Diabetes

Physiology of Serum Glucose Control

- Serum glucose is maintained within a narrow range by the hormones insulin and glucagon.
- Body prefers to use glucose as primary energy source.
- Normal range: 60–100 mg/dL.
 - Usually tightly regulated by the body to remain between 80–90 mg/dL.
- Two pancreatic hormones contribute to maintaining stable serum glucose levels.
 - Insulin
 - Acts to decrease blood glucose levels
 - Glucagon
 - Acts to increase blood glucose levels
- Following a meal, about two thirds of glucose stored in liver and muscle cells as glycogen (storage form of glucose).
- When glucose levels fall, glycogen broken down in process called <u>glycogenolysis</u>, and glucose is released into bloodstream.
- Physiologic actions of insulin
 - Promotes entry of glucose into cells
 - Promotes for storage of glucose, as glycogen
 - Inhibits breakdown of fat and glycogen
 - Increases protein synthesis
 - Inhibits gluconeogenesis (production of new glucose from noncarbohydrate molecules)



Insulin, glucagon, and blood glucose

- Diabetes mellitus United States:
 - 1 in every 400 children and adolescents has diabetes.
 - 9.4% of all people 20 years or older have diabetes.
 - 25% of all people 65 years or older have diabetes.
 - 1.5 million new cases of adult diabetes are diagnosed each year.

Pathophysiology of Diabetes Mellitus: 3 Types of Diabetes

- <u>Type 1 Diabetes</u>
 - characterized by insufficient insulin synthesis by the pancreas, whereas type 2 diabetes is characterized by insulin resistance in the target cells.
 - Less common form of diabetes
 - 5% to 10% of all patients with the disorder
 - Onset most frequently among children and young adults
 - Results from absolute lack of insulin secretion due to destruction of pancreatic beta cells
 - Destruction may result from combination of autoimmune, genetic, and environmental factors.
 - Produces dangerous and potentially life-threatening condition known as diabetic ketoacidosis (DKA)
 - Insufficient insulin results in fatty acids being used as primary energy source instead of glucose
 - Process produces ketones, which accumulate in blood
 - Insulin therapy required in order to survive
- Type 2 diabetes
 - More common form
 - Representing 90% to 95% of all people with diabetes
 - Characterized by insulin resistance
 - Pancreas may be secreting sufficient amounts of insulin but target cells do not recognize it.
 - Blood glucose levels rise, causing pancreas to secrete even more insulin.
 - Insulin resistance
 - Hypersecretion leads to beta cell exhaustion, and ultimately, to beta cell death
 - Progression of disorder leads to insufficient insulin levels and insulin resistance
 - Risk factors
 - Family history of diabetes
 - Obesity BMI> 35
 - Management of disease
 - Initially treated with PO medications
 - Diet: blood sugars can reduce decrease DM coffee tea yogurt and berries. Dash diet or Mediterranean diet recommended. Use a diabetic dinner plate should have no more than a quarter filled with carbs
 - Exercise 60 minutes a day

- Most patients with type 2 diabetes do not require insulin administration, at least initially
 - Condition can be managed with oral antidiabetic drugs
- Loss of beta cells occurs over time and may require insulin administration
- <u>Gestational diabetes</u>
 - Glucose intolerance
 - Onset, or first recognition, during pregnancy
 - Puts woman and fetus at risk
 - Woman at increased risk for diabetes 5 to 10 years after delivery
- Complications of Diabetes Mellitus
 - Serious complications of chronic diabetes include neuropathy, nephropathy, retinopathy, and vascular disease.

