Diabetes Mellitus

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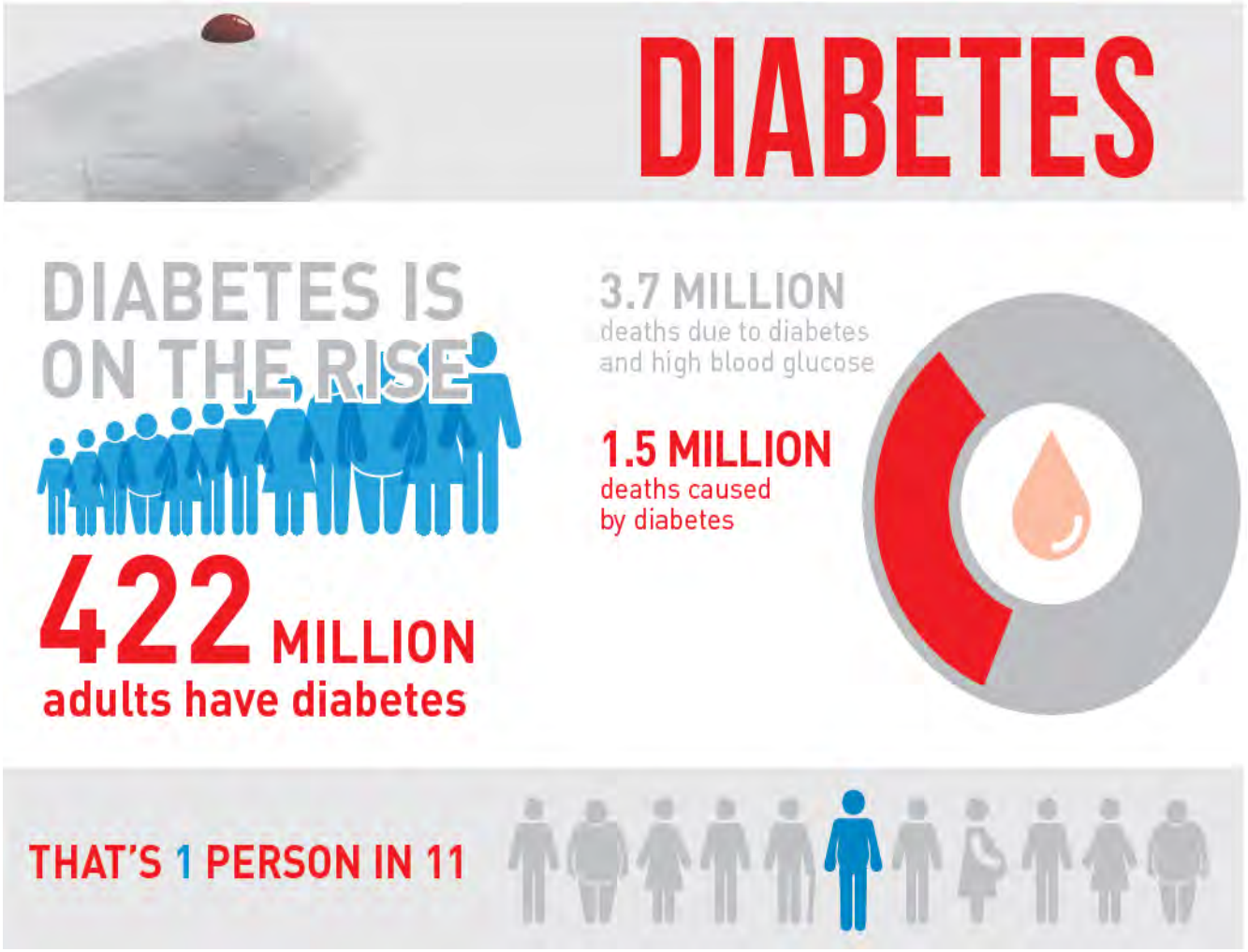
Learning Objectives

- Recognize the role of pharmacists in diabetes care.
- Define diabetes mellitus (DM).
- Compare and contrast type 1 and 2 diabetes presentation, onset, progression, and pathophysiology.
- List the plasma glucose levels that diagnose a patient with: impaired fasting glucose, impaired glucose tolerance, or DM.
- Apply evidence-based recommendations to non-pharmacologic and pharmacologic treatment interventions of DM.
- Identify and describe goals, treatments, and monitoring parameters for common concomitant conditions and complications associated with diabetes mellitus.
- Case Discussion
  - Apply diabetes management concepts to practice relevant cases

Introduction

Diabetes mellitus is one of the most common medical conditions globally.

The number of people with diabetes is increasing due to population growth, aging, urbanization, and increasing prevalence of obesity and physical inactivity.

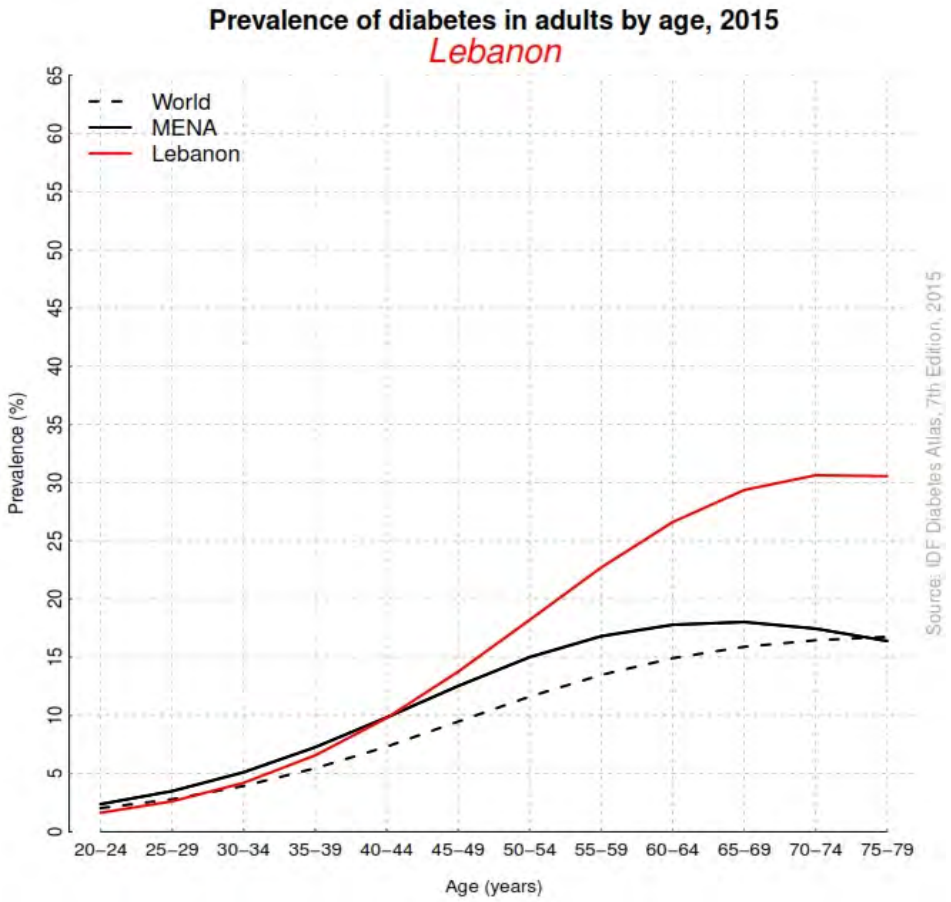


Global report on diabetes. Retrieved February 03, 2017, from http://www.who.int/diabetes/global-report/en/

Introduction

More than 35.4 million people in the MENA Region have diabetes; by 2040 this will rise to 72.1 million.

There were 464,200 cases of diabetes in Lebanon in 2015.



International Diabetes Federation Middle East and North Africa. Lebanon. Retrieved January 26, 2017, from http://www.idf.org/membership/mena/lebanon

Pharmacist Role

- Pharmacists can have a significant impact on diabetes care and education.

- We are trained to do more than just dispense drugs!

Cranor DW, Christenson DB. The Ashville Project: Factors Associated with Outcomes of a Community Pharmacy Diabetes Care Program. J Am Pharm Assoc 2003; 43: 160-72.

Pharmacist Role

The involvement of pharmacists in diabetes management reduced overall costs of care

Specific interventions

- ***Identifying people with diabetes***
  - Acknowledging those people who are aware that they have diabetes; and identifying those who do not know that they have the condition.
- ***Assessment***
- ***Education***
  - Because of their easy access to people with diabetes, they are able to answer doubts and queries about the condition itself, offer guidance on the proper use of medications and other supplies.
- ***Monitoring***

Cranor DW, Christenson DB. The Ashville Project: Factors Associated with Outcomes of a Community Pharmacy Diabetes Care Program. J Am Pharm Assoc 2003; 43: 160-72.

Classification

Type 1 diabetes

- Previously called "insulin dependent" or "juvenile-onset diabetes".
- Accounts for 5–10% of diabetes cases.

Type 2 diabetes

- Previously referred to as "noninsulin-dependent" or "adult-onset diabetes".
- Accounts for 90–95% of diabetes cases.

Gestational diabetes mellitus (GDM)

- Diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation.

Specific types of diabetes due to other causes.

American Diabetes Association. Classification and diagnosis of diabetes. Sec. 2. In Standards of Medical Care in Diabetes 2017. Diabetes Care 2017;40(Suppl. 1):S11–S24

Pathophysiology of Type 1 DM

Autoimmune destruction of the β cells of the pancreas mediated by macrophages and T lymphocytes.

Type 1 diabetes is defined by the presence of one or more of these autoimmune markers:

- Glutamic Acid Decarboxylase Autoantibodies (GADA)
- Tyrosine phosphatases IA-2 and IA-2b
- Zinc transporter (ZnT8)
- Insulin Autoantibodies (IAA)

This process occurs in genetically susceptible subjects.

Usually progresses over many months or years during which the subject is asymptomatic and euglycemic.

Hyperglycemia develops when 80% -90% of β cells are destroyed.

American Diabetes Association. Classification and diagnosis of diabetes. Sec. 2. In Standards of Medical Care in Diabetes 2017. Diabetes Care 2017;40(Suppl. 1):S11–S24

Pathophysiology of Type 1 DM

The rate of progression is dependent on the age at first detection of antibody, number of antibodies, antibody specificity, and antibody titer.

Glucose and A1C levels rise well before the clinical onset of diabetes, making diagnosis feasible well before the onset of Diabetic ketoacidosis (DKA).

