Diabetes Mellitus

Michael D. Rosario, MD

Endocrinology, Diabetes and Metabolism

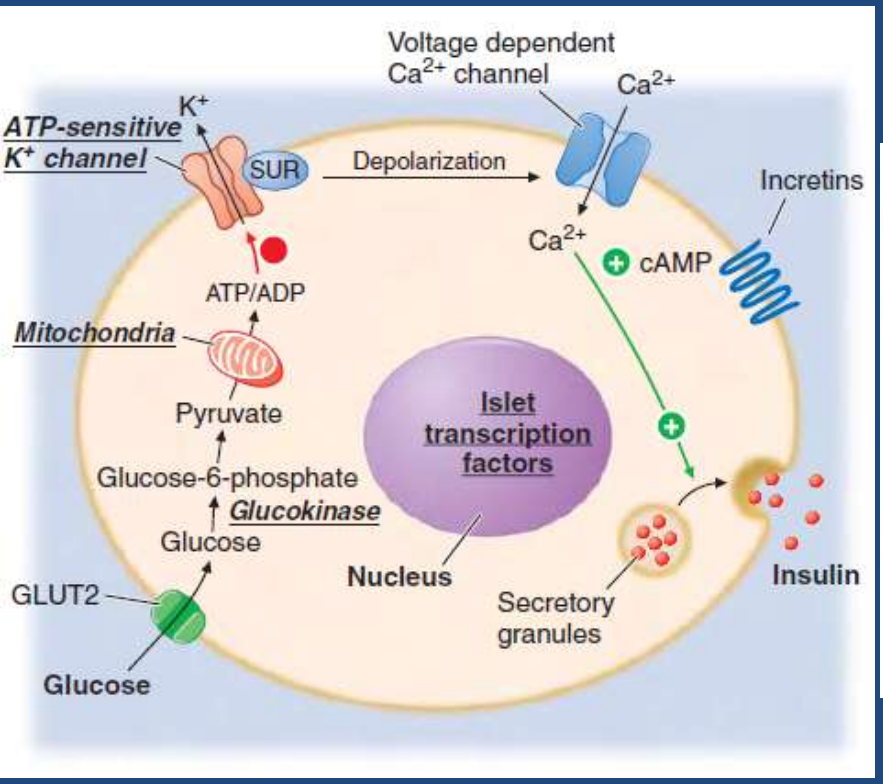
Classification

- Type 1 DM
  - Beta cell destruction leading to absolute insulin deficiency
- Type 2 DM
  - Progressive insulin secretory defect on the background of insulin resistance
- Gestational DM
  - Diagnosed during pregnancy that is not clearly overt diabetes

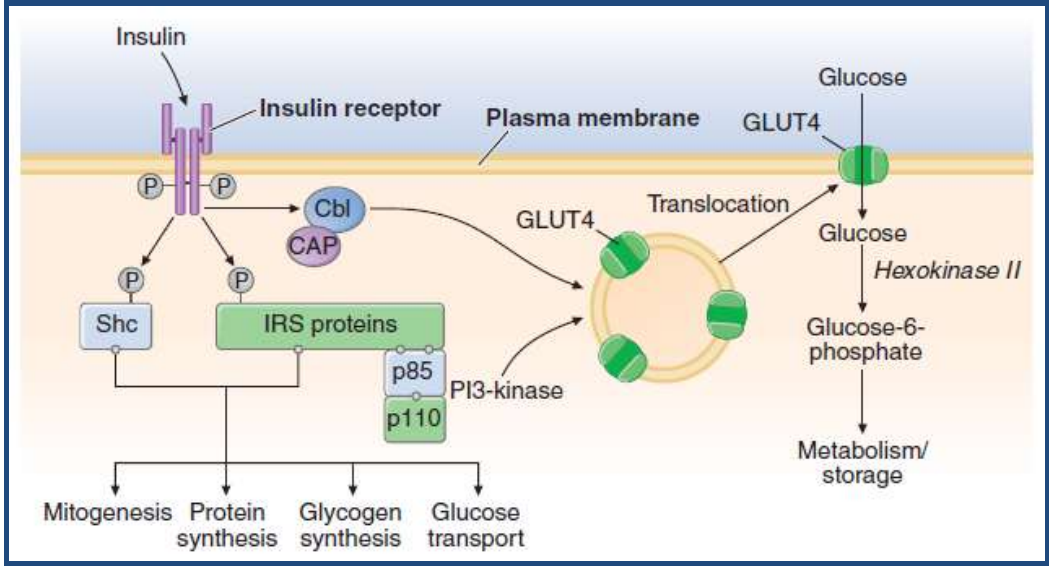
Classification

- Other specific types due to other causes
  - Genetic defects in Beta cell function
  - Genetic defects in Insulin action
  - Diseases of the exocrine pancreas
  - Drug or chemical induced

Insulin action

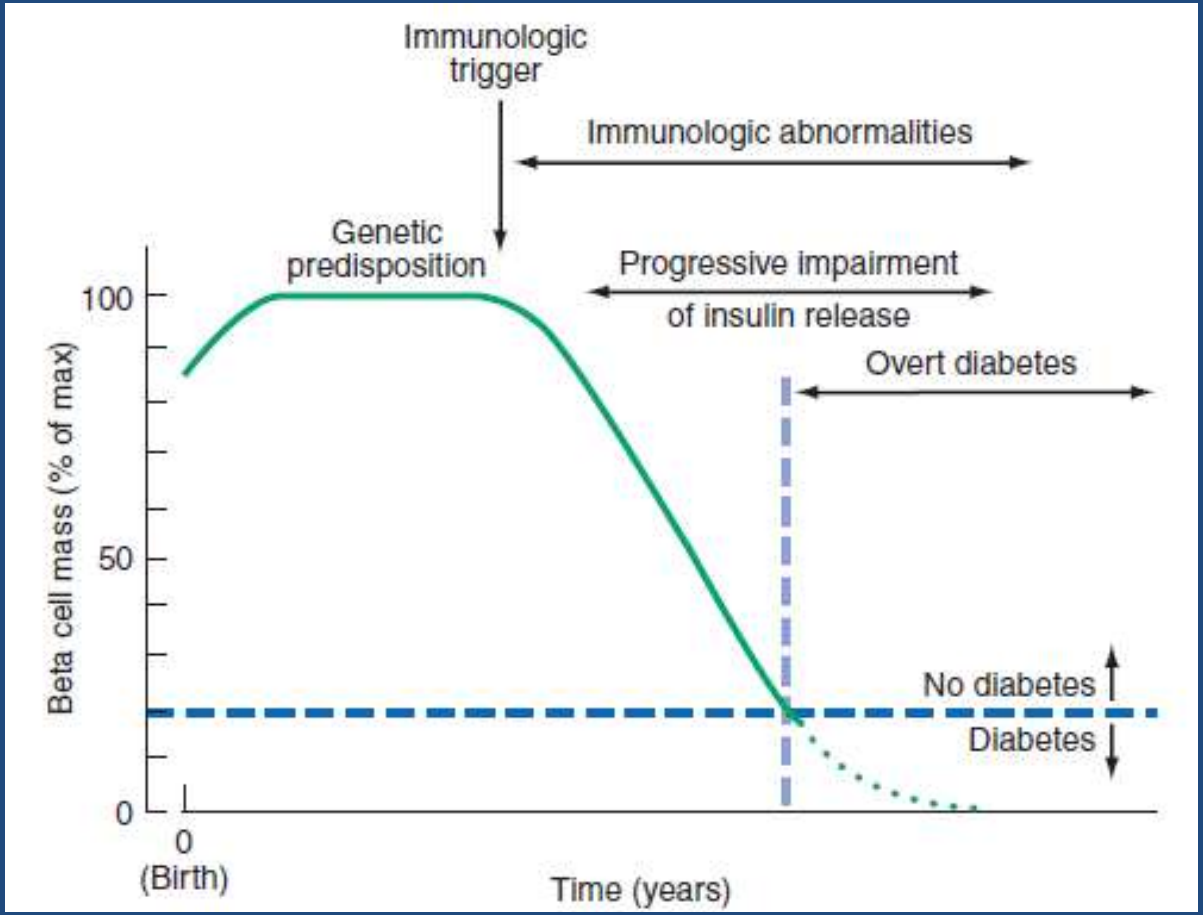


Pancreatic Beta Cell

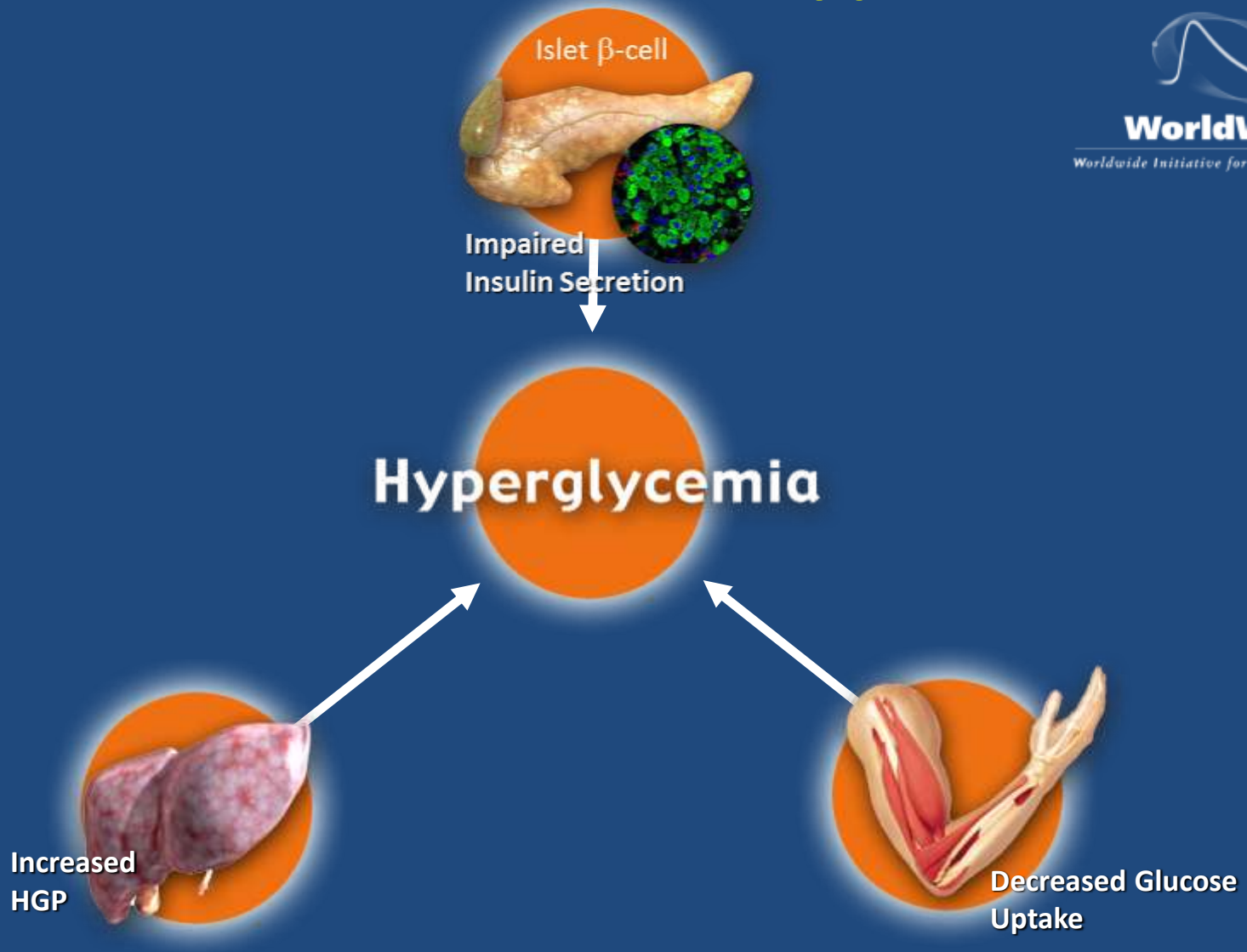


Peripheral Tissues

Type 1 DM


Immunologic trigger
Immunologic abnormalities
Genetic predisposition
Progressive impairment of insulin release
Overt diabetes
100
50
0
Beta cell mass (% of max)
No diabetes
Diabetes
0 (Birth)
Time (years)

