Disease of Endocrine Pancreas and Complications

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Outline

Glucose homeostasis

Hyperglycemia → Diabetes mellitus

- Who should be screened for DM?
- Diagnostic criteria: prediabetes and diabetes
- Classification of DM
- Management

Outline

- ✓ Glucose homeostasis
- Hyperglycemia

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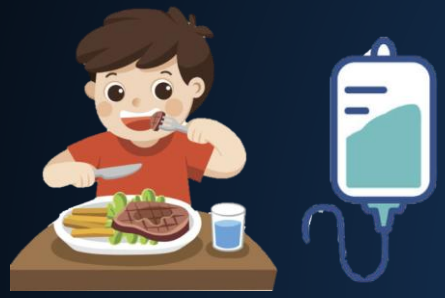
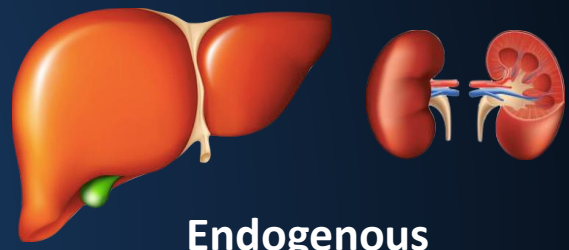
Glucose homeostasis

SI ENDO



Exogenous

Glycogenolysis
Gluconeogenesis



Endogenous

Plasma glucose

Insulin-dependent tissue

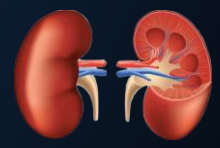
Muscle

Adipose tissue

Insulin-independent tissue

Brain

RBC



Kidney

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Glucose homeostasis

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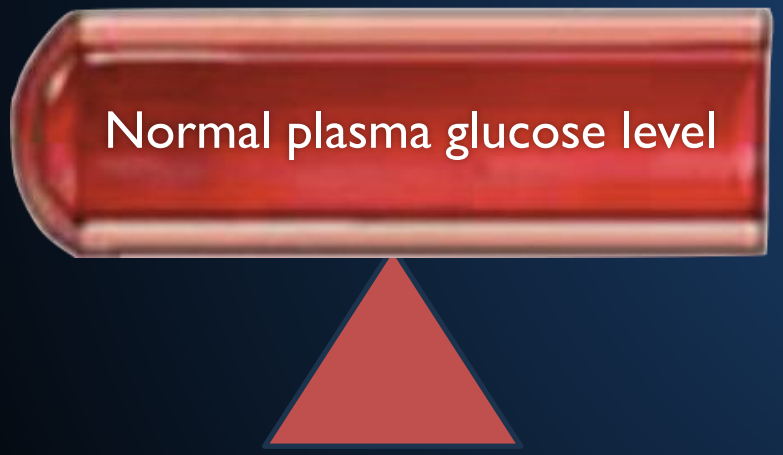
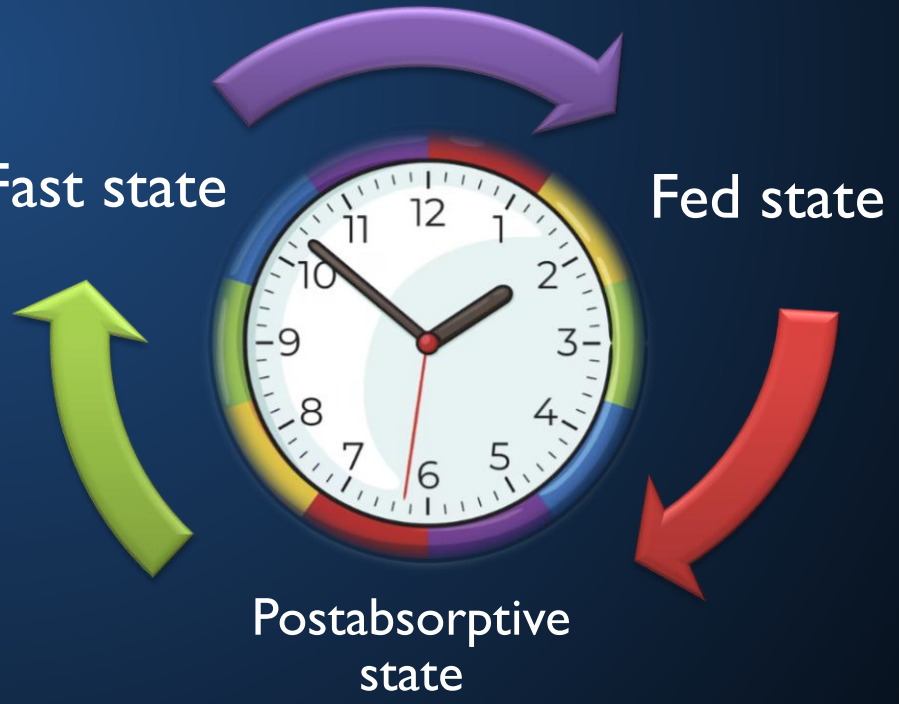
Balance between glucose production and glucose utilization





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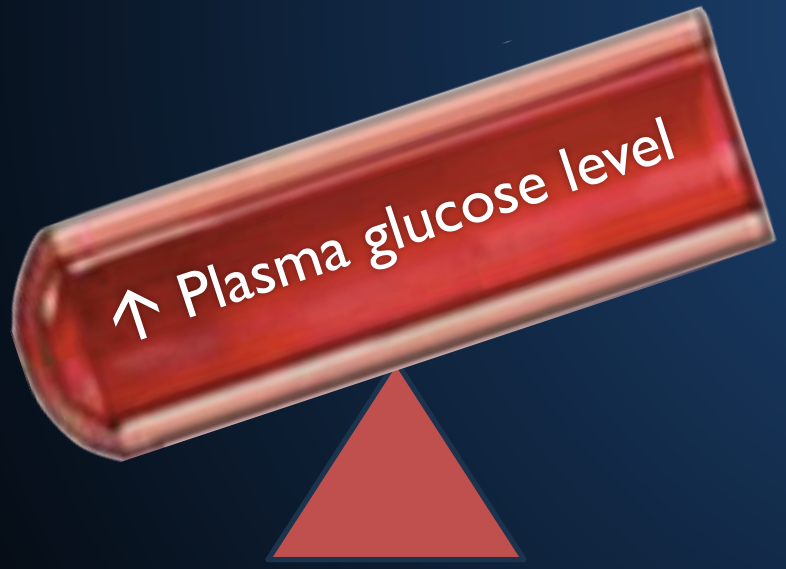
Glucose homeostasis

SI ENDO

Fed state (first 4 hours after meal, active nutrient absorption from GI tract)



↑ insulin secretion

↑ Glucose utilization

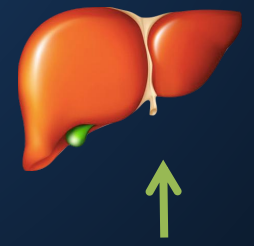
↓ Gluconeogenesis

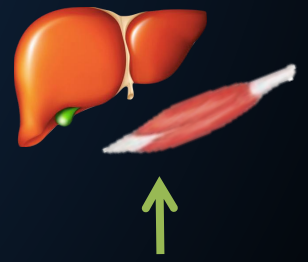
↑ Glycogenesis

↓ Proteolysis

↓ Lipolysis

Insulin-dependent tissue





Parasympathetic (splanchnic)

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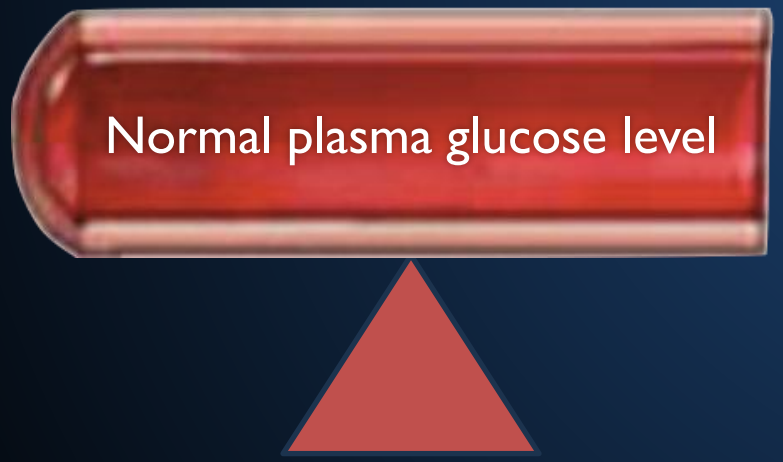
Glucose homeostasis

SI ENDO

Fed state (first 4 hours after meal, active nutrient absorption from GI tract)



↑ insulin secretion

↑ Glucose utilization

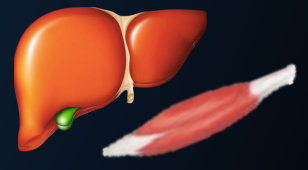
↓ Gluconeogenesis

↑ Glycogenesis

↓ Proteolysis

↓ Lipolysis

Insulin-dependent tissue



Parasympathetic (splanchnic)

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Glucose homeostasis

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Postprandial state (4-8 hours after meal)

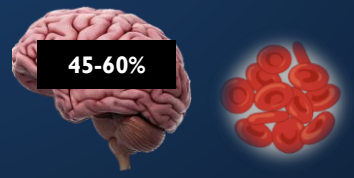
↓ Insulin secretion
↑ Glucagon secretion

