

FINAL CHEAT SHEET: Action Potential & Electrolytes

Phase	Na ⁺	K ⁺	Ca ²⁺	Cl ⁻	Mg ²⁺	Effect on Muscle
Resting (Ready to Fire)	Outside	Inside	Stored in SR	Stabilizing	Blocks extra Ca ²⁺	Relaxed
Depolarization (Firing Up)	Enters cell	Inside	Released from SR	Low	Low	Contracts!
Repolarization (Reset)	Leaves cell	Exits	Pumped out	Stabilizing	Helps relax	Relaxing
Hyperpolarization (Final Reset)	Leaves	Comes back	Pumped out	High	Maintains balance	Ready Again!

Final Memory Trick: Electrolyte Squad & Muscle Action

- **Contraction** = Na⁺ In, K⁺ Out, Ca²⁺ In → Muscles Fire Up
- **Relaxation** = Na⁺ Out, K⁺ In, Ca²⁺ Out, Mg²⁺ High → Muscles Chill

Final Summary: Electrolyte Squad

H⁺ & K⁺ are enemies → One moves in, the other leaves.

K⁺ & Ca²⁺ are besties → If K⁺ is lost, Ca²⁺ follows.

Mg²⁺ is Ca²⁺'s doggo → Mg²⁺ low? Ca²⁺ low too.

Na⁺ is the strict landlord → Keeps K⁺ out, drags H₂O in.

H₂O is madly in love with Na⁺ → Follows it everywhere.

Cl⁻ is the Balance Keeper → Stays with Na⁺ but fights HCO₃⁻

1. SIADH (Syndrome of Inappropriate ADH) = Too Much ADH

- Water is retained → Blood gets diluted
- Na^+ levels drop → Hyponatremia (low sodium)
- More H^+ excreted → Alkalosis (high pH)
 - Example Causes: Lung cancer, brain injury, pain, stress
 - Treatment: Fluid restriction, salt tablets, ADH blockers (Tolvaptan)

2. Diabetes Insipidus (DI) = Too Little ADH

- Water is lost → Severe dehydration
- Na^+ levels rise → Hypernatremia (high sodium)
- H^+ is retained → Acidosis (low pH)
 - Example Causes: Brain damage, alcohol, lithium
 - Treatment: Desmopressin (ADH replacement), IV fluids

1. Vasodilators

- **Nitrates (e.g., Nitroglycerin, Isosorbide dinitrate/mononitrate)** → Venous dilation > arterial dilation, reduces preload. Avoid with PDE-5 inhibitors (e.g., Sildenafil).
 - **CCBs**
 - **Dihydropyridines (e.g., Amlodipine, Nifedipine)** → More vasoselective, cause reflex tachycardia (except Amlodipine).
 - **CCBs - Non-DHPs (e.g., Verapamil, Diltiazem)** → Reduce heart rate & contractility (negative inotropic effect). Verapamil is the most cardioselective.
 - **Hydralazine** → Arterial vasodilator, causes lupus-like syndrome at high doses.
 - **Minoxidil** → Potent vasodilator, causes hypertrichosis (hair growth).
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2. Rate Controllers (HR Slowers)

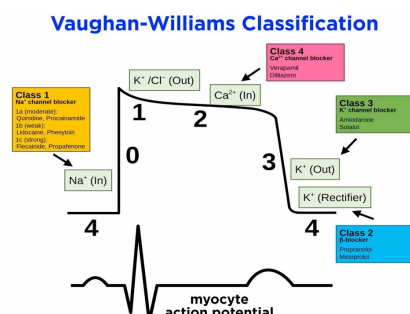
- **Beta-Blockers (BBs)**
 - Cardioselective (e.g., Metoprolol, Atenolol) → Selective for β_1 , preferred in patients with COPD/asthma.
 - Non-Selective (e.g., Propranolol, Carvedilol) → Propranolol crosses BBB (can cause CNS side effects like nightmares).
 - Mixed (e.g., Carvedilol, Labetalol) → Also block α_1 , causing vasodilation.
- **Digoxin** → Positive inotrope, negative chronotrope, narrow therapeutic index (toxicity = visual halos, nausea).
- **Amiodarone** → Contains iodine, long half-life, causes thyroid & pulmonary toxicity.

