

A serene landscape at sunset or sunrise. The sky is a deep, dark blue, and a thin, bright crescent moon is visible in the upper portion. The sun is low on the horizon, creating a bright glow and a reflection on the water below. The water is calm, and the overall scene is peaceful and contemplative.

In The Name Of God

Diabetes

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CLASSIFICATION

Diabetes can be classified into the following general categories:

1. Type 1 diabetes
2. Type 2 diabetes
3. Gestational diabetes mellitus (GDM)
4. Specific types of diabetes due to other causes

Type 1 diabetes

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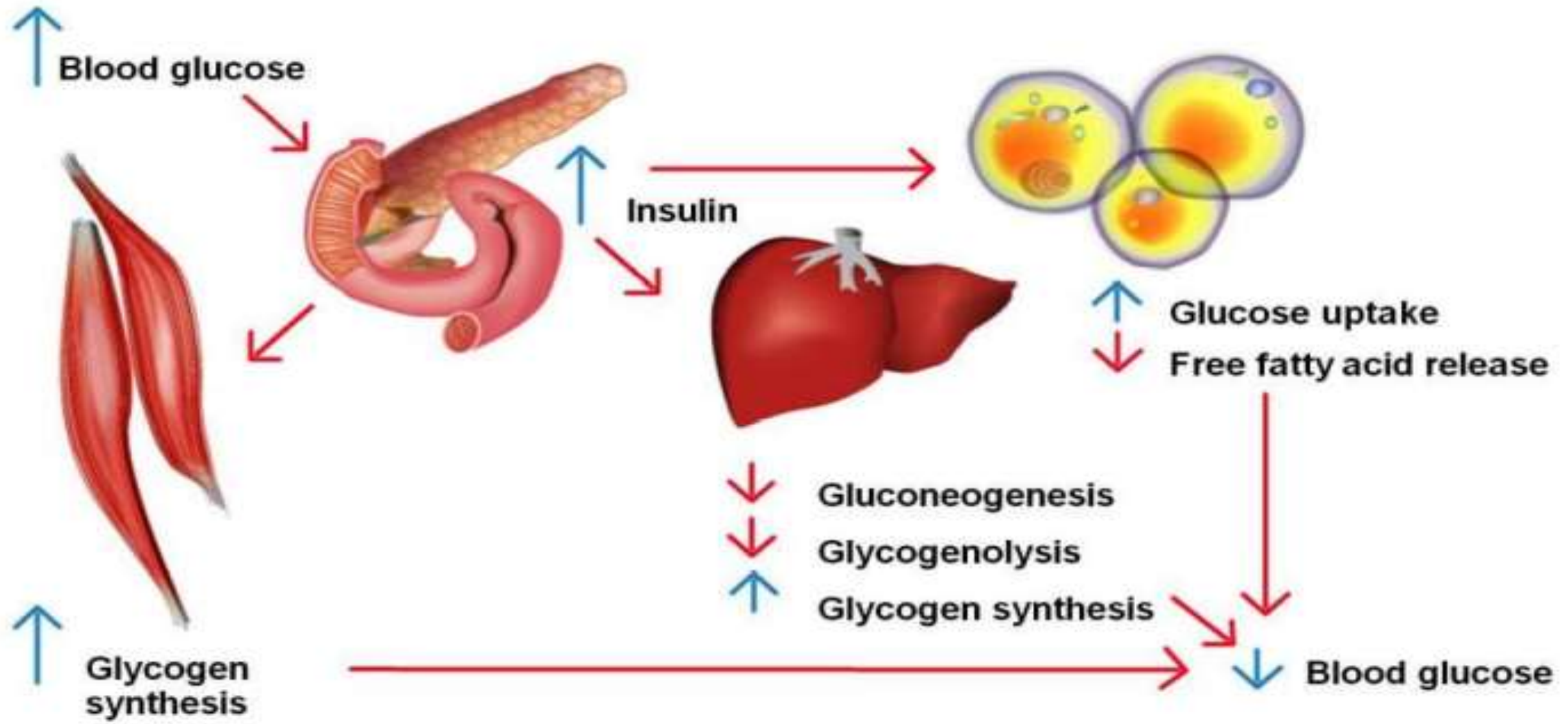
- **autoimmune destruction** of the pancreatic beta cells, leading to absolute insulin deficiency.



- Type 1 diabetes accounts for approximately 5 to 10 percent of diabetes in adults

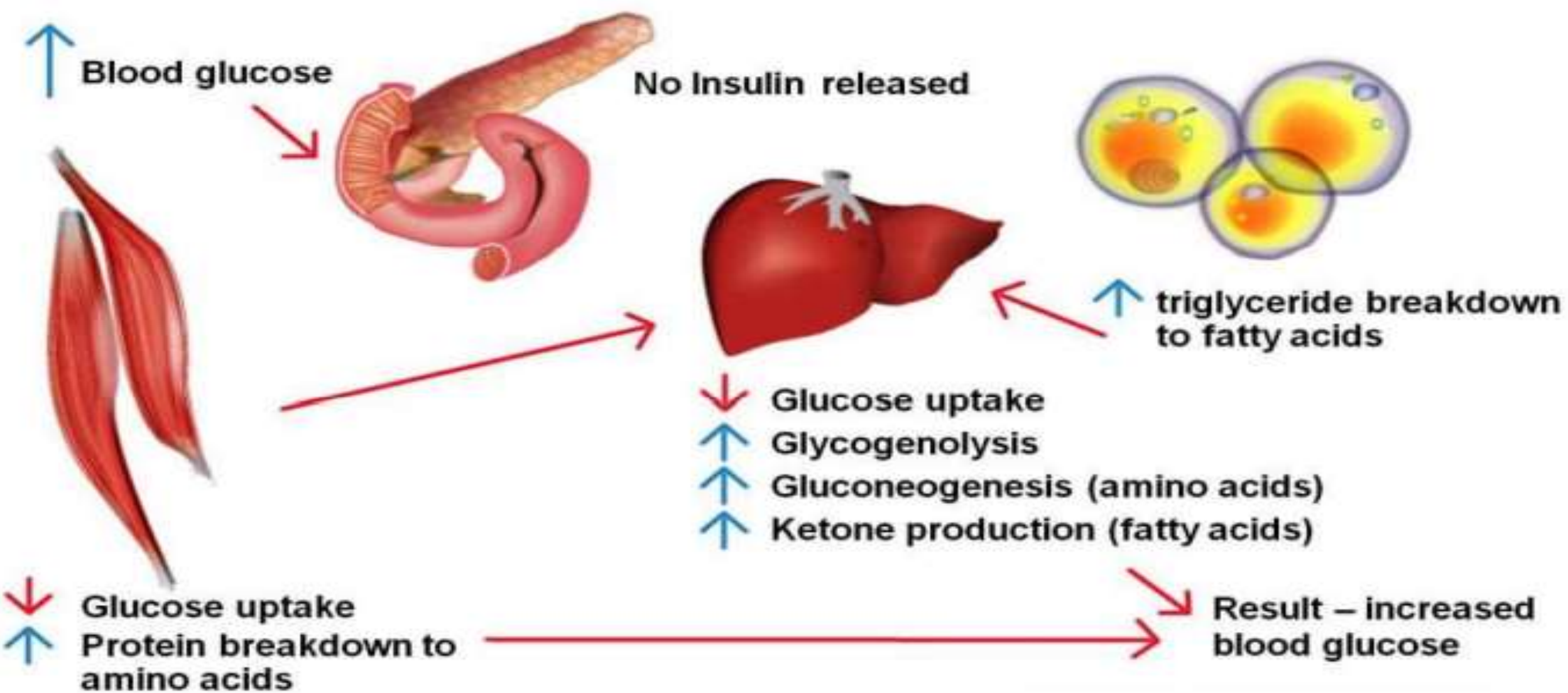
Pathophysiology of diabetes

-Insulin and glucose disposal (without diabetes)



Pathophysiology of diabetes

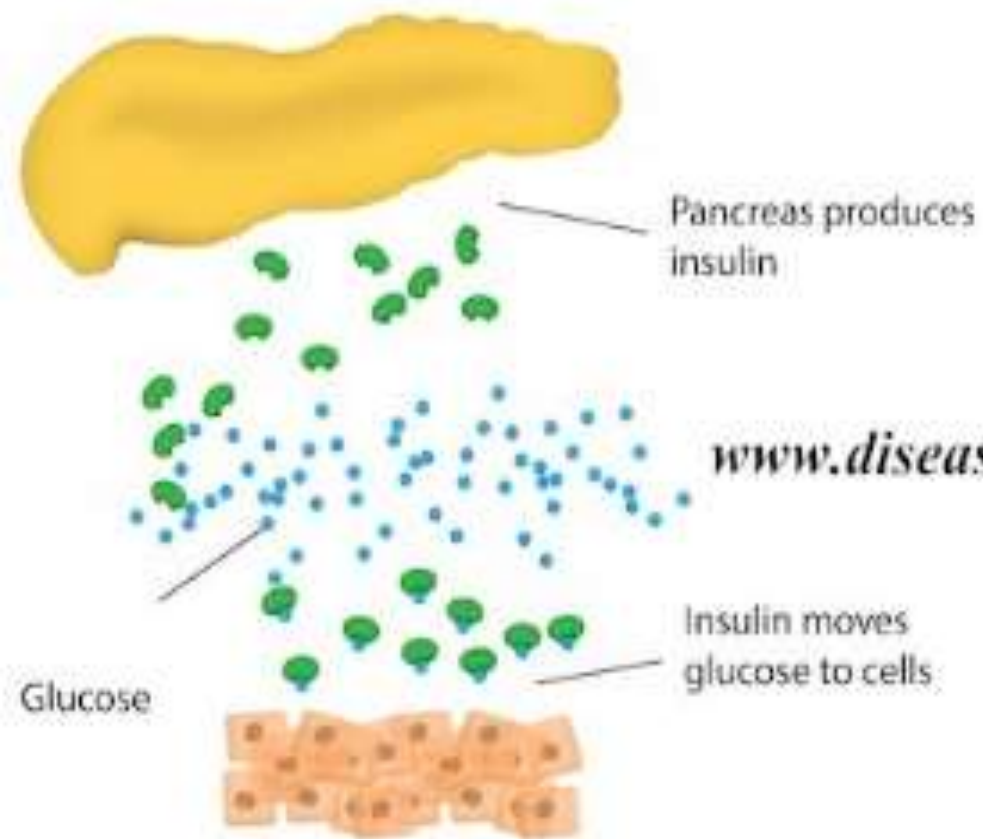
-Insulin and glucose disposal (diabetes)



Type 2 Diabetes

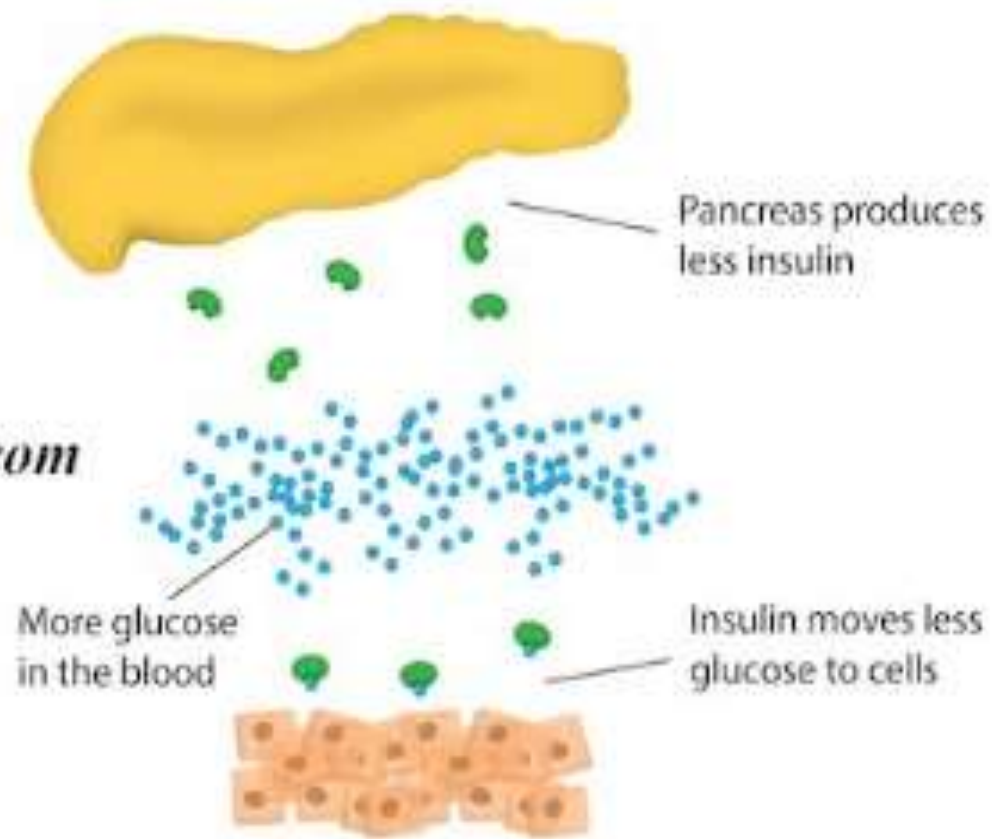
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Normal

