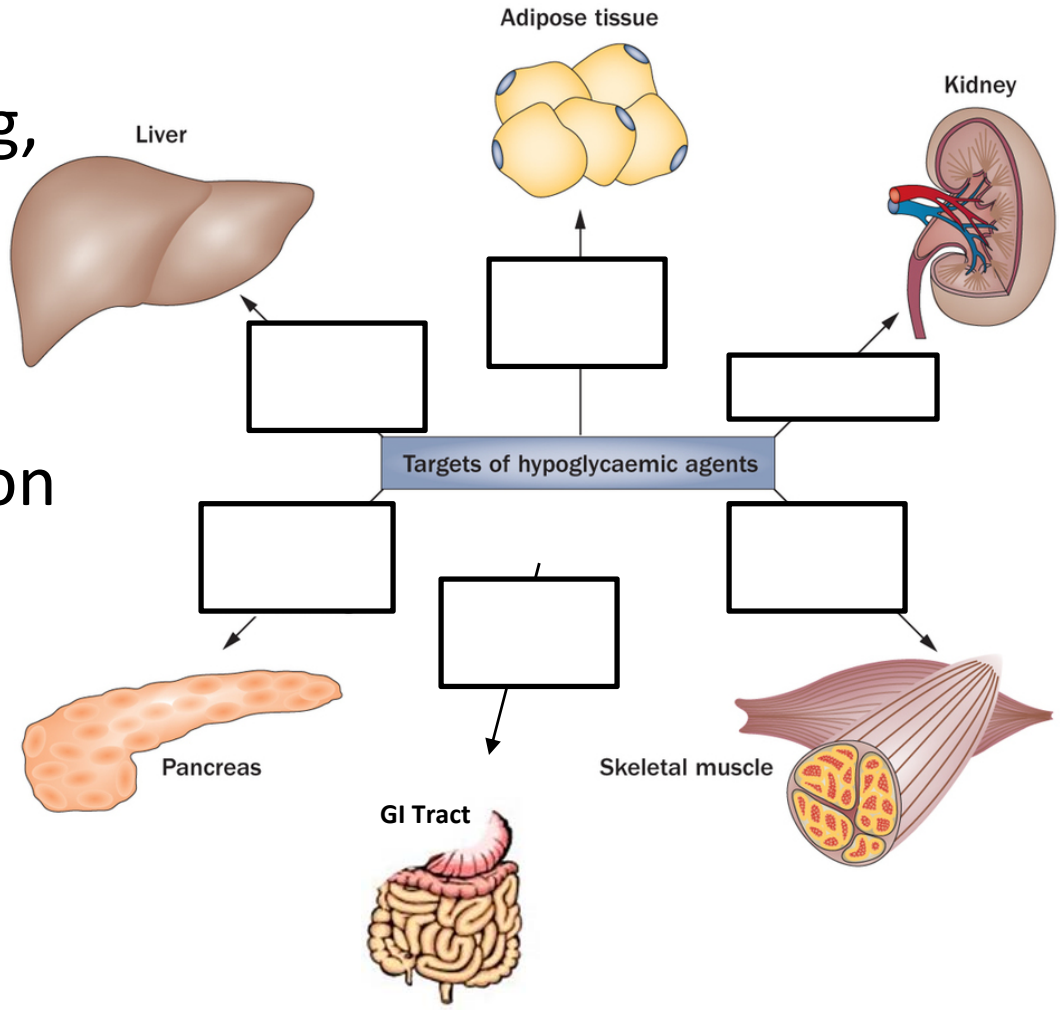
- ❑ List the classes of medications used to treat T2DM
- ❑ Give examples of diabetes medications in each medication class by generic name
- ❑ State significant side-effects of each medication class
- ❑ Give a rough estimate of the cash price for one month of medication in the class

Recap:
Comparison of Drug Classes

Drug Class	Drugs in this Class	Significant Side Effects	Monthly Cost

Recap

On the this drawing, identify the main target organ(s) affected or mechanism of action of each medication class



Jenssen T, Hartmann A. Emerging treatments for post-transplantation diabetes mellitus; Nature Reviews Nephrology 11, Pages:465–477 Year published: (2015) doi:10.1038/nrneph.2015.59

Thank you.