Three distinct stages of type 1 diabetes can be identified:

	Stage 1	Stage 2	Stage 3
Stage	• Autoimmunity • Normoglycemia • Presymptomatic	• Autoimmunity • Dysglycemia • Presymptomatic	• New-onset hyperglycemia • Symptomatic
Diagnostic criteria	• Multiple autoantibodies • No IGT or IFG	• Multiple autoantibodies • Dysglycemia: IFG and/or IGT • FPG 100–125 mg/dL (5.6–6.9 mmol/L) • 2-h PG 140–199 mg/dL (7.8–11.0 mmol/L) • A1C 5.7–6.4% (39–47 mmol/mol) or ≥10% increase in A1C	• Clinical symptoms • Diabetes by standard criteria

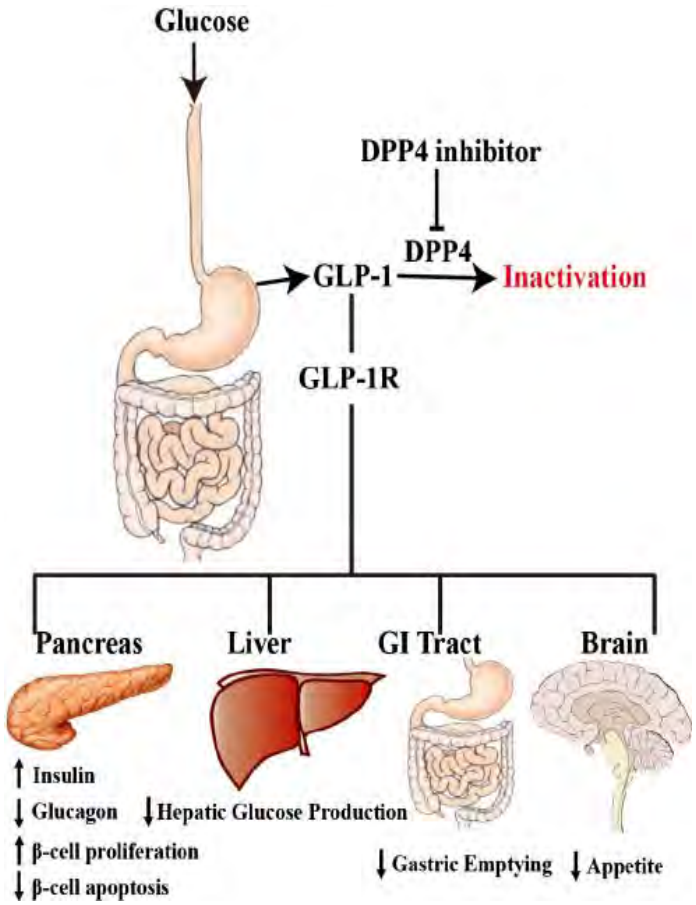
American Diabetes Association. Classification and diagnosis of diabetes. Sec. 2. In Standards of Medical Care in Diabetes 2017. Diabetes Care 2017;40(Suppl. 1):S11–S24

Pathophysiology of Type 2 DM

T2DM is characterized by multiple defects including:

- Relative (rather than absolute) insulin deficiency
- Insulin resistance involving muscle, liver, and the adipocyte
- Excess glucagon secretion
- Glucagon-like peptide-1 (GLP-1) deficiency and possibly resistance

Specific etiologies are not known.



Triplitt CL, Repas T, Alvarez C. Diabetes Mellitus. In: DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey L. eds. Pharmacotherapy: A Pathophysiologic Approach, 10e. New York, NY: McGraw-Hill; 2017.

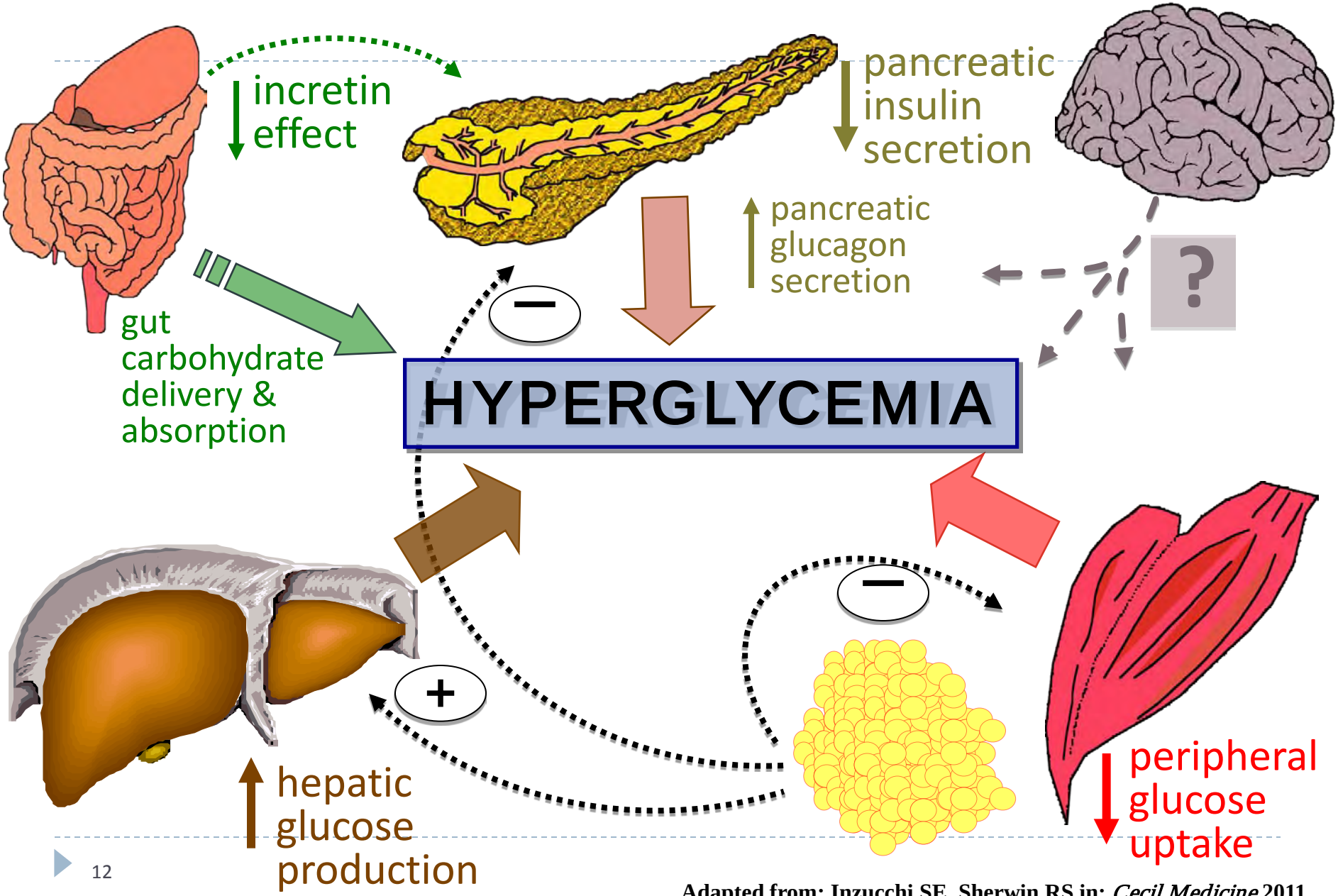
Pathophysiology of Type 2 DM

Impaired Insulin Secretion

- A hallmark finding in T2DM.
- When the insulin released can no longer normalize plasma glucose, dysglycemia, including prediabetes and diabetes, can ensue.
- Both β-cell mass and function in the pancreas are reduced.
  - β-Cell failure is progressive, and starts years prior to the diagnosis of diabetes.
  - People with T2DM lose ~5% to 7% of β-cell function per year of diabetes.
- The reasons for this loss are likely multifactorial including (a) glucose toxicity; (b) lipotoxicity; (c) insulin resistance; (d) age; (e) genetics; and (f) incretin deficiency.
- Glucotoxicity involves glucose levels chronically exceeding 140 mg/dL (7.8 mmol/L).
- The β cell is unable to maintain elevated rates of insulin secretion, and releases less insulin as glucose levels increase.

Triplitt CL, Repas T, Alvarez C. Diabetes Mellitus. In: DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey L. eds. Pharmacotherapy: A Pathophysiologic Approach, 10e. New York, NY: McGraw-Hill; 2017.

Pathophysiology of Type 2 DM



Adapted from: Inzucchi SE, Sherwin RS in: *Cecil Medicine* 2011

Clinical Presentation

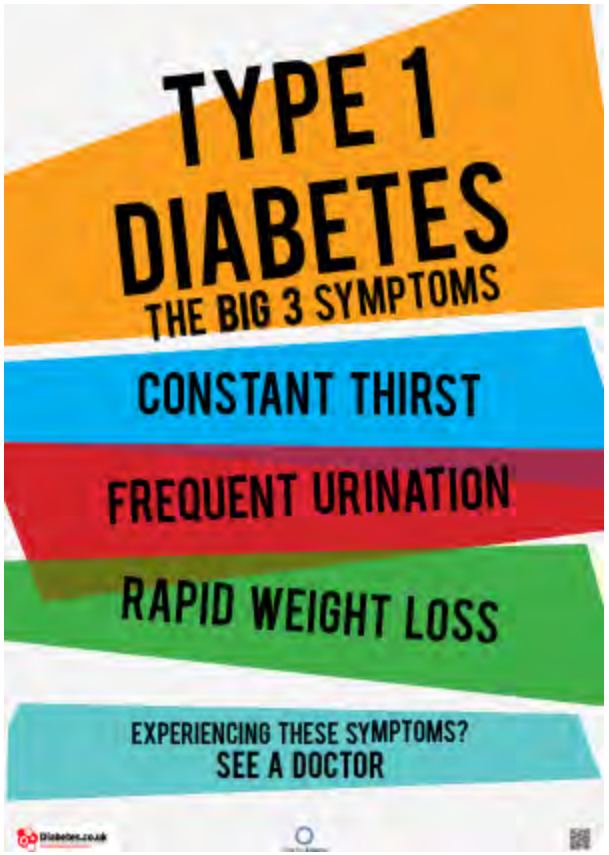
Type 1 DM

- Symptoms such as polyuria, polydipsia, polyphagia, weight loss, and lethargy accompanied by hyperglycemia are the most common.

- The rate of β-cell destruction is quite variable, being rapid in some individuals (mainly infants and children) and slow in others (mainly adults).

Type 2 DM

- Asymptomatic with a slow onset over 5-10 years.
- High frequency of complications.



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Clinical Presentation

Characteristic	Type 1 DM	Type 2 DM
Age	The traditional paradigms of T2DM occurring only in adults and T1DM only in children are no longer accurate, as both diseases occur in both cohorts	
Onset	Abrupt	Gradual
Body habitus	Lean	Most patients are overweight or obese. Or may have an increased % of body fat distributed predominantly in the abdominal region
Insulin resistance	Absent	Present
Autoantibodies	Present	Autoimmune destruction of b-cells does not occur
Symptoms	Symptomatic (Typically children)	Often asymptomatic

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Clinical Presentation

Characteristic	Type 1 DM	Type 2 DM
Ketones at diagnosis	Present (Mainly children)	Ketoacidosis seldom occurs spontaneously. Seen with stress of another illness such as infection.
Need for insulin therapy	Immediate	Years after diagnosis
Microvascular complications at diagnosis	No	Common
Macrovascular complications at or before diagnosis	Rare	Common

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Diagnosis, Screening & Monitoring

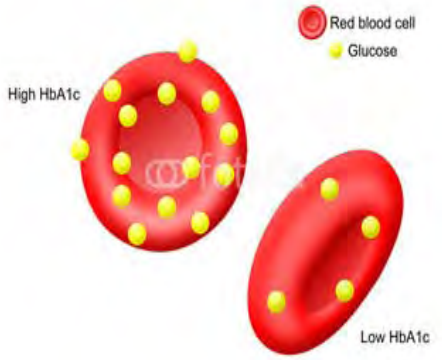
Diagnosis

Plasma glucose

- Fasting plasma glucose (FPG).
- 2-h plasma glucose (2-h PG) value after a 75-g oral glucose tolerance test (OGTT).

HbA1C

- Evaluates the average amount of glucose in the blood over the last 2 to 3 months.
- Greater convenience (fasting not required), greater preanalytical stability, and less day-to-day perturbations during stress and illness.
- Lower sensitivity.
- Greater cost, limited availability of A1C testing in certain regions of the world.
- Consider other factors that may impact hemoglobin glycation independently of glycemia including age, race/ethnicity, and anemia/hemoglobinopathies.



American Diabetes Association. Classification and diagnosis of diabetes. Sec. 2. In Standards ofMedical Care in Diabetesd 2017. Diabetes Care 2017;40(Suppl. 1):S11–S24

Criteria for the Diagnosis of Diabetes

FPG ≥126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.*
OR
2-h PG ≥200 mg/dL (11.1 mmol/L) during an 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 ≥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 ≥200 mg/dL (11.1 mmol/L).
*In the absence of unequivocal hyperglycemia, results should be confirmed by repeat testing.