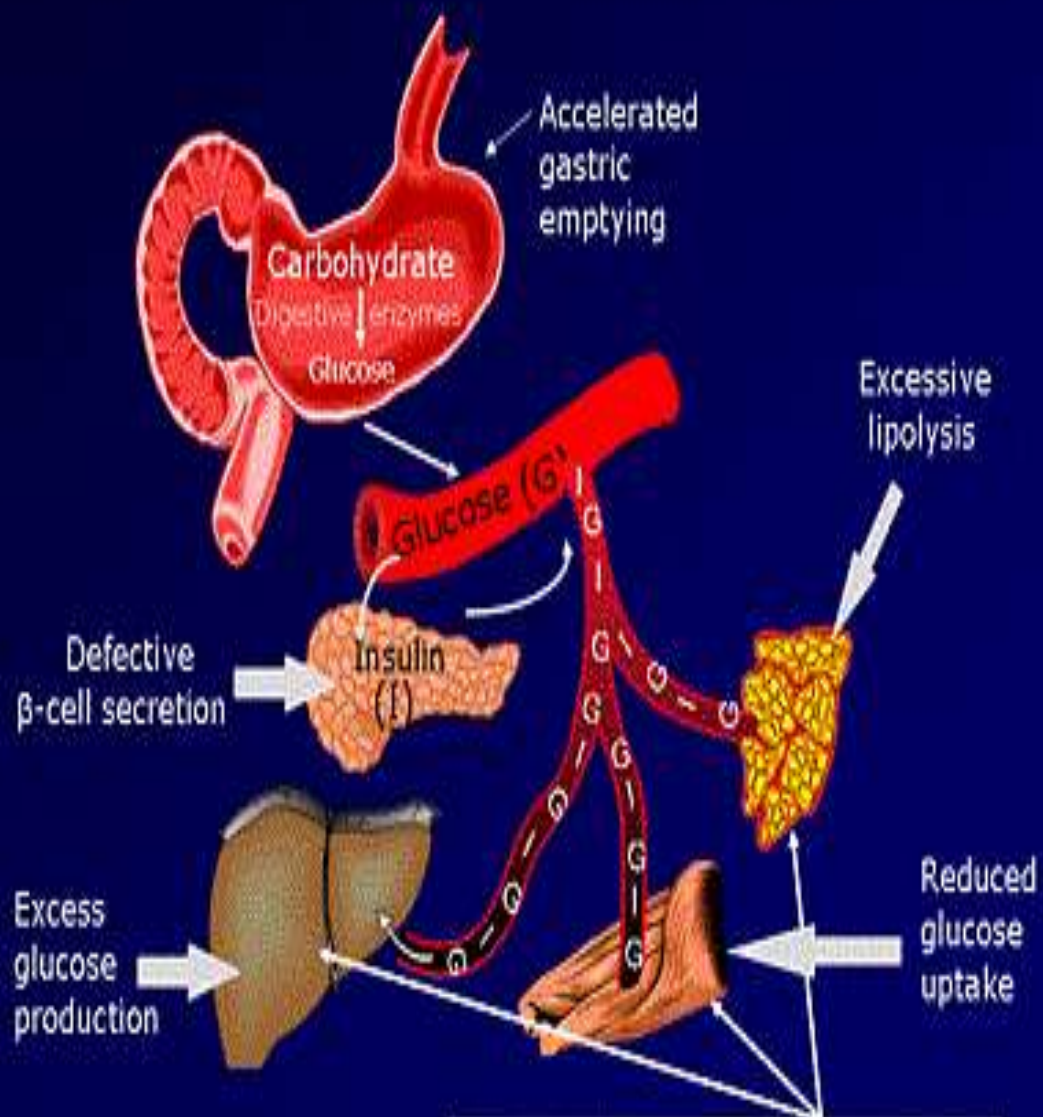


www.diseasesdic.com

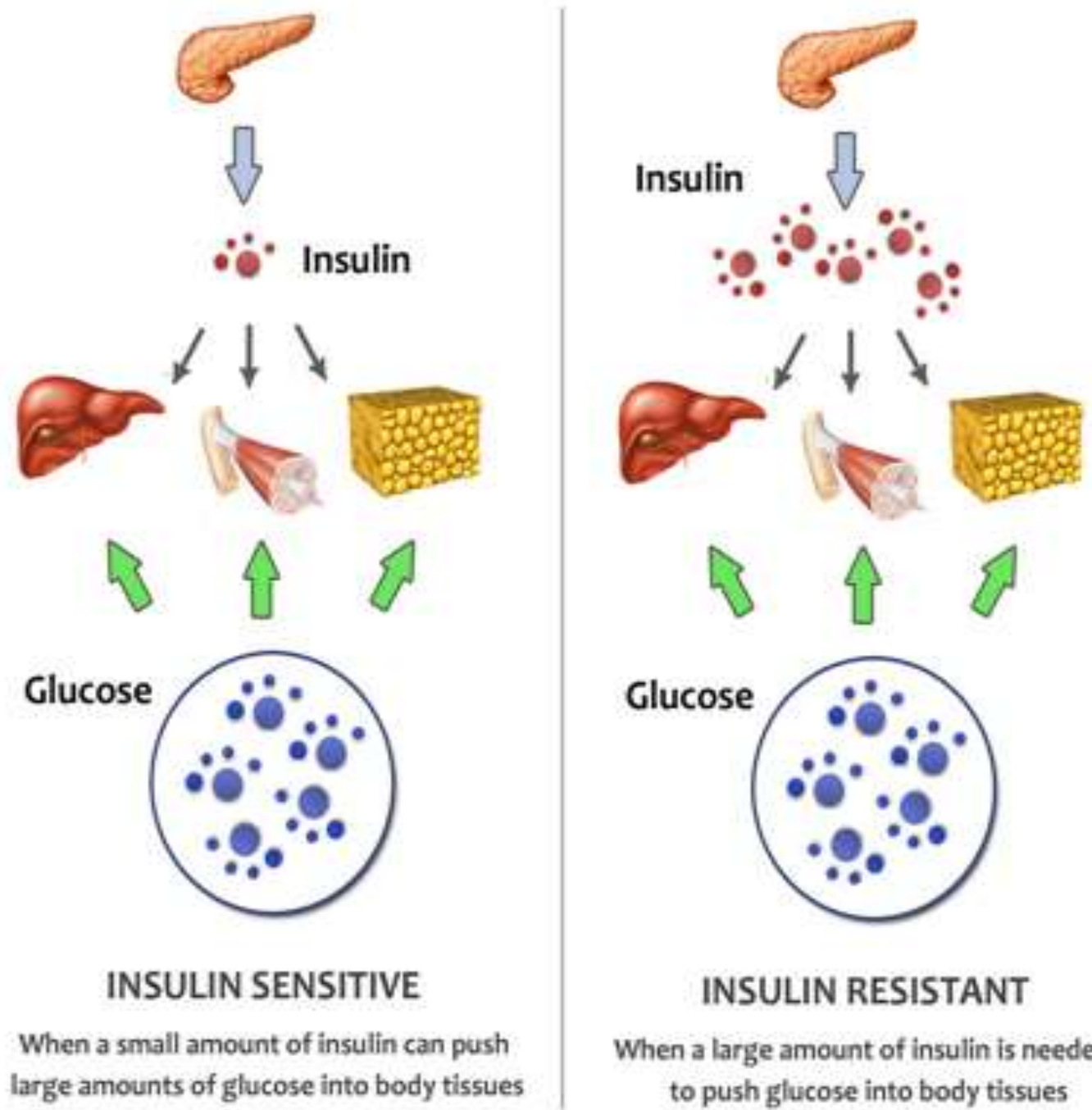
Diabetic



Pathophysiology of Type 2 Diabetes



Resistance to the action of insulin



INSULIN SENSITIVE

When a small amount of insulin can push large amounts of glucose into body tissues

INSULIN RESISTANT

When a large amount of insulin is needed to push glucose into body tissues

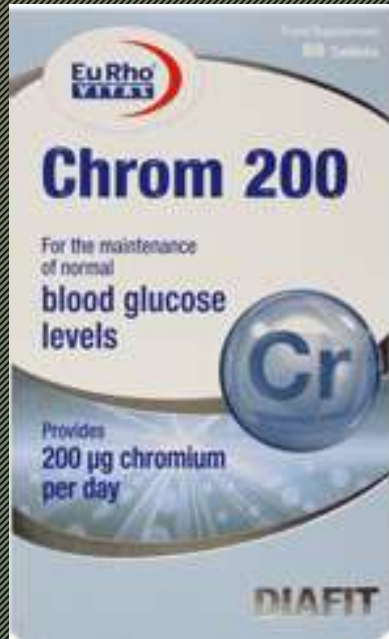
Clinical manifestation

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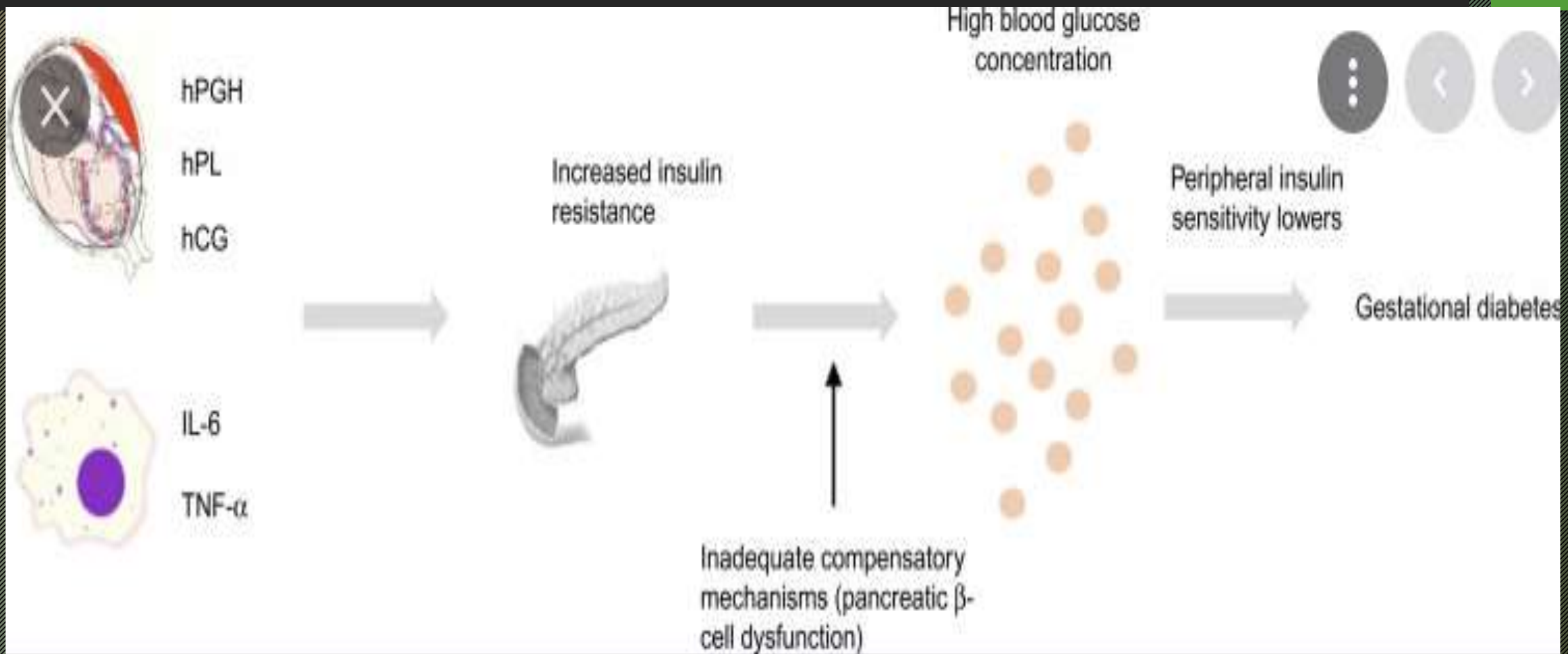


Supplement?