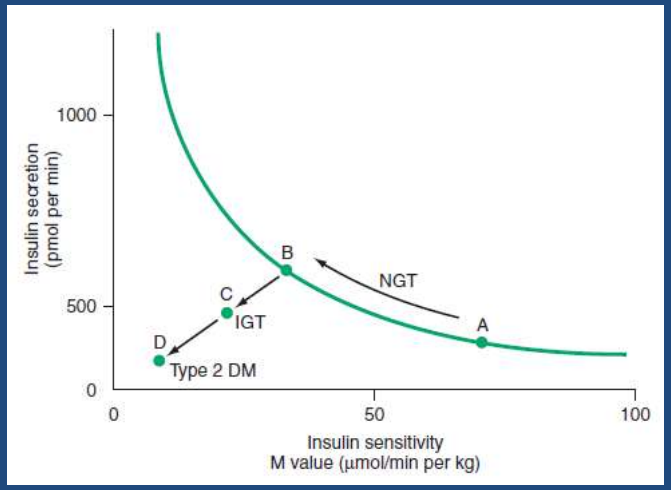
The Triumvirate of Type 2 DM



WorldWIDE
Worldwide Initiative for Diabetes Education

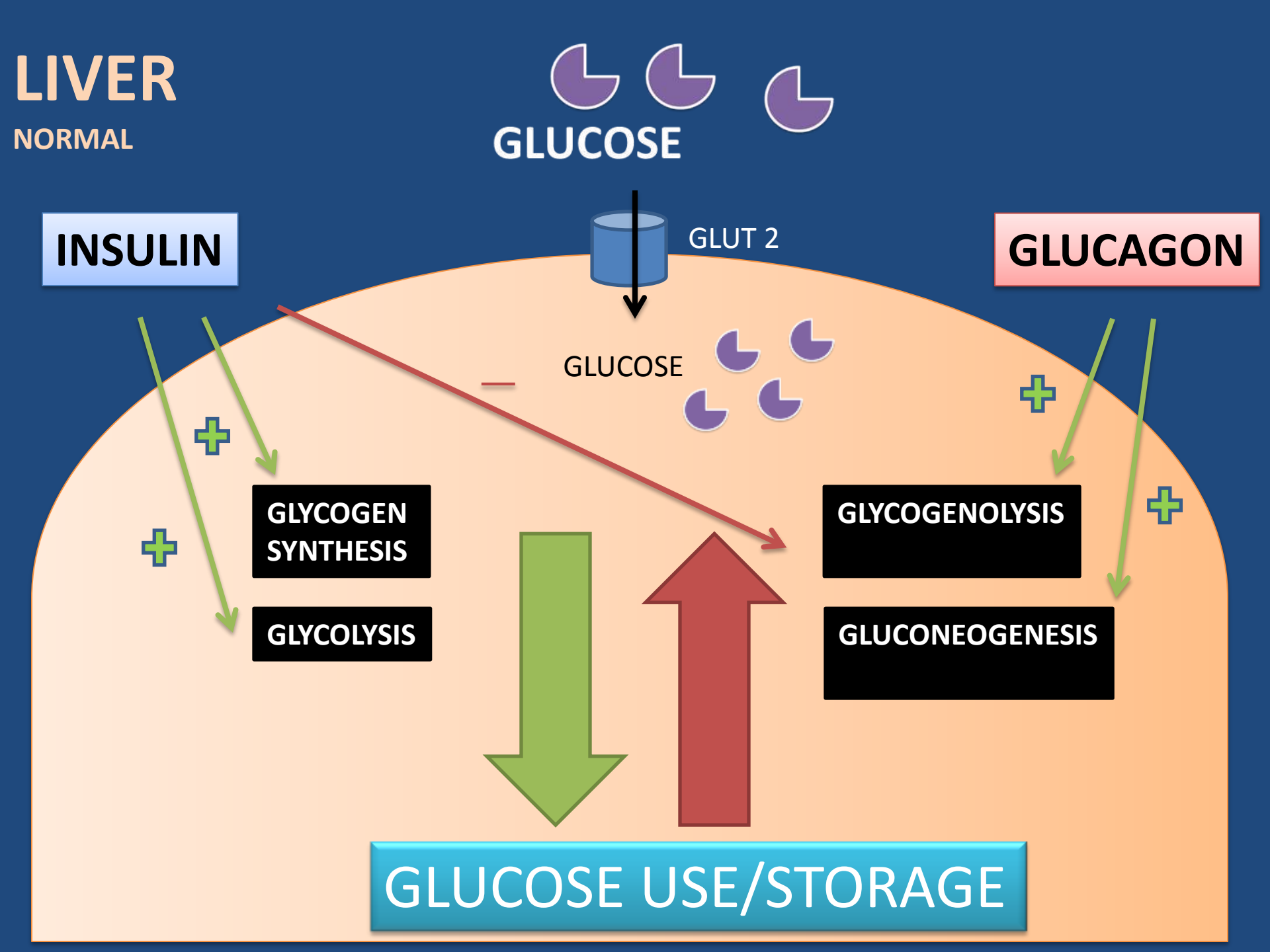
Impaired Insulin Secretion (Beta Cell Failure)

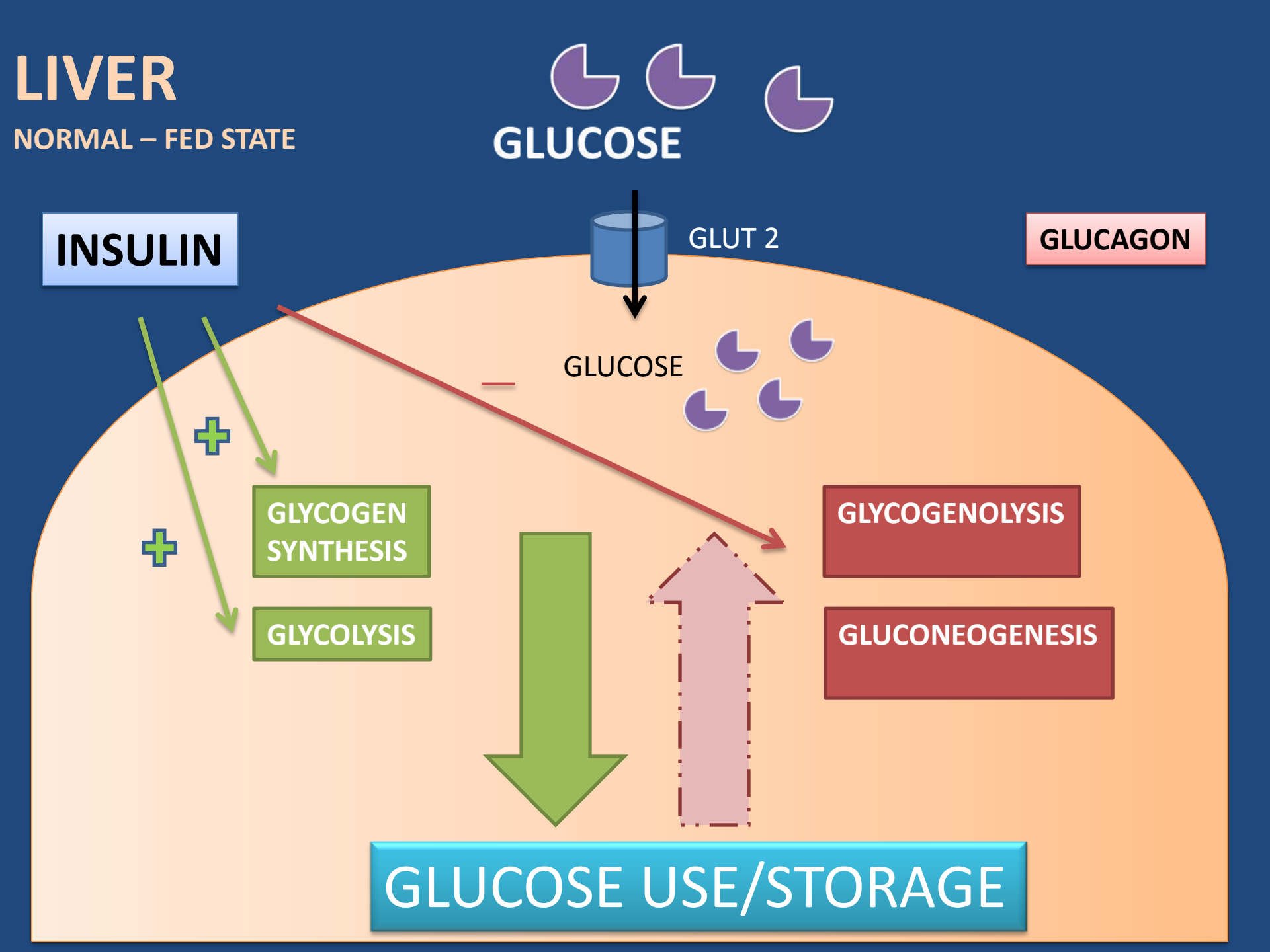
- Aging
- Genes
- Insulin Resistance
  - Same mechanism causing IR will also cause Beta cell failure
- Glucotoxicity
  - Chronic exposure to hyperglycemia impairs insulin secretion
- Incretin Defect
- Lipotoxicity
  - Elevated plasma FFA levels impair insulin secretion
- Hypersecretion of Islet amyloid polypeptide

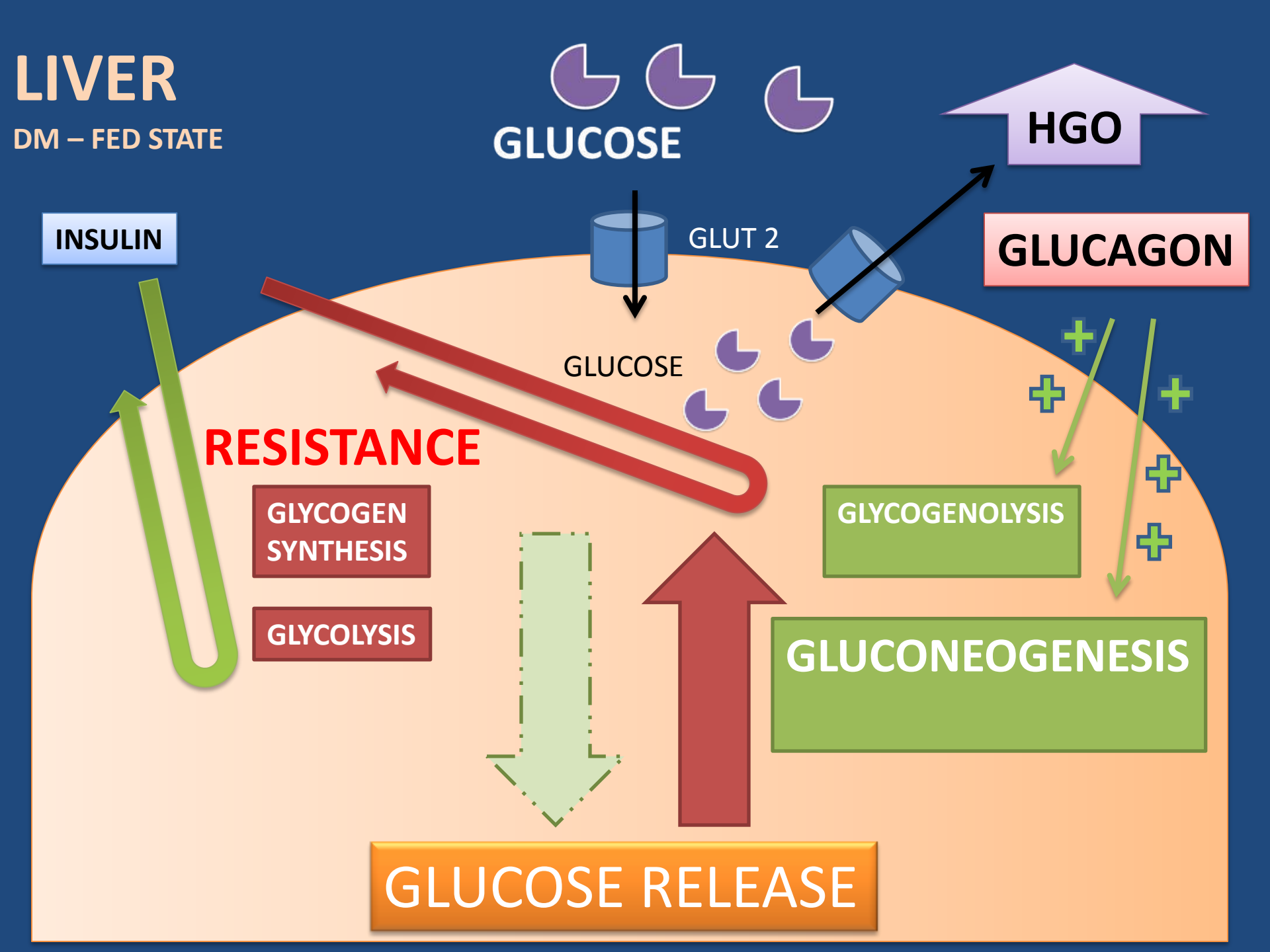


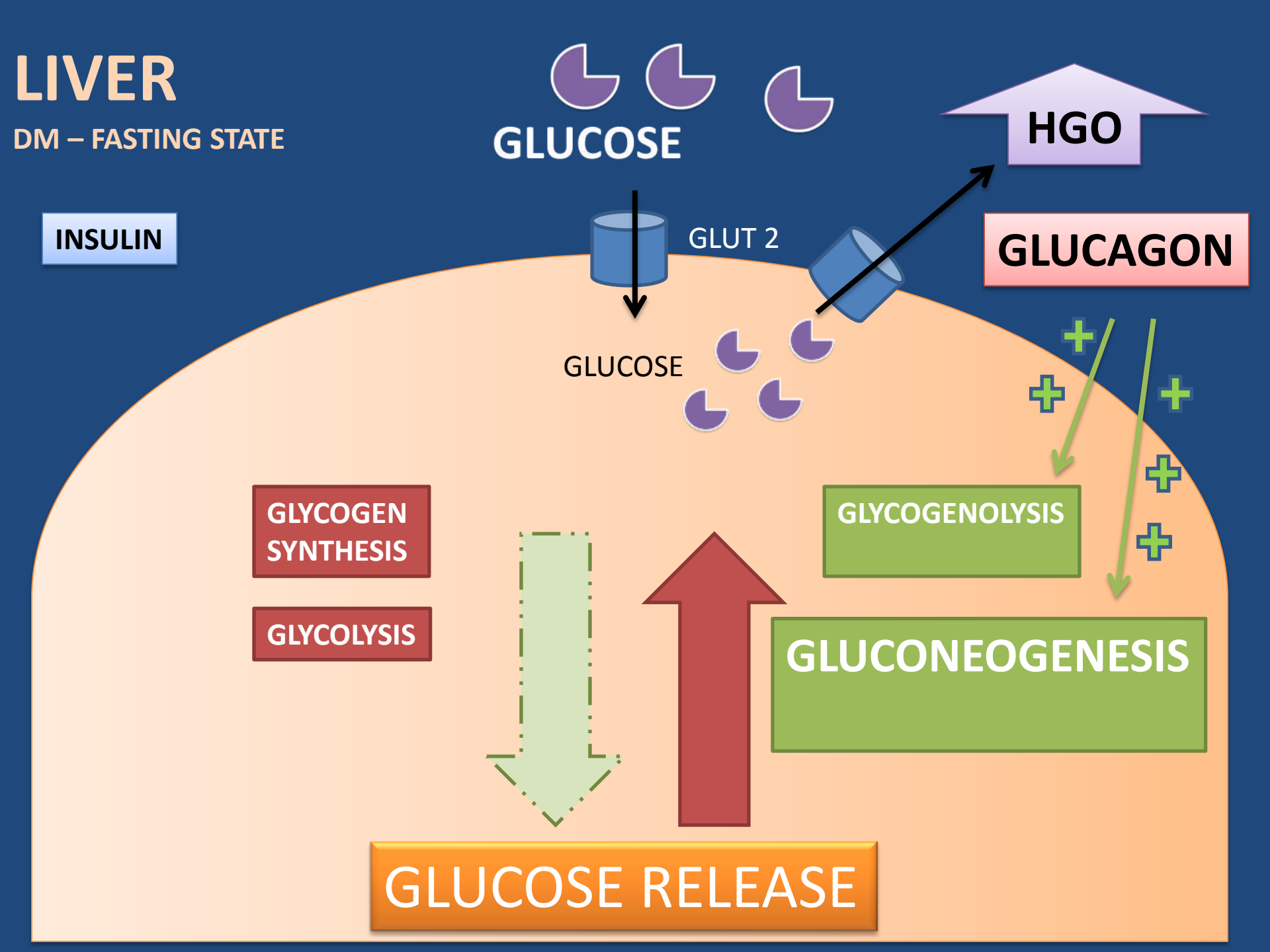
Increased Hepatic Glucose Output (Insulin Resistance in the Liver)