↑ Plasma glucose level

↓ Glucose utilization

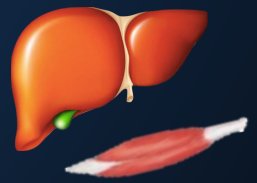
Insulin-dependent tissue

↑ Glucose utilization

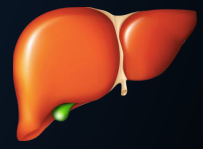


Insulin-independent tissue

↑ Glycogenolysis



↑ Gluconeogenesis



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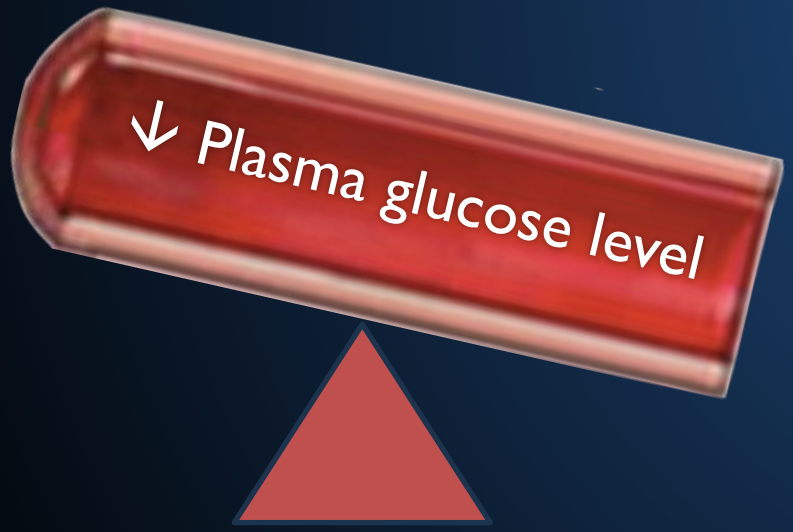
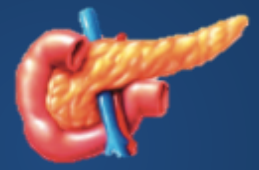
Glucose homeostasis

SI ENDO

Fast state (metabolic condition 10-14 hour after meal)





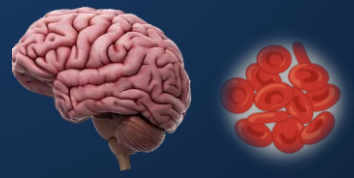
↓ ↓ Insulin secretion (basal plasma insulin)

↑ ↑ Glucagon secretion

↓ ↓ Glucose utilization

Insulin-dependent tissue

↑ ↑ Glucose utilization



Insulin-independent tissue

⇔ Glycogenolysis

↑ ↑ Gluconeogenesis

↑ Ketogenesis

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Gluconeogenesis

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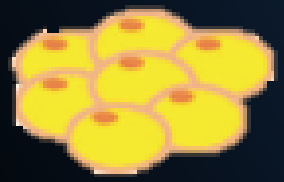
Synthesis of glucose from non-carbohydrate precursors
Occurs mainly in the liver and to a lesser extent in the cortex of the kidney.

Glucose → (Glycolysis) → Pyruvate

Pyruvate → (Anaerobic glycolysis) → Lactate → Glucose-lactate (CORI) cycle

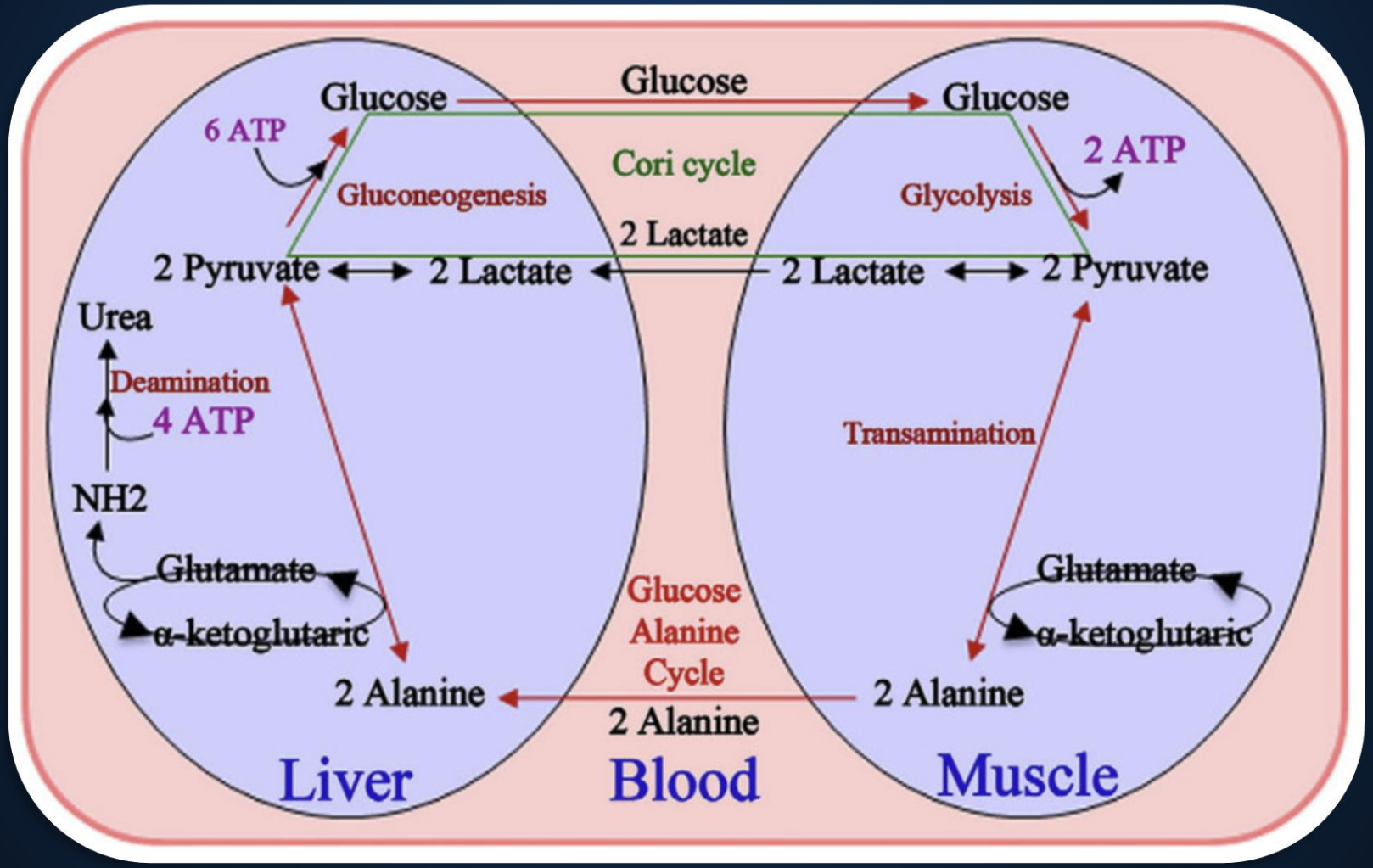
Pyruvate → (Transamination) → Alanine → Glucose-alanine cycle



Hydrolysis of triacylglycerol → FFA + Glycerol → Glycerol → DHAP

DHAP: Dihydroxyacetone phosphate

Cori cycle and glucose-alanine cycle



M. Dashty . Clinical Biochemistry. 2013; 46: 1339–1352

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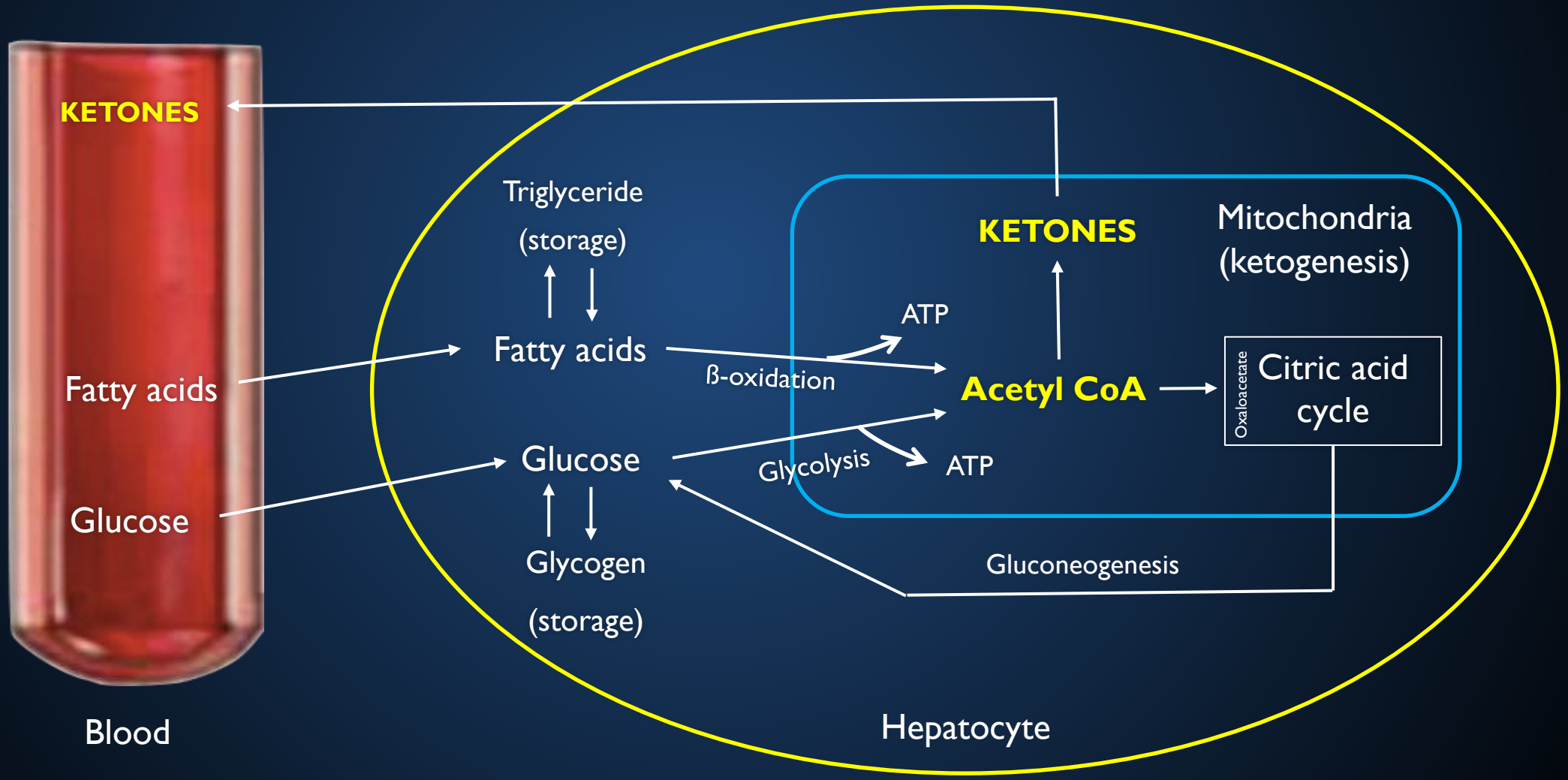
Formation of ketone body