3. Force Controllers (Contractility Reducers)

- **Beta-Blockers (Metoprolol, Carvedilol, Bisoprolol)** → Reduce mortality in heart failure.
- **ACE Inhibitors (Lisinopril, Ramipril)** → First-line for heart failure & hypertension, cause dry cough & hyperkalemia.
- **ARBs (Losartan, Valsartan)** → Similar to ACE-I but no cough.
- **Aldosterone Antagonists (Spironolactone, Eplerenone)** → Cause hyperkalemia, Spironolactone causes gynecomastia.

4. Antiarrhythmics

- **Class I - Sodium Channel Blockers**
 - **IA (Quinidine, Procainamide)** → Prolong QT, cause torsades de pointes.
 - **IB (Lidocaine)** → Best for ischemic tissue (post-MI VT).
 - **IC (Flecainide, Propafenone)** → Contraindicated in structural heart disease (risk of sudden death).
- **Class II - Beta-Blockers** → Reduce mortality in post-MI arrhythmias.
- **Class III - Potassium Channel Blockers (Amiodarone, Sotalol)** → Amiodarone = least proarrhythmic but causes multiple organ toxicities.
- **Class IV - Calcium Channel Blockers (Verapamil, Diltiazem)** → Best for atrial arrhythmias (AFib, SVT).
- **Adenosine** → Used for SVT, causes transient asystole, blocked by caffeine.



5. Antihypertensive

1. RAAS Inhibitors (Renin-Angiotensin-Aldosterone System Blockers)

- Angiotensin-Converting Enzyme Inhibitors (ACE-Is)
 - Lisinopril, Enalapril, Ramipril, Captopril, Perindopril
 - Key Notes: First-line for hypertension, causes dry cough (bradykinin effect), hyperkalemia. Contraindicated in pregnancy and bilateral renal artery stenosis.
- Angiotensin II Receptor Blockers (ARBs)
 - Losartan, Valsartan, Telmisartan, Olmesartan, Candesartan, Irbesartan
 - Key Notes: Similar to ACE-Is but no cough. Used if ACE-Is are not tolerated.
- Direct Renin Inhibitor
 - Aliskiren
 - Key Notes: Blocks renin, reducing angiotensin II production. Used when ACE-Is or ARBs are not tolerated.

2. Diuretics (Increase Sodium & Water Excretion)

- **Thiazide Diuretics**
 - Hydrochlorothiazide (HCTZ), Chlorthalidone, Indapamide
 - Key Notes: First-line for hypertension, causes hypercalcemia, hyperuricemia (can worsen gout), and hypokalemia.
- **Loop Diuretics** (More potent, used in resistant hypertension)
 - Furosemide, Bumetanide, Torsemide, Ethacrynic acid
 - Key Notes: Used for heart failure + hypertension, causes hypokalemia, hypocalcemia, ototoxicity.

- **Potassium-Sparing Diuretics**
 - Spironolactone, Eplerenone (Aldosterone Antagonists)
 - Amiloride, Triamterene (ENaC Inhibitors)
 - Key Notes: Used in resistant hypertension, can cause hyperkalemia. Spironolactone causes gynecomastia.

3. Sympatholytics (Reduce Sympathetic Nervous System Activity)

- **Beta-Blockers (β -Blockers)**
 - **Selective (β_1 -Blockers):** Metoprolol, Atenolol, Bisoprolol, Nebivolol
 - **Non-Selective (β_1 & β_2 Blockers):** Propranolol, Nadolol, Timolol
 - **Mixed α & β Blockers:** Carvedilol, Labetalol
 - Key Notes: Lower BP by reducing heart rate and cardiac output. Avoid non-selective BBs in asthma & COPD. Carvedilol and Labetalol also block α_1 (vasodilation).
- **Alpha-1 Blockers**
 - Prazosin, Doxazosin, Terazosin
 - Key Notes: Used in hypertension with BPH (Benign Prostatic Hyperplasia). Causes first-dose hypotension.
- **Alpha-2 Agonists (Centrally Acting)**
 - Clonidine, Methyldopa, Guanfacine
 - Key Notes: Used in resistant hypertension, Methyldopa is safe in pregnancy. Clonidine causes rebound hypertension if stopped abruptly.