- The purpose of the basal or fasting production of glucose by the liver is to provide glucose for the brain
- In type 2 DM, increased production occurs due to increased Gluconeogenesis despite the presence of elevated insulin
- Other contributing factors to increased HGO
  - Increased glucagon levels and enhanced hepatic sensitivity
  - Lipotoxicity leading to increased expression of gluconeogenic enzymes
  - Glucotoxicity leading to increased production of glucose 6 phosphatase


LIVER
NORMAL
GLUCOSE
INSULIN
GLUT 2
GLUCAGON
GLUCOSE
GLYCOGEN SYNTHESIS
GLYCOLYSIS
GLYCOGENOLYSIS
GLUCONEOGENESIS
GLUCOSE USE/STORAGE

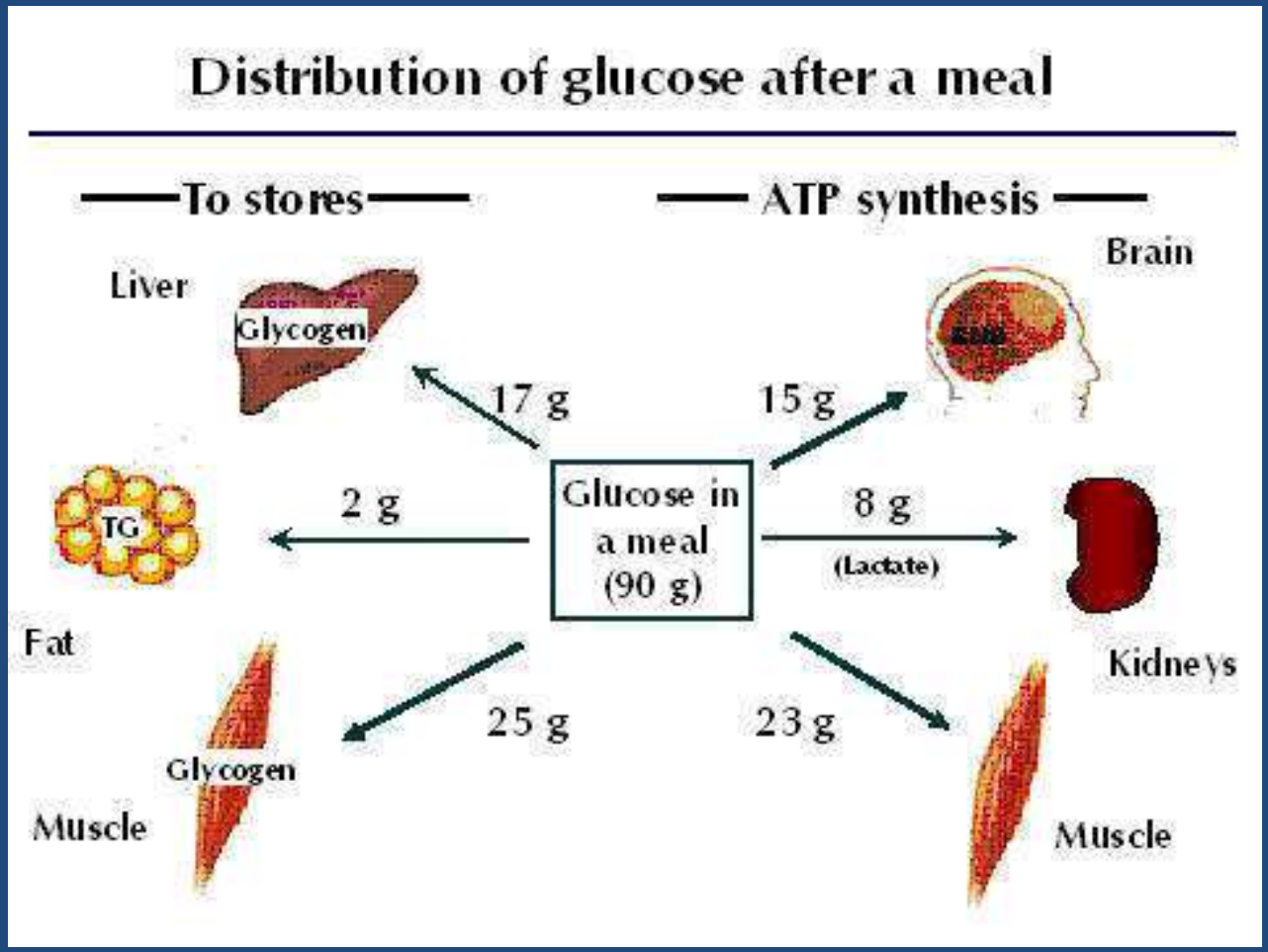

LIVER
NORMAL – FED STATE
GLUCOSE
INSULIN
GLUT 2
GLUCAGON
GLUCOSE
GLYCOGEN SYNTHESIS
GLYCOLYSIS
GLYCOGENOLYSIS
GLUCONEOGENESIS
GLUCOSE USE/STORAGE

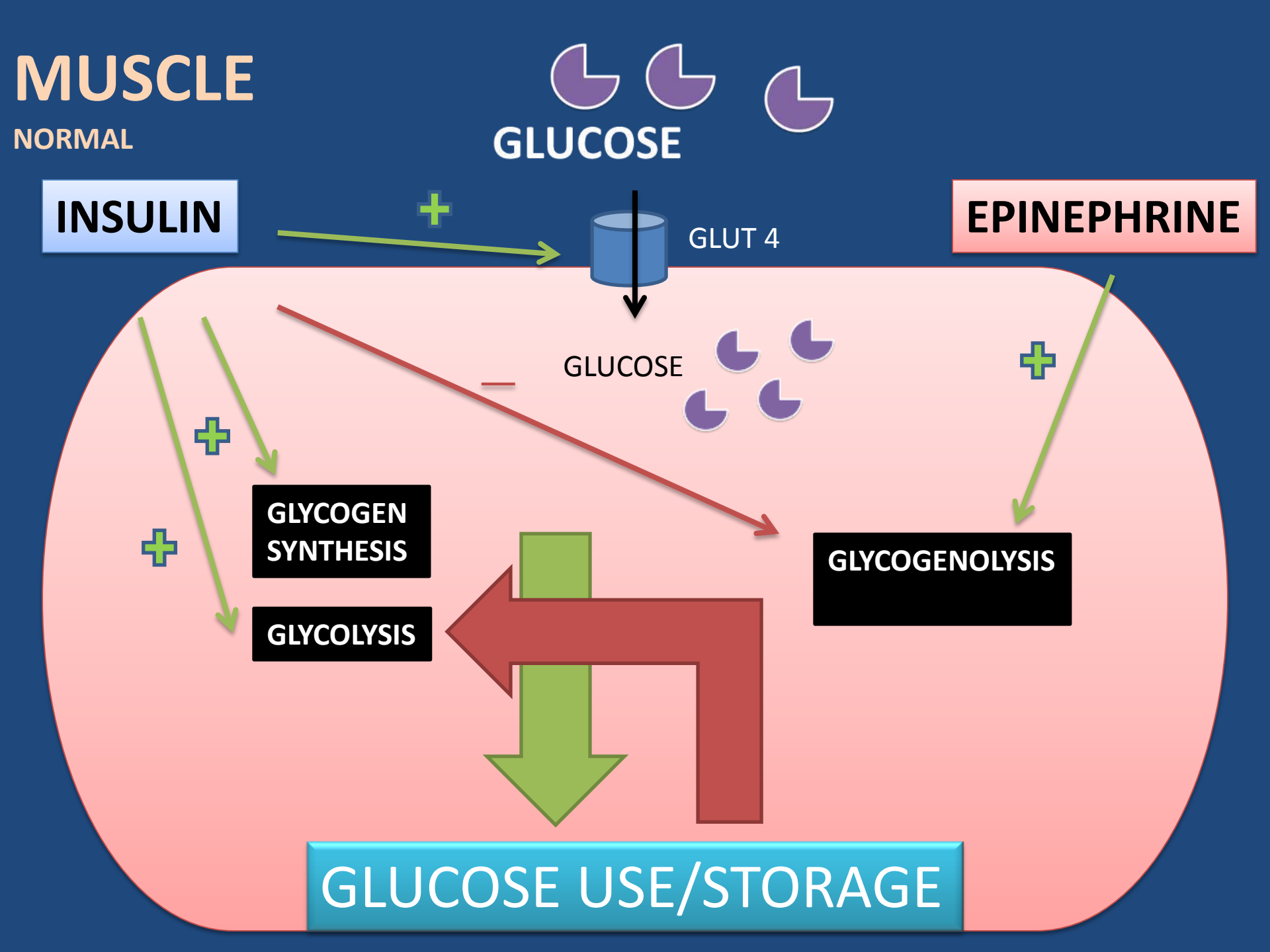

LIVER
DM – FED STATE
GLUCOSE
HGO
INSULIN
GLUT 2
GLUCAGON
GLUCOSE
RESISTANCE
GLYCOGEN SYNTHESIS
GLYCOGENOLYSIS
GLYCOLYSIS
GLUCONEOGENESIS
GLUCOSE RELEASE

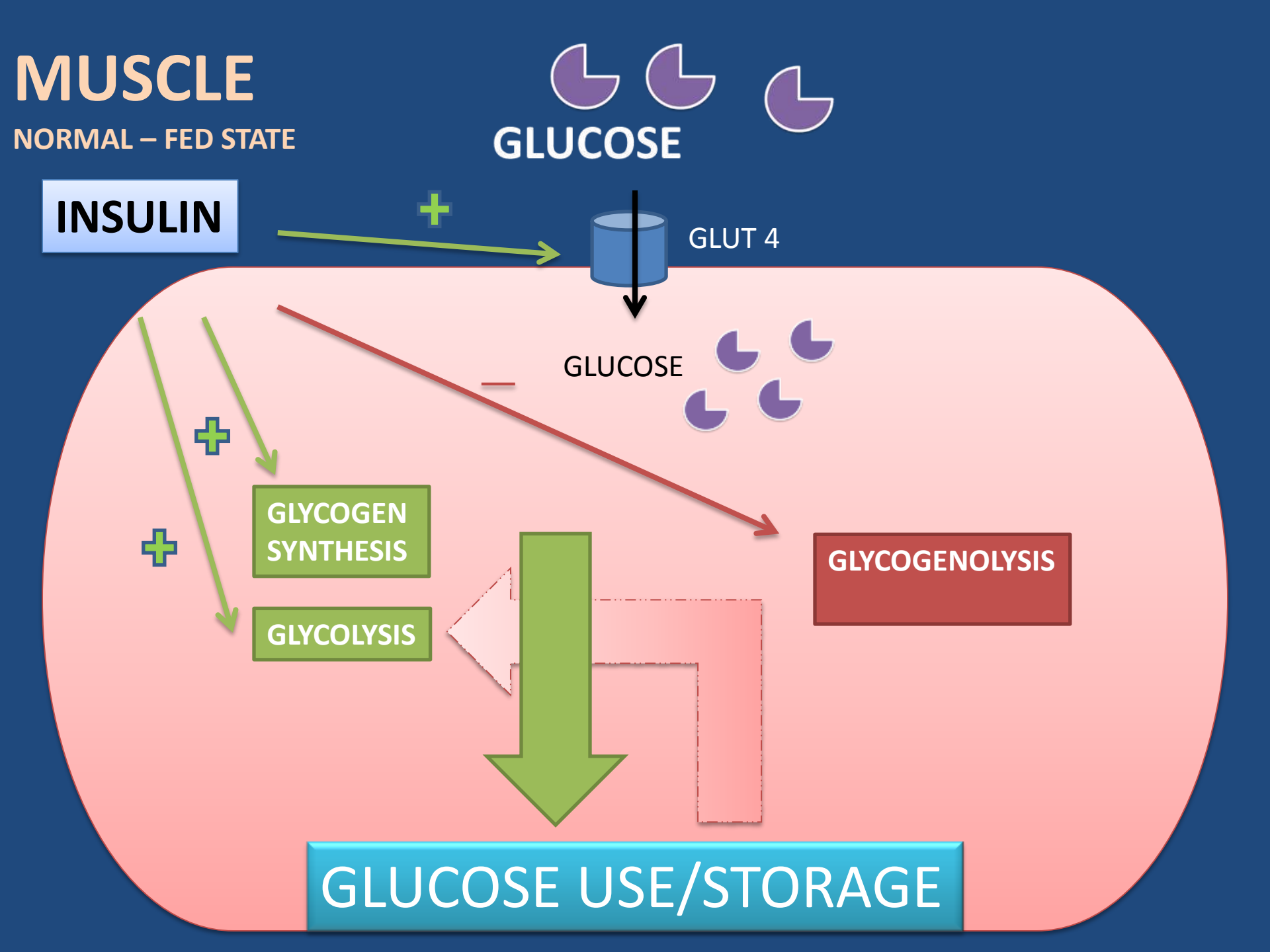

LIVER
DM – FASTING STATE
GLUCOSE
HGO
INSULIN
GLUT 2
GLUCAGON
GLUCOSE
GLYCOGEN SYNTHESIS
GLYCOGENOLYSIS
GLYCOLYSIS
GLUCONEOGENESIS
GLUCOSE RELEASE