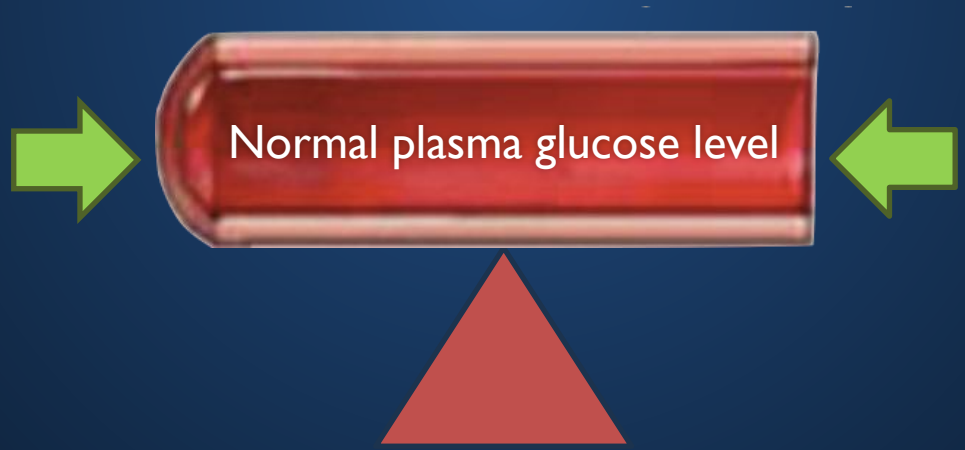


Summary

- Glucose homeostasis: balance between glucose production and glucose utilization

Factors decreasing plasma glucose

- Insulin
- Parasympathetic (splanchnic) nerves to liver
- Hyperglycemia



Factors increasing plasma glucose

- Counterregulatory hormones (glucagon, cortisol, epinephrine, growth hormone)
- Sympathetic (splanchnic) nerve to liver
- Free fatty acid (FFA)

Summary

	Fed state
Insulin secretion	↑↑↑
Counterregulatory hormone secretion	↓↓↓
Source of glucose (%) • Food • Glycogenolysis • Hepatic gluconeogenesis • Renal gluconeogenesis	 100 0 0 0
Glucose utilization by • Insulin-dependent organ (%) • Insulin-independent organ (%)	 >80 <20
Using of other source energy instead of glucose	↓

Outline

Glucose homeostasis

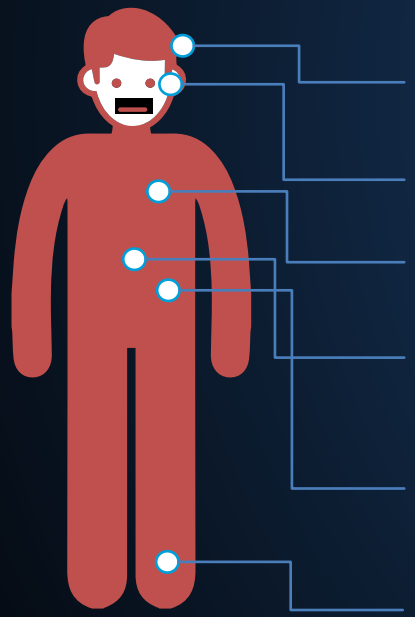
✓ Hyperglycemia ➡ Diabetes mellitus

- Who should be screened for DM?
- Diagnostic criteria: prediabetes and diabetes
- Classification of DM
- Management

Diabetes clinical burden

T2D is a complex, multifactorial disorder with pathophysiological deficits that lead to comorbidities and mortality

Comorbidities



- Cerebrovascular disease; emotional and cognitive challenges
- Diabetic retinopathy
- Hypertension; **cardiovascular disease**
- Obesity; cancer; gastroparesis
- Polyuria; nephropathy**; chronic kidney disease**
- Peripheral vascular disease; neuropathy; skin/foot complications and amputation

Mortality

15% — **All-cause mortality**

14% — **Cardiovascular death**

ADA. Standards of Medical Care in Diabetes - 2019. *Diabetes Care*. 2019;42. ADA. Living with diabetes: complications. http://www.diabetes.org/living-with-diabetes/complications/. Accessed: 9 Sept 2018. Klimek P, et al. *PLoS Comput Biol*. 2015;11:e1004125; Pantalone KM, et al. *BMJ Open Diabetes Res Care*. 2015;3:e000093; Song et al. *Qjm*. 2009;102(11):799-806; Tancredi M, et al. *N Engl J Med*. 2015;373:1720-1732.

Outline

Glucose homeostasis

✓ Hyperglycemia ➡ Diabetes mellitus

- Who should be screened for DM?
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- Classification of DM
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Criteria for screening for diabetes or prediabetes in asymptomatic adults

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1. Testing should be considered in overweight or obese (BMI ≥ 25 kg/m^2 or ≥ 23 kg/m^2 in Asian Americans) adults who have ≥ 1 of the following risk factors:
   - First-degree relative with diabetes
   - High-risk race/ethnicity (e.g. African American, Latino, Native American, Asian American)
   - History of cardiovascular disease
   - Hypertension (≥ 130/80 mmHg or on therapy for hypertension)
   - HDL cholesterol level < 35 mg/dL and/or a triglyceride level > 250 mg/dL
   - Individuals with polycystic ovary syndrome
   - Physical inactivity
   - Other clinical conditions associated with insulin resistance e.g. severe obesity, acanthosis nigricans

Diabetes Care. 2025; 48(Suppl. 1): S1-S321

Criteria for screening for diabetes or prediabetes in asymptomatic adults

2. People who were diagnosed with gestational diabetes mellitus (GDM) should have testing at least every 1-3 years (lifelong).
3. High-risk groups (e.g., HIV, exposure to high-risk medicine, history of pancreatitis) should be closely monitored
4. For all other people, testing should begin at age 35 years.

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.

Patients with **prediabetes** should be tested yearly.

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Diagnosis criteria of diabetes

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1. Fasting plasma glucose ≥ 126 mg/dL ★
   No caloric intake ≥ 8 hours
2. 2-h plasma glucose during 75g-OGTT ≥ 200 mg/dL ★
3. A1C ≥ 6.5% ★
   NGSP certified method
4. Random plasma glucose ≥ 200 mg/dL
   With classic symptoms of hyperglycemia/ hyperglycemic crisis

NGSP = National Glycohemoglobin Standardization Program

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Diagnosis criteria of diabetes

SI ENDO

In the absence of unequivocal hyperglycemia, diagnosis requires **two abnormal test results** obtained at the same time or at two different time points.

1 sample, same time
- **FPG 128 mg/dL**
- **HbA1c 7.0%**

DM

2 different time points
- **FPG 130 mg/dL**
- **FPG 147 mg/dL**

DM

2 different time points
- **FPG 130 mg/dL**
- **HbA1c 6.6 %**

DM

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Diagnosis criteria of diabetes

SI ENDO

If a patient has discordant results from two different tests, then the test result that is above the diagnostic cut point should be repeated.