What questions
do you have?

Medications for Treating Type 2 Diabetes

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Diane.Ogborn@stores.sfdc.com

February 17, 2016

References

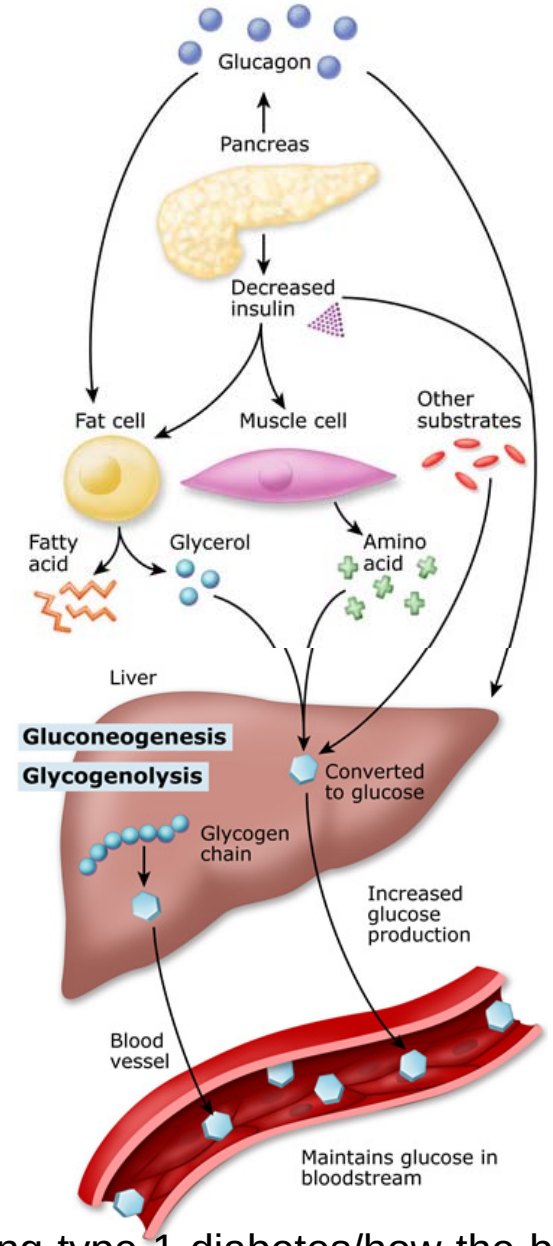
The American Diabetes Association Standards of Medical Care in Diabetes-2015. *Diabetes Care*, January 2015: 38: Supplement 1, pages S41 to S48.

Management of Hyperglycemia in Type 2 Diabetes: A Patient-Centered Approach. Position Statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care*, June 2012: 35: 1364-1379