Insulin Therapy

- Insulin is the cornerstone of therapy for patients with type 1 and gestational diabetes.
- Insulin Therapy
- Pharmacologic goal for patients with type 1 diabetes is to administer insulin as replacement therapy in normal physiological amounts
- Fundamental principle
 - The right amount of insulin must be available to cells when glucose is present in the blood.
- Doses of insulin are highly individualized for the precise control of blood glucose levels in each patient.
- Primary adverse effect of insulin therapy is overtreatment.
 - Results in hypoglycemia
- Prototype drug: Human Regular Insulin (Humulin R, Novolin R)
 - Therapeutic classification
 - Antidiabetic agent, pancreatic hormone
 - Pharmacologic classification
 - Short-acting hypoglycemic agent
 - Therapeutic effects and uses
 - Monotherapy to lower blood glucose levels in patients with type 1 diabetes
 - In combination with oral antidiabetic agents in patients with type 2 diabetes
 - Emergency treatment of DKA or hyperosmolar hyperglycemic state
 - Gestational diabetes
 - Mechanism of action
 - Insulin decreases blood glucose levels by increasing cellular uptake of glucose and stimulating storage of glucose as glycogen.
 - Inhibits release of glucagon
 - Adverse effects
 - Irritation at injection sites
 - Lipohypertrophy
 - Weight gain
 - Drug interactions

- Agents that can produce hypoglycemia
 - Sulfonylureas, meglitinides, beta-adrenergic blockers, salicylates, anabolic steroids, MAOIs, alcohol
- Dextrothyroxine, corticosteroids, epinephrine or norepinephrine, furosemide, thiazide diuretics
- Drug interactions
 - ACE inhibitors
 - Many other drugs can influence blood glucose
 - The nurse should consult current drug references.
- Herbal/Food
 - Potentiate hypoglycemic effect
 - Garlic, chromium, black cohosh, bitter melon, bilberry, ginseng, Potentiate hyperglycemic effect
 - Rosemary, cocoa
- Insulin glargine is pregnancy category C; other forms of insulin are category B.)
- Treatment of overdose
 - Concentrated source of glucose (dextrose), such as D5W or glucagon, by parenteral route
- Insulin aspart (NovoLog)
 - More rapid onset of action and shorter duration of action than regular insulin
- Insulin degludec (Tresiba):
 - A newer long-acting insulin analog approved for both type 1 and type 2 diabetes
 - Long duration of up to 42 hours
 - May be taken at any time of day, regardless of meals
- Insulin detemir (Levemir)
 - Long-acting insulin with a slow onset and dose-dependent duration of action
 - Used to provide basal glycemic control
 - Not injected before meals to control postprandial hyperglycemia
 - Cannot be mixed with any other type of insulin
- Insulin glargine (Basaglar, Lantus, Toujeo)
 - Recombinant insulin analog
 - Constant, long-duration insulin activity
 - Provides for the maintenance of steady blood levels
 - May also help improve the lipid profiles and A1C levels of type 2 diabetes when added to therapy
 - Given by subcutaneous injection only
 - Insulin Therapy
- Insulin glulisine (Apidra)
 - 10–15 minute onset and short duration of 3 to 5 hours
 - Given by subcutaneous injection only

- Insulin lispro (Humalog)
 - Rapid-acting analog of regular insulin
 - Helps control the rise in blood glucose brought on by a meal
 - Cannot be given IV; often used with insulin infusion pumps

• Isophane insulin (Humulin N, NPH)

- Only intermediate-acting insulin
- Has slower onset of action (1 to 4 hours) than regular insulin
- Duration of 18 to 24 hours
- Used to provide a basal level of insulin coverage between meals and at night



Drugs to Treat Type 2 Diabetes

- All medications require some degree of pancreatic insulin secretion.
- Not effective in treating type 1 diabetes •
- Treatment goals (AACE) •
 - A1C level of 6.5% or less
 FPG less than 110 g/dL
- If glycemic control is not achieved with monotherapy, a second medication is added.