FPG 130 mg/dL

HbA1C 6.2%

Repeat FPG

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Criteria defining prediabetes in nonpregnant individuals

Criteria	Value	
Fasting plasma glucose	**100**-125 mg/dL	Impaired fasting glucose (IFG)
2-hr 75 g OGTT	140-199 mg/dL	Impaired glucose tolerance (IGT)
HbA1C	5.7-6.4 %	

OGTT: oral glucose tolerance test

Diabetes Care. 2025; 48(Suppl. 1): S1-S321

Outline

Glucose homeostasis

✓ Hyperglycemia → Diabetes mellitus

- Who should be screened for DM?
- Diagnostic criteria: prediabetes and diabetes
- **Classification of DM**
- Management

Classification of diabetes

WHO 1990

1. Type 1 diabetes
2. Type 2 diabetes
3. Gestational diabetes mellitus (GDM)
4. Other specific types

Classification of diabetes mellitus, WHO 1990

Classification of Diabetes Mellitus WHO 1990

Type	Description
1. Type 1 diabetes • Immune mediated and Idiopathic	**Immune mediated β-cell destruction → absolute insulin deficiency**
2. Type 2 diabetes • Predominantly insulin resistance • Predominantly insulin secretory defects	**Insulin resistance** +/- relative insulin deficiency

Classification of diabetes mellitus, WHO 1990

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Stage of type 1 diabetes

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	Stage 1	Stage 2	Stage 3
Characteristics	• Autoimmunity • Normoglycemia • Presymptomatic	• Autoimmunity • Dysglycemia • Presymptomatic	• Autoimmunity • Overt hyperglycemia • Symptomatic

Diagnosis criteria	• Multiple islet autoantibodies
	• No IGT or IFG, normal A1C
		• Islet autoantibodies (usually multiple)
		• Dysglycemia:
		  • IFG: 100-125 mg/dL or
		  • IGT: 2-h PG 140-199 mg/dL or
		  • A1C 5.7-6.4% or ≥ 10% increase in A1C
			• Autoantibodies may become absent
			• Diabetes by standard criteria

FPG, fasting plasma glucose; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; 2-h PG, 2-h plasma glucose.
Alternative additional stage 2 diagnostic criteria of 30-, 60-, or 90-min plasma glucose on oral glucose tolerance test ≥ 200 mg/dL and confirmatory testing in those aged ≥18 years have been used in clinical trials

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Natural history of T2D

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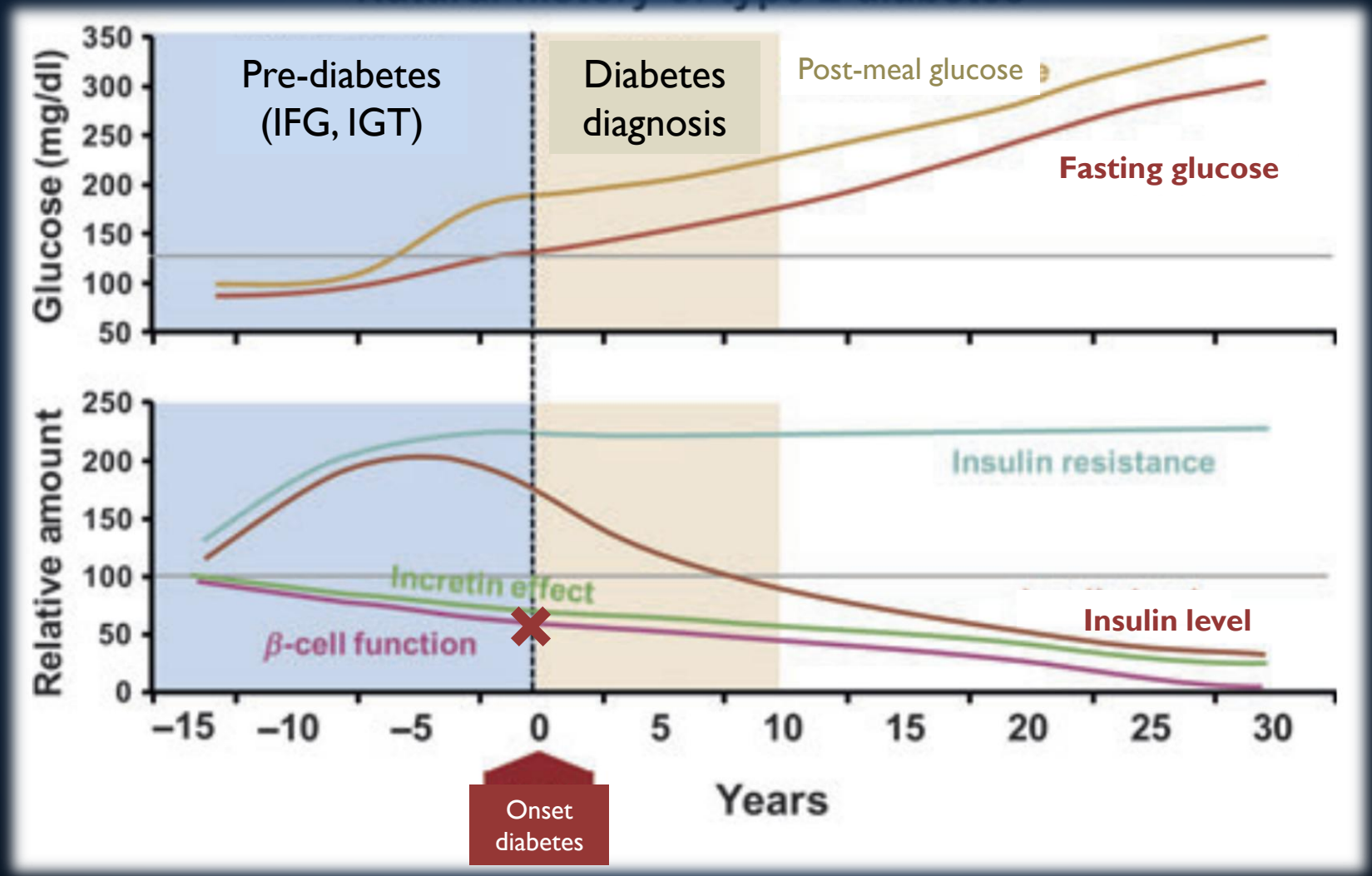

Tobin GS et al. Int J Clin Pract, 2012,; 66(12): 1147–1157.

Clinical comparison

Clinical Features	Type I
Age of onset	< 20-30
Onset	Sudden
Symptoms	Obvious
Body size	Thin
Acanthosis nigricans	No
DKA	Prone
Etiology	Autoimmune
Islet cell Ab	+/-
C-peptide	Low or undetectable
Treatment	Insulin

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Gestational diabetes mellitus

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"defined as any degree of glucose intolerance that was first recognized during pregnancy, regardless of the degree of hyperglycemia."

Diabetes Care. 2025; 48(Suppl. 1): S1-S321

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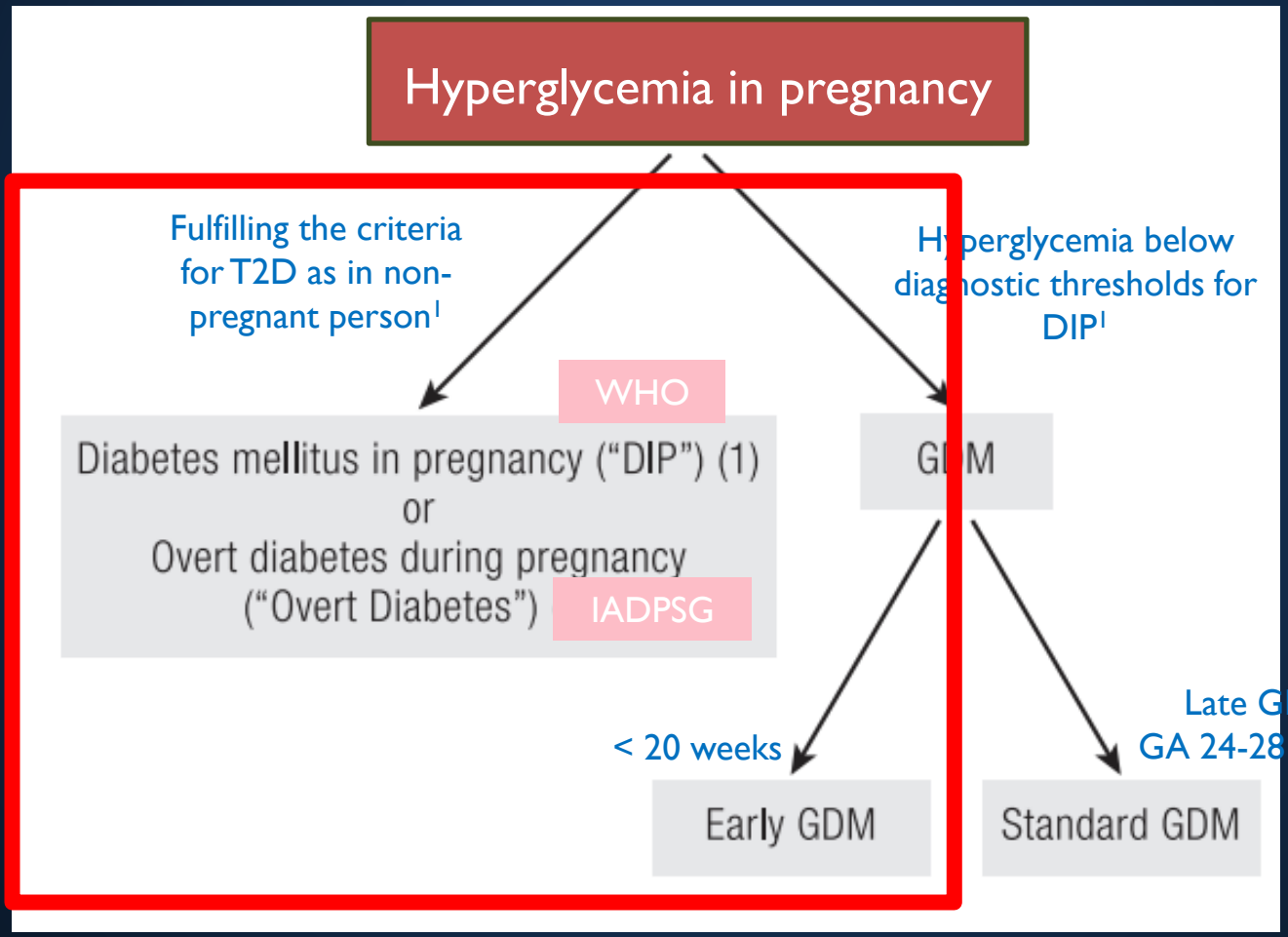
Hyperglycemia in pregnancy

Any degree of glucose intolerance that was first recognized during pregnancy, regardless of the degree of hyperglycemia[2]



IADPSG: International Association of the Diabetes and Pregnancy Study Groups

[1]WHO. Classification of diabetes mellitus. 2019
[2]Diabetes care. 2025; 48(1): 306-320
Sweeting A, et al. Endocrine Reviews, 2022; 43(5): 763-793

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Who and When should be screened?