American Diabetes Association. Classification and diagnosis of diabetes. Sec. 2. In Standards ofMedical Care in Diabetesd 2017. Diabetes Care 2017;40(Suppl. 1):S11–S24

Categories of Increased risk for Diabetes (Prediabetes)*

FPG 100 mg/dL (5.6 mmol/L) to 125 mg/dL (6.9 mmol/L) (IFG)
OR
2-h PG in the 75-g OGTT 140 mg/dL (7.8 mmol/L) to 199 mg/dL (11.0 mmol/L) (IGT)
OR
A1C 5.7–6.4% (39–47 mmol/mol)

*For all three tests, risk is continuous, extending below the lower limit of the range and becoming disproportionately greater at the higher end of the range.

American Diabetes Association. Classification and diagnosis of diabetes. Sec. 2. In Standards of Medical Care in Diabetes 2017. Diabetes Care 2017;40(Suppl. 1):S11–S24

Testing for Type 1 DM

Blood glucose rather than A1C should be used to diagnose the acute onset of type 1 diabetes in individuals with symptoms of hyperglycemia.

Testing for Type 1 Diabetes Risk

- Screening for type 1 diabetes with a panel of autoantibodies is currently recommended only in the setting of a research trial or in first-degree family members of a proband with type 1 diabetes.

American Diabetes Association. Classification and diagnosis of diabetes. Sec. 2. In Standards of Medical Care in Diabetes 2017. Diabetes Care 2017;40(Suppl. 1):S11–S24

Testing for Type 2 DM or Prediabetes in Asymptomatic Adults Criteria

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 one or more of the following risk factors:
   - A1C ≥5.7% (39 mmol/mol), IGT, or IFG on previous testing
   - first-degree relative with diabetes
   - high-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander)
   - women who were diagnosed with GDM
   - history of CVD
   - hypertension (≥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. For all patients, testing should begin at age 45 years.
3. 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 (e.g., those with prediabetes should be tested yearly) and risk status.

American Diabetes Association. Classification and diagnosis of diabetes. Sec. 2. In Standards of Medical Care in Diabetes 2017. Diabetes Care 2017;40(Suppl. 1):S11–S24

Testing for Type 2 DM or Prediabetes in Asymptomatic Children Criteria

- Overweight (BMI >85th percentile for age and sex, weight for height >85th percentile, or weight >120% of ideal for height)

Plus any two of the following risk factors:

- Family history of type 2 diabetes in first- or second-degree relative
- Race/ethnicity (Native American, African American, Latino, Asian American, Pacific Islander)
- Signs of insulin resistance or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome, or small-for-gestational-age birth weight)
- Maternal history of diabetes or GDM during the child's gestation

Age of initiation: age 10 years or at onset of puberty, if puberty occurs at a younger age

Frequency: every 3 years

American Diabetes Association. Classification and diagnosis of diabetes. Sec. 2. In Standards of Medical Care in Diabetes 2017. Diabetes Care 2017;40(Suppl. 1):S11–S24

Diabetes Monitoring

Patients on multiple-dose insulin or insulin pump therapy should do SMBG (self-monitored blood glucose):

Prior to meals and snacks

At bedtime

Prior to exercise

When they suspect low blood glucose

After treating low blood glucose until they are normoglycemic

Prior to critical tasks such as driving

Patients on other therapeutic interventions, including oral agents may perform home blood glucose monitoring.

Quarterly HbA_{Ic} in individuals not meeting glycemic goals, twice yearly in individuals meeting glycemic goals, should be performed.

American Diabetes Association. Glycemic targets. Sec. 6. In Standards of Medical Care in Diabetesd2017. Diabetes Care 2017;40(Suppl. 1):S48–S56

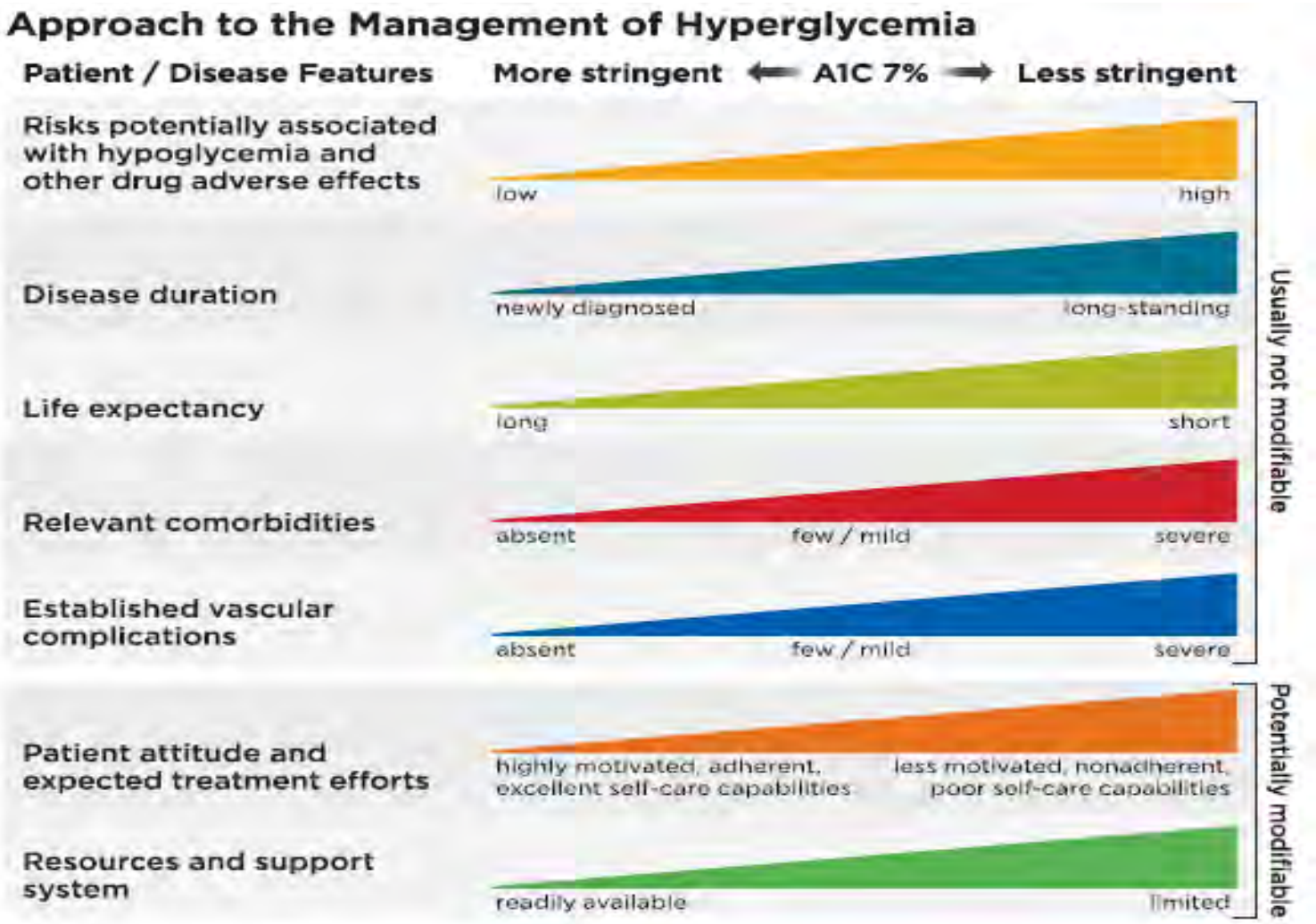
Glycemic Targets

Glycemic Targets

Target Treatment Goals	ADA 2017
AIC	<7%
Fasting glucose	Preprandial capillary plasma glucose: 80-130 mg/dl
Postprandial glucose	Peak postprandial capillary plasma glucose <180 mg/dl

American Diabetes Association. Glycemic targets. Sec. 6. In Standards of Medical Care in Diabetesd2017. Diabetes Care 2017;40(Suppl. 1):S48–S56

Glycemic Targets - HbA1C Goals



American Diabetes Association. Glycemic targets. Sec. 6. In Standards of Medical Care in Diabetesd2017. Diabetes Care 2017;40(Suppl. 1):S48–S56

Glycemic Control & Complications

A1C and Microvascular Complications

- Intensive versus standard glycemic control, showed definitively that better glycemic control is associated with significantly decreased rates of development and progression of microvascular (retinopathy and diabetic kidney disease) and neuropathic complications.

A1C and Cardiovascular Disease Outcomes

- There is evidence for a cardiovascular benefit of intensive glycemic control after long-term follow-up of cohorts treated early in the course of type 1 and type 2 diabetes

American Diabetes Association. Glycemic targets. Sec. 6. In Standards of Medical Care in Diabetesd2017. Diabetes Care 2017;40(Suppl. 1):S48–S56

Hypoglycemia

- Hypoglycemia is the major limiting factor in the glycemic management of type 1 and type 2 diabetes.

- Classification of hypoglycemia:

Level	Glycemic criteria	Description
Glucose alert value (level 1)	≤70 mg/dL (3.9 mmol/L)	Sufficiently low for treatment with fast-acting carbohydrate and dose adjustment of glucose-lowering therapy
Clinically significant hypoglycemia (level 2)	<54 mg/dL (3.0 mmol/L)	Sufficiently low to indicate serious, clinically important hypoglycemia
Severe hypoglycemia (level 3)	No specific glucose threshold	Hypoglycemia associated with severe cognitive impairment requiring external assistance for recovery

American Diabetes Association. Glycemic targets. Sec. 6. In Standards of Medical Care in Diabetesd2017. Diabetes Care 2017;40(Suppl. 1):S48–S56

Hypoglycemia

Severe hypoglycemia can progress to loss of consciousness, seizure, coma, or death..

Treatment:

- Glucose (15–20 g) is the preferred treatment for the conscious individual with hypoglycemia (glucose alert value of ≤ 70 mg/dL)
- Fifteen minutes after treatment, if BG shows continued hypoglycemia, the treatment should be repeated.
- Once BG returns to normal, the individual should consume a meal or snack to prevent recurrence of hypoglycemia.
- Injectable glucagon should be prescribed for all individuals at increased risk of clinically significant hypoglycemia.

American Diabetes Association. Glycemic targets. Sec. 6. In Standards of Medical Care in Diabetesd2017. Diabetes Care 2017;40(Suppl. 1):S48–S56

Diabetes Management

Goals of Therapy

Reduce the risk for microvascular and macrovascular complications

Ameliorate symptoms

Reduce mortality

Improve quality of life

Adherence to therapeutic lifestyle interventions (diet and exercise)

Non-pharmacological Therapy

Medical nutrition therapy

- Weight loss is recommended for all insulin-resistant/overweight or obese individuals. Either low-carbohydrate, low-fat calorie restricted diets.
- Saturated fat should be <7% of total calories.
- Monitoring carbohydrate intake by carbohydrate counting, exchanges, or experienced estimation is recommended to achieve glycemic goals.
- Routine supplementation with antioxidants, such as vitamins E and C is not advised due to lack of efficacy.

American Diabetes Association. Lifestyle management. Sec. 4. In Standards of Medical Care in Diabetesd2017. Diabetes Care 2017;40(Suppl. 1):S33–S43

Non-pharmacological Therapy

Physical activity

- 150 min/week of moderate intensity exercise (brisk walking) spread over at least 3 days and with no more than 2 days without exercise.
- Resistance training of large muscle groups should be ≥2 times/wk.