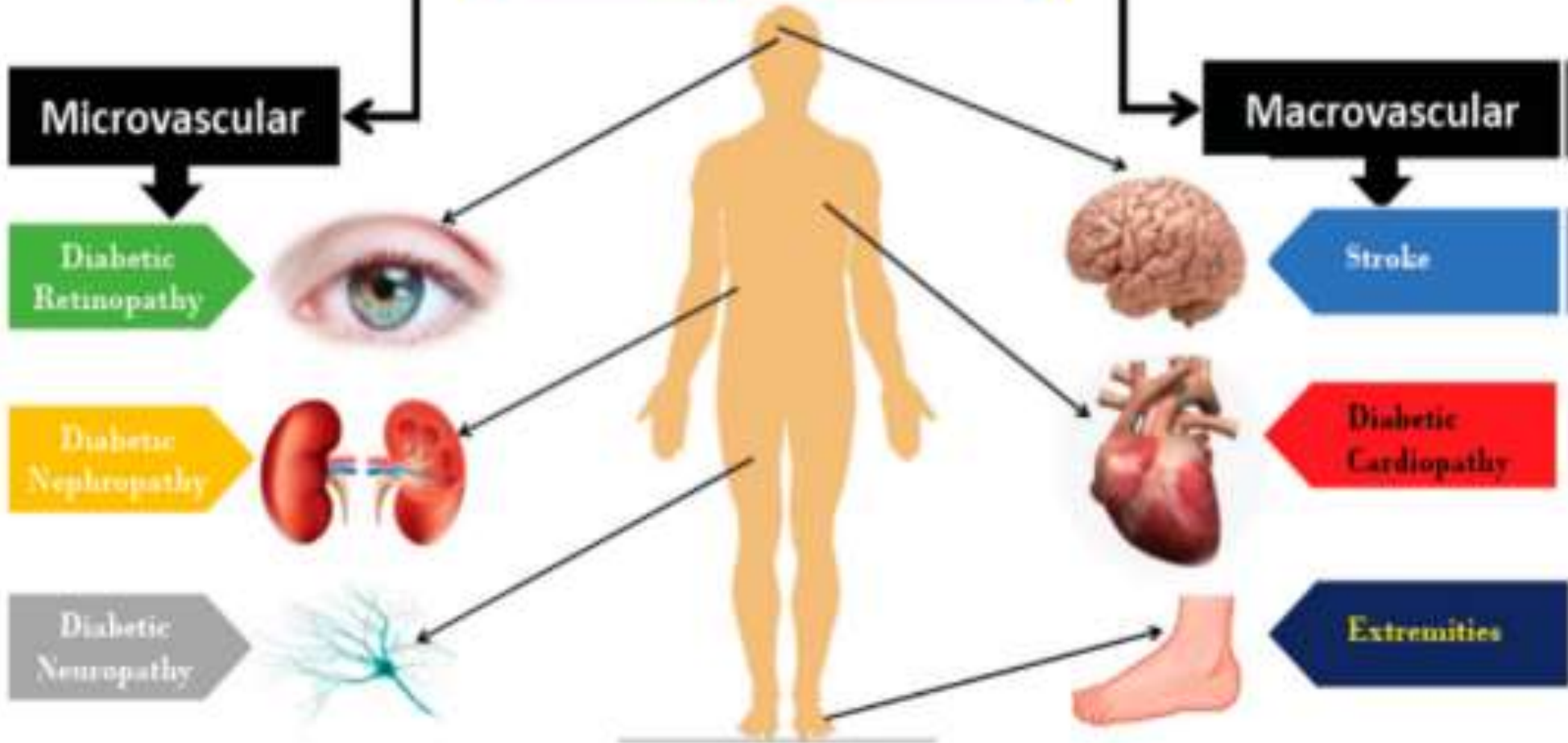


GDM

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Complications of Diabetes



CATEGORIES OF INCREASED RISK FOR DIABETES (PREDIABETES)

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Table 2.3—Criteria for testing for diabetes or prediabetes in asymptomatic adults

1. Testing should be considered in overweight or obese (BMI ≥ 25 kg/m² or ≥ 23 kg/m² in Asian Americans) adults who have one or more of the following risk factors:
 - First-degree relative with diabetes
 - High-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
 - History of CVD
 - Hypertension ($\geq 140/90$ mmHg or on therapy for hypertension)
 - HDL cholesterol level < 35 mg/dL (0.90 mmol/L) and/or a triglyceride level > 250 mg/dL (2.82 mmol/L)
 - Women with polycystic ovary syndrome
 - Physical inactivity
 - Other clinical conditions associated with insulin resistance (e.g., severe obesity, acanthosis nigricans)
2. Patients with prediabetes (A1C $\geq 5.7\%$ [39 mmol/mol], IGT, or IFG) should be tested yearly.
3. Women who were diagnosed with GDM should have lifelong testing at least every 3 years.
4. For all other patients, testing should begin at age 45 years.
5. If results are normal, testing should be repeated at a minimum of 3-year intervals, with consideration of more frequent testing depending on initial results and risk status.

diagnose

diagnose

diagnose

diagnose

diagnose

diagnose

diagnose

diagnose

diagnose

diagnose

diag

nose

CLINICAL PRESENTATION

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The majority of patients are asymptomatic at presentation

The classic symptoms of hyperglycemia (including

- polyuria,
- polydipsia,
- nocturia,
- blurred vision

جدول ۱- اندازه‌گیری و تفسیر قند خون

<p>طبیعی</p> <p>قند خون ناشتای مختل^۱ IFG</p> <p>آزمایش باید تکرار و تأیید شود.</p>	<p>≤ 99</p> <p>۱۰۰-۱۲۵</p> <p>≥ 126</p>	<p>قند خون ناشتا</p> <p>FPG^۱</p> <p>(mg/dl)</p>
<p>طبیعی</p> <p>اختلال تحمل گلوکز^۲ IGT</p> <p>آزمایش باید تکرار و تأیید شود.</p>	<p>≤ 139</p> <p>۱۴۰-۱۹۹</p> <p>≥ 200</p>	<p>آزمایش تحمل گلوکز دو ساعت پس</p> <p>از دریافت ۷۵ گرم گلوکز</p> <p>OGTT^۲</p> <p>(mg/dl)</p>
<p>طبیعی</p> <p>خطر بالا/ پیش دیابت^۳</p> <p>آزمایش باید تکرار و تأیید شود.</p>	<p>$< 1.5\%$</p> <p>۱.۵٪-۱.۶٪</p> <p>$> 1.6\%$</p>	<p>هموگلوبین گلیکوزیله^۳ (HbA_{1c})</p> <p>(به عنوان تست غربالگری)</p>
<p>حضور نشانه‌های هیپرگلیسمی کنترل نشده</p> <p>(پرنوشی، پرادراری، پرخوری) برای</p> <p>تشخیص دیابت ضروری است.</p>	<p>≥ 200</p>	<p>قند خون تصادفی</p> <p>RPG^۴</p> <p>(mg/dl)</p>

DIAGNOSTIC TESTS FOR DIABETES

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Table 2.2—Criteria for the diagnosis of diabetes

FPG \geq 126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.*

OR

2-h PG \geq 200 mg/dL (11.1 mmol/L) during OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75-g anhydrous glucose dissolved in water.*

OR

A1C \geq 6.5% (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*

OR

In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose \geq 200 mg/dL (11.1 mmol/L).

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

Treatment

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- Improved glycemic management lowers the risk of microvascular complications in patients with type 2 diabetes
- Treatment of patients with type 2 diabetes mellitus includes evaluation for micro- and macrovascular complications, attempts to achieve near normoglycemia, minimization of cardiovascular and other long-term risk factors,

جدول ۳- اهداف درمانی کنترل قند خون

هدف	طبیعی	
$<7\%^*$	$<6\%$	هموگلوبین گلیکوزیله (HbA _{1c}) ¹
۹۰-۱۳۰	<100	قند خون ناشتا FPG ² (mg/dl)
<180	<140	قند خون پس از غذا 2h-PP ³ (mg/dl)

¹Hemoglobin A_{1c}, ²Fasting Plasma Glucose, ³2Hour-Post Prandial Glucose

* $HbA_{1c} > 7.5\%$ در افرادی که بیماری قلبی-عروقی، خطر هیپوگلیسمی، ابتلا طولانی مدت به دیابت نداشته و دارای امید به زندگی بالایی باشند.

* $HbA_{1c} < 8\%$ در افرادی که سابقه هیپوگلیسمی شدید، عوارض پیشرفته دیابت، بیماری همراه و دارای امید به زندگی پایین باشند.

GOALS OF THERAPY

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- manage the "ABCs" of diabetes control:



- glycated hemoglobin (**A1C**),
- **b**lood pressure
- low-density lipoprotein (LDL) **c**holesterol

TABLE 30-4 Recommendations for Lipid and Blood Pressure for Most Adults with Diabetes

Lipids/Blood Pressure	Criteria
LDL cholesterol	<100 mg/dl (<2.6 mmol/l) *
HDL cholesterol	
Men	>40 mg/dl (>1.1 mmol/l)
Women	>50 mg/d (>1.4 mmol/l)
Triglycerides	<150 mg/dl (<1.7 mmol/l)
Blood pressure	<140/90 mm Hg

Modified from [American Diabetes Association](#): Standards of medical care in diabetes—2014, *Diabetes Care* 37(S1):S14, 2014.

*In individuals with overt CVD, a lower LDL cholesterol goal of <70 mg/dl (1.8 mmol/l), using a high dose of a statin, is an option.