Normal

If early screening is negative, Repeat screening for GDM at 24-28 weeks of gestation by

- **One-step using 75g OGTT or**
- **Two-step strategy using 50g-GCT, if positive, followed by 100g-OGTT**

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Diagnostic criteria for GDM

SI ENDO

One-step strategy

75-g OGTT (fast 8 hours)

Diagnosis if PG elevated ≥ 1 value

- FPG ≥ 92 mg/dL
- 1-hr PG ≥ 180 mg/dL
- 2-hr PG ≥ 153 mg/dL

Recommended by ADA, Thai, IADPSG, WHO

2008: HAPO study

Two-step strategy

Step 1: 50-g GCT (non-fasting)

- Diagnosis if 1 h PG ≥ 140 mg/dL

Step 2: 100-g OGTT (fasting)

- **Diagnosis if PG elevated ≥ 2 values**

	NDDG	Carpenter-Coustan
Fasting	≥ 105	≥ 95
1 hour	≥ 190	≥ 180
2 hour	≥ 165	≥ 155
3 hour	≥ 145	≥ 140

1964: O'Sullivan and Mahan

Classification of Diabetes Mellitus WHO 1990

Type	Description
1. Type 1 diabetes • Immune mediated and Idiopathic	Immune mediated β-cell destruction → absolute insulin deficiency
2. Type 2 diabetes • Predominantly insulin resistance • Predominantly insulin secretory defects	Insulin resistance +/- relative insulin deficiency
3. Gestational diabetes	
4. Other specific types	
• Genetic defects of β-cell function	• Maturity Onset of Diabetes in the Young (MODY) • Neonatal DM • Mitochondrial
• Genetic defects in insulin action	• Type A insulin resistance, etc
• Diseases of exocrine pancreas	• Pancreatitis, cystic fibrosis, hemochromatosis, etc.
• Endocrinopathies	• Cushing's syndrome, acromegaly, glucagonoma, pheochromocytoma
• Drug or chemical induced	• Glucocorticoids, thiazide, interferon ɣ, etc
• Infection	• Congenital rubella, CMV, etc
• Uncommon forms of immune mediated diabetes	• Anti-insulin receptor Ab
• Other genetic syndromes associated with diabetes	• Down syndrome, Turner, Klinefelter, Prader-Willi syndrome

Classification of diabetes mellitus, WHO 1990

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Classification of diabetes

SI ENDO

WHO 1990

1. Type 1 diabetes
2. Type 2 diabetes
3. Other specific types
4. Gestational diabetes mellitus

WHO 2019

1. Type 1 Diabetes
2. Type 2 Diabetes
3. Hybrid forms of diabetes
4. Other specific types
5. Gestational diabetes mellitus
6. Unclassified diabetes

Classification of diabetes mellitus, WHO 2019

Classification of Diabetes Mellitus

WHO 2019	WHO 1999
Type 1 diabetes T1 subclasses removed	**Type 1 diabetes** A. Immune mediated B. Idiopathic
Type 2 diabetes T2 subclasses removed	**Type 2 diabetes** - Predominantly insulin resistance - Predominantly insulin secretory defects
New	Previously "LADA" Latent Autoimmune Diabetes of Adults
Other specific types	Presents with ketosis and insulin deficiency but later does not require insulin; common episodes of ketosis, not immune-mediated
New	
Hyperglycemia first detected during pregnancy • Diabetes mellitus in pregnancy • Gestational diabetes mellitus	**Gestational diabetes**

Outline

Glucose homeostasis

✓ Hyperglycemia → Diabetes mellitus

- Who should be screened for DM?
- Diagnostic criteria for diabetes and prediabetes
- Classification of DM
- **Management**

Goals treatment of DM

- Relieve from hyperglycemic symptoms
- Prevention and treatment of acute complication
- Prevention or treatment of chronic complications
  - Macrovascular (CAD, CVD, PVD)
  - Microvascular (eyes, kidneys, nerve)
- Improve quality of life (optimal overall health and well-being)

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Complications of DM

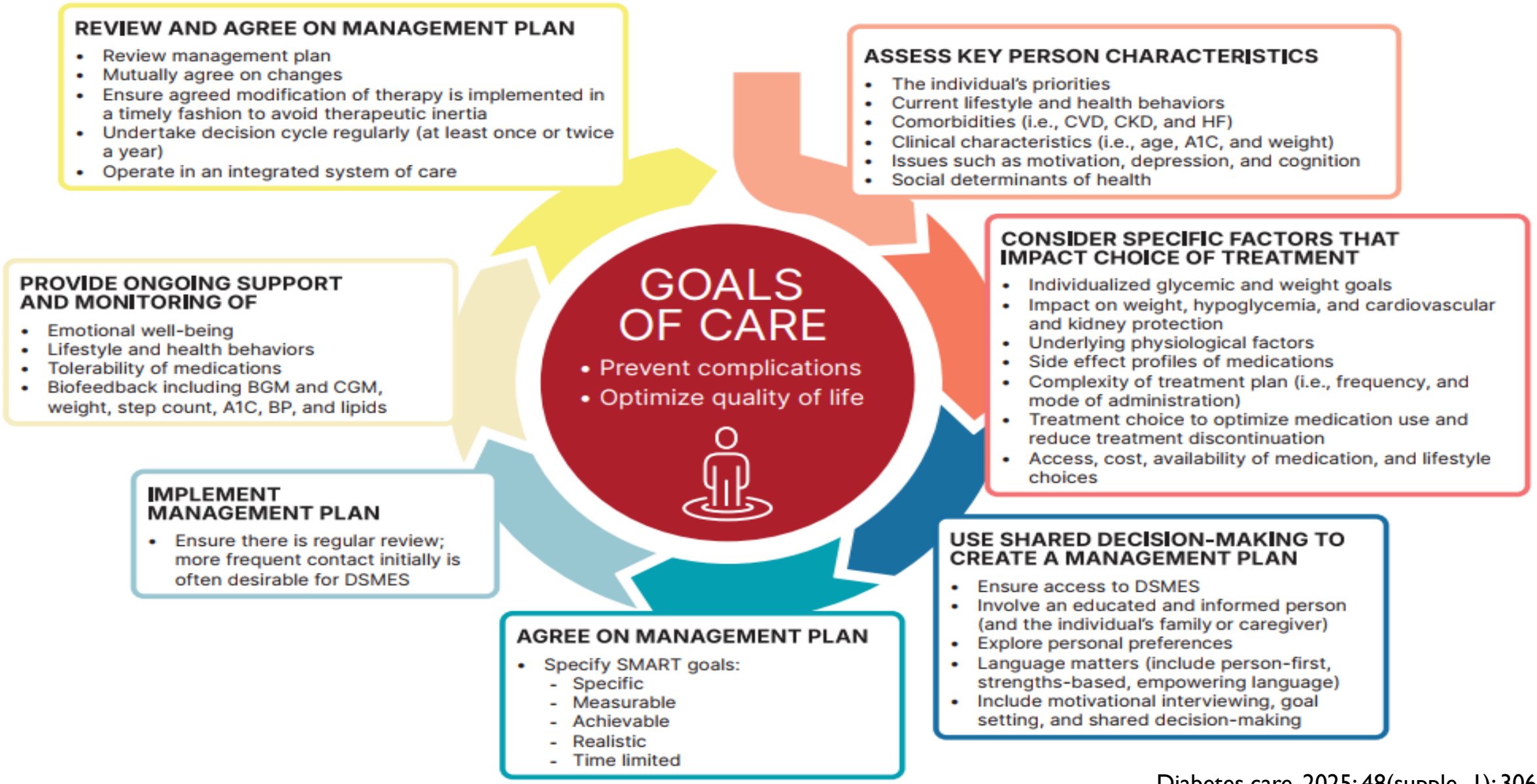
Acute complications

- Hypoglycemia
- Diabetic ketoacidosis (DKA)
- Hyperglycemic hyperosmolar syndrome (HHS)

Chronic complications

- Macrovascular
  - Coronary artery disease
  - Cerebrovascular disease
  - Peripheral vascular disease
- Microvascular
  - Retinopathy
  - Nephropathy
  - Neuropathy