American Diabetes Association. Lifestyle management. Sec. 4. In Standards of Medical Care in Diabetesd2017. Diabetes Care 2017;40(Suppl. 1):S33–S43

Non-pharmacological Therapy

Prevention of type 2 diabetes

- Patients with IGT, IFG, or an A_{1C} of 5.7%-6.4% should be referred to an intensive diet and physical activity behavioral counseling program.
- Targeting loss of 7% of body weight and increasing moderate-intensity physical activity to > 150 min/wk.
- Metformin may be considered with IGT, IFG, or an A_{1C} 5.7%-6.4% , especially in obese, <60-year-old patients, and women with prior GDM.

American Diabetes Association. Lifestyle management. Sec. 4. In Standards of Medical Care in Diabetesd2017. Diabetes Care 2017;40(Suppl. 1):S33–S43

Key Points to Consider When Selecting Pharmacotherapy for Type 2 DM

The A1C target must be individualized.
Glycemic control targets include fasting and postprandial glucoses.
The choice of therapies must be individualized on basis of patient characteristics, impact of net cost to patient, formulary restrictions, personal preferences, etc.
Minimizing risk of hypoglycemia is a priority.
Minimizing risk of weight gain is a priority.
Combination therapy is usually required and should involve agents with complementary actions.
Comprehensive management includes lipid and blood pressure therapies and related comorbidities.
Therapy must be evaluated frequently until stable (e.g., every 3 months) and then less often.
The therapeutic regimen should be as simple as possible to optimize adherence.

Noninsulin Agents Available for Type 2 DM

Class	Primary Mechanism of Action	Agent(s)
α-Glucosidase inhibitors	• Delay carbohydrate absorption from intestine	Acarbose (100 mg) Miglitol (100 mg)
Amylin analogue	• Decrease glucagon secretion • Slow gastric emptying • Increase satiety	Pramlintide (120 mcg pen)
Biguanide	• Decrease HGP • Increase glucose uptake in muscle	Metformin (500,800, 1000 mg)
Bile acid sequestrant	• Decrease HGP? • Increase incretin levels?	Colesevelam (625 mg tabs)
DPP-4 inhibitors	• Increase glucose-dependent insulin secretion • Decrease glucagon secretion	Alogliptin (25 mg) Linagliptin (5 mg) Saxagliptin (5 mg) Sitagliptin (100 mg)
Dopamine-2 agonist	• Activates dopaminergic receptors	Bromocriptine (0.8 mg)
Glinides	• Increase insulin secretion	Nateglinide (120 mg) Repaglinide (2 mg)

HGP = hepatic glucose production.

American Diabetes Association.Pharmacologic approaches to glycemic treatment. Sec. 8. In Standards of Medical Care in Diabetes 2017. Diabetes Care 2017; 40(Suppl. 1):S64–S74

Noninsulin Agents Available for Type 2 DM

Class	Primary Mechanism of Action	Agent(s)
GLP-1 receptor agonists	• Increase glucose-dependent insulin secretion • Decrease glucagon secretion • Slow gastric emptying • Increase satiety	Albiglutide (50 mg pen) Dulaglutide (1.5/0.5 mL pen) Exenatide (10 mcg pen) Exenatide XR (2 mg) Liraglutide (18 mg/3 mL pen)
SGLT2 inhibitors	• Increase urinary excretion of glucose	Canagliflozin (300 mg) Dapagliflozin (10 mg) Empagliflozin (25 mg)
Sulfonylureas	• Increase insulin secretion	Glimepiride (4 mg) Glipizide (10 mg) Glyburide (5, 6 mg)
Thiazolidinediones	• Increase glucose uptake in muscle and fat • Decrease HGP	Pioglitazone (45 mg) Rosiglitazone (4 mg)

American Diabetes Association.Pharmacologic approaches to glycemic treatment. Sec. 8. In Standards of Medical Care in Diabetes 2017. Diabetes Care 2017; 40(Suppl. 1):S64–S74

Noninsulin Agents Available for Type 2 DM

Class	Advantages	Disadvantages
α-Glucosidase inhibitors	• Rare hypoglycemia • ↓ Postprandial glucose • excursions • ? ↓ CVD events in prediabetes • Nonsystemic	• Generally modest A1C efficacy • Gastrointestinal side effects • (flatulence, diarrhea) • Frequent dosing schedule
Amylin analogue	• ↓ Postprandial glucose excursions • ↓ Weight	• Modest A1C efficacy • Gastrointestinal side effects • (nausea/vomiting) • Hypoglycemia unless insulin dose is simultaneously reduced • Injectable • Frequent dosing schedule • Training requirements

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Properties of Glucose-Lowering Agents

Class	Advantages	Disadvantages
Biguanide	• Extensive experience • Rare hypoglycemia • ↓ CVD events (UKPDS) • Relatively higher A1C efficacy	• Gastrointestinal side effects (diarrhea, abdominal cramping, nausea) • Vitamin B12 deficiency • Contraindications: eGFR ,30 mL/min/1.73 m2, acidosis, hypoxia, dehydration, etc. • Lactic acidosis risk (rare)
Bile acid sequestrant	• Rare hypoglycemia • ↓ LDL-C	• Modest A1C efficacy • Constipation • ↑ Triglycerides • May ↓ absorption of other • Medications

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Properties of Glucose-Lowering Agents

Class	Advantages	Disadvantages
DPP-4 inhibitors	• Rare hypoglycemia • Well tolerated	• Angioedema/urticaria and other immune-mediated dermatological effects • ? Acute pancreatitis • ↑ Heart failure hospitalizations (saxagliptin; ? alogliptin)
Dopamine-2 agonist	• Rare hypoglycemia • ? ↓ CVD events • (Cycloset Safety Trial)	• Modest A1C efficacy • Dizziness/syncope • Nausea • Fatigue • Rhinitis
Glinides	• ↓ Postprandial glucose • excursions • Dosing flexibility	• Hypoglycemia • ↑ Weight • Frequent dosing schedule

American Diabetes Association.Pharmacologic approaches to glycemic treatment. Sec. 8. In Standards of Medical Care in Diabetesd2017. Diabetes Care 2017; 40(Suppl. 1):S64–S74

Properties of Glucose-Lowering Agents

Class	Advantages	Disadvantages
GLP-1 receptor agonists	• Rare hypoglycemia • ↓ Weight • ↓ Postprandial glucose excursions • ↓ Some cardiovascular risk factors • Associated with lower CVD event rate and mortality in patients with CVD (liraglutide LEADER)	• Gastrointestinal side effects (nausea/vomiting/diarrhea) • ↑ Heart rate • ? Acute pancreatitis • C-cell hyperplasia/medullary thyroid tumors in animals • Injectable • Training requirements
SGLT2 inhibitors	• Rare hypoglycemia • ↓ Weight • ↓ Blood pressure • Associated with lower CVD event rate and mortality in patients with CVD (empagliflozin EMPA-REG OUTCOME)	• Genitourinary infections • Polyuria • Volumedepletion/hypotension /dizziness • ↑ LDL-C • ↑ Creatinine (transient) • DKA, urinary tract infections leading to urosepsis, pyelonephritis

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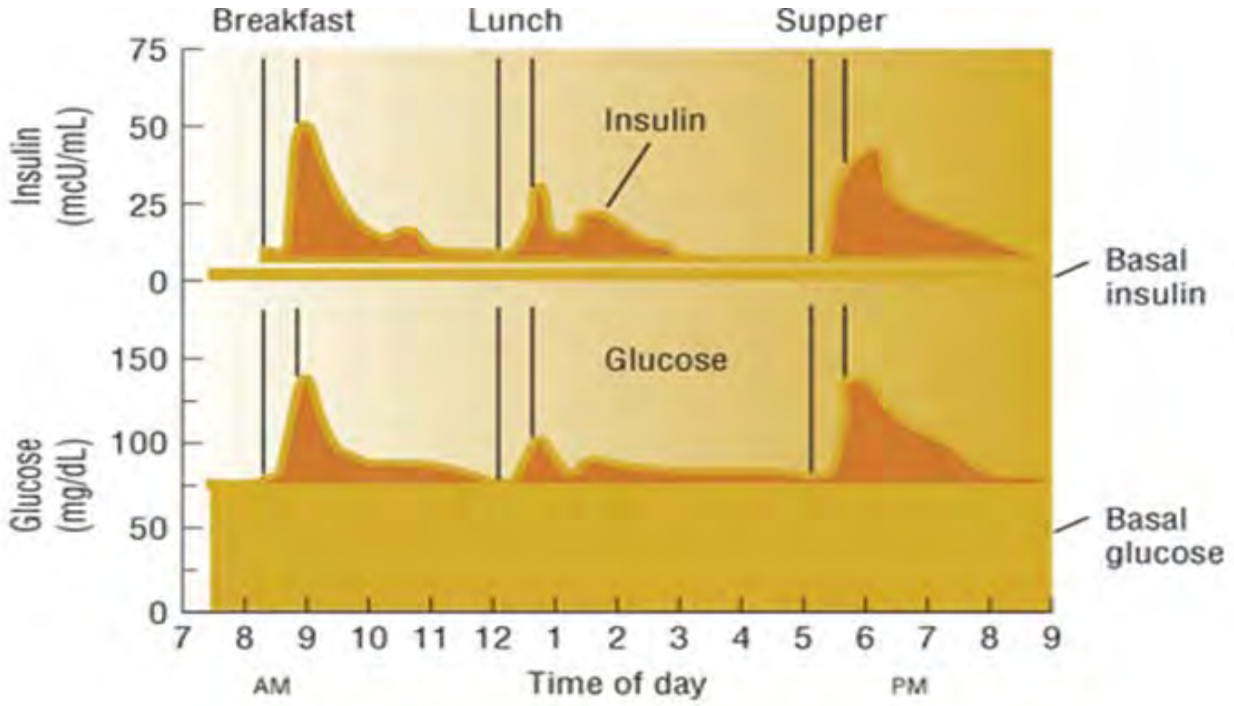
Properties of Glucose-Lowering Agents

Class	Advantages	Disadvantages
Sulfonylureas	• Extensive experience • ↓ Microvascular risk • Relatively higher A1C efficacy	• Hypoglycemia • ↑ Weight
Thiazolidinediones	• Rare hypoglycemia • Relatively higher A1C efficacy • Durability • ↓ Triglycerides (pioglitazone) • ? ↓ CVD events (PROactive, pioglitazone) • ↓ Risk of stroke and MI in patients without diabetes and with insulin resistance and history of recent stroke or TIA (IRIS study, pioglitazone)	• ↑ Weight • Edema/heart failure • Bone fractures • ↑ LDL-C (rosiglitazone)

American Diabetes Association.Pharmacologic approaches to glycemic treatment. Sec. 8. In Standards of Medical Care in Diabetesd2017. Diabetes Care 2017; 40(Suppl. 1):S64–S74

Insulin

- Normal physiologic secretion of insulin can be divided into:
  - Relatively constant background level of insulin ("basal") during the fasting and postabsorptive period
  - Prandial spikes of insulin after eating ("bolus" or "prandial")



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Insulin

The timing of insulin onset, peak, and duration of effect must match meal patterns and exercise schedules to achieve near-normal blood glucose values throughout the day.

One or two injections daily of any one insulin formulation will in no way mimic normal physiology, and therefore is unacceptable.

How insulin is delivered should be based on the patient's preferences and lifestyle behaviors as well as clinician preferences and available resources.