Nutritional considerations in type 2 diabetes mellitus

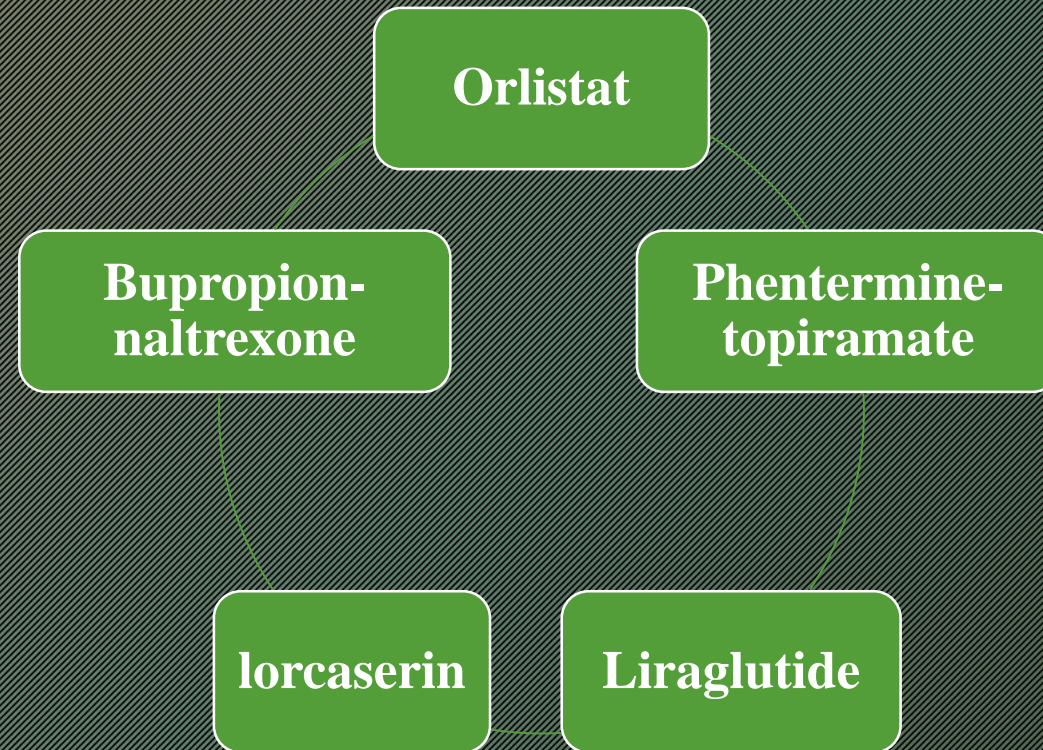
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- The strongest evidence for diabetes prevention comes from the Diabetes Prevention Program (DPP)
- The two major goals of the DPP intensive, behavioral, lifestyle intervention were to achieve and maintain a minimum of **7% weight loss and 150 min of physical activity per week**
- **Uptodate:** Diet is one of the most important behavioral aspects of diabetes treatment

- If weight loss cannot be achieved, weight maintenance (rather than gain) is an important goal.
- Pharmacologic therapy for weight loss and weight loss surgery can be effective but are not considered initial therapy

Drugs available as adjuncts to diet and exercise for treatment of obesity

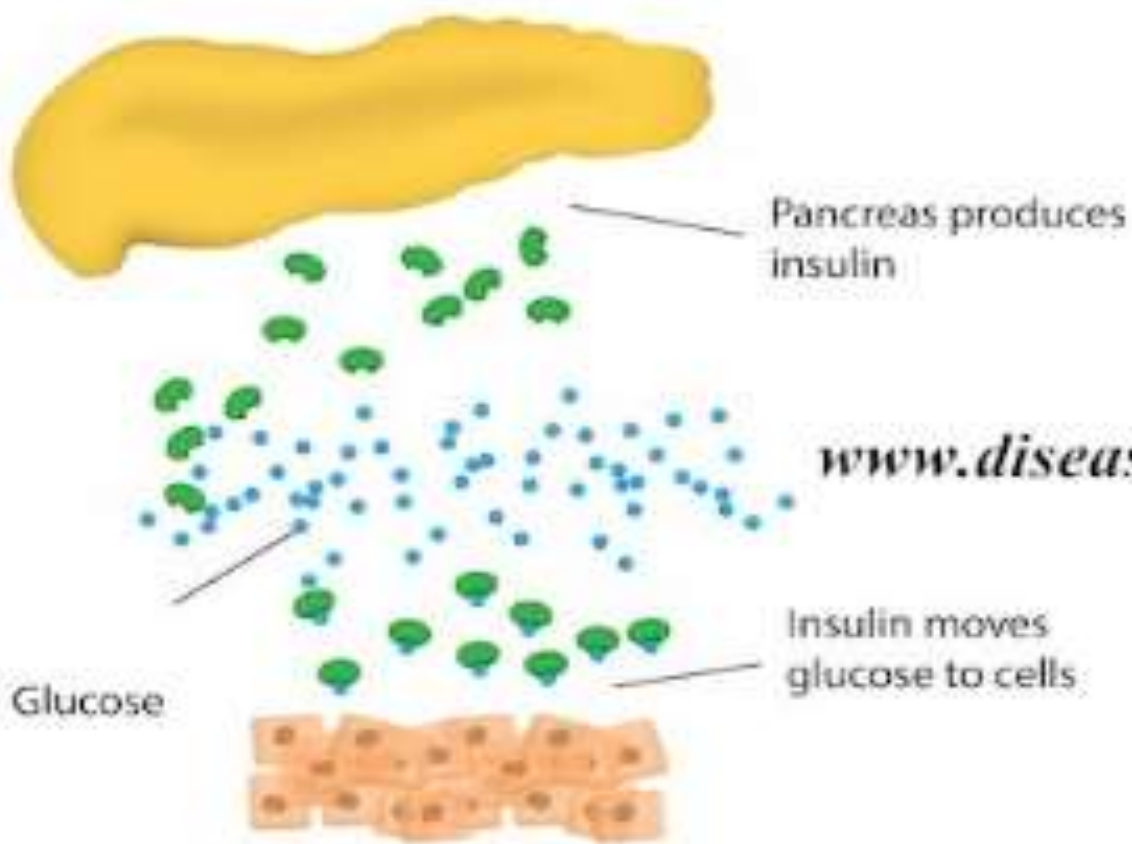
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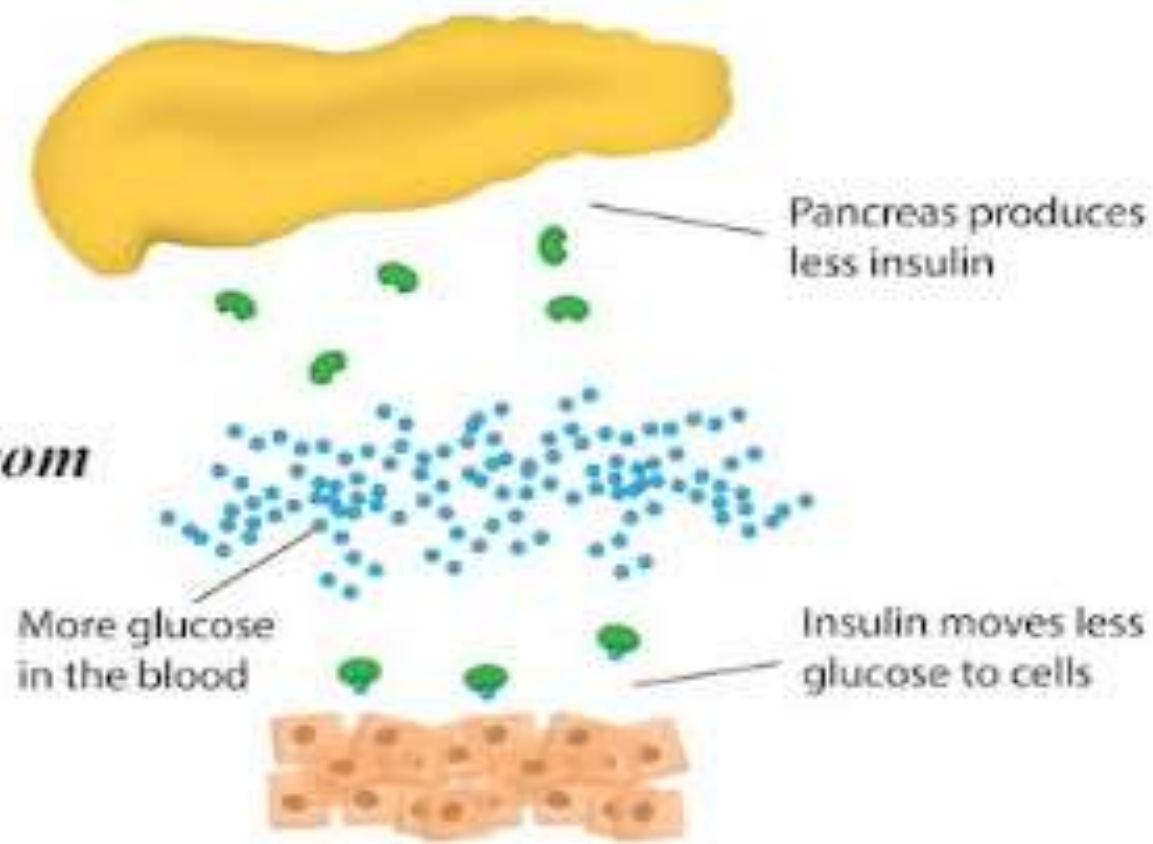


Type 2 Diabetes

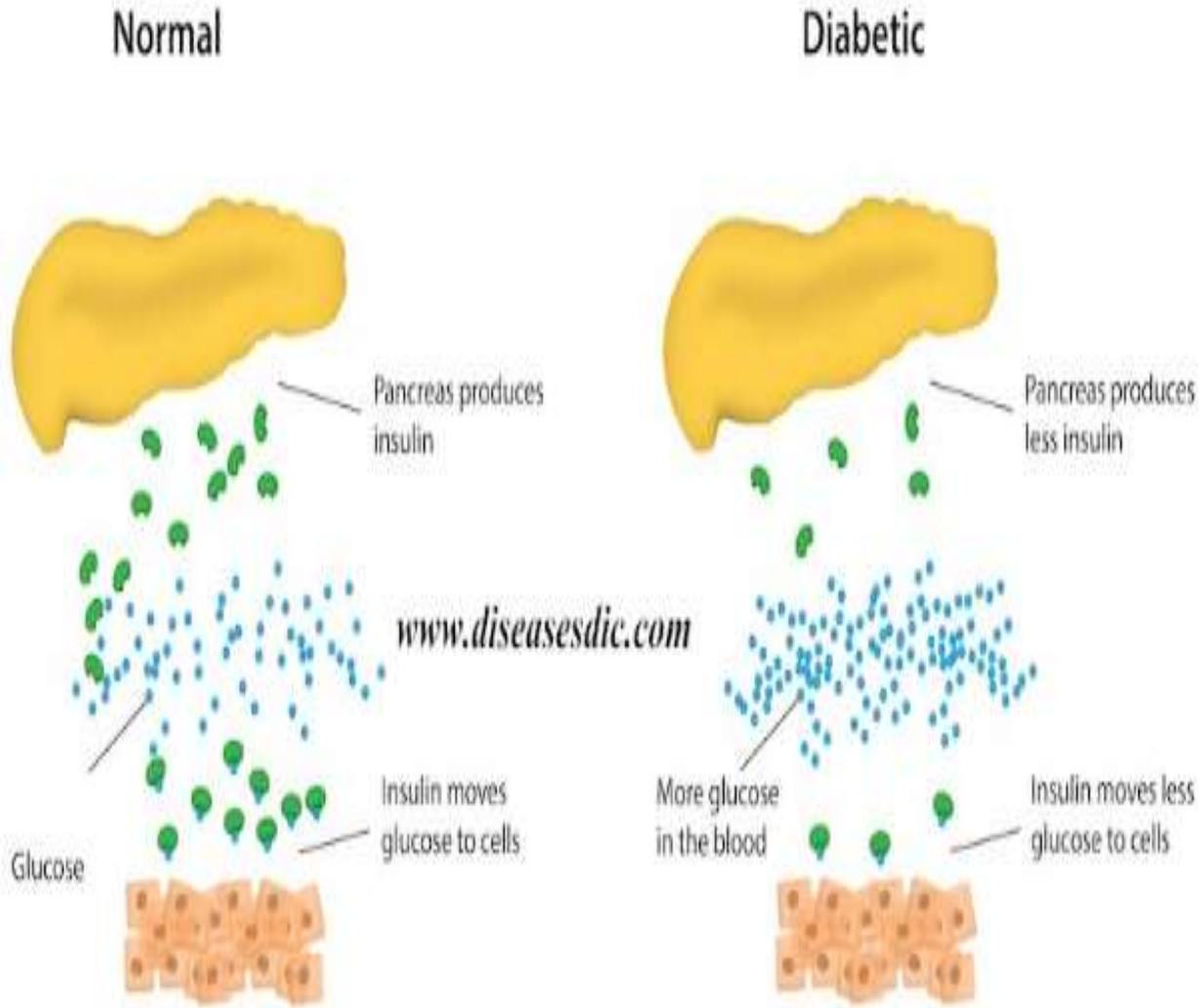
Normal



Diabetic



Type 2 Diabetes



Sulfonylureas (2nd generation)

- Glyburide
- Glipizide
- Glimepiride

Meglitinides (glinides)