4. Calcium Channel Blockers (CCBs)

- **Dihydropyridines (Vasoselective)**
 - Amlodipine, Nifedipine, Felodipine, Nicardipine, Clevidipine
 - Key Notes: First-line for hypertension, cause reflex tachycardia (except Amlodipine), can cause peripheral edema.

- **Non-Dihydropyridines (Cardioselective)**
 - Verapamil, Diltiazem
 - Key Notes: Lower HR & BP (used in atrial fibrillation + hypertension).
Avoid in heart failure due to negative inotropic effects.
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5. Direct Vasodilators

- **Hydralazine**
 - Key Notes: Arterial vasodilator, used in hypertension during pregnancy.
Causes lupus-like syndrome at high doses.
 - **Minoxidil**
 - Key Notes: Potent vasodilator, used in refractory hypertension. Causes hypertrichosis (hair growth) (used in Rogaine for hair loss).
 - **Sodium Nitroprusside**
 - Key Notes: Used in hypertensive emergencies, short-acting, risk of cyanide toxicity.
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6. Hypertensive Emergency Drugs (IV Medications)

Used in hypertensive crisis (BP >180/120 mmHg) with organ damage.

- **Sodium Nitroprusside** (Arterial & venous vasodilation, risk of cyanide toxicity)
 - **Labetalol** (Mixed α & β blocker, no reflex tachycardia)
 - **Nicardipine/Clevidipine** (IV CCBs, safe for stroke patients)
 - **Fenoldopam** (Dopamine agonist, improves renal perfusion)
 - **Esmolol** (Short-acting β 1-blocker, used perioperatively)
 - **Hydralazine** (Used in eclampsia/preeclampsia)
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7. Antihypertensives Used in Pregnancy

- First-line: **Methyldopa, Labetalol, Nifedipine**
 - Second-line: **Hydralazine**
 - **Avoid:** ACE-Is, ARBs, Direct Renin Inhibitors (Aliskiren), Diuretics (risk of fetal hypoperfusion).
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Quick Mnemonics for Easy Recall

"ABCD" for First-Line Hypertension Treatment:

- **A** = ACE-Is/ARBs
- **B** = Beta-Blockers
- **C** = Calcium Channel Blockers
- **D** = Diuretics (Thiazides)

"PALS" for Pregnancy-Safe Antihypertensives:

- **P** = Prazosin
- **A** = Alpha-Methyldopa
- **L** = Labetalol
- **S** = Slow-release Nifedipine

"The 4 Ds for Direct Vasodilators:"

- **D** = Dihydropyridines (CCBs)
 - **D** = Direct Vasodilators (Hydralazine, Minoxidil)
 - **D** = Dopamine Agonist (Fenoldopam)
 - **D** = Danger (Sodium Nitroprusside - Cyanide Toxicity)
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Summary

Class	Example Drugs	Key Notes
ACE-Is	Lisinopril, Ramipril	First-line, causes dry cough
ARBs	Losartan, Valsartan	No cough, alternative to ACE-Is
Thiazide Diuretics	HCTZ, Chlorthalidone	First-line, hypercalcemia, hyperuricemia
Loop Diuretics	Furosemide	Strong diuresis , hypokalemia
Potassium-Sparing	Spironolactone	Hyperkalemia, gynecomastia
Beta-Blockers	Metoprolol, Carvedilol	HR control, avoid in asthma (non-selective BBs)
CCBs - DHPs	Amlodipine, Nifedipine	Vasoselective, peripheral edema
CCBs - Non-DHPs	Verapamil, Diltiazem	Lower HR & BP, avoid in heart failure
Alpha-1 Blockers	Prazosin	BPH + Hypertension, first-dose hypotension
Alpha-2 Agonists	Clonidine, Methyldopa	Used in resistant HTN, pregnancy-safe (Methyldopa)
Direct Vasodilators	Hydralazine, Minoxidil	Reflex tachycardia, lupus-like syndrome (Hydralazine)
Hypertensive Emergency Drugs	Nitroprusside, Labetalol	IV-only, rapid BP control

6. Anticoagulants and Antiplatelets

1. Anticoagulants (Prevent Clot Formation & Growth)

Used in deep vein thrombosis (DVT), pulmonary embolism (PE), atrial fibrillation (AF), stroke prevention, and mechanical heart valves.