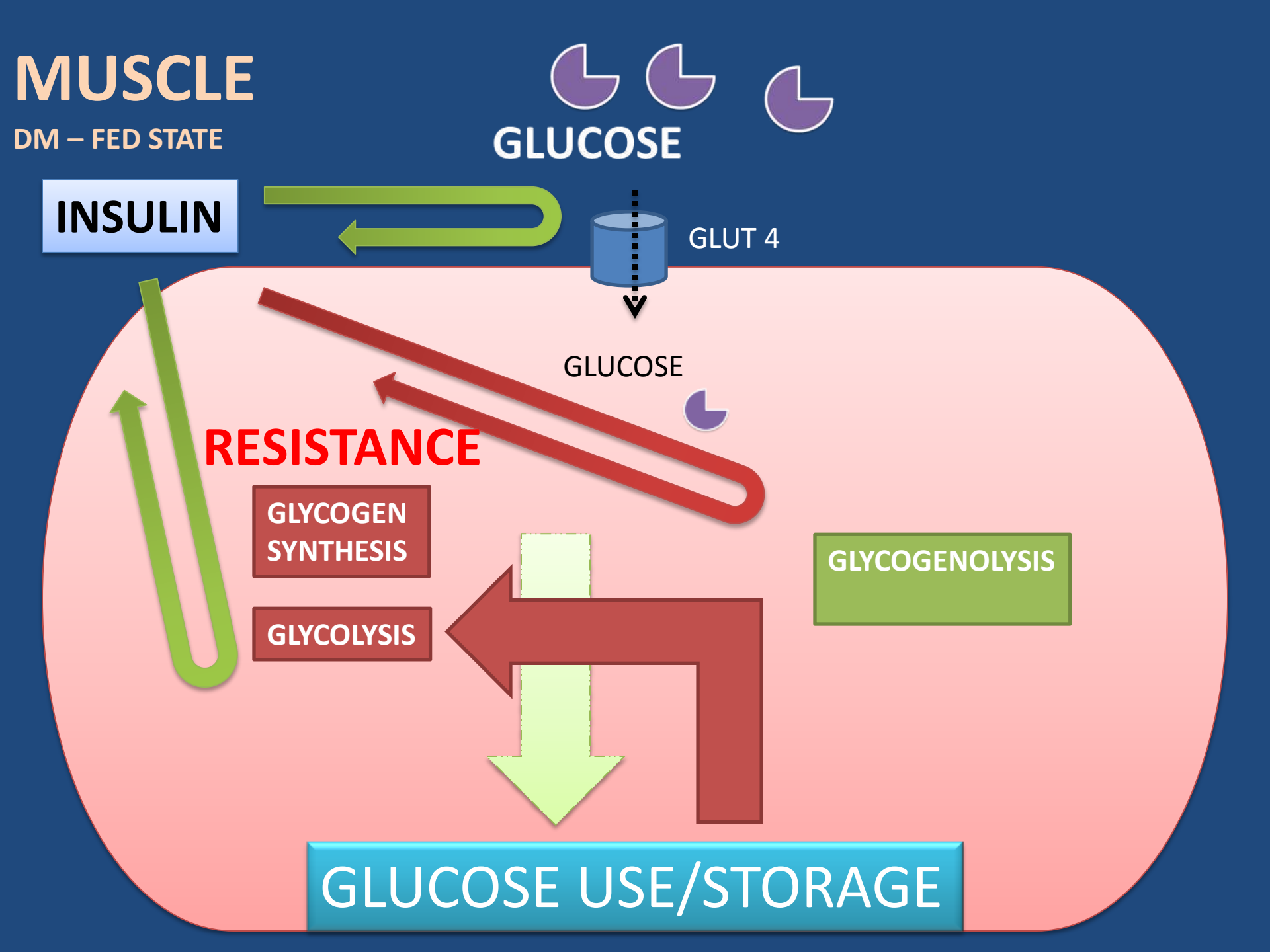
Decreased Glucose Uptake in Peripheral Tissues

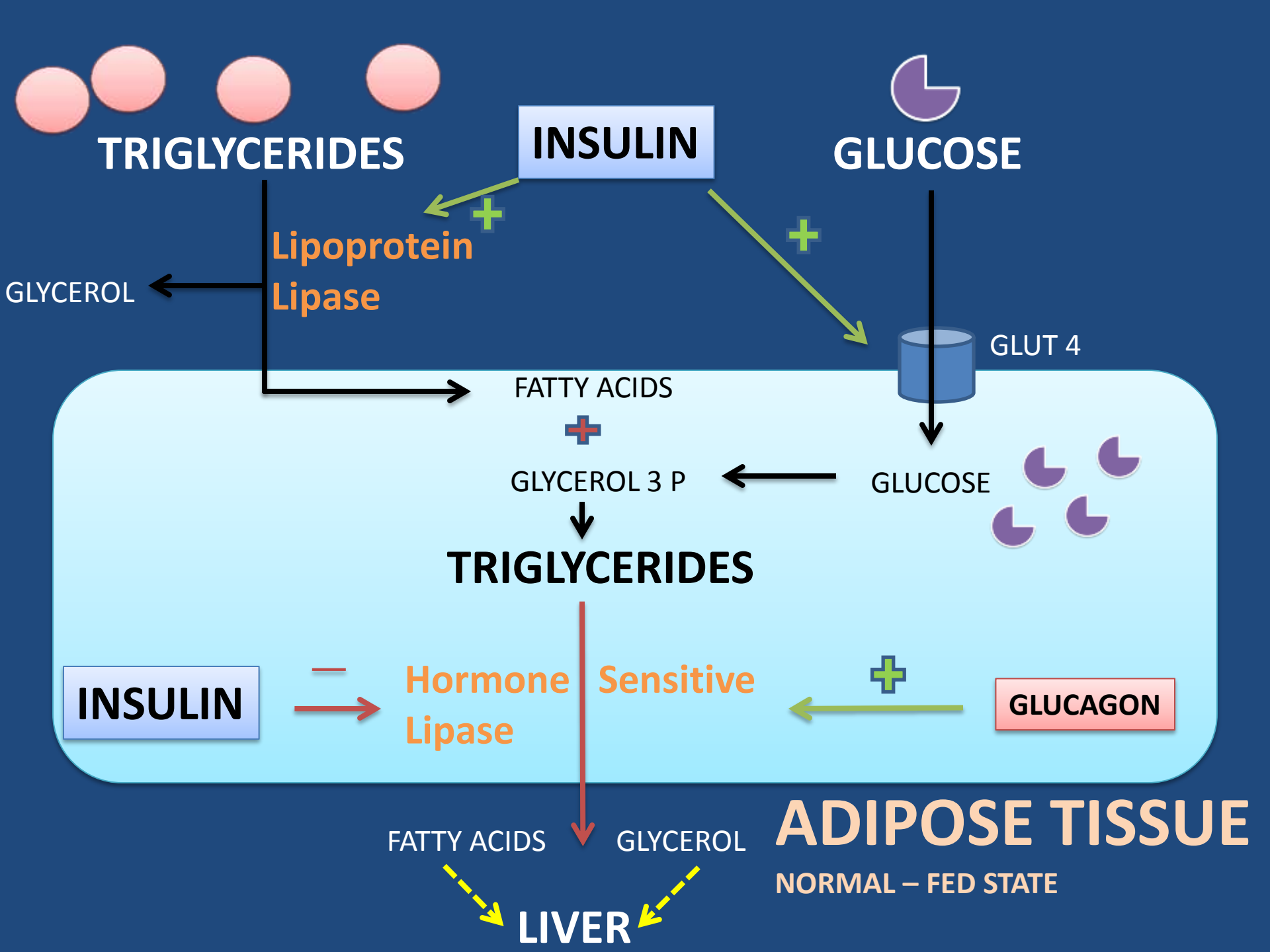
- Defects in insulin action
- Defect in insulin signal transduction system
  - Defect in tyrosine phosphorylation of Insulin Receptor Substrate 1 (IRS-1)
  - Leads to decreased glucose uptake
  - Resultant hyperglycemia leads to increased insulin secretion
  - MAP kinase pathway in the cell retains insulin sensitivity; leads to activation of pathways involved in inflammation and atherogenesis

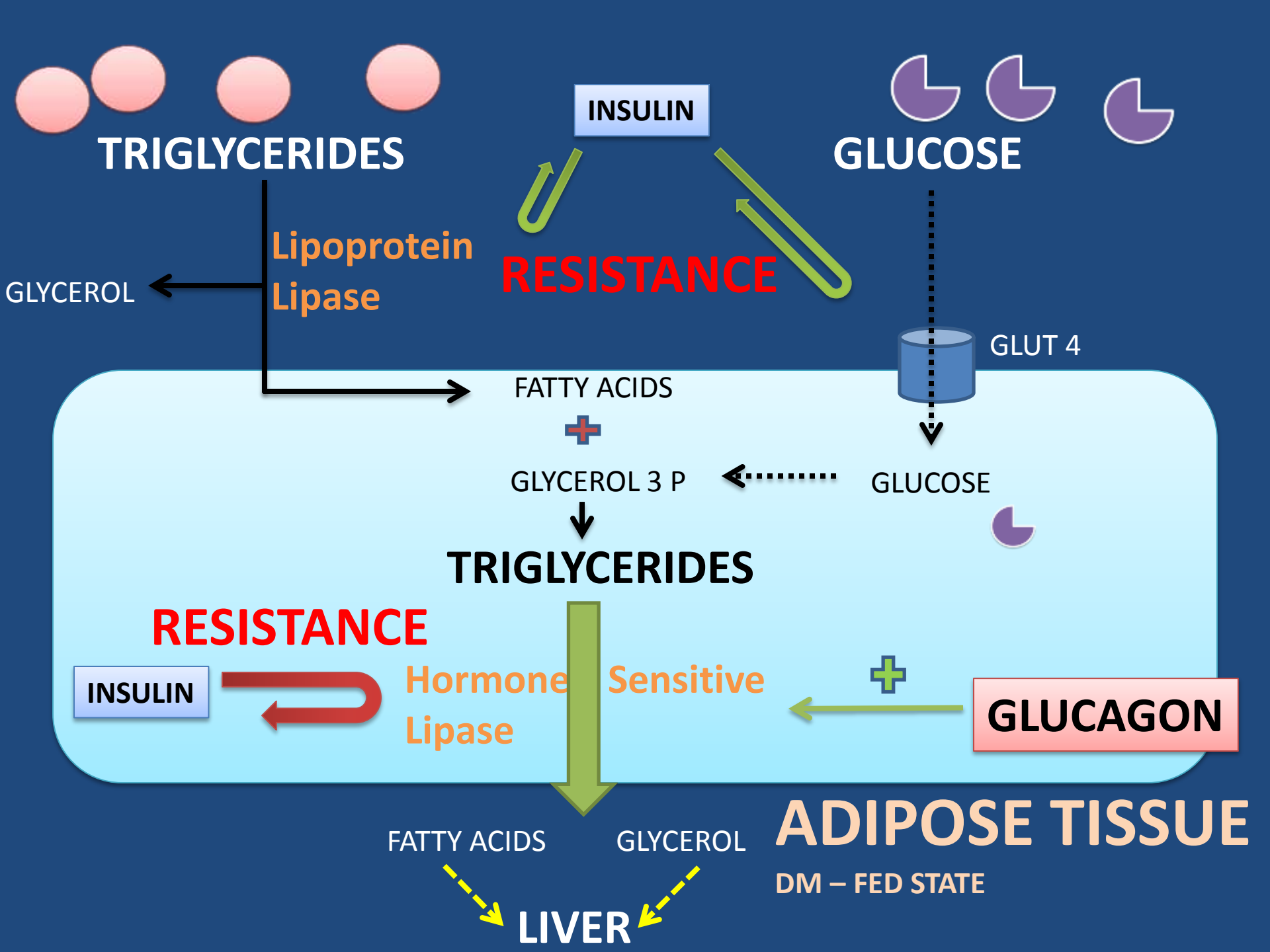

Distribution of glucose after a meal
To stores
ATP synthesis
Liver
Glycogen
Brain
17 g
15 g
2 g
TG
Glucose in a meal (90 g)
8 g
(Lactate)
Fat
Kidneys
25 g
23 g
Glycogen
Muscle
Muscle


MUSCLE
NORMAL
GLUCOSE
INSULIN
GLUT 4
EPINEPHRINE
GLUCOSE
GLYCOGEN SYNTHESIS
GLYCOLYSIS
GLYCOGENOLYSIS
GLUCOSE USE/STORAGE


MUSCLE
NORMAL – FED STATE
GLUCOSE
INSULIN
GLUT 4
GLUCOSE
GLYCOGEN SYNTHESIS
GLYCOLYSIS
GLYCOGENOLYSIS
GLUCOSE USE/STORAGE


MUSCLE
DM – FED STATE
GLUCOSE
INSULIN
GLUT 4
GLUCOSE
RESISTANCE
GLYCOGEN SYNTHESIS
GLYCOLYSIS
GLYCOGENOLYSIS
GLUCOSE USE/STORAGE


TRIGLYCERIDES
INSULIN
GLUCOSE
Lipoprotein Lipase
GLYCEROL
GLUT 4
FATTY ACIDS
GLYCEROL 3 P
GLUCOSE
TRIGLYCERIDES
INSULIN
Hormone Sensitive Lipase
GLUCAGON
FATTY ACIDS
GLYCEROL
LIVER
ADIPOSE TISSUE
NORMAL – FED STATE