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Insulin

Cellular Mechanism	Primary Action
• Activates insulin receptors	• ↑ Glucose disposal • ↓ Hepatic glucose • production • Suppresses ketogenesis

Advantages	Disadvantages
• Nearly universal response • Theoretically unlimited efficacy • ↓ Microvascular risk	• Hypoglycemia • Weight gain • Training requirements • Patient and provider reluctance • Injectable (except inhaled insulin) • Pulmonary toxicity (inhaled insulin)

American Diabetes Association.Pharmacologic approaches to glycemic treatment. Sec. 8. In Standards of Medical Care in Diabetesd2017. Diabetes Care 2017; 40(Suppl. 1):S64–S74

Pharmacokinetics of Insulin Administered Subcutaneously

Type of Insulin	Onset	Peak (Hours)	Duration (Hours)	Maximum Duration (Hours)	Appearance
Rapid Acting					
Aspart	15–30 minutes	1–2	3–5	5–6	Clear
Lispro	15–30 minutes	1–2	3–4	4–6	Clear
Glulisine	15–30 minutes	1–2	3–4	5–6	Clear
Technosphere (inhaled)	5-10 minutes	0.57-1	3	3	Powder
Short Acting					
Regular	0.5–1 hours	2–3	4–6	6–8	Clear
Intermediate Acting					
NPH	2–4 hours	4–8	8–12	14–18	Cloudy
Long Acting					
Detemir	2 hours	—[a]	14–24	24	Clear
Glargine	4–5 hours	—[a]	22–24	24	Clear
Degludec	2 hours	—[a]	30-36	36	Clear

Glargine is considered "flat" though there may be a slight peak in effect at 8-12 hours, and with detemir at ~8 hours, but both have exhibited peak effects during comparative testing, and these peak effects may necessitate changing therapy in a minority of type 1 DM patients. Degludec appears to have less peak effect.

Insulin Preparations

Generic Name	Analog	Administration Options	Room Temperature Expiration
Rapid-acting insulins			
insulin lispro	Yes	Insulin pen 3-mL, 3-mL and 10-mL vial, or 3-mL pen cartridge	28 days
insulin aspart	Yes	Insulin pen 3-mL, 10-mL vial, or 3-mL pen cartridge	28 days
insulin glulisine	Yes	Insulin pen 3-mL, 10-mL vial	28 days
Short-acting insulins			
regular U-100	No	10-mL vial, 3-mL vial	28 days
regular	No	10-mL vial	42 days
Long-acting insulins			
Insulin glargine	Yes	10-mL vial, Insulin pen 3-mL	28 days
Insulin detemir	Yes	10-mL vial, Insulin pen 3-mL	42 days
Insulin degludec	Yes	Insulin pen 3-mL	56 days

American Diabetes Association.Pharmacologic approaches to glycemic treatment. Sec. 8. In Standards of Medical Care in Diabetesd2017. Diabetes Care 2017; 40(Suppl. 1):S64–S74

Insulin Preparations

Generic Name	Analog	Administration Options	Room Temperature Expiration
Premixed insulins			
Premixed insulin analogs			
75% neutral protamine lispro, 25% lispro	Yes	10-mLvial, Insulin pen 3-mL	Vial: 28 days; pen: 10 days
70% aspart protamine suspension, 30% aspart	Yes	10-mL vial, Insulin pen 3-mL	Vial: 28 days; pen: 14 days
50% neutral protamine lispro/50% lispro	Yes	10-mL vial, Insulin pen 3-mL	Vial: 28 days; pen:10 days
Insulin degudec 70/ Aspart 30	Yes	pen 3-mL	28 days
Inhaled insulin			
Technosphere insulin	No	4 unit and 8 unit cartridges	Sealed-unopened blister card/strip 10 days Opened- 3 days

American Diabetes Association.Pharmacologic approaches to glycemic treatment. Sec. 8. In Standards of Medical Care in Diabetesd2017. Diabetes Care 2017; 40(Suppl. 1):S64–S74

Insulin Counseling Tips

To inject SC, patient should be instructed to:

- Firmly pinch up the area to be injected and quickly insert the needle perpendicularly (90°) into the center of this area and 45° used for infants and individuals with little SC fat.
- Then, skin pinch is released and insulin is injected.

Rotate injection site within the same anatomic region.

- Recommended to avoid lipodystrophy effect

Abdominal area injection site is the least affected by exercise and the most predictable.

Factors altering SC absorption: site of injection, exercise of injected area, temperature, local massage, smoking, lipohypertrophy, insulin preparation.

Triplitt CL, Repas T, Alvarez C. Diabetes Mellitus. In: DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey L. eds. Pharmacotherapy: A Pathophysiologic Approach, 10e. New York, NY: McGraw-Hill; 2017.

Pharmacologic Therapy for Type 1 DM

Most people with type 1 diabetes should be treated with multiple daily injections of prandial insulin and basal insulin or continuous subcutaneous insulin infusion

- The starting insulin dose is based on weight, with doses ranging from 0.4 to 1.0 units/kg/ day of total insulin
- 0.5 units/kg/day is the typical starting dose in patients who are metabolically stable.
- Approximately 50% of total daily insulin replacement should be basal insulin, and the other 50% will be bolus insulin, divided into doses before meals.

Pramlintide, FDA approved for use in adults with type 1 diabetes.

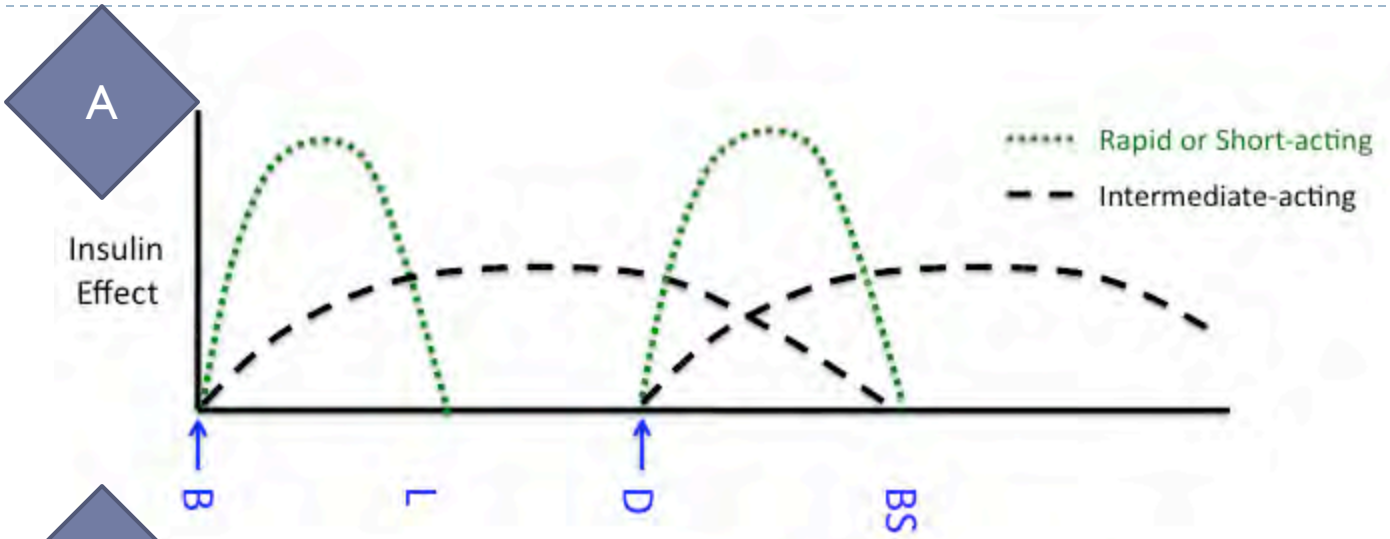
- It has been shown to induce weight loss and lower insulin doses.
- Concurrent reduction of prandial insulin dosing is required to reduce the risk of severe hypoglycemia.

Investigational Agents

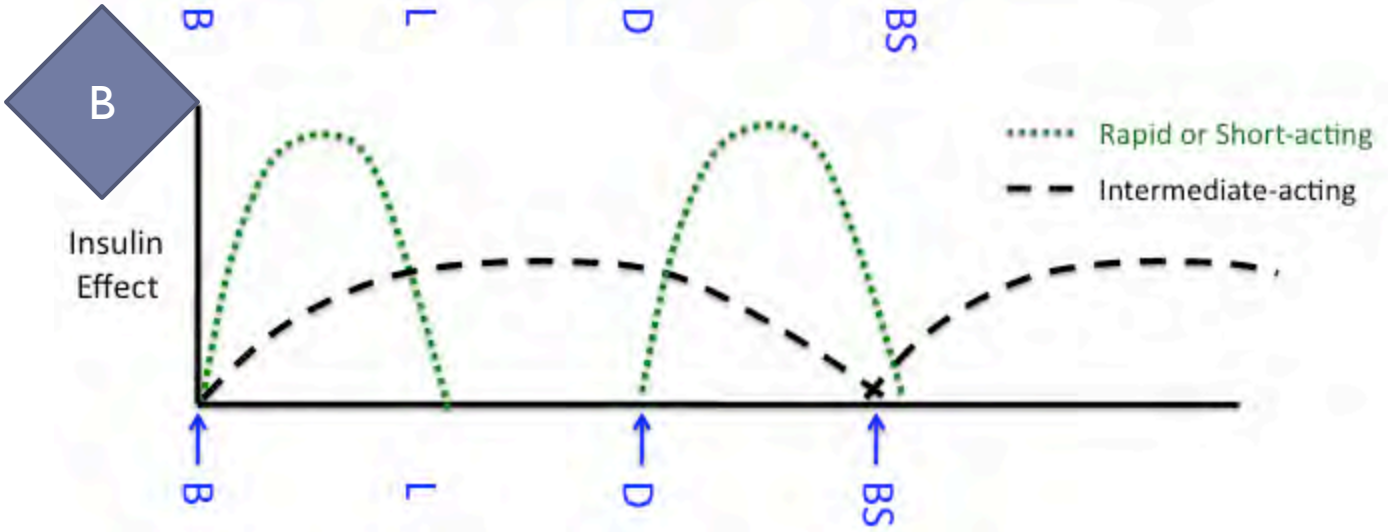
- Metformin
  - Adding metformin to insulin therapy may reduce insulin requirements and improve metabolic control in overweight/obese patients with poorly controlled type 1 diabetes
  - Not FDA-approved for use in patients with type 1 diabetes.

American Diabetes Association.Pharmacologic approaches to glycemic treatment. Sec. 8. In Standards of Medical Care in Diabetesd2017. Diabetes Care 2017; 40(Suppl. 1):S64–S74