Drug	Action(s)	Nursing Considerations			
Alpha- Glucosidase Inhibitors	Interfere with carbohydrate breakdown and absorption; act locally in the GI tract with little systemic absorption	Common GI effects; hypoglycemia can occur if combined with another oral drug; if this occurs, treat with glucose, not sucrose; take with meals			
Biguanides	Decrease production and release of glucose from the liver; increase cellular uptake of glucose; lower lipid levels; promote weight loss	Common GI adverse effects; risk for lactic acidosis (rare); avoid alcohol; low risk for hypoglycemia			
Incretin Enhancers	Slow the breakdown of insulin, keeping it circulating in the blood longer; slow the rate of digestion, which increases satiety	Well tolerated; minor nausea, vomiting, and diarrhea; some weight loss is likely; low risk for hypoglycemia			
Meglitinides	Stimulate insulin release	Can cause hypoglycemia, GI effects; well tolerated; administer shortly before meals			
Sulfonylureas	Stimulate insulin release; decrease insulin resistance	Can cause hypoglycemia, GI disturbances, rash; cross sensitivity with sulfa drugs and thiazide diuretics; possible disulfiram response with alcohol			
Thiazolidinedione	Decrease production and release of glucose from the liver; increase insulin sensitivity in fat and muscle tissue	Can cause fluid retention and worsening of heart failure; therapeutic effects take several weeks to develop			
Drug	Route and Adult Dose (Maximum Dose Where Indicated)	Adverse Effects			
Alpha-Glucosidase Inhibitors					
acarbose (Precose)	PO: 25–100 mg tid (max: 300 mg/day)	Flatulence, diarrhea, abdominal distention			
miglitol (Glyset)	PO: 25-100 mg tid (max: 300 mg/day)	<u>Hypoglycemia (tremors, palpitations, sweating)</u>			
		swedung			
Biguanide		sweating			

Drug	Route and Adult Dose (Maximum Dose Where Indicated)	Adverse Effects		
Incretin Mimetics (GLP-1 Receptor Agonists)				
albiglutide (Tanzeum)	Subcutaneous: 30-50 mg once weekly	Nausea, vomiting, diarrhea, headache, nervousness		
dulaglutide (Trulicity)	Subcutaneous: 0.75–1.5 mg once weekly			
exenatide (Byetta)	Subcutaneous: 5–10 mcg bid 60 min prior to morning and evening meals	Hypoglycemia (tremors, palpitations, sweating), antibody formation, pancreatitis, CKD		
liraglutide (Victoza)	Subcutaneous: 0.6–1.8 mg once daily, any time of day	(exenatide). thyroid tumors (liraglutide. albiglutide)		
lixisenatide (Adlyxin)	Subcutaneous: 10–20 mcg once daily prior to morning meal			
Drug	Route and Adult Dose (Maximum Dose Where Indicated)	Adverse Effects		
ncretin Enhancers (DPP-4 Inhibitors)				
alogliptin (Nesina)	PO: 25 mg once daily	Headache, upper respiratory and urinary tract infections		
linagliptin (Tradjenta)	PO: 5 mg once daily			
saxagliptin (Onglyza)	PO: 2.5–5 mg once daily	<u>Hypoglycemia (tremors, palpitations,</u> sweating), anaphylaxis, peripheral		
sitagliptin (Januvia)	PO: 100 mg once daily	edema. exfoliative dermatitis. Stevens- Johnson syndrome		
Meglitinides				
nateglinide (Starlix)	PO: 60–120 mg tid, 1–30 min prior to meals	Flulike symptoms, upper respiratory infection, back pain		
epaglinide (Prandin)	PO: 0.5–4 mg bid–gid, 1–30 min prior to meals (max: 16 mg/day)	Hypoglycemia (tremors. palpitations. sweating), anaphylaxis, pancreatitis		