TRIGLYCERIDES
INSULIN
GLUCOSE
Lipoprotein Lipase
GLYCEROL
RESISTANCE
GLUT 4
FATTY ACIDS
GLYCEROL 3 P
GLUCOSE
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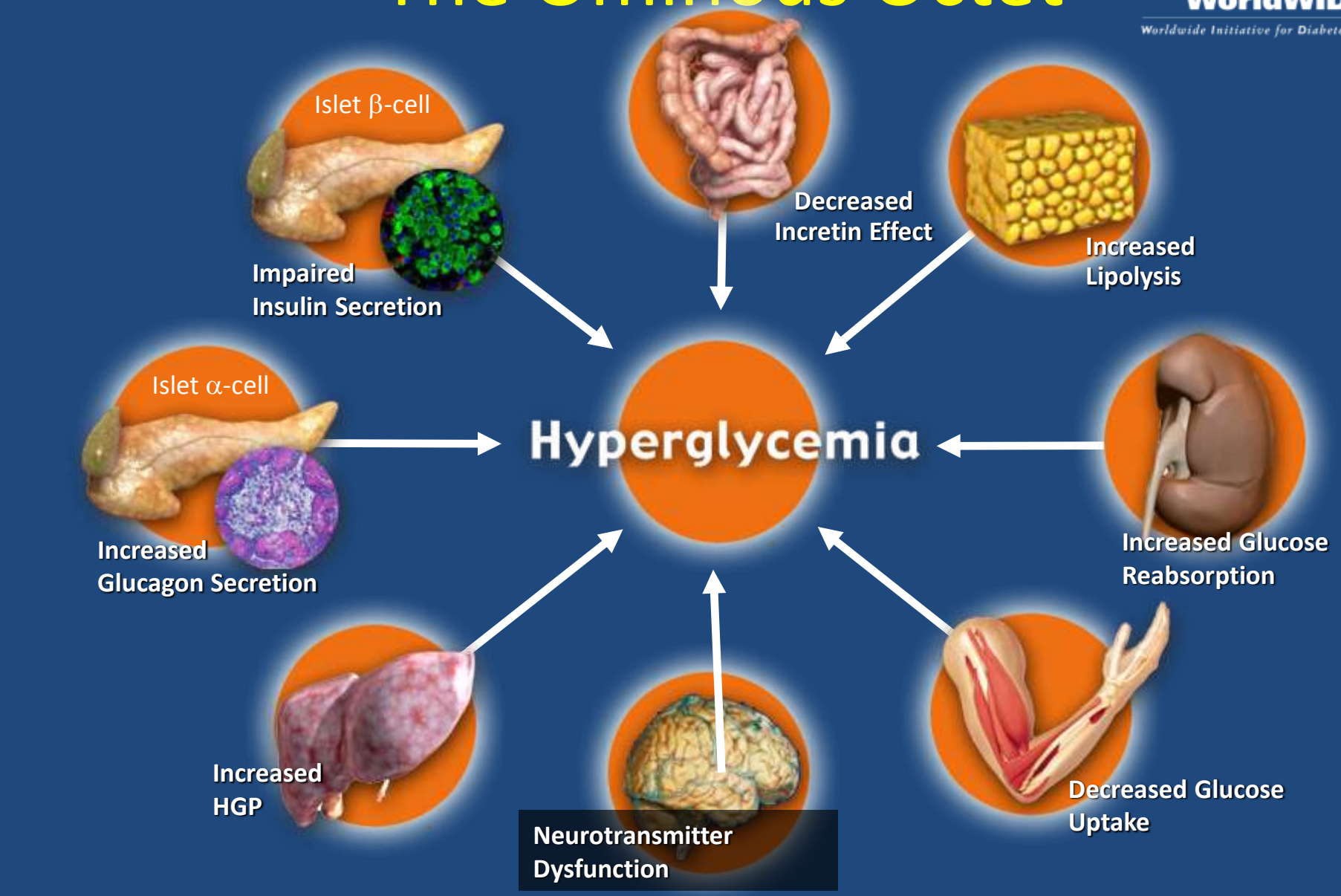
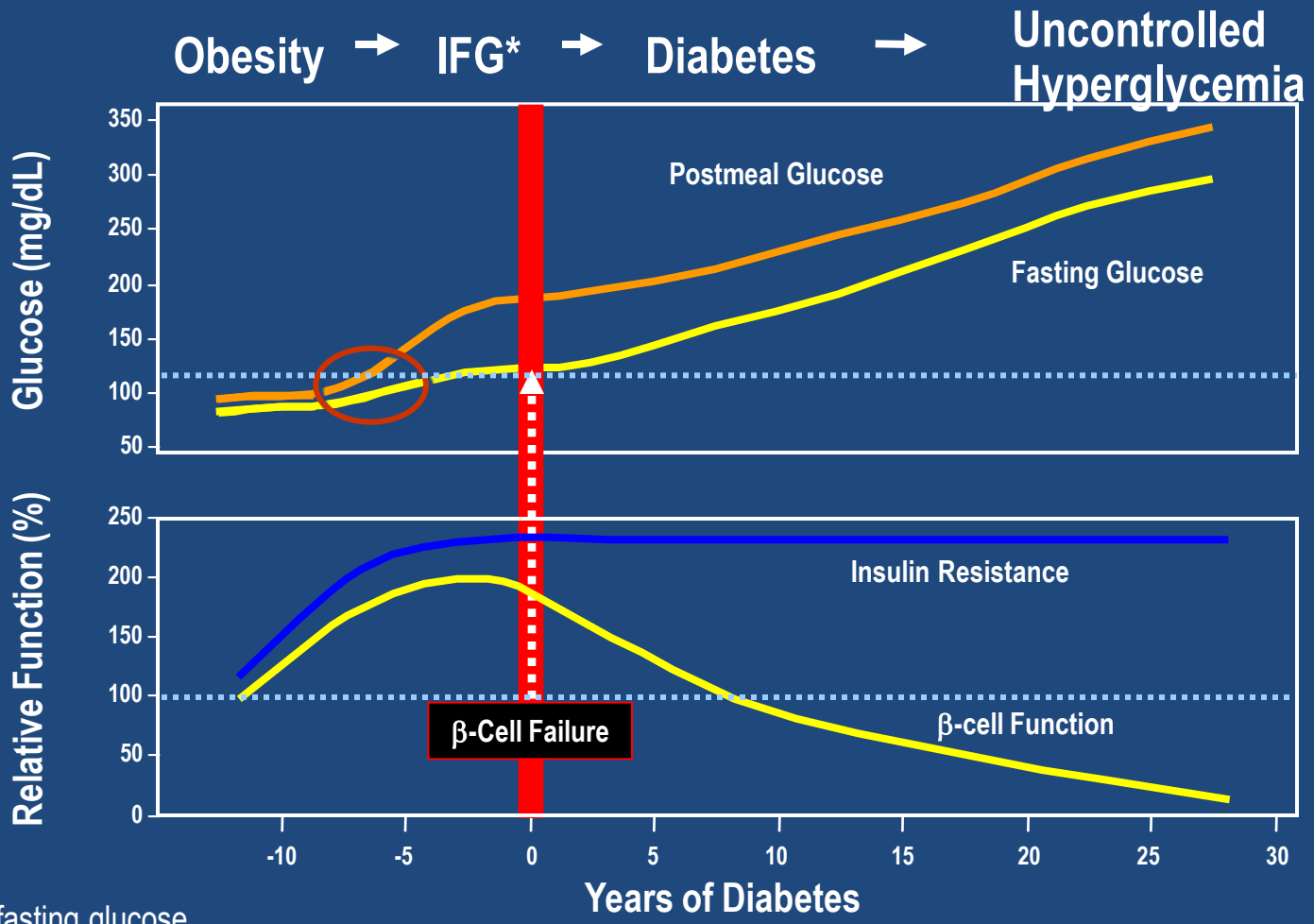
Hormone Sensitive Lipase
GLUCAGON
FATTY ACIDS
GLYCEROL
LIVER
ADIPOSE TISSUE
DM – FED STATE

The Ominous Octet

WorldWIDE
Worldwide Initiative for Diabetes Education



Natural History of Type 2 Diabetes



*IFG=impaired fasting glucose.

Who to screen for Diabetes?

- Testing should be considered in all adults who are overweight (BMI > 25 kg/m^2) plus additional risk factors (see next slide).
  - Body Mass Index (BMI) is computed using the formula below
    - Weight in kilograms

      $(\text{Height in meters})^2$

Who to screen for Diabetes?

- Testing should be considered in all adults who are overweight (BMI > 25 kg/m^2) plus additional risk factors.
  - Physical inactivity
  - First degree relative with Diabetes
  - Women who delivered a baby weighing > 9 lbs or were diagnosed with Gestational Diabetes Mellitus
  - Hypertension

Standards of Medical Care in Diabetes—2011 *DIABETES CARE, VOLUME 34, SUPPLEMENT 1, JANUARY 2011*

Who to screen for Diabetes?

- Testing should be considered in all adults who are overweight (BMI > 25 kg/m^2) plus additional risk factors.
  - Abnormal Lipid Profile (Dyslipidemia)
    - HDL < 35 mg/dl or triglycerides > 250 mg/dl
  - Women with polycystic ovary syndrome
  - AIC > 5.7%, IGT or IFG on previous testing
  - History of cardiovascular disease

When to start screening for Diabetes? (Asymptomatic)

1. At any age when you are overweight plus other additional risk factors
2. In the absence of the previous criteria, screening should begin at age 45 years old
3. If results are normal, testing should be repeated at least at 3 year intervals; more frequent if indicated.

Standards of Medical Care in Diabetes—2011 *DIABETES CARE, VOLUME 34, SUPPLEMENT 1, JANUARY 2011*

How to screen for Diabetes?

- A1C 6.5%
  - The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*

or

- FPG 126 mg/dl (7.0 mmol/l)
  - Fasting is defined as no caloric intake for at least 8 h.*

or

- 2-h plasma glucose 200 mg/dl (11.1 mmol/l) during an OGTT.
  - The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.*

*In the absence of unequivocal hyperglycemia, result should be confirmed by repeat testing.

How to screen for Diabetes? (Symptomatic)

- In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose 200 mg/dl (11.1mmol/l)

Pre-Diabetes

- IFG
  - FPG 100–125 mg/dl (5.6–6.9 mmol/l)

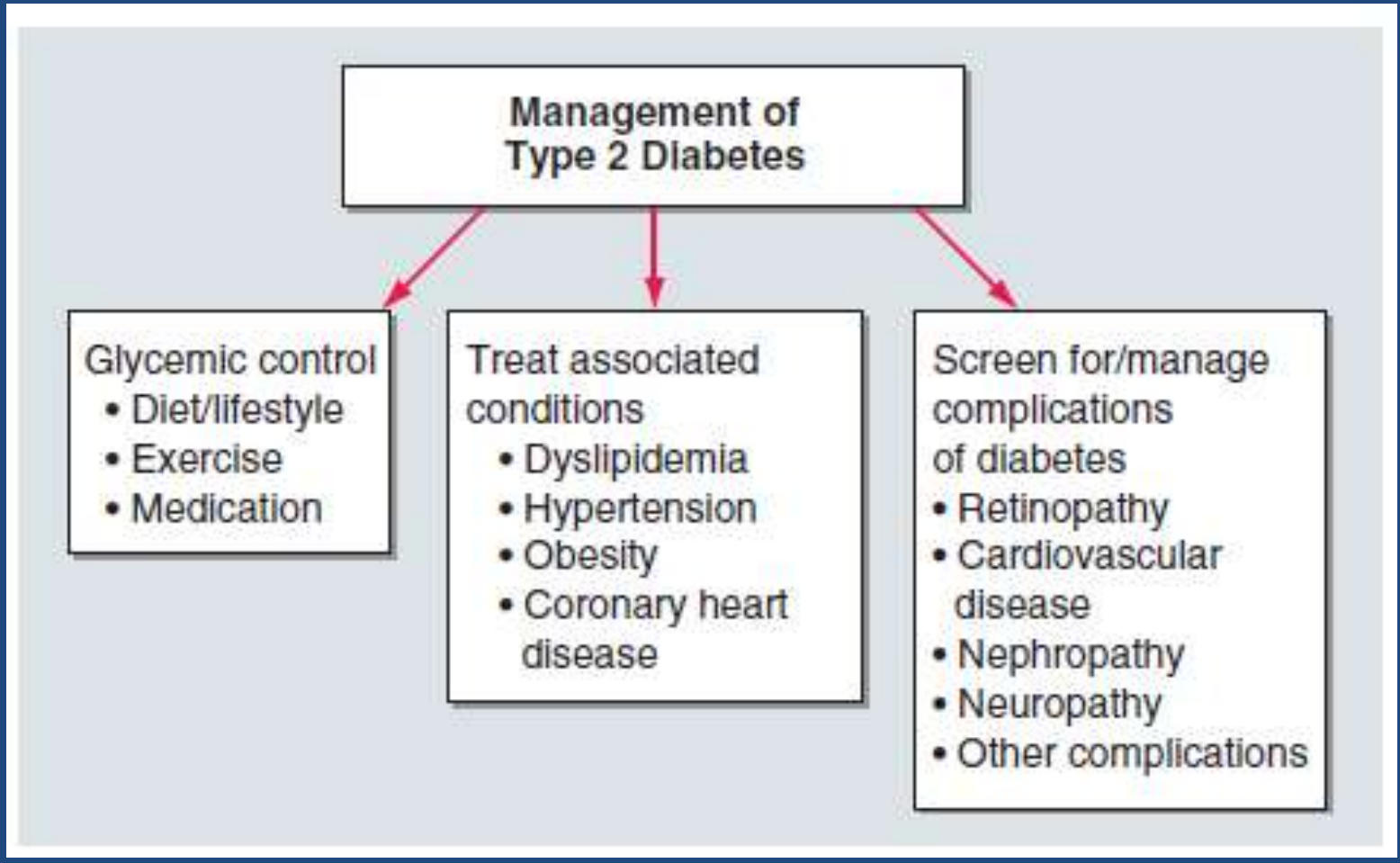
    Or
- IGT
  - 2-h plasma glucose in the 75-g OGTT 140–199 mg/dl (7.8–11.0 mmol/l)

    Or
- A1C 5.7–6.4%
- Should not be viewed as clinical entities in their own right but rather risk factors for diabetes as well as cardiovascular disease (CVD)

Pre–Diabetes Management

- Patients with IGT (A), IFG (E), or an A1C of 5.7–6.4% (E) should be referred to an effective ongoing support program targeting weight loss of 7% of body weight and increasing physical activity to at least 150 min/week of moderate activity such as walking.
- Follow-up counseling appears to be important for success. (B)
- Metformin therapy for prevention of type 2 diabetes may be considered in those at the highest risk for developing diabetes, such as those with multiple risk factors, especially if they demonstrate progression of hyperglycemia (e.g., A1C 6%) despite lifestyle interventions. (B)
- Monitoring for the development of diabetes in those with prediabetes should be performed every year. (E)

Overview of Diabetes Management



Glycemic Goals

Table 10—*Summary of glycemic recommendations for many nonpregnant adults with diabetes*

A1C	<7.0%*
Preprandial capillary plasma glucose	70–130 mg/dl* (3.9–7.2 mmol/l)
Peak postprandial capillary plasma glucose†	<180 mg/dl* (<10.0 mmol/l)
• Goals should be individualized based on*:	
• duration of diabetes	
• age/life expectancy	
• comorbid conditions	
• known CVD or advanced microvascular complications	
• hypoglycemia unawareness	
• individual patient considerations	
• More or less stringent glycemic goals may be appropriate for individual patients.	
• Postprandial glucose may be targeted if A1C goals are not met despite reaching preprandial glucose goals.	

Postprandial glucose measurements should be made 1–2 h after the beginning of the meal, generally peak levels in patients with diabetes.