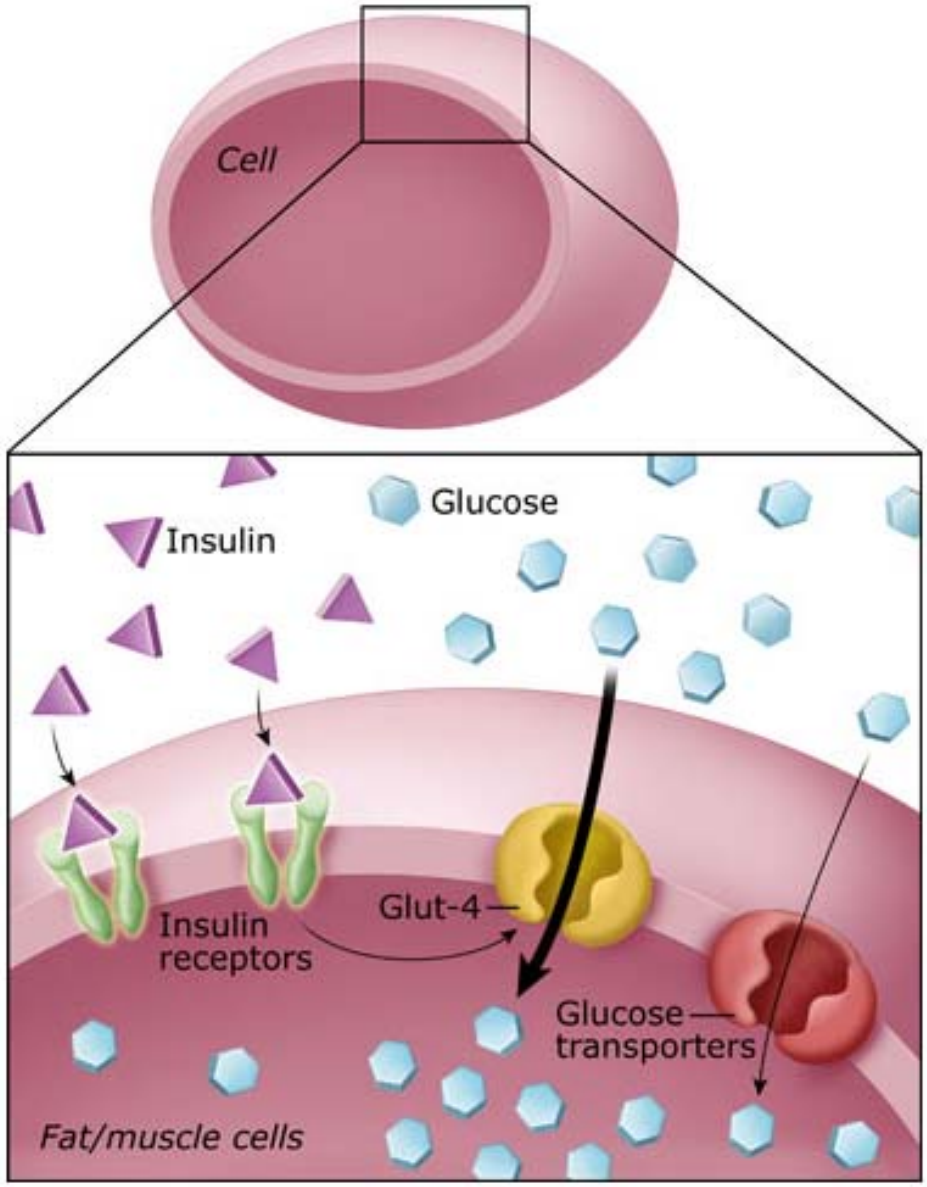
The approximate cash price of the drugs in this presentation are estimates of averages that were collected in January 2016.