Drug	Route and Adult Dose (Maximum Dose Where Indicated)		Adverse Effects		
Sulfonylureas, First Generation					
chlorpropamide (Diabinese)	PO: 100–500 mg/day (max: 750 mg/day)		Nausea, heartburn, dizziness, headache, drowsiness		
tolazamide (Tolinase) tolbutamide (Orinase)	PO: 100–500 mg 1–2 times/day (ma 1 g/day) PO: 250–1500 mg 1–2 times/day (m 3 g/day)	 <u>Hypoglycemia (tremors, palpitation</u> <u>sweating), cholestatic jaundice, blo</u> <u>dyscrasias</u> 			
Sulfonylureas, Second Generation					
glimepiride (Amaryl)	PO: 1–4 mg/day (max: 8 mg/day)	Nausea, heartburn, dizziness, headache, drowsiness			
glipizide (Glucotrol)	PO: 2.5–20 mg 1–2 times/day (max: mg/day)	Hypoglycemia (tremors, palpitations, sweating), cholestatic jaundice, bloo dyscrasias			
glyburide (DiaBeta) glyburide micronized (Glynase)	PO: 1.25–10 mg 1–2 times/day (ma: 20 mg/day) PO: 0.75–12 mg 1–2 times/day (ma: 12 mg/day)	x: x:			
Drug	Route and Adult Dose (Maximum Dose Where Indicated)	Ad	verse Effects		
Thiazolidinediones					
pioglitazone (Actos)	PO: 15–30 mg/day (max: 45 mg/day)	Up) hea	per respiratory infection, myalgia, adache, edema, weight gain		
rosiglitazone (Avandia)	PO: 4–8 mg 1–2 times/day (max: 8 mg/day)	Hyr swe her failu	poglycemia (tremors. palpitations. eating). patotoxicity. bone fractures. heart ure. MI		
Miscellaneous Drugs					
bromocriptine (Cycloset)	PO: 0.8–4.8 mg/day upon awakening	Na hea	usea, fatigue, dizziness, vomiting, and adache		
		Hyp	potension, psychosis, drowsiness		
canagliflozin (Invokana)	PO: 100 mg once daily (max: 300 mg/day) taken before first meal	Fer trac	male genital mycotic infections, urinary ct infection, and <u>nasopharyngitis</u>		
dapagliflozin (Farxiga)	PO: 5–10 mg once daily in the morning, with or without food	<u>Hyp</u> hyp	potension, CKD, hyperkalemia, poglycemia		
empagliflozin (Jardiance)	PO: 10–25 mg once daily in the morning, with or without food				

Trade-Name Drug	Generic Drug Combination	Route and Adult Dose (Maximum Dose Where Indicated)		
Actoplus Met	pioglitazone/metformin	PO: 15 mg/500–850 mg bid (regular release) or 15–30 mg/1000 mg once daily (extended release)		
Avandamet	rosiglitazone/metformin	PO: 4 mg/1000 mg daily in divided doses		
Duetact	pioglitazone/glimepiride	PO: Start with 30 mg/2 mg once daily (max: 45 mg/8 mg daily)		
Glucovance	glyburide/metformin	PO: 1.25–5 mg/250–500 mg once or twice daily with a meal (max: 20 mg/2000 mg daily)		
Janumet	sitagliptin/metformin	PO: Starting dose 50 mg/500 mg bid (regular release) or 100 mg/1000 mg once daily (extended release) (max: 100 mg/2000 mg/day)		
Jentadueto	linagliptin/metformin	PO: 2.5 mg/500–1000 mg bid (regular release) or 5 mg/1000 mg once daily (extended release) with meals		
Trade-Name Drug	Generic Drug Combination	Route and Adult Dose (Maximum Dose Where Indicated)		
Kazano	alogliptin/metformin	PO: 12.5 mg/500 mg bid with meal		
Oseni	alogliptin/pioglitazone	PO: 25 mg/15 mg once daily with or without food		
PrandiMet	repaglinide/metformin	PO: 1 mg/500 mg bid, 15 min before meals (max: 10 mg/2500 mg daily)		
Qtern	dapagliflozin/saxagliptin	PO: 10 mg/5 mg once daily with morning meal		
Synjardy	empagliflozin/metformin	PO: 12.5 mg/1000 mg bid with meals (regular release) or 25 mg/2000 mg once daily with morning meal (extended release)		

* Dosage levels are determined individually according to patient response and glycemic laboratory results.