Insulin Regimens



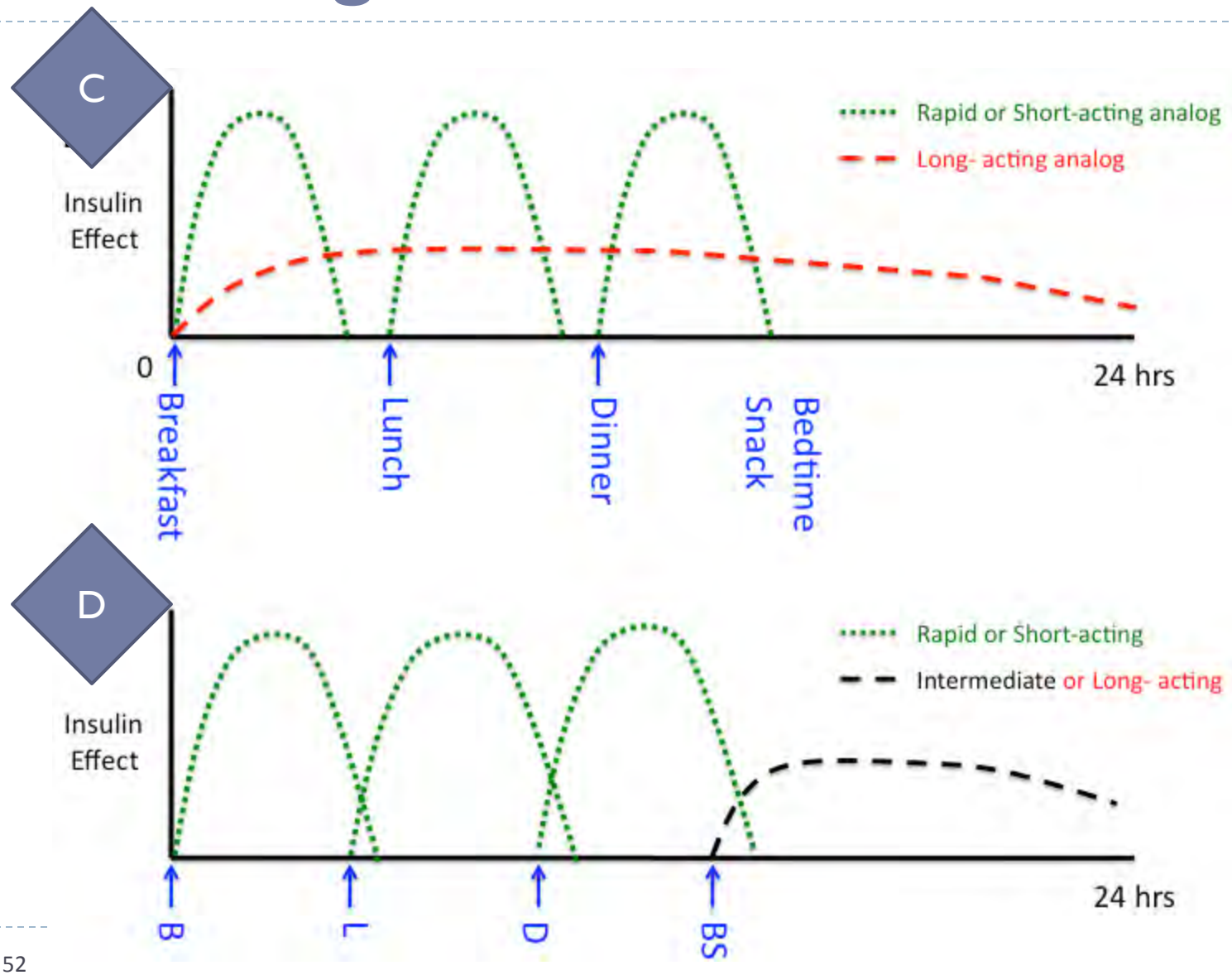
Split-mixed



Modified split-mixed

Insulin Regimens

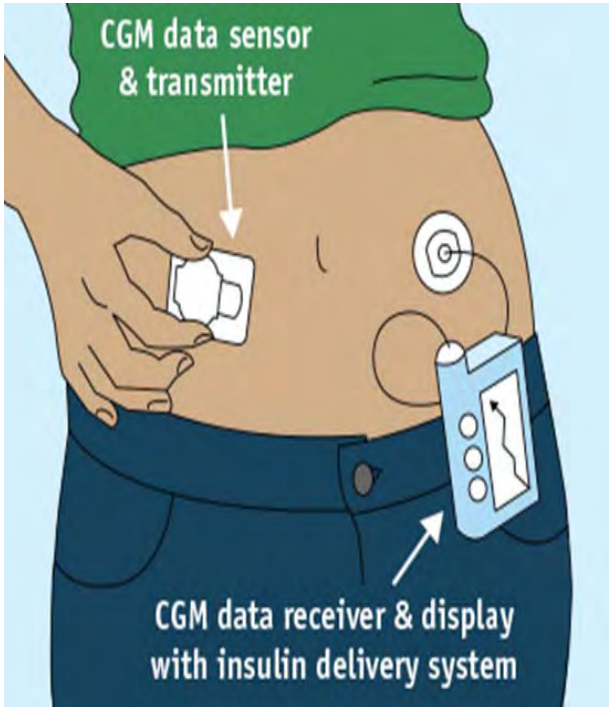
Basal-Bolus



Insulin Pump

Insulin Pump therapy: continuous SC infusion of insulin (CSII)

- Most precise way to mimic normal insulin secretion
- Battery operated pump and computer that deliver predetermined amounts of regular insulin, lispro, or aspart from a reservoir.
- Delivers various basal amounts of insulin as well meal related boluses which is released 30 min. before food ingestion.
- Basal infusion rate adjusted depending on situation: decreased in midnight and increased before awakening to avoid hyperglycemia.



Treatment Algorithms
ADA 2017

Start with Monotherapy unless:

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 — Metformin — Lifestyle Management

EFFICACY*	high
HYPO RISK	low risk
WEIGHT	neutral/loss
SIDE EFFECTS	GI/lactic acidosis
COSTS*	low

If A1C target not achieved after approximately 3 months of monotherapy, proceed to 2-drug combination (order not meant to denote any specific preference — choice dependent on a variety of patient- & disease-specific factors):

Dual Therapy — Metformin + — Lifestyle Management

	Sulfonylurea	Thiazolidinedione	DPP-4 inhibitor	SGLT2 inhibitor	GLP-1 receptor agonist	Insulin (basal)
EFFICACY*	high	high	intermediate	intermediate	high	highest
HYPO RISK	moderate risk	low risk	low risk	low risk	low risk	high risk
WEIGHT	gain	gain	neutral	loss	loss	gain
SIDE EFFECTS	hypoglycemia	edema, HF, fxs	rare	GU, dehydration, fxs	GI	hypoglycemia
COSTS*	low	low	high	high	high	high

If A1C target not achieved after approximately 3 months of dual therapy, proceed to 3-drug combination (order not meant to denote any specific preference — choice dependent on a variety of patient- & disease-specific factors):

Triple Therapy — Metformin + — Lifestyle Management

Sulfonylurea +	Thiazolidinedione +	DPP-4 inhibitor +	SGLT2 inhibitor +	GLP-1 receptor agonist +	Insulin (basal) +
TZD	SU	SU	SU	SU	TZD
or DPP-4-i	or DPP-4-i	or TZD	or TZD	or TZD	or DPP-4-i
or SGLT2-i	or SGLT2-i	or SGLT2-i	or DPP-4-i	or SGLT2-i	or SGLT2-i
or GLP-1-RA	or GLP-1-RA	or Insulin[§]	or GLP-1-RA	or Insulin[§]	or GLP-1-RA
or Insulin[§]	or Insulin[§]		or Insulin[§]		

If A1C target not achieved after approximately 3 months of triple therapy and patient (1) on oral combination, move to basal insulin or GLP-1 RA, (2) on GLP-1 RA, add basal insulin, or (3) on optimally titrated basal insulin, add GLP-1 RA or mealtime insulin. Metformin therapy should be maintained, while other oral agents may be discontinued on an individual basis to avoid unnecessarily complex or costly regimens (i.e., adding a fourth antihyperglycemic agent).

Combination Injectable Therapy (See Figure 8.2)

Pharmacologic Therapy for Type 2 DM

Metformin monotherapy should be started at diagnosis of type 2 diabetes unless there are contraindications

If noninsulin monotherapy at maximal tolerated dose does not achieve or maintain the A1C target over 3 months, add a second oral agent

Consider starting dual therapy when A1C is 9%

Consider starting combination injectable therapy when blood glucose is ≥ 300 mg/dL and/or A1C is ≥ 10%, especially if symptomatic or catabolic features are present.

American Diabetes Association.Pharmacologic approaches to glycemic treatment. Sec. 8. In Standards of Medical Care in Diabetes 2017. Diabetes Care 2017; 40(Suppl. 1):S64–S74

Pharmacologic Therapy for Type 2 DM

The choice should be individualized according to efficacy in A1C lowering, unique benefits, dosing frequency, side effect profiles, and cost.

The A1C lowering capacity is:

- Greatest for metformin and sulfonylureas (average 1–2%)
- Next greatest for GLP-1 agonists and thiazolidinediones (average 1–1.5%)
- Least for meglitinides, dipeptidyl peptidase 4 (DPP-4) inhibitors, alpha-glucosidase inhibitors (AGIs), and colesevelam (average 0.5–1%)

American Diabetes Association.Pharmacologic approaches to glycemic treatment. Sec. 8. In Standards of Medical Care in Diabetesd2017. Diabetes Care 2017; 40(Suppl. 1):S64–S74

Pharmacologic Therapy for Type 2 DM

Available Combination Antihyperglycemic Products

Medication	Combined with:
Metformin and/or metformin extended release	Pioglitazone Rosiglitazone Sitagliptin Saxagliptin Linagliptin Alogliptin Glyburide Glipizide Repaglinide Canagliflozin Dapagliflozin Empagliflozin
Linagliptin	Empagliflozin
Glimepiride	Pioglitazone Rosiglitazone
Pioglitazone	Alogliptin

Triplitt CL, Repas T, Alvarez C. Diabetes Mellitus. In: DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey L. eds. Pharmacotherapy: A Pathophysiologic Approach, 10e. New York, NY: McGraw-Hill; 2017.

Pharmacologic Therapy for Type 2 DM Transitioning to Insulin

Although many patients are reluctant to start insulin therapy, thorough counseling, encouragement, and support can assist in the transition.

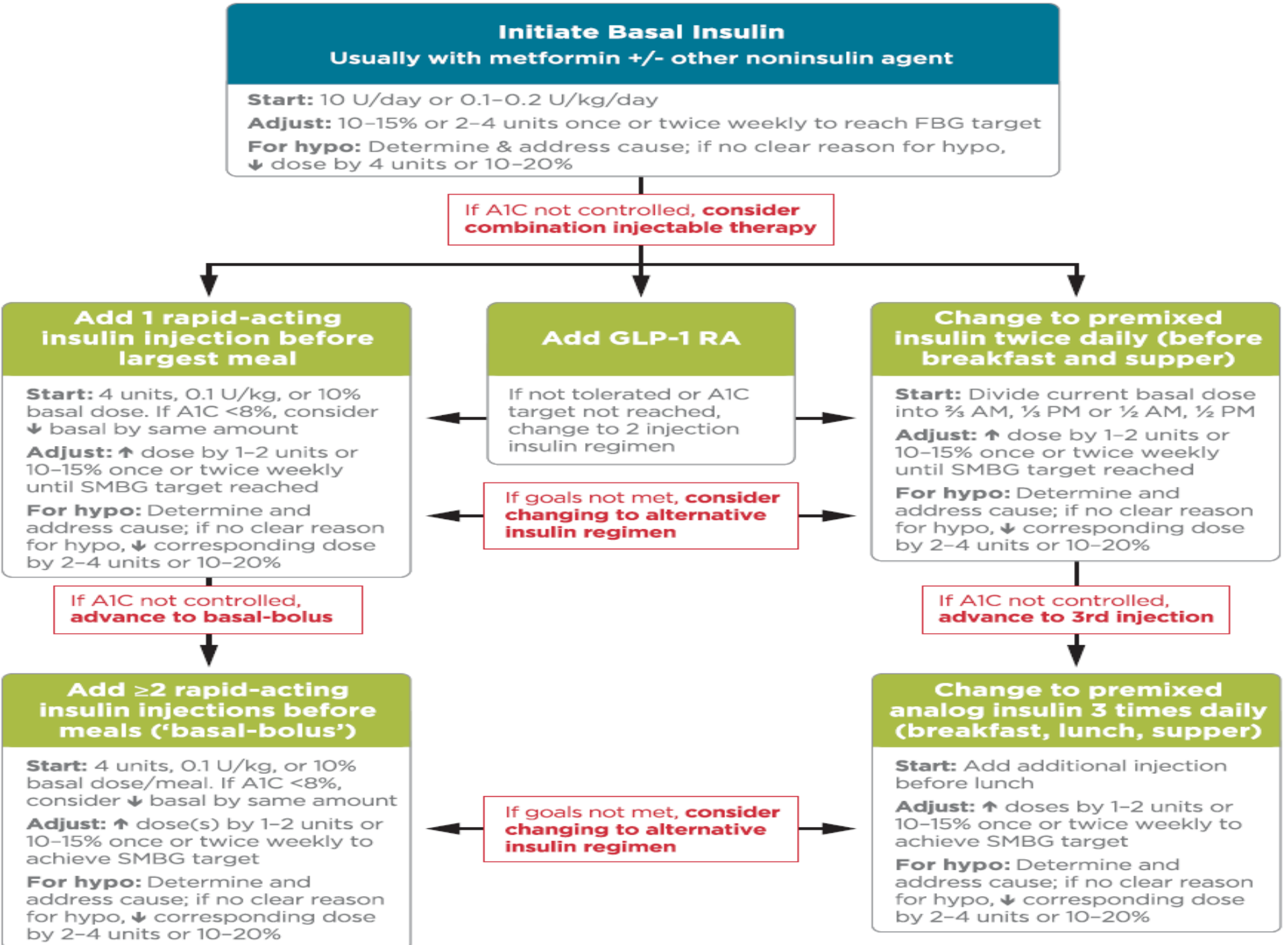
A basal insulin is usually begun at a low dose, such as 0.1–0.2 units per kg per day.