Decision Cycle for Person-Centered Glycemic Management in Type 2 Diabetes



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Glycemic target

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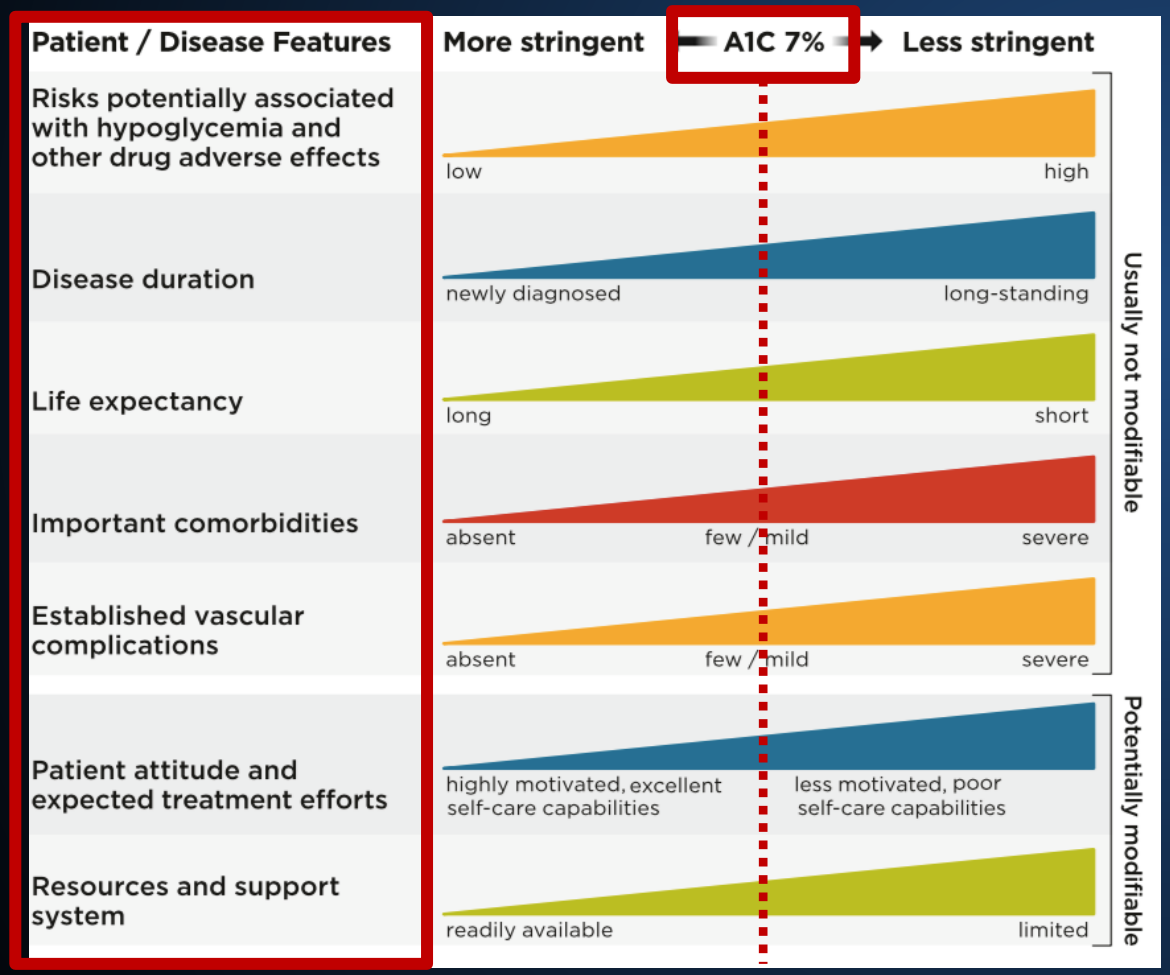

Individualized target HbA_1C

General glycemic recommendations for many nonpregnant adult with diabetes

- HbA1C **< 7%**
- Pre-prandial plasma glucose **80-130 mg/dL**
- Peak postprandial plasma glucose **< 180 mg/dL**

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How to achieve glycemic target?

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How to achieve glycemic target?

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Non Pharmacological treatment

Pharmacological treatment

- **Diabetes education**
- **Lifestyle modification**

- **Oral antidiabetic agent**
- **Insulin treatment**

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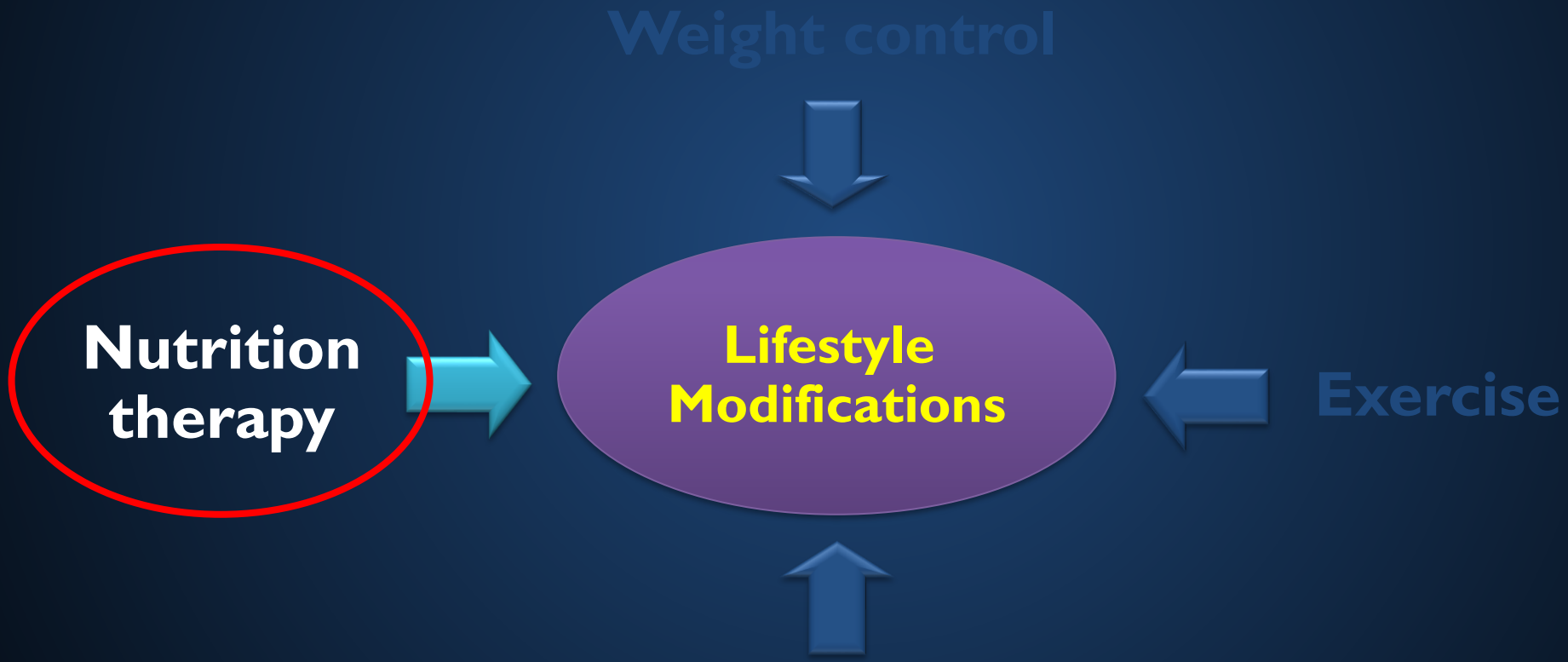
Lifestyle Modifications

AIC reduction 0.5-2%



Nutritional therapy

Diabetes care. 2025; 48(supple_1): 306-320, สมาคมโรคเบาหวานแห่งประเทศไทย

Diet	Recommendations
Carbohydrate	• Emphasize minimally processed, nutrient-dense, high-fiber sources of carbohydrate (at least 14 g fiber /1,000 kcal) • Regardless of diabetes classification, individuals treated with SGLT2i should avoid a ketogenic eating pattern (increased risk of DKA)
Proteins	• Incorporate more **plant-based protein sources** (e.g., nuts, seeds, and legumes) as part of an overall diverse eating pattern to reduce cardiovascular disease risk. • Mediterranean eating pattern, which is rich in monounsaturated and polyunsaturated fats and long-chain fatty acids such as fatty fish, nuts, and seeds, to reduce cardiovascular disease risk and improve glucose metabolism.
Fats	Limit intake of foods high in saturated fat (e.g.,red meat, full-fat dairy, butter, and coconut oil) to help reduce cardiovascular disease risk.
Micronutrients and herbal supplements	Dietary supplement with vitamins, minerals, herbs or spices are **not recommended** for glycemic benefits.
Sodium	Limit sodium consumption to < 2.3 g/day
Alcohol	Male ≤ 2 drinks/day, female ≤ 1 drink/day (one drink is equal to a 12-oz beer, a 5-oz glass of wine, or 1.5 oz of distilled spirits)
Nonnutritive sweetener	Water is recommended over nutritive and nonnutritive sweetened beverages. The use of nonnutritive sweeteners in moderation is acceptable if it reduces overall calories and carbohydrate intake.