Glycemic Goals - Remarks

- Lowering A1C to below or around 7% has been shown to reduce microvascular and neuropathic complications of diabetes and, if implemented soon after the diagnosis of diabetes, is associated with long-term reduction in macrovascular disease (B)
- Small but incremental benefit in microvascular outcomes with A1C values closer to normal, providers might reasonably suggest more stringent A1C goals for selected individual patients, if this can be achieved without significant hypoglycemia or other adverse effects of treatment. Such patients might include those with short duration of diabetes, long life expectancy, and no significant CVD. (B)
- Conversely, less stringent A1C goals may be appropriate for patients with a history of severe hypoglycemia, limited life expectancy, advanced microvascular or macrovascular complications, extensive comorbid conditions, and those with longstanding diabetes in whom the general goal is difficult to attain despite DSME, appropriate glucose monitoring, and effective doses of multiple glucose-lowering agents including insulin. (C)

Medical Nutrition Therapy

TABLE 338-9 NUTRITIONAL RECOMMENDATIONS FOR ADULTS WITH DIABETES[a]

- Fat
  - 20–35% of total caloric intake
  - Saturated fat < 7% of total calories
  - <200 mg/day of dietary cholesterol
  - Two or more servings of fish/week provide ω-3 polyunsaturated fatty acids
  - Minimal trans fat consumption
- Carbohydrate
  - 45–65% of total caloric intake (low-carbohydrate diets are not recommended)
  - Amount and type of carbohydrate important[b]
  - Sucrose-containing foods may be consumed with adjustments in insulin dose
- Protein
  - 10–35% of total caloric intake (high-protein diets are not recommended)
- Other components
  - Fiber-containing foods may reduce postprandial glucose excursions
  - Nonnutrient sweeteners

[a]See text for differences for patients with type 1 or type 2 diabetes. As for the general population, a healthy diet includes fruits, vegetables, and fiber-containing foods.
[b]Amount of carbohydrate determined by estimating grams of carbohydrate in diet; glycemic index reflects how consumption of a particular food affects the blood glucose.
Source: Adapted from American Diabetes Association, 2007.

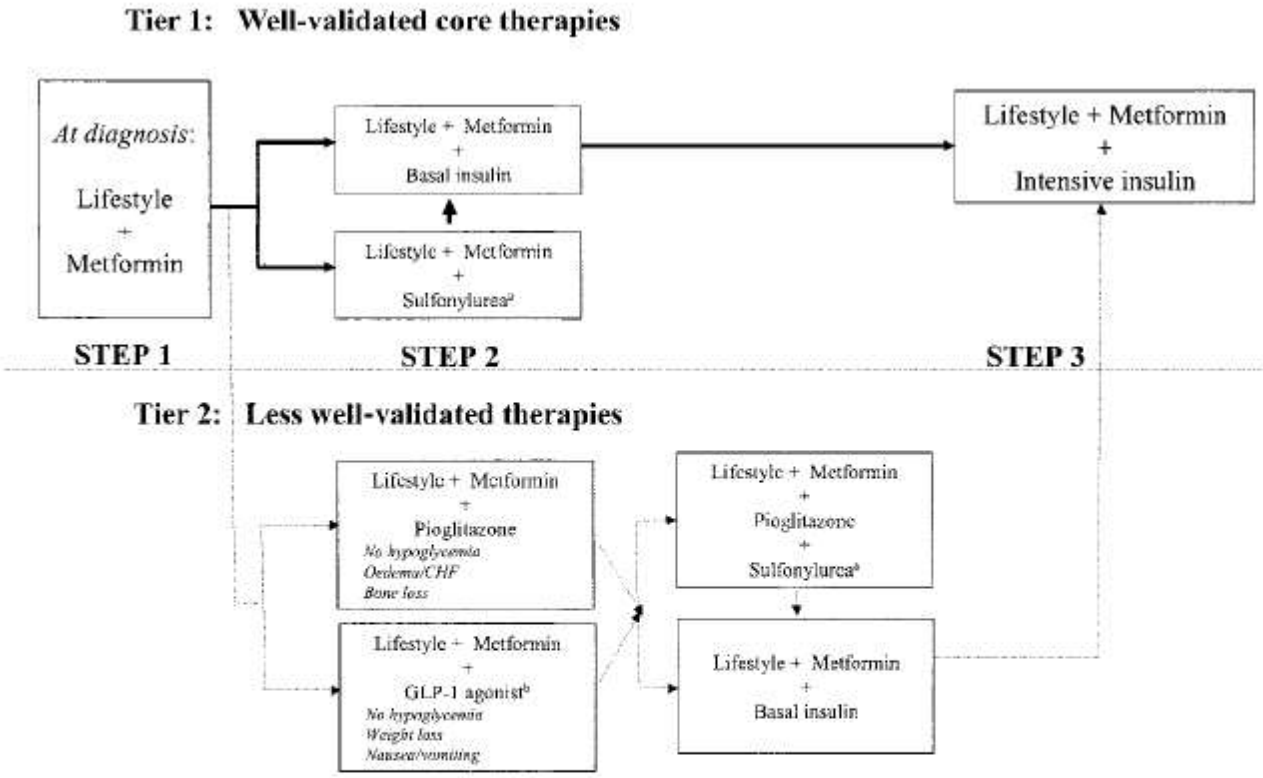


Figure 2—*Algorithm for the metabolic management of type 2 diabetes; Reinforce lifestyle interventions at every visit and check A1C every 3 months until A1C is <7% and then at least every 6 months. The interventions should be changed if A1C is ≥7%. [a]Sulfonylureas other than glyburide (glyburide) or chlorpropamide. [b]Insufficient clinical use to be confident regarding safety. See text box, entitled* TITRATION OF METFORMIN. *See Fig. 1 for initiation and adjustment of insulin. CHF, congestive heart failure.*

INSULIN SECRETAGOGUES
Sulfonylureas

1ST GENERATION

Acetohexamide

Chlorpropamide

Tolbutamide

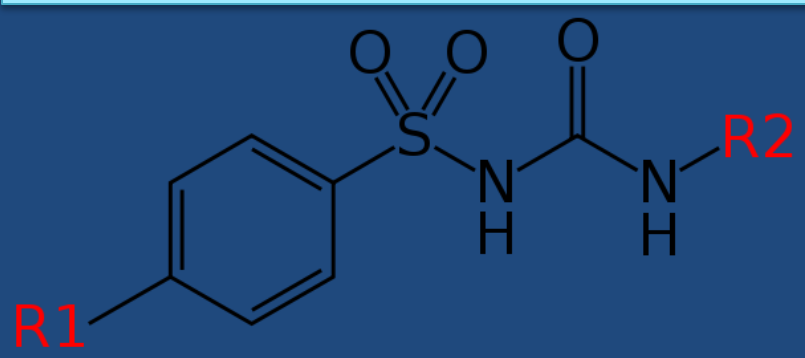
2nd GENERATION

Glipizide

Gliclazide

Glibenclamide

Glimepiride



Mechanism of Action:

Acts on sulfonylurea receptor on Potassium channel. Leads to depolarizaion of cell which promotes calcium influx which triggers insulin secretion

ADVANTAGES:

Rapidly Effective

DISADVANTAGES:

Hypoglycemia & Weight Gain

A1C Lowering : 1.0 – 2.0

INSULIN SECRETAGOGUES
Meglitinides

Repaglinide
Nateglinide

Mechanism of Action:
Acts on another receptor on Potassium channel. Leads to depolarizaion of cell which promotes calcium influx which triggers insulin secretion

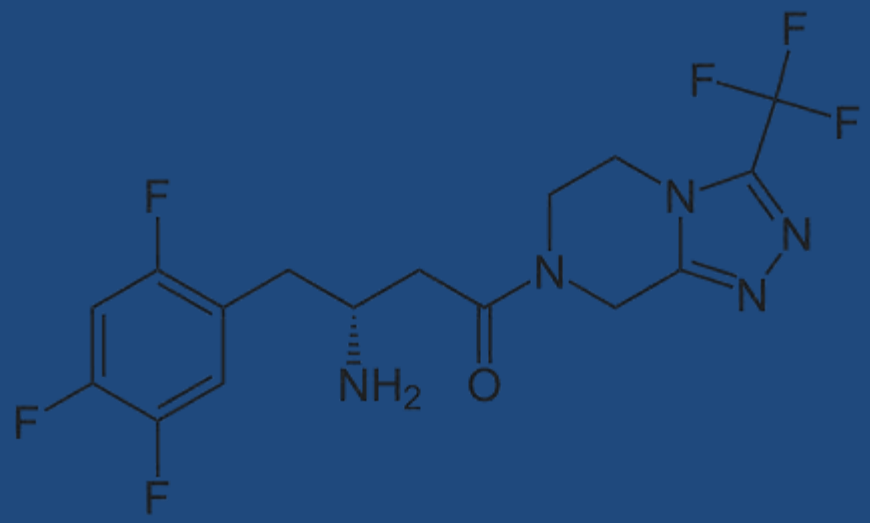
ADVANTAGES:
Rapid onset especially in postprandial phase

DISADVANTAGES:
Hypoglycemia & Weight Gain

A1C Lowering : 1.0 – 2.0

DPP IV INHIBITORS

Alogiptin
Linagliptin
Saxagliptin
Sitagliptin
Vildagliptin



Mechanism of Action:

Prevents GLP 1 breakdown by inhibiting DPP IV enzyme. GLP 1 promotes insulin secretion by a glucose dependent manner. Improves alpha cell sensitivity (Glucagon release).

ADVANTAGES:

Weight Neutral and Low risk for Hypoglycemia

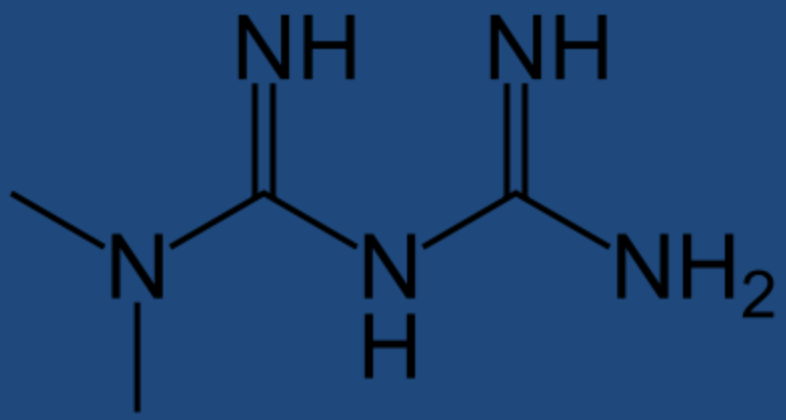
DISADVANTAGES:

Not as effective in lowering A1C

A1C Lowering : 0.5 – 0.8

BIGUANIDES

Metformin
Phenformin



Mechanism of Action:
Reduces Hepatic Glucose Output by inhibiting Hepatic Gluconeogenesis. Weak sensitizer in muscle

ADVANTAGES:
Weight Neutral/Loss

DISADVANTAGES:
GIT disturbances. Avoid in renal disease

A1C Lowering : 1.0 – 2.0

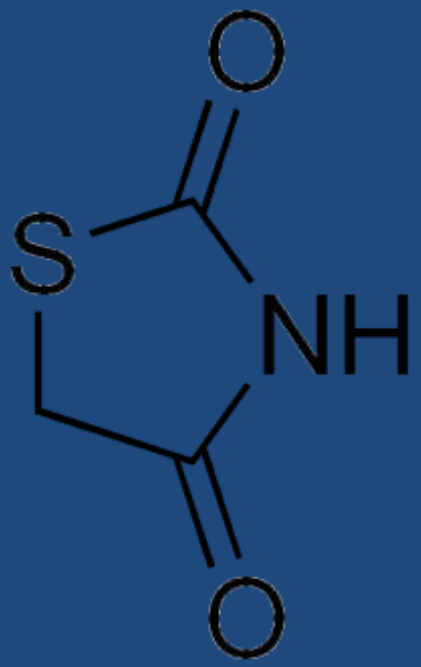
How to start Metformin

TITRATION OF METFORMIN

1. Begin with low-dose metformin (500 mg) taken once or twice per day with meals (breakfast and/or dinner) or 850 mg once per day.
2. After 5–7 days, if gastrointestinal side effects have not occurred, advance dose to 850, or two 500 mg tablets, twice per day (medication to be taken before breakfast and/or dinner).
3. If gastrointestinal side effects appear as doses advanced, decrease to previous lower dose and try to advance the dose at a later time.
4. The maximum effective dose can be up to 1,000 mg twice per day but is often 850 mg twice per day. Modestly greater effectiveness has been observed with doses up to about 2,500 mg/day. Gastrointestinal side effects may limit the dose that can be used.
5. Based on cost considerations, generic metformin is the first choice of therapy. A longer-acting formulation is available in some countries and can be given once per day.

THIAZOLIDINEDIONES

Pioglitazone
Rosiglitzaone
Troglitazone



Mechanism of Action:

Acts on a nuclear receptor Peroxisome Proliferator activated receptor (PPAR γ)

Improves peripheral insulin sensitivity

ADVANTAGES:

Improves lipid profile.