Biguanides

- <u>Metformin (Glucophage)</u> is the only drug in this class.
 - Preferred drug for managing type 2 diabetes due to effectiveness and safety
- Antidiabetic Drugs for Type 2 Diabetes
- Prototype drug: <u>Metformin (Glucophage, Glumetza, others)</u>
 - Therapeutic classification
 - Antidiabetic drug
 - Pharmacologic classification
 - Biguanide
 - Therapeutic effects and uses
 - Lowers blood glucose levels in patients with type 2 diabetes who are unable to control glucose levels by diet and exercise

- Off-label to treat women with polycystic ovary syndrome
- Mechanism of action
 - Reduces blood glucose levels by reducing gluconeogenesis, thereby suppressing hepatic production of glucose
 - Decreases intestinal reabsorption of glucose and increases the cellular uptake of glucose
- Adverse effects
 - GI-related effects
 - Nausea, vomiting, abdominal discomfort, metallic taste, diarrhea, anorexia, moderate weight loss
 - Headache
- Adverse effects
 - Dizziness
 - Agitation
 - Fatigue
- Black box warning
 - Lactic acidosis
- Contraindications/precautions
 - Severe CKD
 - Heart failure, liver failure, history of lactic acidosis
 - Concurrent serious infection
 - Any condition that predisposes patient to hypoxemia
- Contraindications/precautions
 - 2 days prior to, and 2 days after, receiving IV radiographic contrast
 - Anemia, diarrhea, vomiting, dehydration, fever, gastroparesis, GI obstruction
 - Older adults
 - Hyperthyroidism, pituitary insufficiency, trauma
 - Pregnancy and lactation
- Drug interactions
 - Alcohol
 - Captopril, furosemide, nifedipine
 - IV radiographic contrast
 - Amiloride, cimetidine, digoxin, dofetilide, midodrine, morphine, procainamide, quinidine, ranitidine, triamterene, trimethoprim, vancomycin
- Drug interactions
 - Use with other antidiabetic drugs potentiates hypoglycemic effects
- Herbal/Food
 - Vitamin B₁₂ and folic acid
 - Garlic and ginseng
- Pregnancy category B
- Treatment of overdose
 - Hemodialysis
- Antidiabetic Drugs for Type 2 Diabetes

- Prototype drug: <u>*Repaglinide (Prandin)</u>*</u>
 - Therapeutic classification
 - Antidiabetic drug
 - Pharmacologic classification
 - Meglitinide
 - Therapeutic effects and uses
 - Lowers blood glucose levels in patients with type 2 diabetes as an adjunct to diet and exercise
 - Mechanism of action
 - Lowers glucose levels by stimulating insulin release from pancreatic beta cells

Thiazolidinediones

- Reduce blood glucose by decreasing insulin resistance and inhibiting hepatic gluconeogenesis
- Hypoglycemia does not occur with this class.
- Antidiabetic Drugs for Type 2 Diabetes
- Prototype drug: <u>Rosiglitazone (Avandia)</u>
 - Therapeutic classification
 - Antidiabetic drug
 - Pharmacologic classification
 - Thiazolidinedione

Alpha-Glucosidase Inhibitors

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- Block enzymes in the small intestine are responsible for breaking down complex carbohydrates into monosaccharides.
- Hypoglycemia may occur when these drugs are combined with insulin or a sulfonylurea.
- Prototype drug: <u>Acarbose (Precose)</u>
 - Therapeutic classification
 - Antidiabetic drug
 - Pharmacologic classification
 - Alpha-glucosidase inhibitor

Incretin Therapies

- Incretin therapies offer a different approach to treating type 2 diabetes.
- Glucagon-like peptide (GLP-1) acts rapidly to produce:
 - Increased amount of insulin secreted by pancreas
 - Decreased amount of glucagon secreted by pancreas
 - Delayed gastric emptying
 - Decreased food intake
- Two groups
 - Activating GLP-1 receptor
 - Inhibiting dipeptidyl peptidase 4 (DPP-4)
- Incretin Therapies
- Prototype drug: *Sitagliptin (Januvia)*