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Lifestyle Modifications

AIC reduction 0.5-2%

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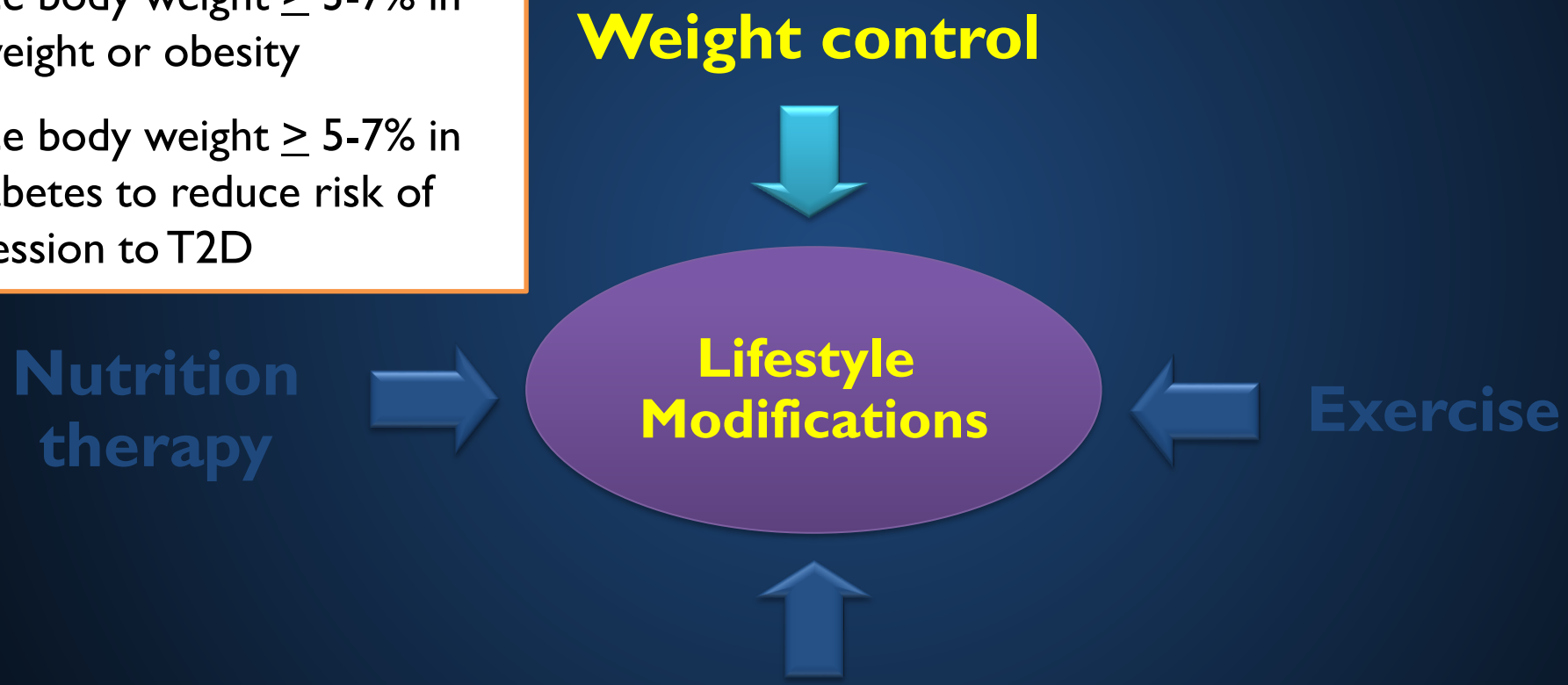
- Reduce body weight ≥ 3-7% in overweight or obesity
- Reduce body weight ≥ 5-7% in prediabetes to reduce risk of progression to T2D



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Lifestyle Modifications

AIC reduction 0.5-2%

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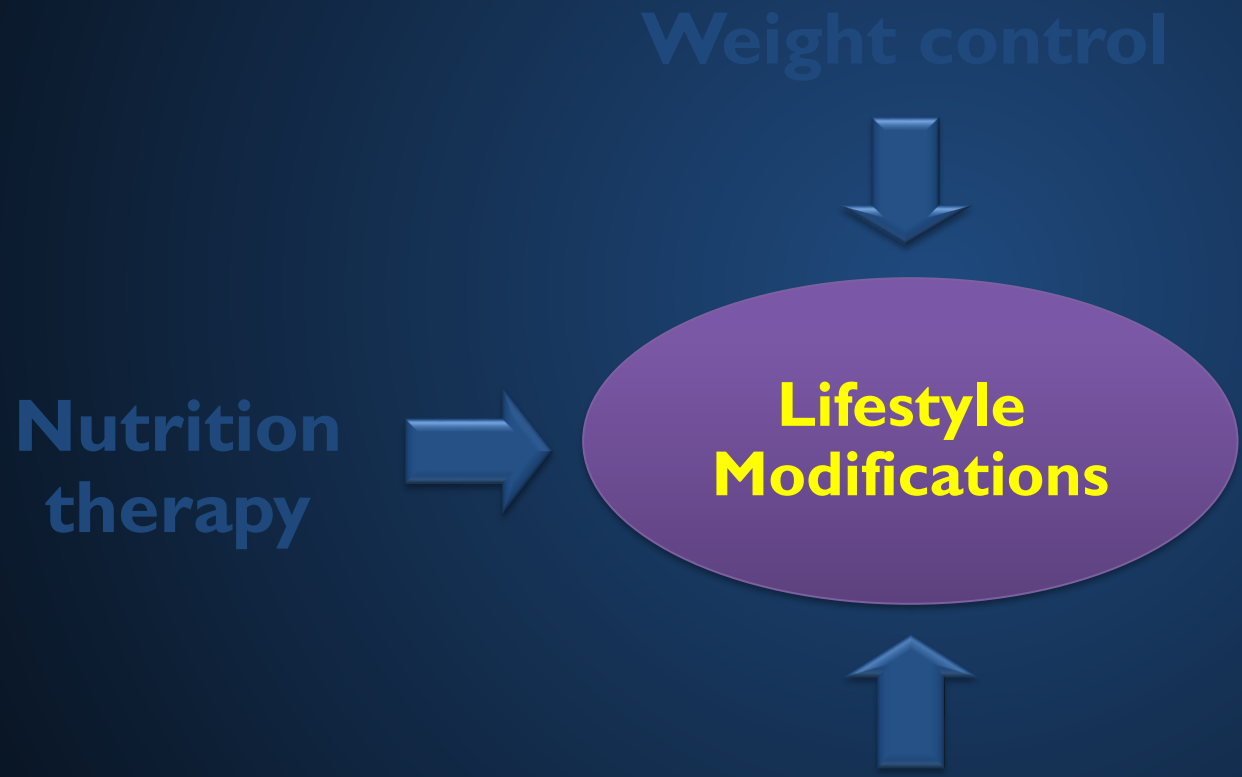

"Aerobic exercise"

- Moderate to vigorous-intensity aerobic activity ≥ 60 mins/day with muscle strengthening and bone strengthening ≥ 3 days/wk with < 2 consecutive days without exercise

"Resistance training" should be encouraged: 2-3 sessions/wk of nonconsecutive days

"Flexibility and balance training" 2-3 times/week for older adults (Yoga, Tai chi)

"Prolonged sitting" should be interrupted every 30 mins

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How to achieve glycemic target?

- **Oral antidiabetic agents**
- **Injection therapy**

(insulin, GLP-1 analog, combination injectable therapy)

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Pathophysiology of T2D with Treatment Options

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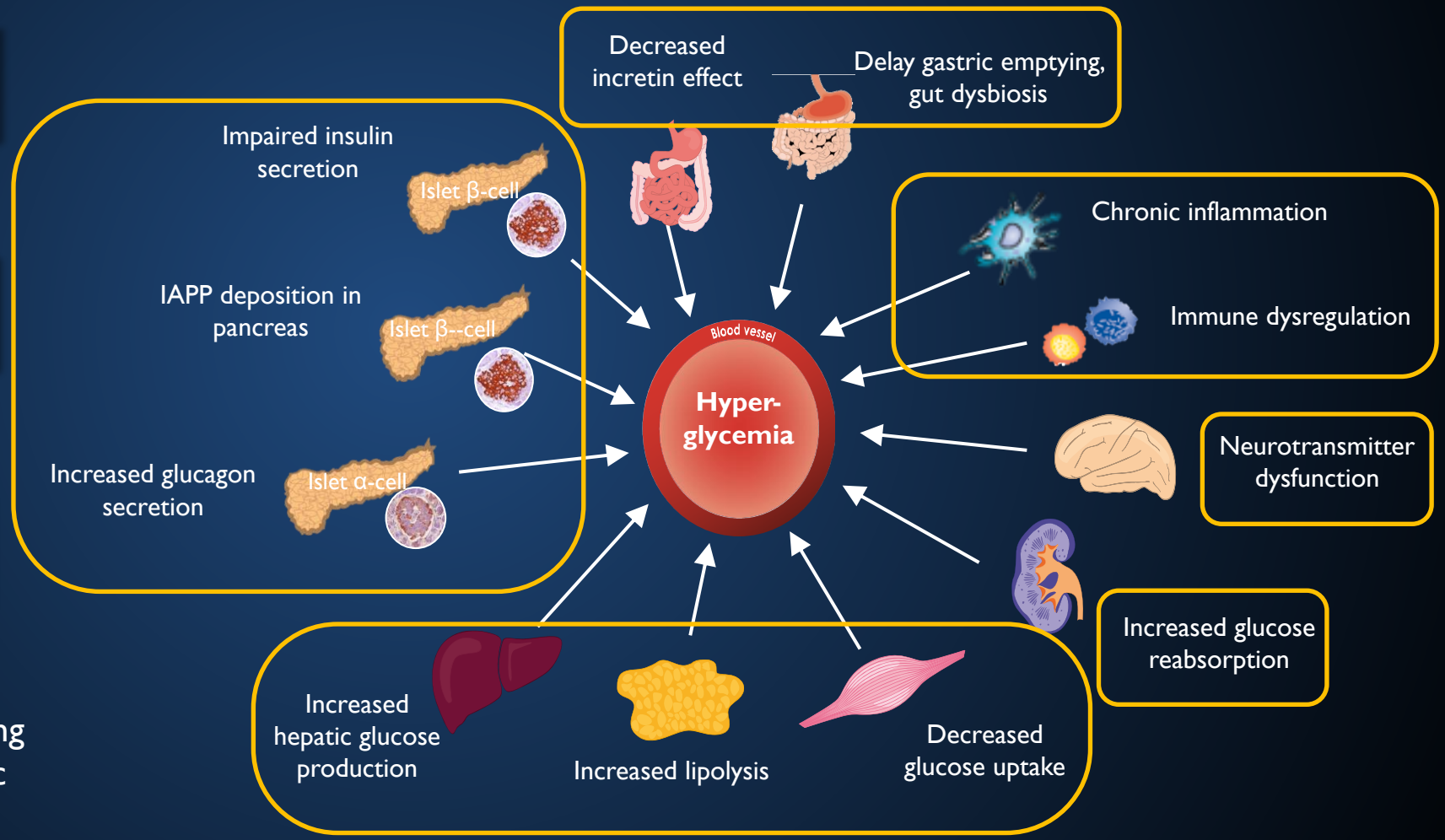
Ominous Octet