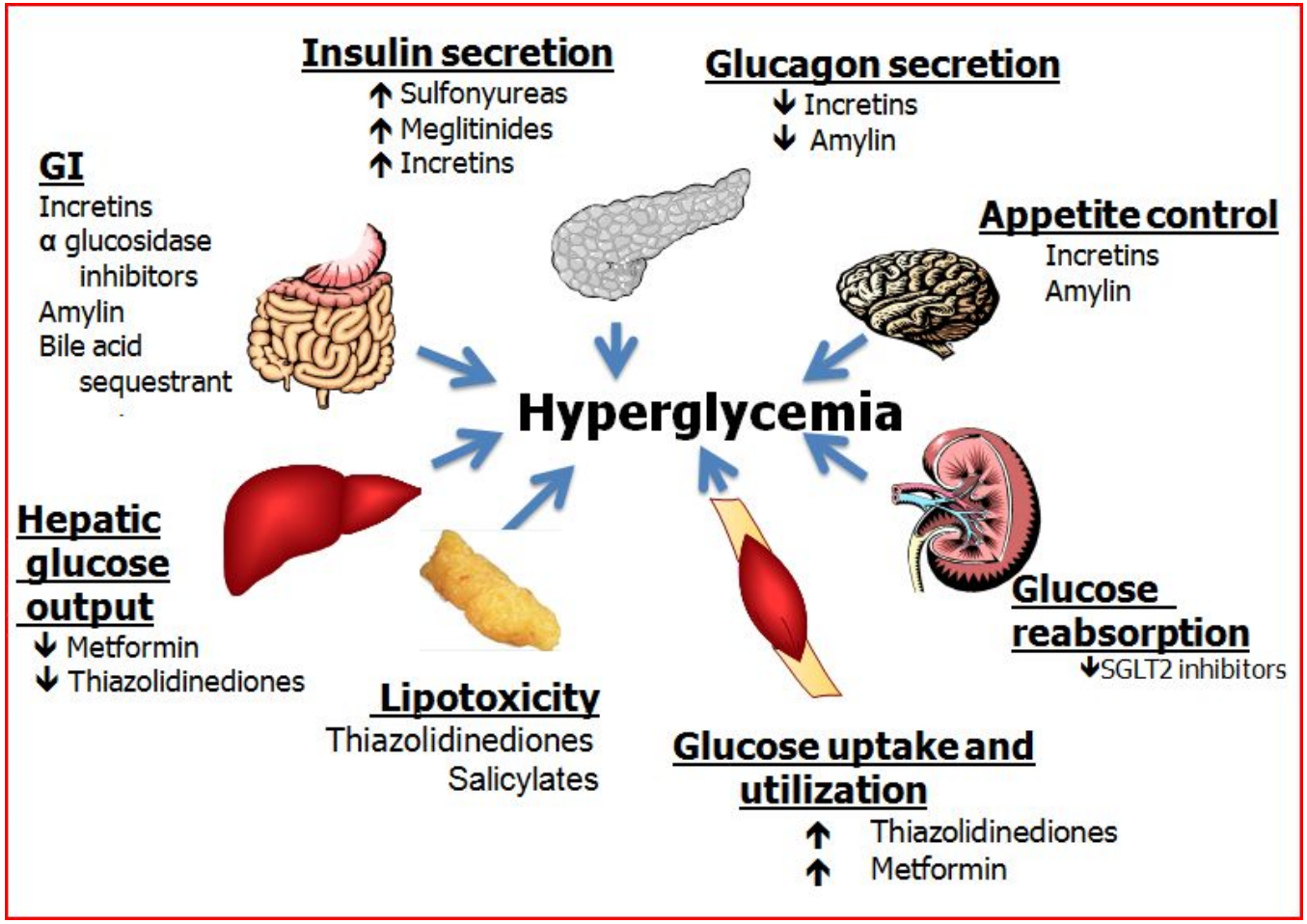
- Walmart.com
- Costco.com
- Smith's Food and Drug, Inc.

Please note that these prices are subject to change due to market pricing.



http://dtc.ucsf.edu/types-of-diabetes/type1/understanding-type-1-diabetes/how-the-body-processes-sugar/the-liver-blood-sugar/


Cell
Glucose
Insulin
Insulin receptors
Glut-4
Glucose transporters
Fat/muscle cells


Insulin secretion
↑ Sulfonyureas
↑ Meglitinides
↑ Incretins
Glucagon secretion
↓ Incretins
↓ Amylin
GI
Incretins
α glucosidase inhibitors
Amylin
Bile acid sequestrant
Appetite control
Incretins
Amylin
Hyperglycemia
Hepatic glucose output
↓ Metformin
↓ Thiazolidinediones
Glucose reabsorption
↓SGLT2 inhibitors
Lipotoxicity
Thiazolidinediones
Salicylates
Glucose uptake and utilization
↑ Thiazolidinediones
↑ Metformin