- For example, glargine (10 units) is typically started for many patients.

At this time, oral regimens should be evaluated for continuation with insulin initiation.

- Continuing metformin is usually reasonable and effective for most patients.
- Oral agents that enhance insulin secretion (i.e., sulfonylureas and meglitinides) are usually stopped, or the dose decreased, to eliminate increased risk of hypoglycemia.
- If postprandial blood glucose levels are elevated, bolus insulin (or a GLP-1 agonist as an alternative) could be started prior to meals.
- The class of TZDs could increase weight gain in combination with insulin and are usually avoided when starting injections as well.

American Diabetes Association.Pharmacologic approaches to glycemic treatment. Sec. 8. In Standards of Medical Care in Diabetesd2017. Diabetes Care 2017; 40(Suppl. 1):S64–S74


Initiate Basal Insulin
Usually with metformin +/- other noninsulin agent
Start: 10 U/day or 0.1–0.2 U/kg/day
Adjust: 10–15% or 2–4 units once or twice weekly to reach FBG target
For hypo: Determine & address cause; if no clear reason for hypo, ↓ dose by 4 units or 10–20%
If A1C not controlled, consider combination injectable therapy
Add 1 rapid-acting insulin injection before largest meal
Start: 4 units, 0.1 U/kg, or 10% basal dose. If A1C <8%, consider ↓ basal by same amount
Adjust: ↑ dose by 1–2 units or 10–15% once or twice weekly until SMBG target reached
For hypo: Determine and address cause; if no clear reason for hypo, ↓ corresponding dose by 2–4 units or 10–20%
If A1C not controlled, advance to basal-bolus
Add ≥2 rapid-acting insulin injections before meals ('basal-bolus')
Start: 4 units, 0.1 U/kg, or 10% basal dose/meal. If A1C <8%, consider ↓ basal by same amount
Adjust: ↑ dose(s) by 1–2 units or 10–15% once or twice weekly to achieve SMBG target
For hypo: Determine and address cause; if no clear reason for hypo, ↓ corresponding dose by 2–4 units or 10–20%
Add GLP-1 RA
If not tolerated or A1C target not reached, change to 2 injection insulin regimen
If goals not met, consider changing to alternative insulin regimen
If goals not met, consider changing to alternative insulin regimen
Change to premixed insulin twice daily (before breakfast and supper)
Start: Divide current basal dose into ⅔ AM, ⅓ PM or ½ AM, ½ PM
Adjust: ↑ dose by 1–2 units or 10–15% once or twice weekly until SMBG target reached
For hypo: Determine and address cause; if no clear reason for hypo, ↓ corresponding dose by 2–4 units or 10–20%
If A1C not controlled, advance to 3rd injection
Change to premixed analog insulin 3 times daily (breakfast, lunch, supper)
Start: Add additional injection before lunch
Adjust: ↑ doses by 1–2 units or 10–15% once or twice weekly to achieve SMBG target
For hypo: Determine and address cause; if no clear reason for hypo, ↓ corresponding dose by 2–4 units or 10–20%

Treatment of Concomitant Conditions and Complications

Hypertension/Blood Pressure Control

Screening and Diagnosis

- BP should be measured at every routine visit.

Goals

- Patients with diabetes and hypertension should be treated to a systolic blood pressure goal of < 140 mmHg and a diastolic blood pressure goal of < 90 mmHg.
- Lower systolic and diastolic blood pressure targets, such as 130/80 mmHg, may be appropriate for individuals at high risk of cardiovascular disease.
- In pregnant patients with diabetes and chronic hypertension, blood pressure targets of 120–160/80–105 mmHg

American Diabetes Association. Cardiovascular disease and risk management. Sec. 9. In Standards of Medical Care in Diabetesd2017. Diabetes Care 2017;40(Suppl. 1): S75–S87

Hypertension/Blood Pressure Control

Treatment

- Patients blood pressure > 140/90 mmHg should, in addition to lifestyle therapy, have prompt initiation of pharmacologic therapy.
- Patients with blood pressure > 160/100mmHg should, in addition to lifestyle therapy, have prompt initiation of two drugs or a single pill combination of drugs.
- Drug classes proven to reduce cardiovascular events in patients with diabetes (ACE inhibitors, angiotensin receptor blockers, thiazide- like diuretics, or dihydropyridine calcium channel blockers).
- An ACEi or ARB at the maximum tolerated dose indicated for blood pressure treatment, is the recommended first-line treatment for hypertension in patients with diabetes and urinary albumin–to– creatinine ratio ≥ 300 mg/g creatinine or 30–299 mg/g creatinine.

American Diabetes Association. Cardiovascular disease and risk management. Sec. 9. In Standards of Medical Care in Diabetesd2017. Diabetes Care 2017;40(Suppl. 1): S75–S87

Lipid Management

Dyslipidemia

- Obtain a lipid profile at the time of diabetes diagnosis at an initial medical evaluation, and every 5 years thereafter, or more frequently if indicated.
- Lifestyle modification focusing on the reduction of saturated fat, trans fat, and cholesterol intake; increase omega-3 acids, viscous fiber, and plant sterols; weight loss if indicated, and increase physical activity should be recommended.
- For patients with diabetes aged <40 years with additional CVD risk factors, consider using moderate or high-intensity statin.
- For patients with diabetes aged >40 without additional CVD risk factors, consider using moderate-intensity statin.
- If with additional risk factors, high-intensity statin.

American Diabetes Association. Cardiovascular disease and risk management. Sec. 9. In Standards of Medical Care in Diabetesd2017. Diabetes Care 2017;40(Suppl. 1): S75–S87

Diabetic Kidney Disease

Screening

- At least once a year
- Assess urinary albumin and estimated glomerular filtration rate in patients with type 1 diabetes with duration of ≥ 5 years, in all patients with type 2 diabetes, and in all patients with comorbid hypertension.

Treatment

- Optimize glucose control.
- Optimize blood pressure control.
- In patients with diabetes and hypertension, either an ACE inhibitor or an ARB is recommended

- ACEi or ARB for prevention is not recommended for the primary prevention of diabetic kidney disease in patients with diabetes who have normal blood pressure or normal GFR.

- Patients should be referred for evaluation for renal replacement treatment if they have an estimated glomerular filtration rate < 30 mL/min.

American Diabetes Association. Microvascular complications and foot care. Sec. 10. In Standards of Medical Care in Diabetesd2017. Diabetes Care 2017;40(Suppl. 1): S88–S98

Diabetic Retinopathy

Optimize glycemic control.

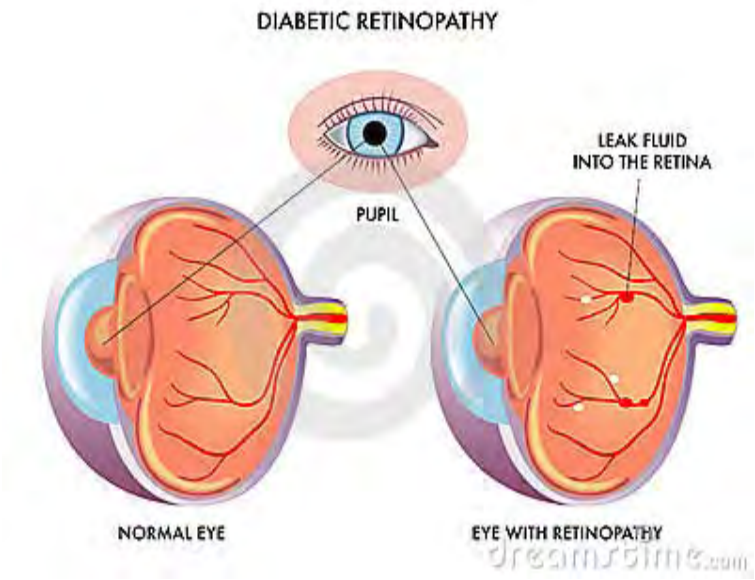
Optimize blood pressure and serum lipid control.

Screening

- Adults with type 1 DM should have an initial examination within 5 years after the onset of diabetes.
- Patients with type 2 DM should have initial eye examination at the time of the diabetes diagnosis.
- If there is no evidence of retinopathy, then exams every 2 years may be considered.
- If any level of diabetic retinopathy is present, examinations should be repeated at least annually.

Treatment

- Laser photocoagulation
- Lucentis® (ranibizumab injection into the eye)
  - Approved diabetic macular edema.



American Diabetes Association. Microvascular complications and foot care. Sec. 10. In Standards of Medical Care in Diabetesd2017. Diabetes Care 2017;40(Suppl. 1): S88–S98

Neuropathy

Screening

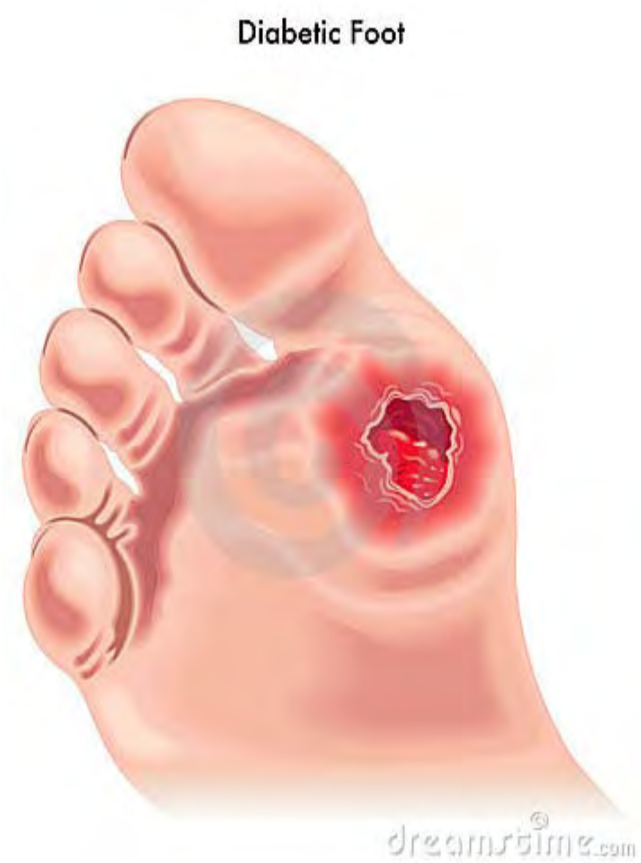
- All patients should be assessed for diabetic peripheral neuropathy starting at diagnosis of type 2 diabetes and 5 years after the diagnosis of type 1 diabetes and at least annually thereafter.

- All patients should have annual testing to identify feet at risk for ulceration and amputation.