- Repaglinide
- Nateglinide



Weight time

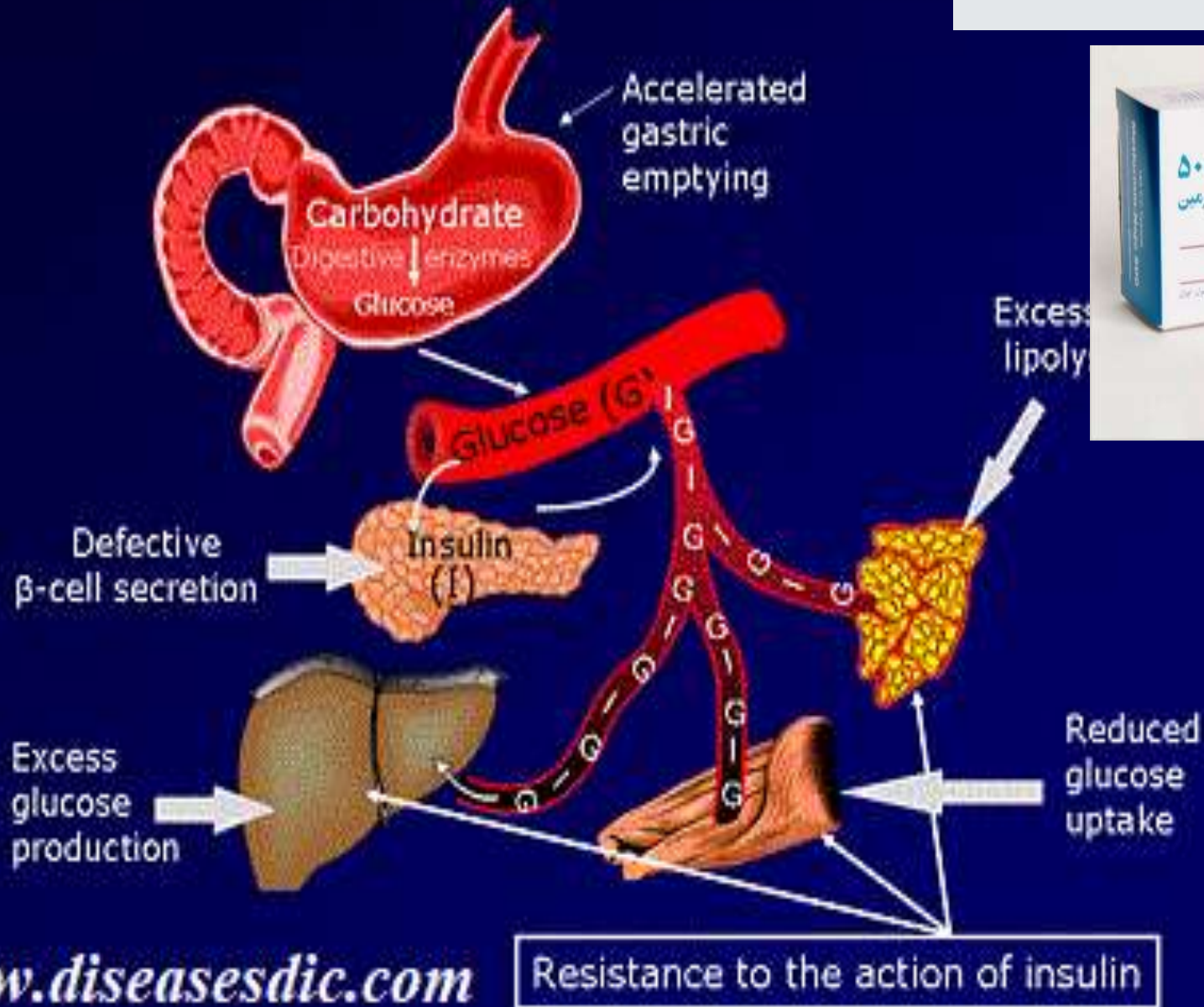
Pathophysiology of Type 2 Diabetes

Biguanides

• Metformin

Activates AMP kinase (? other)

↓ Hepatic glucose production



مان راست؟



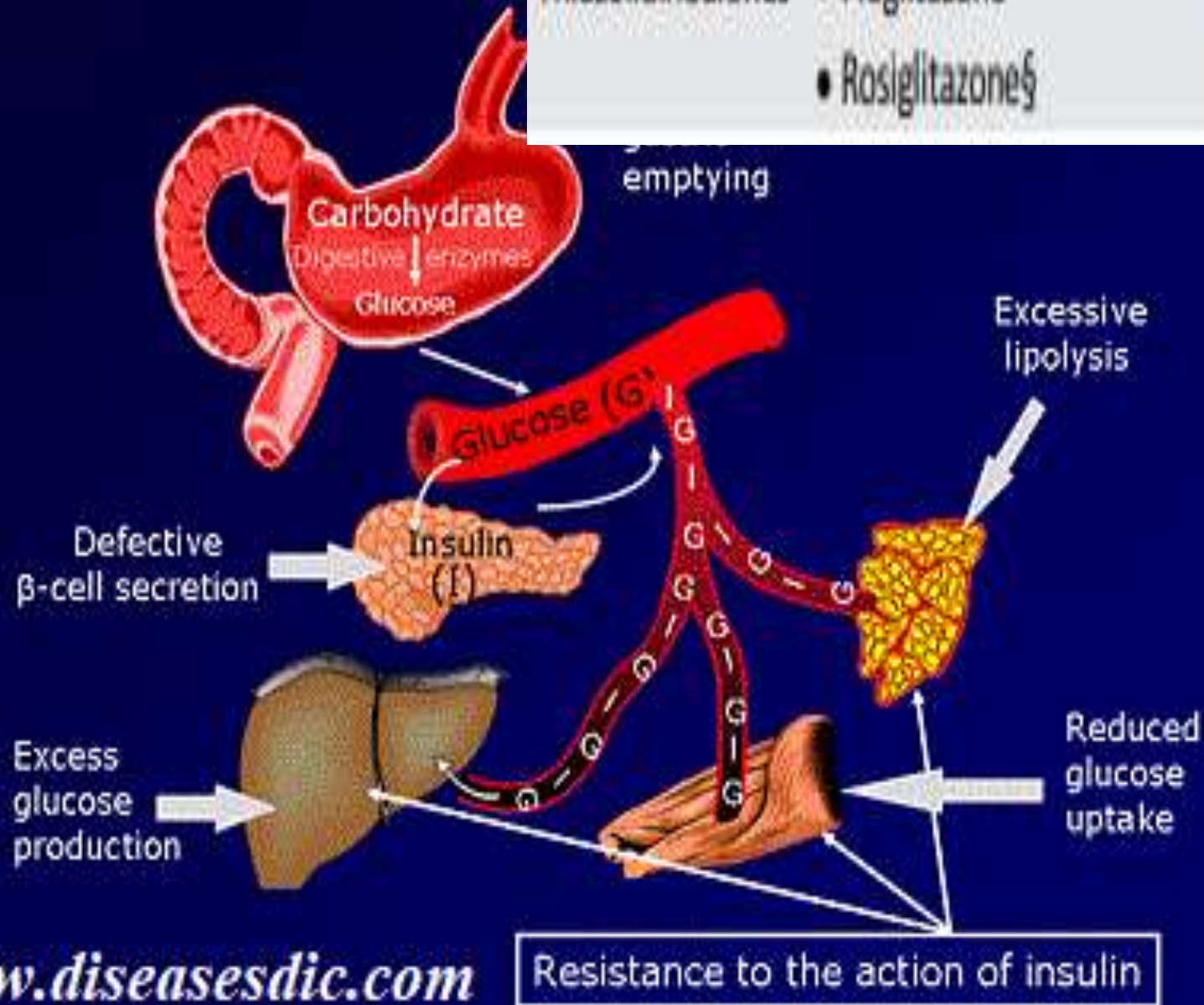
Weight?
Vitamin?