- Therapeutic classification
 - Antidiabetic drug
- Pharmacologic classification
 - DPP-4 inhibitor, incretin enhancer

Diabetic Drugs

<u>Metformin:</u>

- MOA:
 - Decreases hepatic glucose production
 - Decreases intestinal absorption of glucose
 - Improves insulin sensitivity
- Side Effects:
 - GI Upset
 - Diarrhea
 - Nausea
 - Vomiting
 - Weight gain/loss
 - Lactic acidosis
- Precautions:
 - Black box warning: Risk of lactic acidosis resulting in death. Risk factors include renal impairment, concomitant use of certain drugs (e.g. topiramate), > 65 years old, excess alcohol intake.
- Contraindications
 - Hypersensitivity
 - chronic heart failure
 - metabolic acidosis with or without coma
 - diabetic ketoacidosis (DKA)
 - severe renal disease
 - abnormal creatinine clearance resulting from shock
 - o septicemia
 - myocardial infarction
 - lactation
 - Nursing Considering:
 - This is the preferred 1st line treatment for clients with T2DM
 - Clients may need to be titrated up on this medication to mitigate adverse effects
 - Avoid in chronic kidney disease (eGFR < 45)
- Common Key Generics (Brand)
 - Metformin (Glucophage)

<u>Sulfonylurea</u>

- MOA:
 - Stimulates insulin release in pancreatic beta cells
- Side Effects:

- Hypoglycemia: These medications stimulate the release of insulin regardless of glucose intake. Taking alongside insulin dramatically increases hypoglycemic risk.
- Weight gain
- Sulfa allergies
- Photosensitivity
- Precautions:
 - Sulfa moiety contained in these compounds avoid these medications in clients with sulfa allergies
 - Increased risk of hypoglycemia in clients with chronic kidney disease
- Nursing Considering:
 - Hypoglycemia is less common with glipizide
 - Use with caution in clients on insulin
 - Use with caution in clients with "sulfa allergies"
 - Use with caution in clients with severe renal disease
 - Common Key Generics (Brands)
 - Glyburide (Glynase)
 - Glipizide (Glucotrol)
 - Glimepiride (Amaryl)

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0	Humalog or Lispro	< 15 min	60-90 min	3-5 hrs	Taiast 10,15 min bafasa menliina	
API	Novolog or Aspart	< 15 min	60-120 min	3-5 hrs	Inject 10-15 min before meanine Typically used in conjunction with longer-acting insulin	
e c	Apidra or Glulisine	< 15 min	60-90 min	1-2.5 hrs	- Typically used in conjunction manifest dealing insulin.	
HORT	Regular (R) Humulin, Actrapid or Novolin	30-60 min	2-5 hrs	6-8 hrs	Inject at least 20-30 minutes before mealtime	
S	Velosulin	30-60 min	2-3 hrs	2-3 hrs		
INTERMEDIATE	NPH (N)	1-2 hrs	4-12 hrs	18-24 hrs	Commonly used twice daily	
	Lente (L)	1-2.5 hrs	3-10 hrs	18-24 hrs	Often combined with rapid- or short-acting insulin	
U	Ultralente (U)	30 min- 3 hrs	10-20 hrs	20-36 hrs	 Covers insulin needs for 24 hrs 	
Š	Lantus or Glargine	1-1.5 hrs	No Peak	20-24 hrs	 If needed, often combined with rapid- or short-acting 	
-	Levemir or Detemir	1-2 hrs	6-8 hrs	Up to 24 hrs	insulin	
0	Humulin 70/30	30 min	2-4 hrs	14-24 hrs		
XEC	Novolin 70/30	30 min	2-12 hrs	Up to 24 hrs	Combination of intermediate, and short acting insulin	
Ē.	Novolog 70/30	10-20 min	1-4 hrs	Up to 24 hrs	Component used twice daily before mealtime	
PRE	Humulin 50/50	30 min	2-5 hrs	18-24 hrs	Commonly used twice daily before meanine	
	Humalog 75/25	15 min	30 min-2.5 hrs	16-20 hrs		

Monitoring Blood sugar while on Insulin



Dietary advice for Type II diabetes.