Egregious Eleven

Deleterious Dozen

12 pathophysiological defects contributing to β-cell failure in T2D with therapeutic options for individual pathways



↑=increase. ↓=decrease. DPP-4=dipeptidyl peptidase 4. GLP-1=glucagon-like peptide-1. IAPP=islet amyloid polypeptide. MRA=mineralocorticoid receptor antagonist. SGLT2=sodium-glucose cotransporter 2. *Not the primary mechanism of action

Adapted from: Ahmad E, et al. Lancet. 2022; 400:1803-20

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Antidiabetic agents

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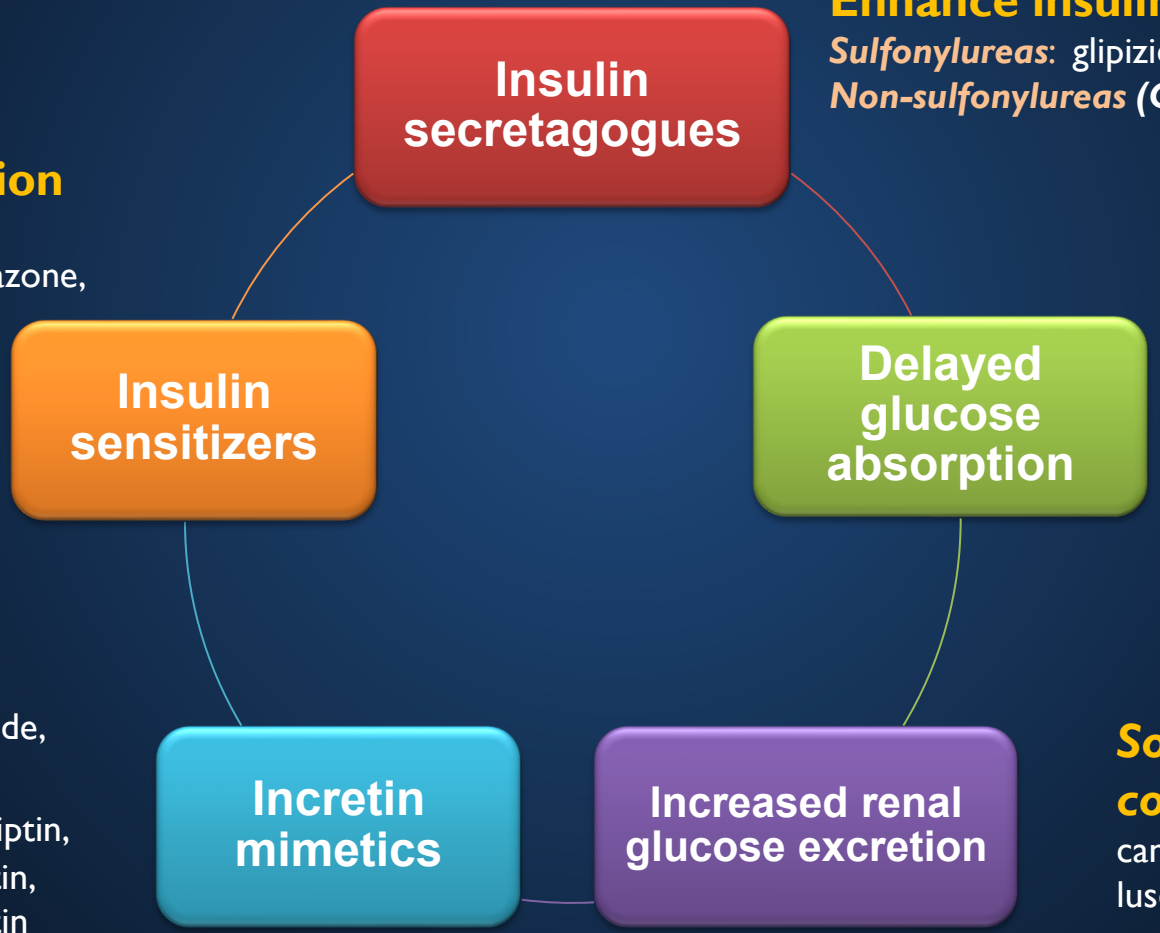

Enhance insulin secretion
Sulfonylureas: glipizide, glibenclamide, gliclazide, glimepiride
Non-sulfonylureas (Glinides): repaglinide, nateglinide

Alpha-Glucosidase inhibitors: acarbose, voglibose

Sodium glucose cotransporter 2 inhibitors: canagliflozin, dapagliflozin, empagliflozin, luseogliflozin

Enhance insulin action
Biguanide: metformin
Thiazolidinediones: pioglitazone, (rosiglitazone)

GLP-1 agonist: liraglutide, dulaglutide, semaglutide
DPP IV inhibitor: sitagliptin, vildagliptin, saxagliptin, linagliptin, alogliptin. gemigliptin, trelagliptin

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Indications for Insulin Therapy

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- Type II diabetes mellitus who has one of the following conditions
  - Very high blood glucose
  - Poor glycemic controlled despite the use of high or maximal tolerated dose of 2-3 oral anti-diabetic agents
  - Under stress condition i.e., severe infection, severe injury, steroid used, etc.
  - During surgery or pregnancy
  - Renal and hepatic impairment
  - Allergy to oral anti-diabetic agents
- Type I diabetes mellitus
- Diabetes emergency (DKA, HHS)
- Gestational diabetes (uncontrolled by lifestyle modification)
- Pancreatic diabetes i.e. chronic pancreatitis, post-pancreatectomy

Thai Clinical Practice Guideline for Diabetes 2023

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Treatment for reduce complications

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Alphabet strategy

- A: Advice (diabetes education)
- B: Blood pressure (<130/80)
- C: Cholesterol (considered statin therapy)

Optimized metabolic parameters

- D: Diabetes control and DN screening
- E: Eye examination
- F: Feet care

Annual screening

Immunization for adults with diabetes

Vaccine	Recommended ages	Schedule
COVID-19	All individuals age ≥ 6 months	Initial vaccination and boosters
Hepatitis B	< 60 years ≥ 60 years may be administered	-
Influenza	All individuals age ≥ 6 months	Annual
Pneumonia (PPSV23)	19-64 years: one dose if previously received PCV13 ≥ 65 years: one dose if previously received PCV13	≥ 1 year after last dose of PCV13
PCV20 or PCV15	19-64 years with immunocompromise: one dose of PCV15 or PCV20 ≥ 65 years: one dose if previously received PCV13	≥ 1 year after last dose of vaccine
Tetanus, diphtheria, pertussis	All adults	Booster every 10 years
Zoster	≥ 50 years of age	Two-dose Shingrix, even if previously vaccinated
Respiratory syncytial virus (RSV)	≥ 60 years of age	May receive a single dose of an RSV vaccine

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Summary

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- ✓ Glucose homeostasis
- ✓ Who should be screened for prediabetes or diabetes mellitus
- ✓ Diagnosis criteria for diabetes mellitus and prediabetes
- ✓ Identified type of diabetes
- ✓ Set and achieve individualized target HbA1C
  - Lifestyle modification or pharmacological therapy
  - Oral medication or insulin
- ✓ Prevention or treatment of acute and chronic complications
- ✓ Optimal treatment of associated disease: HT, dyslipidemia, obesity
- ✓ Prolonged life expectancy and improve quality of life

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Recommended reading

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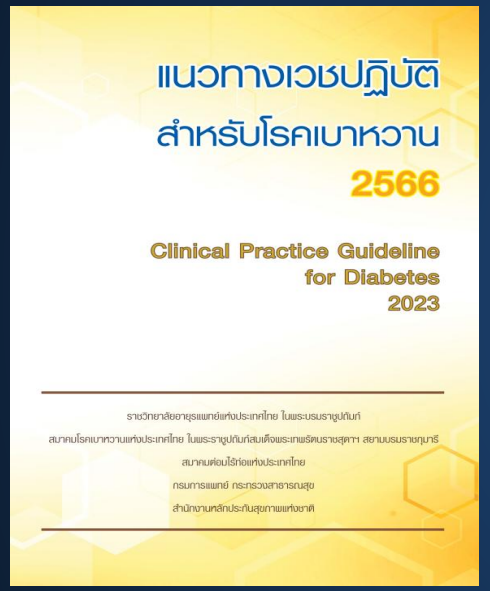

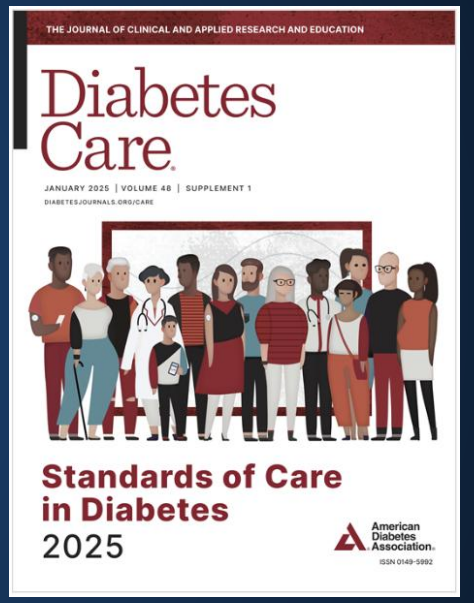

Thai Clinical Practice Guideline for Diabetes 2023.
สมาคมโรคเบาหวานแห่งประเทศไทย,
สมาคมต่อมไร้ท่อแห่งประเทศไทย

Standards of Care in Diabetes. American Diabetes Association. Diabetes care 2025;
48 (Supplement_1): S1-S352

Disease of Endocrine Pancreas and Complications

THANK YOU

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