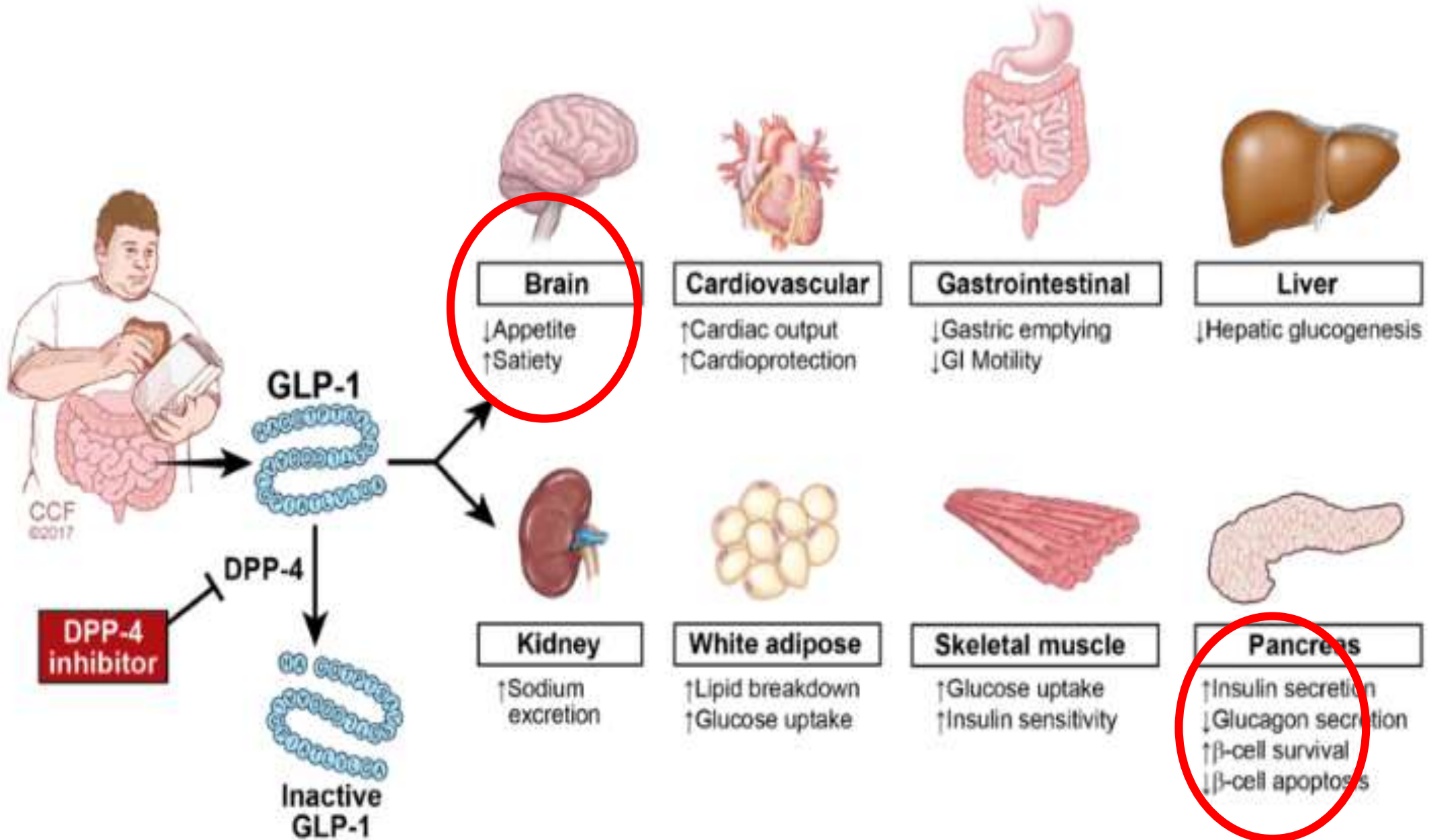
Pathophysiology of Type 2 Diabetes

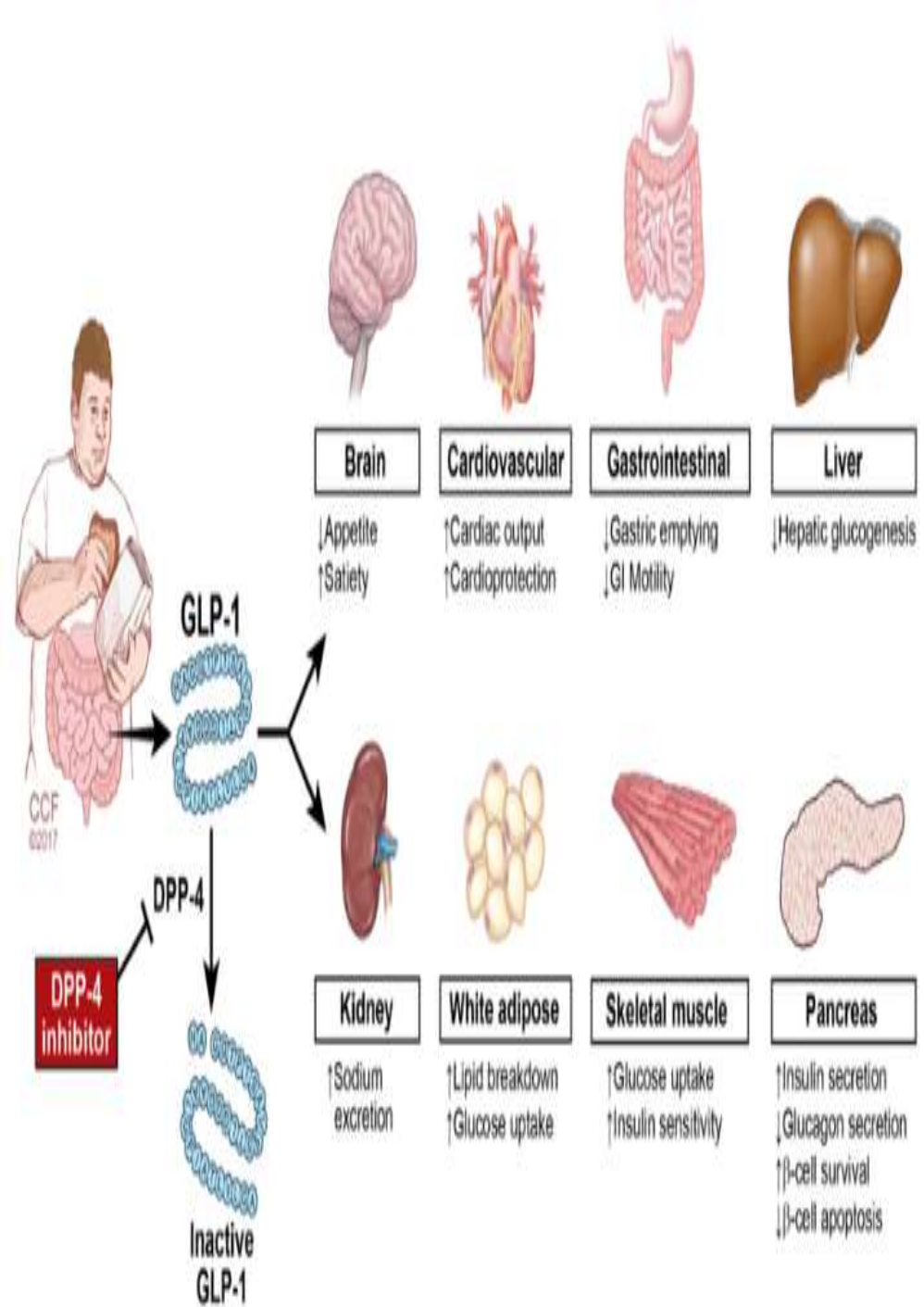
Thiazolidinediones • Pioglitazone
• Rosiglitazone

Activates the nuclear
transcription factor PPAR- γ

↑ Insulin sensitivity







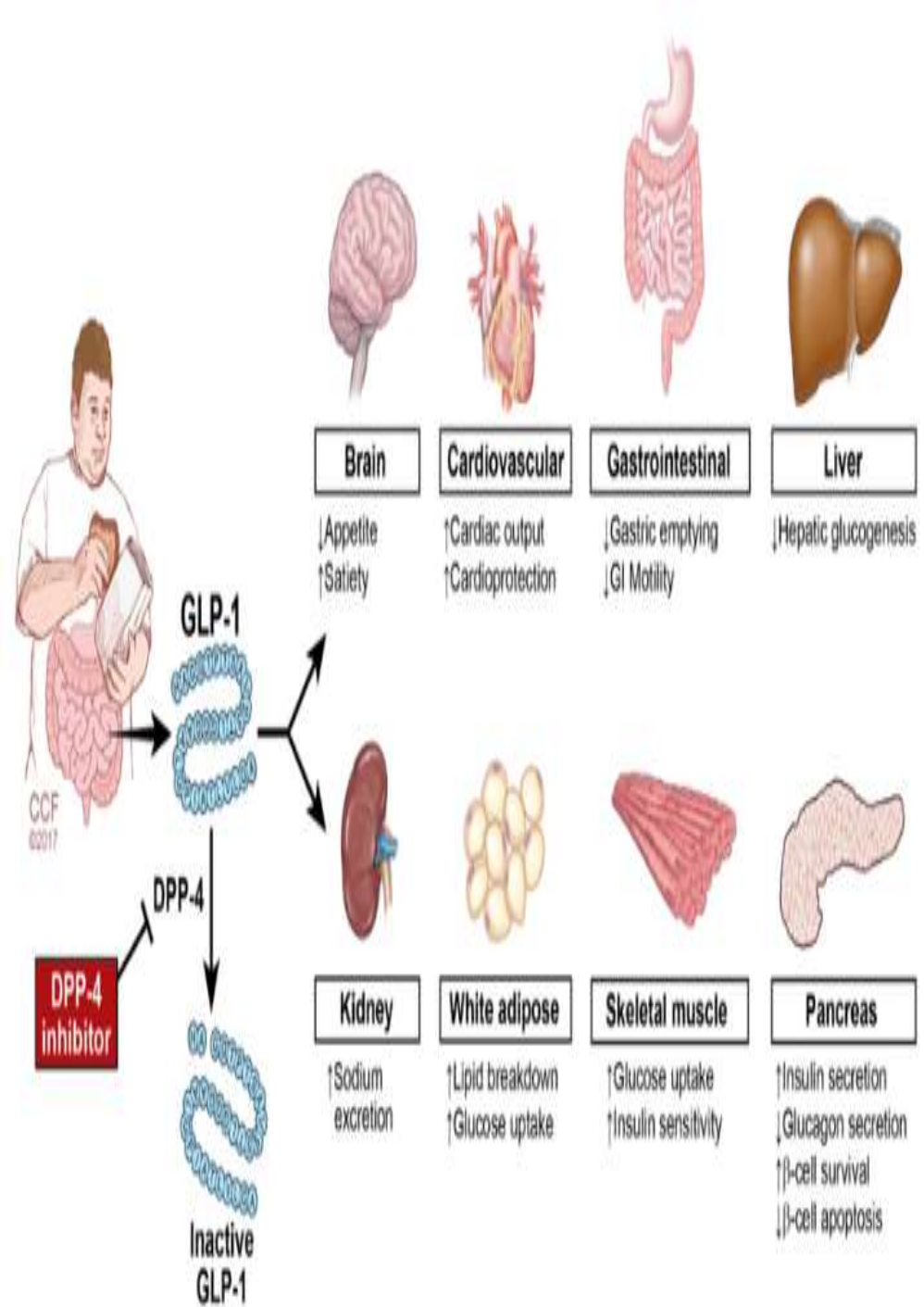
DPP-4 inhibitors

- Sitagliptin
- Saxagliptin
- Linagliptin
- Alogliptin

Inhibits DPP-4 activity, increasing postprandial incretin (GLP-1, GIP) concentrations

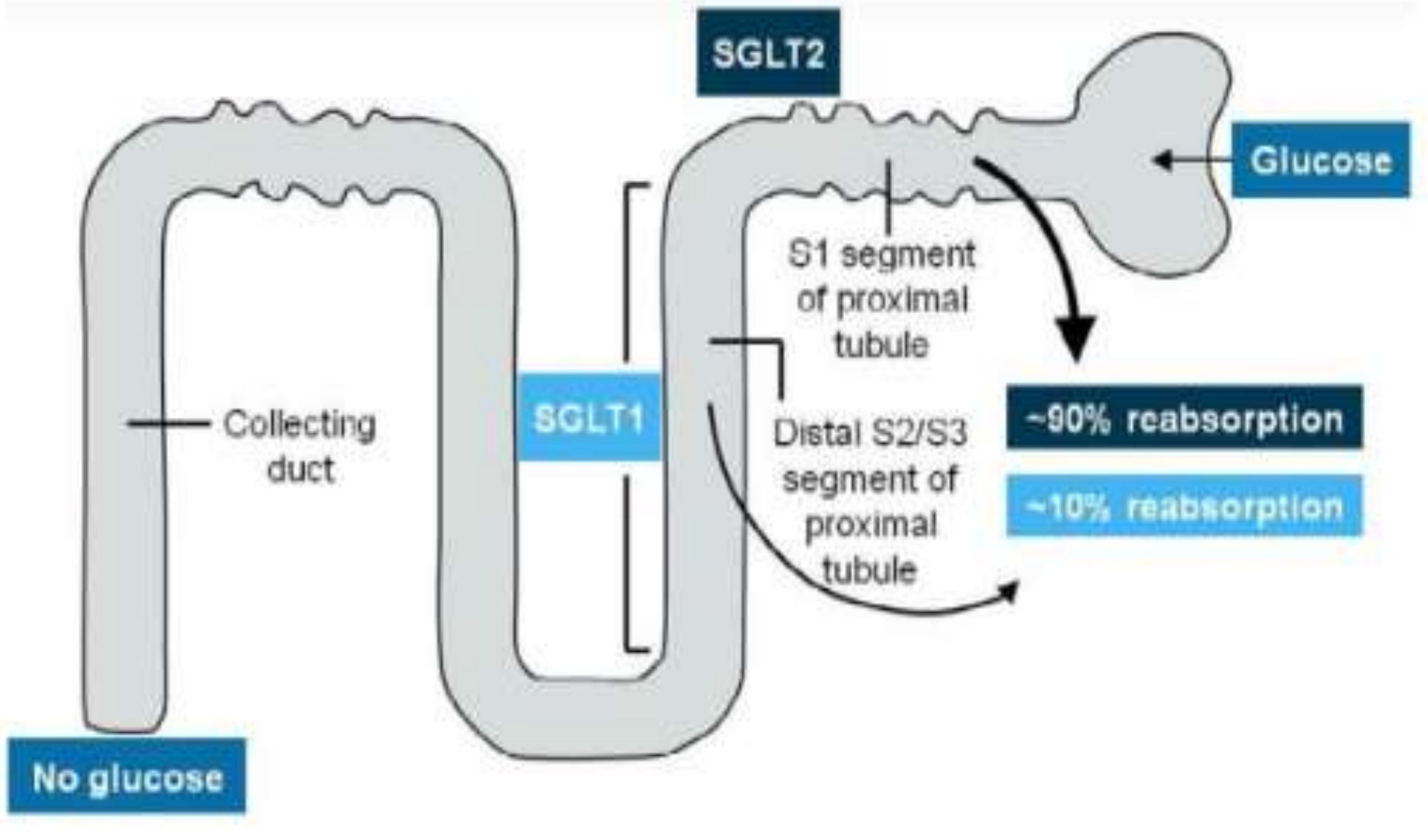
↑ Insulin secretion (glucose dependent);
↓ Glucagon secretion (glucose dependent)





- GLP-1 receptor agonists**
- Exenatide
 - Exenatide extended release
 - Liraglutide
 - Albiglutide
 - Lixisenatide
- Activates GLP-1 receptors**
- ↑ Insulin secretion (glucose dependent)
 - ↓ Glucagon secretion (glucose dependent);
 - Slows gastric emptying;
 - ↑ Satiety