The basic technique for following low GI guidelines is simply a "this for that" approach -i.e.: replacing high GI foods with low GI foods. One need not count numbers or do any sort of mental arithmetic to make sure they are eating a healthy, low GI diet. Some tips include:

- Increasing the consumption of whole grains, nuts, legumes, fruit, and non-starchy vegetables
- Decreasing the consumption of starchy high-glycemic index foods like potatoes, white rice, and white bread
- Decreasing the consumption of sugary foods like cookies, cakes, candy, and soft-drinks

Choose My Plate

Choose My Plate replaces the retired USDA Food Pyramid and contains general, simple guidelines for healthy eating using a small plate to visually illustrate foods and portion control. An explanation and picture of the guide is listed earlier in this chapter.

Mediterranean-Style Eating

The Mediterranean-style eating pattern derived from the Mediterranean region of the world has been observed to improve glycemic control and cardiovascular disease risk factors. The Mediterranean eating pattern includes:

- Vegetables, fruits, nuts, seeds, legumes, potatoes, whole grains, breads, herbs, spices, fish, seafood and extra virgin olive oil. Emphasis is placed on use of minimally processed foods, seasonal fresh and locally grown foods
- Olive oil is the primary fat, replacing other fats and oils (including butter and margarine)
- Total fat ranging from 25% to 35% of total energy, with saturated fat no more than 7% of calories
- Low-to-moderate amounts of cheese and yogurt
- Twice-weekly consumption of fish and poultry; approximately seven eggs/week
- Fresh fruit as daily dessert; sweets only a few times/week
- Red meat a few times/month (limited to 12 oz to 16 oz per month)
- Regular physical activity to promote a healthy weight, fitness and well-being
- Moderate consumption of wine, normally with meals; approximately two glasses/day for men and one glass/day for women

Medications affecting someone's ability to recognize hypoglycemia

• Beta-blockers have the potential for masking symptoms of hypoglycemia. The catecholamine-mediated neurogenic hypoglycemic symptoms masked by this class of medications include tremor and palpitations.



American Diabetic Association (2020) Pharmacologic approaches to Glycemic Treatment



- Empegliflozin, canagliflozin and dapagliflozin have shown reduction in HF and to reduce CKD progression in CVOTs. Canagliflozin has primary renal outcome data from CREDENCE. Dapagliflozen has primary heart failure outcome data from DAPA-HF
- 4. Degludec or U100 glargine have demonstrated CVD safety

5. Low dose may be better tolerated though less well studied for CVD effects

† Actioned whenever these become new clinical of

SU⁶ • TZD⁵ • Basal insulin

8. Semaplutide > liraquitide > dulaquitide > exenatide > lixisenatide If no specific comorbidities (i.e. no established CVD, low risk of hypog and lower priority to avoid weight gain or no weight-related comorbidi

Consider country- and region-specific cost of drugs. In some countries TZDs relatively more expensive and DPP-4i relatively cheaper

LVH = Left Ventricular Hypertrophy; HFrEF = Heart Failure reduced Ejection Fra UACR = Urine Albumin-to-Cm e Ratio: LVEF = Left Ventricular Ei



1. Consider insulin as the first injectable if evidence of ongoing catabolism, symptoms of hyperglycemia are present, when A1C levels (>10% [86 mmol/mol]) or blood glucose levels (>300 mg/dL [16.7 mmol/L]) are very high, or a diagnosis of type 1 diabetes is a possibility.