Treatment

- Optimize glucose control to prevent or delay the development of neuropathy in patients with type 1 diabetes and to slow the progression of neuropathy in patients with type 2 diabetes.

- Either pregabalin or duloxetine are recommended as initial pharmacologic treatments for neuropathic pain in diabetes.



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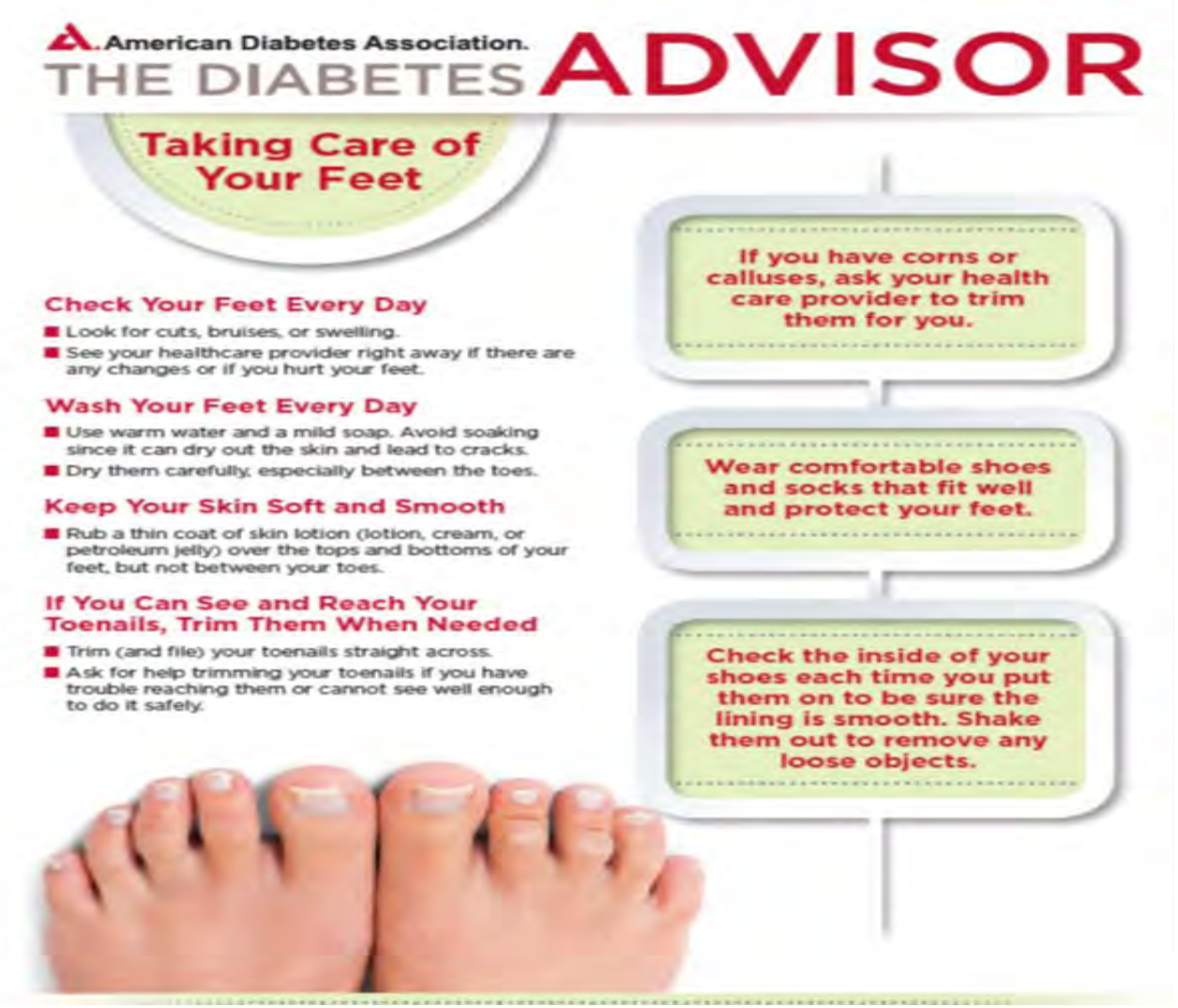
Foot Care



American Diabetes Association. Microvascular complications and foot care. Sec. 10. In Standards of Medical Care in Diabetes 2017. Diabetes Care 2017;40(Suppl. 1): S88–S98

Traveling With Diabetes

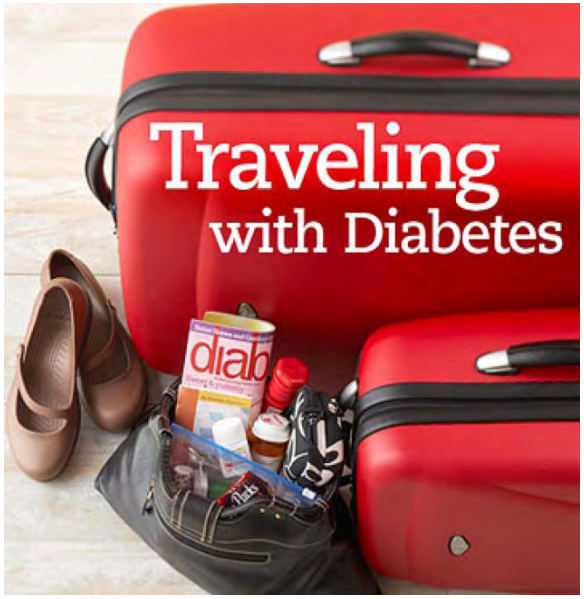
Supplies: plentiful back-up supply of insulin, syringes, blood-testing supplies (extra battery), and glucose tablets. Carry also drugs and prescription for emergency cases.

Identification: medical alert bracelet that aids in diagnosis in emergency cases.

Foot Care: well fit shoes should be worn.

Meal Planning: maintain regularity in diet (time and amounts).

Insulin Doses: use insulin lispro or aspart to cover meals since they provide maximum flexibility to patients.



Case Discussion

Case

- MF is 52 year old Lebanese man who comes to the community pharmacy to refill his medications. He also asks for assistance with selecting an OTC weight loss product since he wants to lose at least 14 Kg.

- Home medications:
  - Hydrochlorothiazide 25 mg daily
  - Amlodipine 10 mg daily
  - Allopurinol 300 mg daily
  - Fluticasone/salmeterol one inhalation twice daily

- You observe that he appears to be approximately 180 cm tall and 90 kgs or more with central adiposity. He is also a current smoker.

Case

1. What risk factors for diabetes does MF have?
   a. Age
   b. Hypertension
   c. Asthma/COPD
   d. Gout
   e. Obesity
   f. More than one. Specify….

Case

- Because MF has several risk factors for DM, you ask him if he has ever been tested. He says he doesn't know if his physician has screened for diabetes. He mentions that his mother has DM treated with insulin.

- Next month, MF comes back to the pharmacy for his monthly refills. He says that he has been diagnosed with pre-diabetes.

2. Which of the following meet the diagnostic criteria for pre-diabetes?
   a. FPG 100-125 mg/dl
   b. HbA1C 5.7%-6.4%
   c. OGTT 140-199 mg/dl
   d. All of the above

Case

3. Which treatment(s) should be recommended for MF at this point for his prediabetes?
   a. No therapy is needed. He has prediabetes and not overt diabetes at this time.
   b. Intensive therapeutic lifestyle changes.
   c. Metformin
   d. Acarbose
   e. More than one. Specify….

Case

- MF does well making lifestyle changes as directed and is able to maintain HbA1C between 5.7% and 6.2% for 5 years. He was eventually diagnosed with type 2 DM. Today he comes in for his medication refills and brings his recent lab results to show you. (Age 57 yrs, Weight 85 kg)

	Na	K	Cl	BUN	Scr	FBG	ALT	AST	HbA 1C
Todays Value	146	4.6	106	24	2.8	186	21	26	8.2%

4. According to the current clinical practice guideline, which of the following medications is/are NOT recommended for MF at this time?
   a. Metformin
   b. Sulfonylureas
   c. Pioglitazone
   d. Liraglutide
   e. Pramlintide
   f. Saxagliptin

Case

	Met	GLP1RA	SGLT2I	DPP4I	TZD	AGI	Coles	BCR-QR	SU/ Glinide	Insulin	Pram
Renal impair-ment/ GU	eGFR 30-45 Not recommended to initiate treatment <30 Cl	Exenatide contra-indicated CrCl <30 mg/mL	GU infection risk	Dose adjust-ment (except lina-gliptin)	May worsen fluid retention	Neutral	Neutral	Neutral	Increased hypo-glycemia risk	Increased risks of hypo-glycemia and fluid retention	Neutral
GI adverse effects	Mod	Mod*	Neutral	Neutral*	Neutral	Mod	Mild	Mod	Neutral	Neutral	Mod
CHF	Neutral	Neutral	Neutral	Neutral†	Mod	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral
CVD	Possible benefit	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Safe	?	Neutral	Neutral
Bone	Neutral	Neutral	Bone loss	Neutral	Mod bone loss	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral

AGI = α-glucosidase inhibitors; BCR-QR = bromocriptine quick release; Coles = colesevelam; CHF = congestive heart failure; CVD = cardiovascular disease; DPP4I = dipeptidyl peptidase 4 inhibitors; GI = gastrointestinal; GLP1RA = glucagon-like peptide 1 receptor agonists; GU = genitourinary; Met = metformin; Mod = moderate; SGLT2I = sodium-glucose cotransporter 2 inhibitors; SU = sulfonylureas; TZD = thiazolidinediones.

*Caution in labeling about pancreatitis.

†Caution: possibly increased CHF hospitalization risk seen in CV safety trial.

Case

- After discussing pharmacotherapy with MF, he is concerned about gaining weight. He states “I am already a little pudgy in the belly and don’t want the medication to make it worse.”

5. Which of the following agents will not cause weight gain as a side effect?
   a. Glipizide
   b. Pioglitazone
   c. Sitagliptin
   d. Liraglutide
   e. Insulin
   f. Empagliflozin

Case

	Met	GLP1RA	SGLT2I	DPP4I	TZD	AGI	Coles	BCR-QR	SU/ Glinide	Insulin	Pram
Hypo-glycemia	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	Neutral	SU: mod to severe Glinide: mild to mod	Mod to severe*	Neutral
Weight	Slight loss	Loss	Loss	Neutral	Gain	Neutral	Neutral	Neutral	Gain	Gain	Loss

AGI = α-glucosidase inhibitors; BCR-QR = bromocriptine quick release; Coles = colesevelam; DPP4I = dipeptidyl peptidase 4 inhibitors; GLP1RA = glucagon-like peptide 1 receptor agonists; Met = metformin; Mod = moderate; NAFLD, nonalcoholic fatty liver disease; SGLT2I = sodium-glucose cotransporter 2 inhibitors; SU = sulfonylureas; TZD = thiazolidinediones.

*Especially with short/ rapid-acting or premixed.

Take Home Message

The pharmacist should try to help patient achieve A1C <7%.

The pharmacist should try to achieve specific goals for concomitant disease states such as hypertension, dyslipidemia, and other cardiovascular diseases.

Essential counseling points include:

- Action to take when experiencing hypoglycemia and hyperglycemia
- Medical nutrition therapy& exercise
- Medication use and adherence
- Self-management with checking blood glucose readings
- Proper foot care
- Insulin injection technique and storage (if applicable).

Oral agents, starting with metformin, can be effective in reducing the A1C in most type 2DM patients.

Patients with a high baseline A1C will not achieve goal through oral medication therapy, insulin therapy should be started.

Frequent follow-up, patient education, and simplification of medication regimens using combination products are helpful.

THANK YOU FOR YOUR ATTENTION

ANY QUESTIONS?