SGLT2 inhibitors

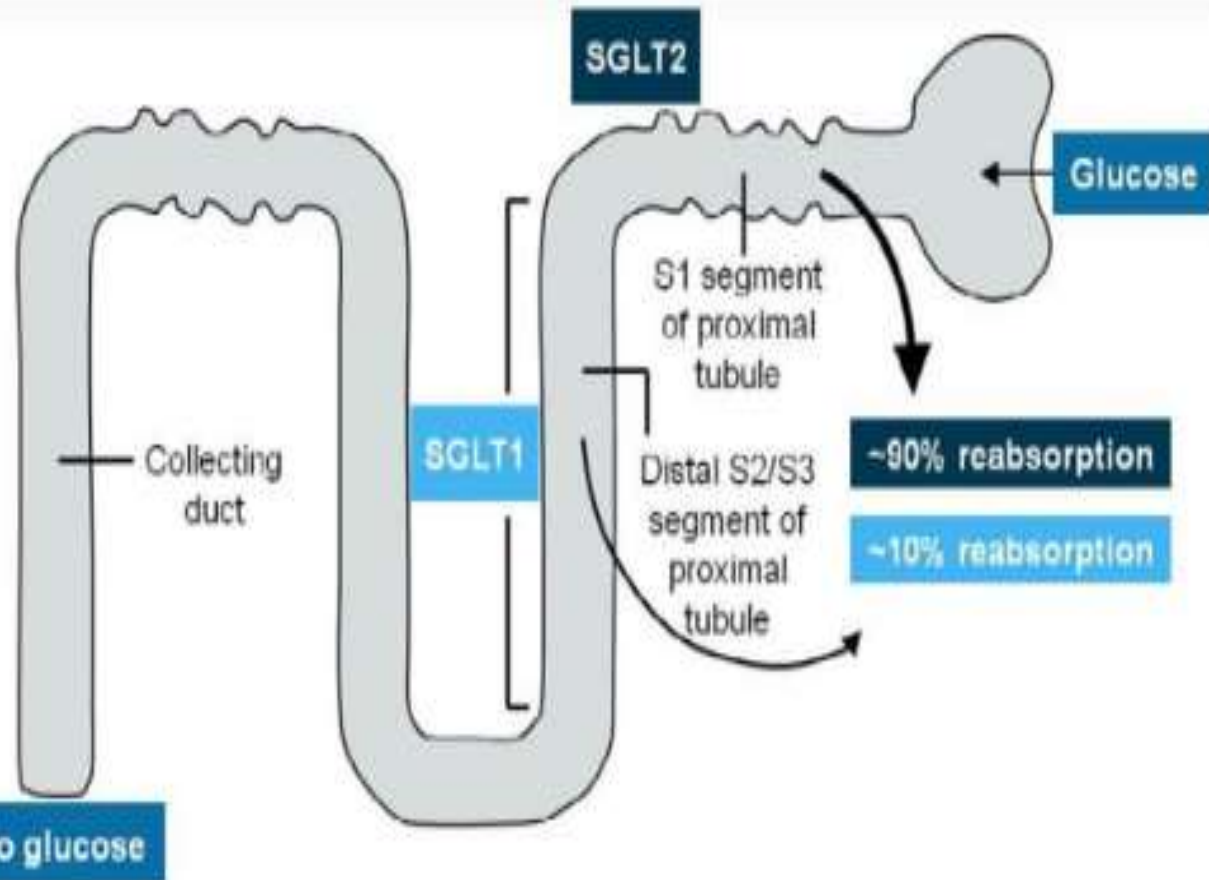
- Canagliflozin

Inhibits SGLT2 in the proximal nephron

Blocks glucose reabsorption by the kidney, increasing glucosuria

- Dapagliflozin

- Empagliflozin



	Efficacy*	Hypoglycemia	Weight Change						
				DPP-4 Inhibitors	Intermediate	No	Neutral	Neutral	Potential Risk: saxagliptin, alogliptin
Metformin	High	No	Neutral (Potential for Modest Loss)	Thiazolidinediones	High	No	Gain	Potential Benefit: pioglitazone	Increased Risk
SGLT-2 Inhibitors	Intermediate	No	Loss	Sulfonylureas (2nd Generation)	High	Yes	Gain	Neutral	Neutral
GLP-1 RAs	High	No	Loss	Insulin					
				Human Insulin	Highest	Yes	Gain	Neutral	Neutral
				Analog					

Antihyperglycemic Therapy in Adults with Type 2 Diabetes

At diagnosis, initiate lifestyle management, set A1C target, and initiate pharmacologic therapy based on A1C:

A1C is less than 9%, **consider Monotherapy.**

A1C is greater than or equal to 9%, **consider Dual Therapy.**

A1C is greater than or equal to 10%, blood glucose is greater than or equal to 300 mg/dL, or patient is markedly symptomatic, **consider Combination Injectable Therapy** (See Figure 8.2).

Monotherapy

Lifestyle Management + Metformin

Initiate metformin therapy if no contraindications* (See Table 8.1)

**A1C at target
after 3 months
of monotherapy?**

- Yes:** - Monitor A1C every 3–6 months
- No:** - Assess medication-taking behavior
- Consider Dual Therapy

Dual Therapy

Lifestyle Management + Metformin + Additional Agent

ASCVD?

Yes:

- Add agent proven to reduce major adverse cardiovascular events and/or cardiovascular mortality (see recommendations with * on p. S75 and **Table 8.1**)

No:

- Add second agent after consideration of drug-specific effects and patient factors (See Table 8.1)

Dual Therapy Lifestyle Management + Metformin + Additional Agent

ASCVD? **Yes:** - Add agent proven to reduce major adverse cardiovascular events and/or cardiovascular mortality (see recommendations with * on p. S75 and **Table 8.1**)
No: - Add second agent after consideration of drug-specific effects and patient factors (See Table 8.1)

Yes: - Monitor A1C every 3–6 months
No: - Assess medication-taking behavior
- Consider Triple Therapy

Lifestyle Management + Metformin + Two Additional Agents

Add third agent based on drug-specific effects and patient factors[#] (See Table 8.1)

A1C at target after 3 months of triple therapy? **Yes:** - Monitor A1C every 3–6 months
No: - Assess medication-taking behavior
- Consider Combination Injectable Therapy (See Figure 8.2)

Yes:

- Monitor A1C every 3–6 months

No:

- Assess medication-taking behavior
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Lifestyle Management + Metformin + Two Additional Agents

Add third agent based on drug-specific effects and patient factors[#] (See Table 8.1)

A1C at target after 3 months of triple therapy?

Yes:

- Monitor A1C every 3–6 months

No:

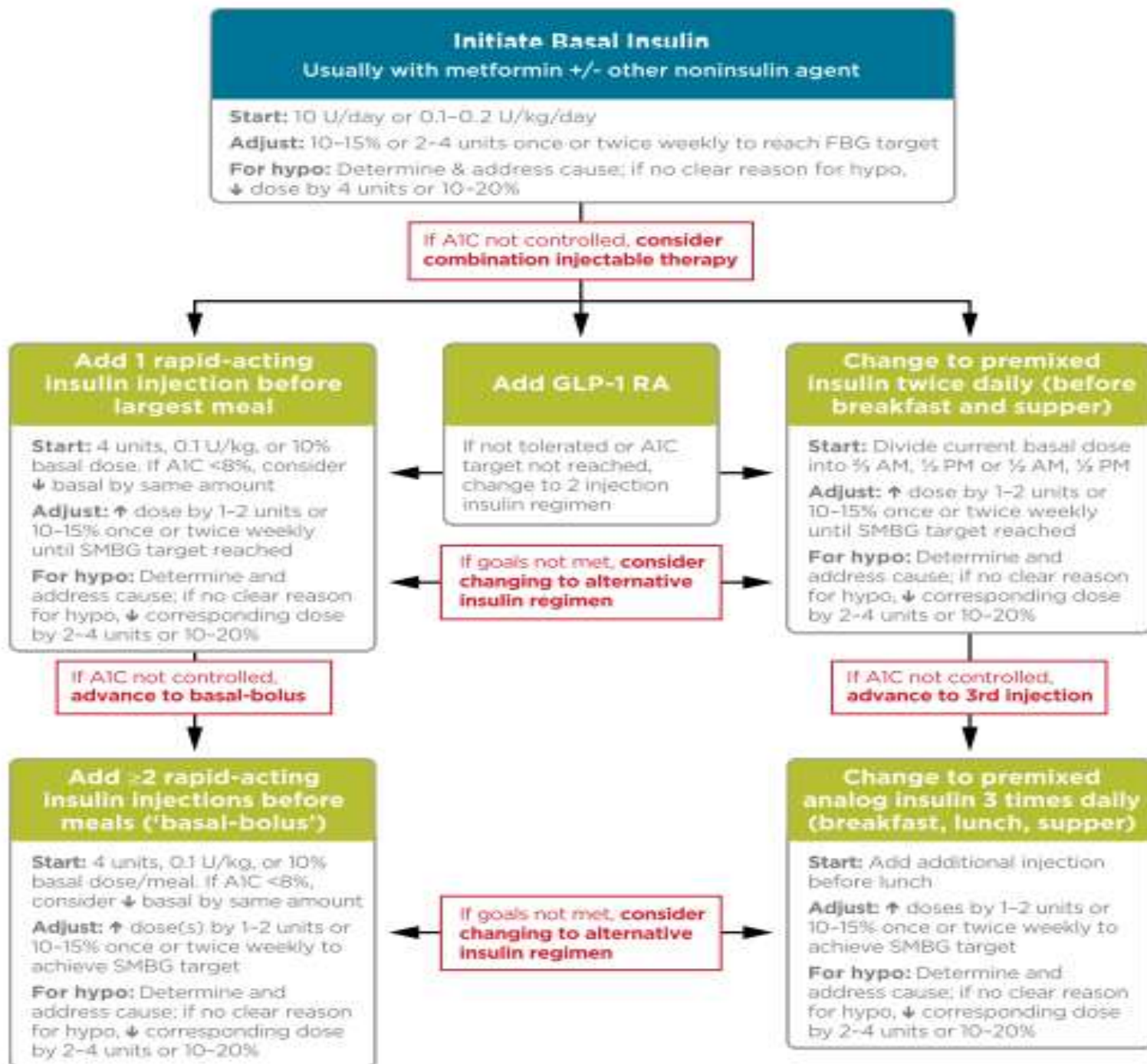
- Assess medication-taking behavior
- Consider Combination Injectable Therapy (See Figure 8.2)



- Gloripa
- Glorenta
- Gloria







insulin

PREPARATION & brand names	TIME OF ACTION		
	ONSET, h	PEAK, h	EFFECTIVE DURATION, h
Short-acting: provide post-prandial needs			
Aspart	<0.25	0.5-1.5	3-4
Glulisine	<0.25	0.5-1.5	3-4
Lispro	<0.25	0.5-1.5	3-4
Regular	0.5-1.0	2-3	4-6
Long-acting: provide daily insulin needs			
Detemir	1-4	— ^a	20-24
Glargine	1-4	— ^a	20-24
NPH	1-4	6-10	10-16
Insulin combinations			
75/25-75% protamine lispro, 25% lispro	<0.25	1.5 h	Up to 10-16
70/30-70% protamine aspart, 30% aspart	<0.25	1.5 h	Up to 10-16
50/50-50% protamine lispro, 50% lispro	<0.25	1.5 h	Up to 10-16
70/30-70% NPH, 30% regular	0.5-1	Dual ^b	10-16