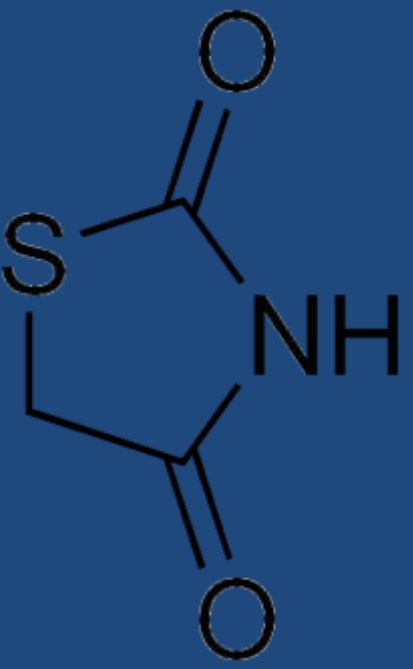
Reduces insulin requirements

DISADVANTAGES:

Weight Gain, Edema, Bone Loss

A1C Lowering : 0.5 – 1.4

THIAZOLIDINEDIONES

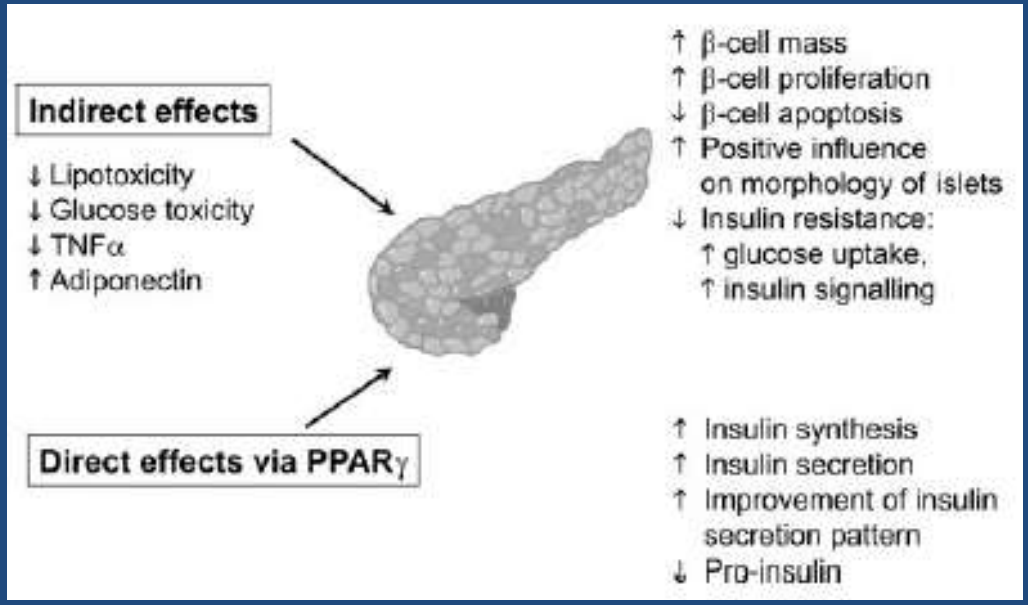


ADIPOCYTES

INCREASED ADIPOCYTE DIFFERENTIATION
- Increased number of small sensitive Adipocytes leading to increased glucose uptake

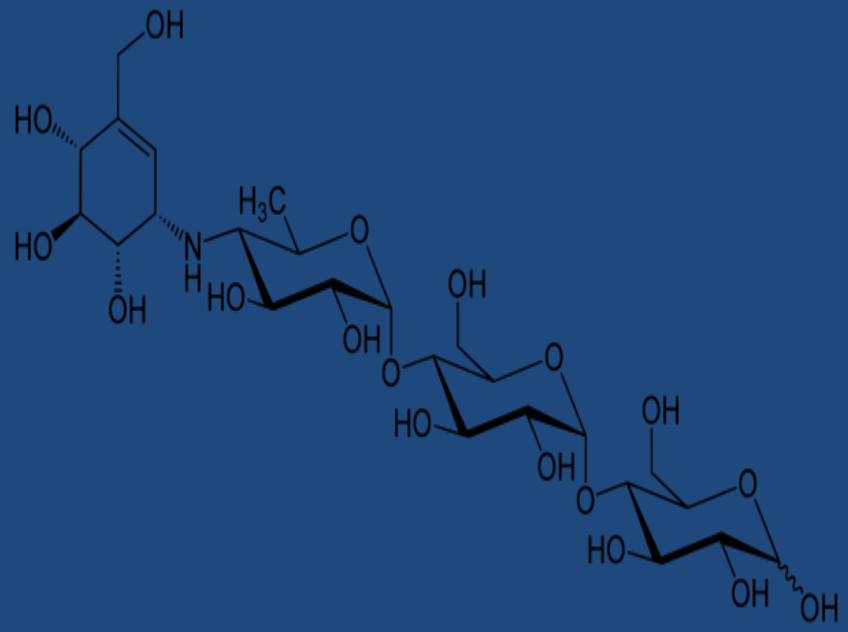
DECREASED LIPOLYSIS
- Due to increased insulin sensitivity
- Decreased fatty acid release

BETA CELLS



ALPHA GLUCOSIDASE INHIBITORS

Acarbose
Miglitol



Mechanism of Action:
Reversible inhibition of alpha glucosidase in the intestinal brush border. Decrease intestinal absorption of glucose.

ADVANTAGES:
No Hypoglycemia

DISADVANTAGES:
GIT disturbances.

A1C Lowering : 0.5 – 0.8

TABLE 383-11 GLUCOSE-LOWERING THERAPIES FOR TYPE 2 DIABETES

	Mechanism of Action	Examples	A1C Reduction (%)[a]	Agent-Specific Advantages	Agent-Specific Disadvantages	Contraindications/ Relative Contraindications
Oral						
Biguanides	↓ Hepatic glucose production, weight loss, glucose, utilization, insulin resistance	Metformin	1–2	Weight loss	Lactic acidosis, diarrhea, nausea	Serum creatinine >1.5 mg/dL (men) >1.4 mg/dL (women), CHF, radiographic contrast studies, seriously ill patients, acidosis
α–Glucosidase inhibitors	↓ Glucose absorption	Acarbose, Miglitol	0.5–0.8	Reduce postprandial glycemia	GI flatulence, liver function tests	Renal/liver disease
Dipeptidyl peptidase IV inhibitors	Prolong endogenous GLP-1 action	Sitagliptin	0.5–1.0	Does not cause hypoglycemia		Reduce dose with renal disease
Insulin secretagogues—sulfonylureas	↑ Insulin secretion	Table 338-12	1–2	Lower fasting blood glucose	Hypoglycemia, weight gain	Renal/liver disease
Insulin secretagogues—nonsulfonylureas	↑ Insulin secretion	Table 338-12	1–2	Short onset of action, lowers postprandial glucose	Hypoglycemia	Renal/liver disease
Thiazolidinediones	↓ Insulin resistance, ↑ glucose utilization	Rosiglitazone, Pioglitazone	0.5–1.4	Lower insulin requirements	Peripheral edema, CHF, weight gain, fractures, macular edema; rosiglitazone may increase risk of MI	Congestive heart failure, liver disease
Parenteral						
Insulin	↑ Glucose utilization and other anabolic actions	Table 323-11	No limit	Known safety profile	Injection, weight gain, hypoglycemia	
GLP-1 agonist	↑ Insulin, ↓ Glucagon, slow gastric emptying	Exenatide	0.5–1.0	Weight loss	Injection, nausea, ↑ risk of hypoglycemia with insulin secretagogues	Renal disease, agents that also slow GI motility
Amylin agonist[b]	Slow gastric emptying, ↓ Glucagon	Pramlintide	0.25–0.5	Reduce postprandial glycemia, weight loss	Injection, nausea, ↑ risk of hypoglycemia with insulin	Agents that also slow GI motility
Medical nutrition therapy and physical activity	↓ Insulin, resistance, ↑ insulin secretion	Low-calorie, low-fat diet, exercise	1–2	Other health benefits	Compliance difficult, long-term success low	

[a]A1C reduction depends partly on starting A1C.
[b]Amylin agonist is approved for use in type 1 and type 2 diabetes.

Complications - CVD

- Screen and treat for co-existent CVD or its risk factors
  - Hypertension
  - Dyslipidemia
  - Antiplatelet therapy
  - Smoking

Hypertension

- Screening and diagnosis
  - Blood pressure should be measured at every routine diabetes visit. Patients found to have systolic blood pressure 130 mmHg or diastolic blood pressure 80 mmHg should have blood pressure confirmed on a separate day. Repeat systolic blood pressure 130 mmHg or diastolic blood pressure 80 mmHg confirms a diagnosis of hypertension. (C)

- Treatment
  - Patients with a systolic blood pressure of 130–139 mmHg or a diastolic blood pressure of 80–89mmHgmay be given lifestyle therapy alone for a maximum of 3 months and then, if targets are not achieved, be treated with addition of pharmacological agents. (E)
  - Patients with more severe hypertension (systolic blood pressure 140 or diastolic blood pressure 90 mmHg) at diagnosis or follow-up should receive pharmacologic therapy in addition to lifestyle therapy. (A)

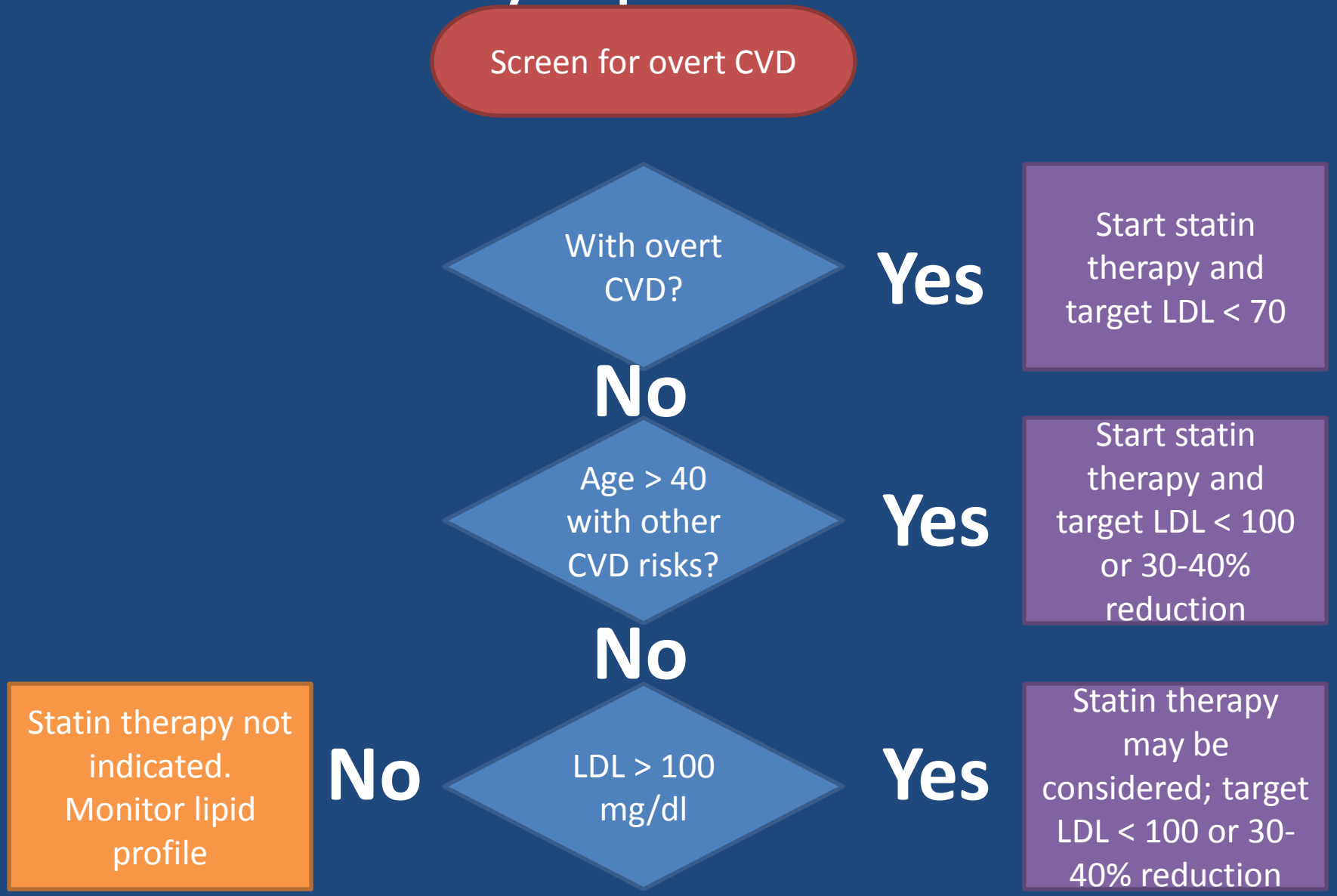
Hypertension

- Treatment
  - Lifestyle therapy for hypertension consists of: weight loss, if overweight; Dietary Approaches to Stop Hypertension (DASH)-style dietary pattern includingreducing sodium and increasing potassium intake; moderation of alcohol intake; and increased physical activity. (B)
  - Pharmacologic therapy for patients with diabetes and hypertension should be with a regimen that includes either an ACE inhibitor or an ARB. If one class is not tolerated, the other should be substituted. If needed to achieve blood pressure targets, a thiazide diuretic should be added to those with an estimated GFR (eGFR) (see below) 30 ml/min/1.73 m2 and a loop diuretic for those with an eGFR 30 ml/min/1.73 m2. (C)
  - Multiple drug therapy (two or more agents at maximal doses) is generally required to achieve blood pressure targets. (B)