2. When selecting GLP-1 RA, consider: patient preference, A1C lowering, weight-lowering effect, or frequency of injection. If CVD, consider GLP-1 RA with proven CVD benefit.

3. For patients on GLP-1 RA and basal insulin combination, consider use of a fixed-ratio combination product (iDegLira or iGlarLixi).

4. Consider switching from evening NPH to a basal analog if the patient develops hypoglycemia and/or frequently forgets to administer NPH in the evening and would be better managed with an AM dose of a long-acting basal insulin.

5. If adding prandial insulin to NPH, consider initiation of a self-mixed or premixed insulin regimen to decrease the number of injections required.

	Efficacy	Hypoglycemia	Weight	CV effe	ects	Cost	Renal		Qral/SO Rena		Oral/SQ Ret		effects	Additional considerations
			change	ASCVD	HF			Progression of DKD	Dosing/use considerations*	Additional considerations				
Metformin	High	No	Neutral (potential for modest loss)	Potential benefit	Neutral	Low	Oral	Neutral	 Contraindicated with eGFR <30 mL/min/1.73 m² 	 Gastrointestinal side effects common (diarrhea, nausea) Potential for B12 deficiency 				
SGLT-2 inhibitors	Intermediate	No	Loss	Benefit: empagliflozin†, canagliflozin	Benefit: empagliflozin†, canagliflozin†, dapagliflozin‡	High	Oral	Benefit: canagliflozinş, empagliflozin,dapagliflozin	 Renal dose adjustment required (canagliflozin, dapagliflozin, empagliflozin, ertugliflozin) 	FDA Black Box: Risk of amputation (canagifficatin) Risk of boxe fractures (canagifficatin) DKA risk (all sepents, rare in TZDM) Genitourinary infections Risk of volume depletion, hypotension - PtDL choisterol Risk of forumier's gangrene				
GLP-1 RAs	High	No	Loss	Neutral: lixisenatide Benefit: See label indication of reducing CVD events	Neutral	High	SQ; oral (semaglutide)	Benefit: liragiutide	Renal dose adjustment required (exenatide, lixisenatide) Caution when initiating or increasing dose due to potential risk of acute kidney injury	FDA Black Box: Risk of thyroid C-cell tumors (liregituide, albiglutide, dulagituide, exenatide extended release) Gastrointestinal side effects common (nausea, vomiting, diarrhea) Injection site reactions ?Acute pancreatitis risk				
DPP-4 inhibitors	Intermediate	No	Neutral	Neutral	Potential risk: saxagliptin	High	Oral	Neutral	 Renal dose adjustment required (sitagliptin, saxagliptin, alogliptin); can be used in renal impairment No dose adjustment required for linagliptin 	Potential risk of acute pancreatitis Joint pain				
Thiazolidinediones	High	No	Gain	Potential benefit: pioglitazone	Increased risk	Low	Oral	Neutral	No dose adjustment required Generally not recommended in renal impairment due to potential for fluid retention	FDA Black Box: Congestive heart failure: [plogiltazone, rssigiltazone] Fluid retention (edema; heart failure) Benefit in NASH Risk of bone fractures Risk of bone fractures Bidder cancer (pirgiltazone) HDL cholesteroil (osigiltazone)				
Sulfonylureas (2nd generation)	High	Yes	Gain	Neutral	Neutral	Low	Oral	Neutral	 Glyburide: not recommended Glipizide and glimepiride: initiate conservatively to avoid hypoglycemia 	FDA Special Warning on increased risk of cardiovascular mortality based on studies of an older sulfonylurea (tolbutamide)				
Insulin Human insulin	Highest	Yes	Gain	Neutral	Neutral	Low	SQ; inhaled	Neutral	 Lower insulin doses required with a decrease in eGFR; titrate per clinical response 	 Injection site reactions Higher risk of hypoglycemia with human insulin (NPH or premixed formulations) vs. analoas 				
Analogs						High	SQ		Per annou response					