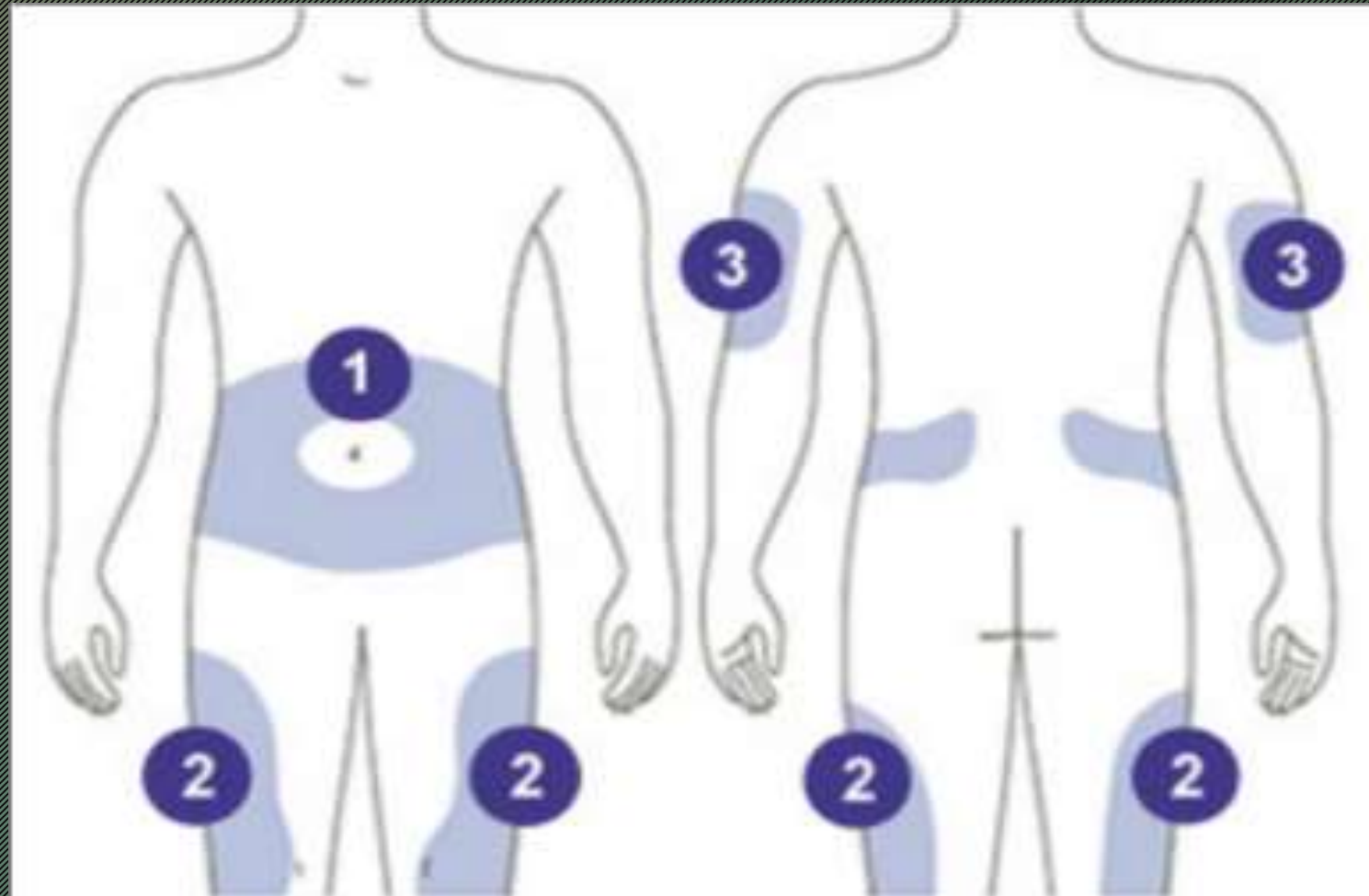


- ۱- انسولین نوومیکس Novomix یا قلم سرمه ای
- ۲- انسولین لانتوس یا گلارژین Glargine یا Lantus یا قلم طوسی/بنفش کم رنگ
- ۳- انسولین اسپارت یا نوورپید Novorapid یا قلم سرمه ای / نارنجی
- ۴- انسولین اپیدرا Apidra یا گلولیزین Glulisine با قلم رنگ ابی



PREPARATION & brand names	ONSET, h	PEAK, h	ACTION
Short-acting: provide post-prandial needs			
Aspart	<0.25	0.5-1.5	3-4
Glulisine	<0.25	0.5-1.5	
Lispro	<0.25	0.5-1.5	
Regular	0.5-1.0	2-3	4-6
Long-acting: provide daily insulin needs			
Detemir	1-4	—	
Glargine	1-4	—	
NPH	1-4	6-10	10-16
Insulin combinations			
75/25-75% protamine lispro, 25% lispro	<0.25	1.5 h	
70/30-70% protamine aspart, 30% aspart	<0.25	1.5 h	
50/50-50% protamine lispro, 50% lispro	<0.25	1.5 h	
70/30-70% NPH, 30% regular	0.5-1	Dual ^b	10-16

- Side effect
- absorb



Insulin to Carbohydrate Ratio (ICR)

1- Insulin (bolus)/CHO

مثال ۱: ۶ واحد انسولین R و ۶ واحد NPH قبل نهار تزریق کرده
نهار مصرفی: ۹۰ گرم نان + ۱۲۰ گرم جوجه کباب + گوجه فرنگی ۱ عدد + ۲ لیوان دوغ
نسبت انسولین به کربو؟

- Insulin (bolus)/CHO

- مثال ۲: آقای ۶۰ ساله، میزان انسولین دریافتی روزانه بشرح زیر است
لانتوس ۱۵ واحد شب ها
نورویپید ۶ واحد قبل نهار/ ۶ واحد قبل شام
در کل روز ۱۳ واحد کربوهیدرات دریافت کرده است
- نسبت انسولین به کربو؟

- Total daily dose/30

• مثال ۳: نسبت انسولین به کربوهیدرات در فردی که روزانه ۶۰ واحد انسولین N/R دریافت میکند را محاسبه کنید.

- ۴۵۰ OR 500/Total Daily Dose
- انسولین آنالوگ : 500
- 45۰ (N/R) انسولین انسانی :

• مثال ۴: نسبت انسولین به کربوهیدرات با استفاده از این قانون در فردی که ۵۰ واحد انسولین لانتوس/نوورپید تزریق میکند چه میزان است؟



ISF (insulin sensitivity factor)

- 1500 or 1700-1800/TDD
- 1500: انسولین انسانی (N/R)
- 1700-1800: انسولین آنالوگ
- مثال ۵: در فردی که ۵۰ واحد انسولین (N/R) مصرف میکند هر واحد انسولین چه میزان قند خونس را کاهش میدهد <

• مثال ٦:

TDD: 30 unit (N/R)

Target glucose level: 100

Premeal glucose level: 250

60 gram carbohydrate are to be consumed

- TDD: 30 unit (N/R)
- Target glucose level: 100
- Premeal glucose level: 250
- 60 gram carbohydrate are to be consumed

$$\text{ISF: } 1500/30=50$$

$$250-100=150$$

$150/50=3$ UNIT to decrease high glucose level

$$450/30= 15 \text{ gr}$$

$$60/15=4 \text{ unit ins}$$

$$3+ 4= 7 \text{ unit insulin}$$

- آقای ۴۵ ساله با دیابت نوع ۱، با وزن ۶۲ کیلوگرم و قد ۱۷۰ مراجعه کرده است
- رژیم دارویی فرد: صبح ها ۱۶ واحد NPH، ۶ واحد رگولار
- شب ها ۸ واحد NPH، ۶ واحد رگولار
- یاد آمد غذایی فرد نشان داده است ۱۰ واحد کربو مصرف میکند

FBS: 210 HbA1C: 9% TG: 317 LDL-c: 70 Chol: 180

قند هدف: ۱۰۰

حذف واحدهای از سه روز بعد، معام غذا را لازم دارد؟

- TDD: 36
- Ins (bolus)/cho: $12/10=1.2$
- TDD/30: $36/30= 1.2$
- CHO count: 4 unit $4*1.2=4.8$
- ISF: $1500/\text{TDD}: 1500/36=41.6$
- $210-100=110$
- $110/41.6=2.6$
- $2.6+ 4.8=7.4$
-

Table 6.2—Summary of glycemic recommendations for many nonpregnant adults with diabetes

A1C	<7.0% (53 mmol/mol)*
Preprandial capillary plasma glucose	80–130 mg/dL* (4.4–7.2 mmol/L)
Peak postprandial capillary plasma glucose†	<180 mg/dL* (10.0 mmol/L)

*More or less stringent glycemic goals may be appropriate for individual patients. Goals should be individualized based on duration of diabetes, age/life expectancy, comorbid conditions, known CVD or advanced microvascular complications, hypoglycemia unawareness, and individual patient considerations. †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.

The nutritional goals for people with type 2 diabetes are to

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- Maintain blood glucose levels as near-normal as possible by balancing food intake with activity and medications or insulin
- Achieve optimal blood pressure and lipid levels
- Provide appropriate calories for achieving and maintaining a healthy, desirable body weight
- Manage risk factors and prevent complications of diabetes, both acute (hypoglycemia) and long term (gastroparesis, [CVD], renal disease, and other consequences of micro- and macrovascular disease)



MNT for type 2 diabetes should consider five key aspects:

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- Weight management and increased physical activity
 - Caloric intake (balanced with caloric expenditure)
 - Consistency in day-to-day carbohydrate intake at meals and snacks
 - Nutritional content
 - Timing of meals and snacks
-
- Meal content, quantity, and timing are particularly important for patients who are treated with insulin secretagogues or traditional insulin regimens.

Weight loss goals

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For patients with type 2 diabetes who are overweight (BMI ≥ 25 to 29.9 kg/m^2) or obese (BMI $\geq 30 \text{ kg/m}^2$), initial recommendations for weight loss and physical activity are to lose 5 to 10 percent of initial body weight

- and to accumulate at least 30 minutes of moderate physical activity over the course of most days of the week

Other supplements

60

- some minerals and nutritional supplements have purportedly improved glycemic control in patients with type 2 diabetes
- As an example, in some randomized trials, **chromium** supplementation improved glycemia among patients with diabetes but not among those with normal glucose tolerance



- Cinnamon supplementation
- However, meta-analyses have shown conflicting results



- A variety of eating patterns (Mediterranean, low fat, low carbohydrate, vegetarian) are acceptable.
- Fat quality is more important than fat quantity.
- Trans fats contribute to coronary heart disease, while mono- and polyunsaturated fats (eg, those found in fish, olive oil, nuts) are relatively protective.
- Trans fatty acid consumption should be kept as low as possible.

- Protein intake goals should be individualized but not lower than 0.8 g/kg body weight per day (the recommended daily allowance).
- Patients should be encouraged to substitute lean meats, fish, eggs, beans, peas, soy products, and nuts and seeds for red meat

- **Fiber intake** should be at least 14 grams per 1000 calories daily; higher fiber intake may improve glycemic control.
- A reduced **sodium** intake of 2300 mg per day with a diet high in fruits, vegetables, and low-fat dairy products is prudent and has demonstrated beneficial effects on blood pressure

Hypoglycemia

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- Patients taking insulin or oral hypoglycemic medications that increase insulin secretion should be well trained in methods to treat hypoglycemia, for example during or after exercise, to prevent overcompensation.
- In the long-term, it is better to adjust medications or insulin to compensate for increased activity (or a reduced calorie intake) rather than add extra snacks in patients with type 2 diabetes, as most are trying to lose weight or manage weigh

- Advise patients to carry a snack with 10 to 15 grams of carbohydrate to prevent hypoglycemia or to treat hypoglycemia.

blood glucose	carbohydrate
51 to 70 mg/dL	10 to 15 g
≤50 mg/dL	20 to 30 g

- Retest 15 minutes after ingestion and repeat treatment as needed based on blood glucose levels

ملاحظات تغذیه ای در اصول رژیم نویسی برای بیماران دیابتی

رژیم نویسی در بیماران دیابتی مشابه با بیماران غیردیابتی است و تنها تفاوت در نحوه توزیع کربوهیدرات بین وعده های غذایی است - کمترین افزایش قندخون بعد از هر وعده غذایی - جلوگیری از هیپوگلیسمی ناشی از تجویز انسولین یا قرص های کاهنده قندخون جهت توزیع کربوهیدرات بین وعده های، بعد از محاسبه کل کربوهیدرات مورد نیاز روزانه، بصورت درصدهای زیر بین وعده های غذایی توزیع میکنیم:

صبحانه	میان وعده صبح	نهار	میان وعده عصر	شام	میان وعده آخرشب
%۱۵	%۱۳	%۲۲	%۱۳	%۲۲	%۱۵
%۱۵	%۱۳	%۲۴	%۱۳	%۲۴	%۱۱

Weight consequences of diabetes medications

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- Thiazolidinedione therapy ([pioglitazone](#) and [rosiglitazone](#)) is associated with significant weight gain.
- It is both dose dependent and time dependent, and it can be substantial. Some weight gain from thiazolidinediones may be associated with fluid retention, which is of significant concern in patients with congestive heart disease

- in contrast, the use of glucagon-like peptide-1 (GLP-1) agonists and sodium-glucose co-transporter 2 (SGLT2) inhibitors are associated with moderate weight loss.
- Metformin and dipeptidyl peptidase-4 (DPP-4) inhibitors are generally weight neutral

A grayscale illustration of a desk setup. In the top left, there is a white mug filled with dark coffee. Below it, a pair of glasses with oval lenses and a thin frame lies on the surface. To the right, an open book is shown, with its pages filled with text. The entire scene is rendered in a soft, painterly style with a grayscale palette.

THE END