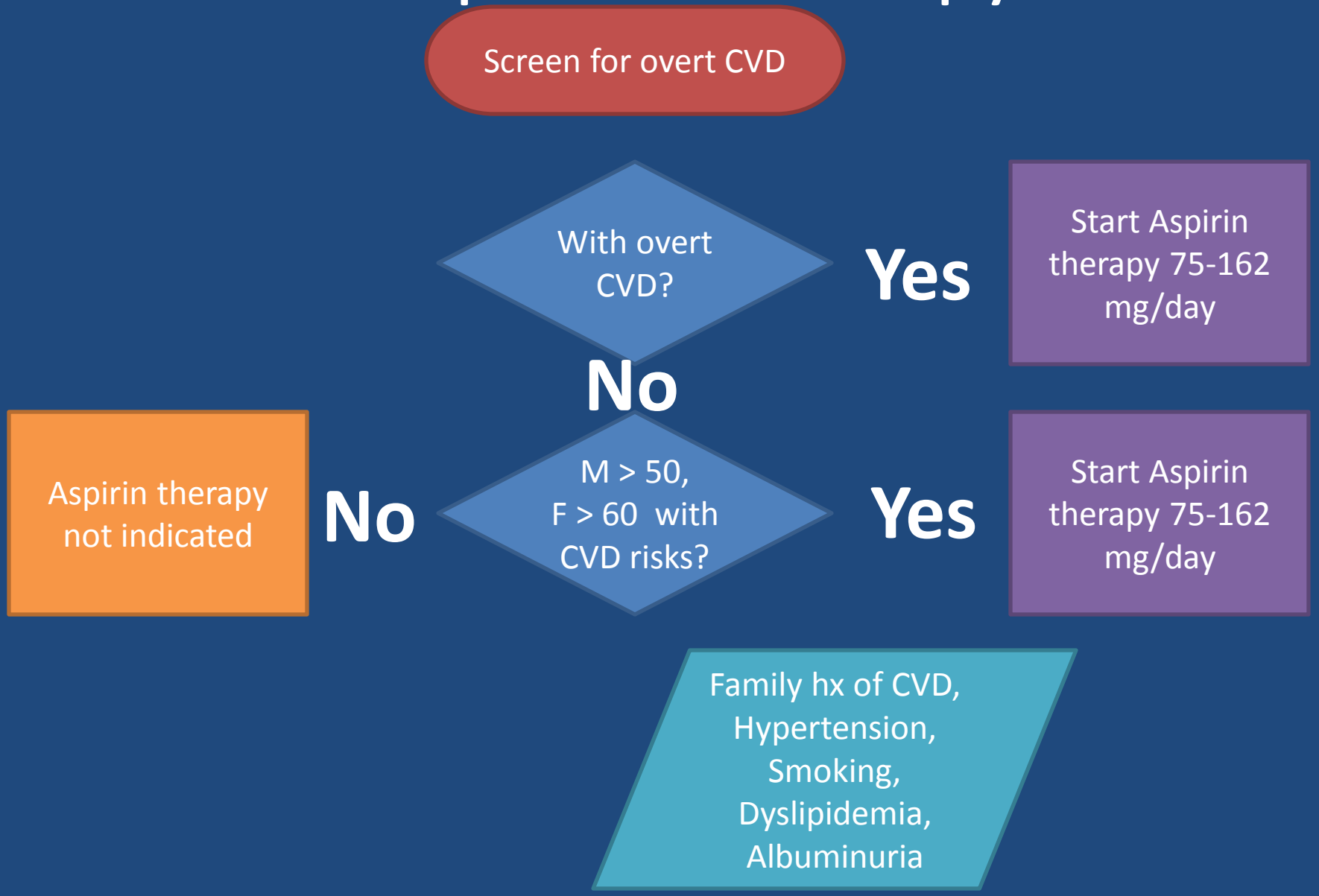
Dyslipidemia

- Screening
  - In most adult patients, measure fasting lipid profile at least annually. In adults with low-risk lipid values (LDL cholesterol 100 mg/dl, HDL cholesterol 50 mg/dl, and triglycerides 150 mg/dl), lipid assessments may be repeated every 2 years. (E)

Dyslipidemia



Antiplatelet therapy



Smoking

- Advise all patients not to smoke

Complications - Nephropathy

- Screening
  - Perform an annual test to assess urine albumin excretion in type 1 diabetic patients with diabetes duration of 5 years and in all type 2 diabetic patients starting at diagnosis. (E)
  - Measure serum creatinine at least annually in all adults with diabetes regardless of the degree of urine albumin excretion. The serum creatinine should be used to estimate GFR and stage the level of chronic kidney disease (CKD), if present. (E)

Table 13—*Definitions of abnormalities in albumin excretion*

Category	Spot collection (μg/mg creatinine)
Normal	<30
Microalbuminuria	30–299
Macro (clinical)-albuminuria	≥300

Complications - Nephropathy

- Treatment
  - In the treatment of the nonpregnant patient with micro- or macroalbuminuria, either ACE inhibitors or ARBs should be used. (A)
  - Reduction of protein intake to 0.8 –1.0 g kg body wt/day in individuals with diabetes and the earlier stages of CKD and to 0.8 g kg body wt/day in the later stages of CKD may improve measures of renal function (urine albumin excretion rate, GFR)and is recommended. (B)

Complications - Nephropathy

Table 15—*Management of CKD in diabetes*

GFR (ml/min/ 1.73 m^2)	Recommended
All patients	Yearly measurement of creatinine, urinary albumin excretion, potassium
45–60	Referral to nephrology if possibility for nondiabetic kidney disease exists (duration type 1 diabetes <10 years, heavy proteinuria, abnormal findings on renal ultrasound, resistant hypertension, rapid fall in GFR, or active urinary sediment)
	Consider need for dose adjustment of medications
	Monitor eGFR every 6 months
	Monitor electrolytes, bicarbonate, hemoglobin, calcium, phosphorus, parathyroid hormone at least yearly
	Assure vitamin D sufficiency
	Consider bone density testing
	Referral for dietary counselling
30–44	Monitor eGFR every 3 months
	Monitor electrolytes, bicarbonate, calcium, phosphorus, parathyroid hormone, hemoglobin, albumin, weight every 3–6 months
	Consider need for dose adjustment of medications
<30	Referral to nephrologist

Adapted from http://www.kidney.org/professionals/KDOQI/guideline_diabetes/.

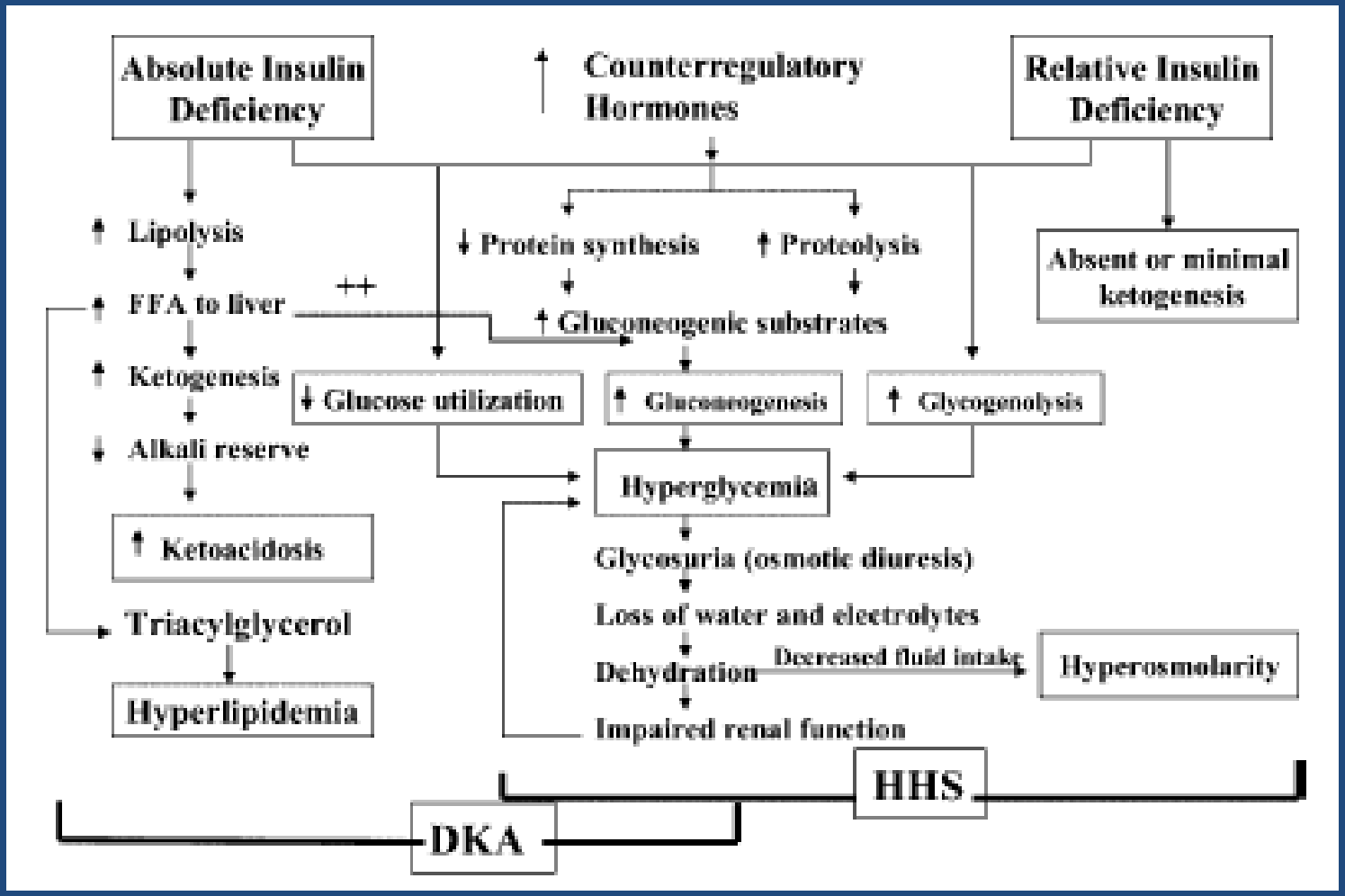
Complications - Retinopathy

- Screening
  - Adults and children aged 10 years or older with type 1 diabetes should have an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist within 5 years after the onset of diabetes. (B)
  - Patients with type 2 diabetes should have an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist shortly after the diagnosis of diabetes. (B)
  - Subsequent examinations for type 1 and type 2 diabetic patients should be repeated annually by an ophthalmologist or optometrist. Less frequent exams (every 2–3 years) may be considered following one or more normal eye exams. Examinations will be required more frequently if retinopathy is progressing.(B)
- Treatment
  - The presence of retinopathy is not a contraindication to aspirin therapy for cardioprotection, as this therapy does not increase the risk of retinal hemorrhage.(A)

Complications - Neuropathy

- All patients should be screened for distal symmetric polyneuropathy (DPN) at diagnosis and at least annually thereafter, using simple clinical tests. (B)
- Electrophysiological testing is rarely needed, except in situations where the clinical features are atypical. (E)
- Screening for signs and symptoms of autonomic neuropathy should be instituted at diagnosis of type 2 diabetes and 5 years after the diagnosis of type 1 diabetes. Special testing is rarely needed and may not affect management or outcomes. (E)
- Medications for the relief of specific symptoms related to DPN and autonomic neuropathy are recommended, as they improve the quality of life of the patient. (E)

Acute Complications - Pathogenesis

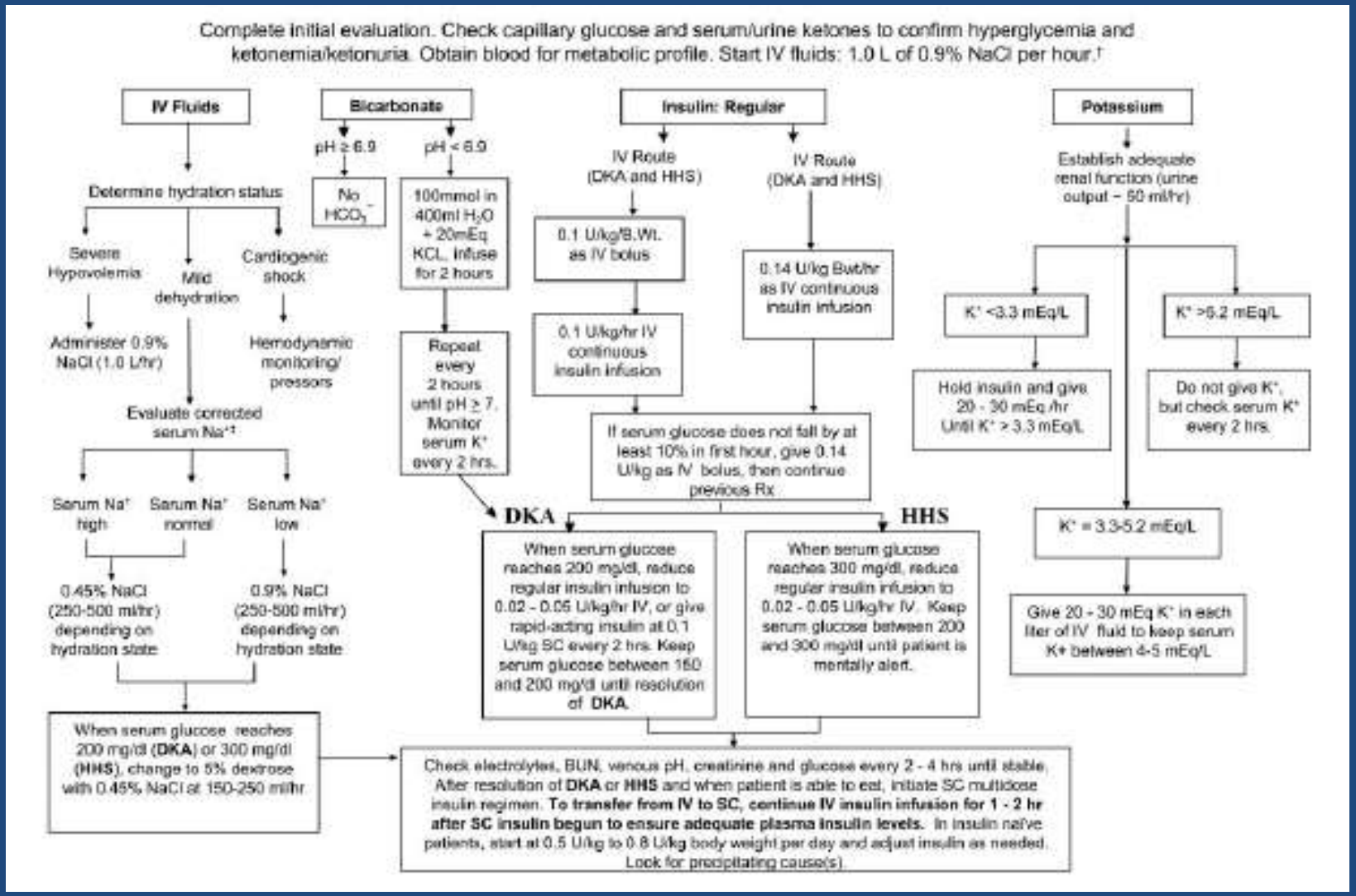


Acute Complications – Diagnostic Criteria

Table 1—*Diagnostic criteria for DKA and HHS*

	DKA			HHS
	Mild (plasma glucose >250 mg/dl)	Moderate (plasma glucose >250 mg/dl)	Severe (plasma glucose >250 mg/dl)	Plasma glucose >600 mg/dl
Arterial pH	7.25–7.30	7.00 to <7.24	<7.00	>7.30
Serum bicarbonate (mEq/l)	15–18	10 to <15	<10	>18
Urine ketone*	Positive	Positive	Positive	Small
Serum ketone*	Positive	Positive	Positive	Small
Effective serum osmolality†	Variable	Variable	Variable	>320 mOsm/kg
Anion gap†	>10	>12	>12	Variable
Mental status	Alert	Alert/drowsy	Stupor/coma	Stupor/coma

Acute Complications - Treatment



Sources

- Harrison's Principles of Internal Medicine
- Standards of Medical Care 2011 – American Diabetes Association
- Hyperglycemic crises in Adult patients with Diabetes – consensus statement from American Diabetes Association
- ADA EASD Management Algorithm 2009