A. Parenteral Anticoagulants (Injectable)

- Unfractionated Heparin (UFH)
 - **Key Notes:** Fast-acting, requires aPTT monitoring, antidote = Protamine sulfate, risk of heparin-induced thrombocytopenia (HIT).
- Low-Molecular-Weight Heparins (LMWH)
 - Enoxaparin (Lovenox), Dalteparin, Tinzaparin
 - **Key Notes:** More predictable than UFH, no aPTT monitoring, renal clearance (avoid in severe CKD).
- Fondaparinux
 - **Key Notes:** Factor Xa inhibitor, **safe in HIT** (does not cause platelet activation).

B. Oral Anticoagulants

- Vitamin K Antagonist (Warfarin)
 - **Key Notes:** Blocks Factor II, VII, IX, X synthesis, requires INR monitoring, interacts with diet (green leafy vegetables - vitamin K), antidote = Vitamin K.
- Direct Oral Anticoagulants (DOACs) / NOACs
 - Factor Xa Inhibitors → Apixaban, Rivaroxaban, Edoxaban, Betrixaban

- **Direct Thrombin Inhibitor → Dabigatran**
 - **Key Notes:** No INR monitoring needed, rapid onset, antidote for dabigatran = Idarucizumab, antidote for Xa inhibitors = Andexanet alfa.
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2. Antiplatelet Drugs (Prevent Platelet Aggregation)

Used for acute coronary syndrome (ACS), post-stroke, post-percutaneous coronary intervention (PCI), and secondary prevention of cardiovascular disease.

- **A. COX-1 Inhibitor**
 - **Aspirin (Acetylsalicylic Acid - ASA)**
 - **Key Notes:** Irreversible COX-1 inhibitor, prevents thromboxane A2 formation, reduces MI & stroke risk, risk of GI ulcers and bleeding. Avoid in children (Reye's syndrome).
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B. P2Y12 Receptor Inhibitors (ADP Receptor Blockers)

- **Thienopyridines (Irreversible inhibitors)**
 - **Clopidogrel (Plavix), Prasugrel (Effient), Ticlopidine (rarely used due to side effects)**
 - **Key Notes:** Clopidogrel activated by CYP2C19, slow onset, alternative to aspirin in aspirin allergy.
 - **Non-Thienopyridines (Reversible inhibitors)**
 - **Ticagrelor (Brilinta), Cangrelor (IV)**
 - **Key Notes:** Faster onset than Clopidogrel, Ticagrelor can cause dyspnea.
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C. Glycoprotein IIb/IIIa Inhibitors (IV-Only, Used in PCI)

- **Abciximab, Tirofiban, Eptifibatide**
- **Key Notes:** Used during PCI or STEMI, most potent antiplatelets, risk of bleeding & thrombocytopenia.

D. Phosphodiesterase (PDE) Inhibitors

- **Dipyridamole + Aspirin (Aggrenox)**
 - **Key Notes:** Used in **stroke prevention**, weak antiplatelet effect.
 - **Cilostazol**
 - **Key Notes:** Used in **peripheral artery disease (PAD)**, causes **vasodilation**.
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3. Fibrinolytics (Clot Busters - Used in Acute Stroke & MI)

- **Tissue Plasminogen Activators (tPA)**
 - **Alteplase, Tenecteplase, Reteplase**
 - **Key Notes:** Used in **ischemic stroke (<4.5h window)**, **STEMI**, **massive PE**, **contraindicated** in recent bleeding, history of **hemorrhagic stroke**.
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Quick Mnemonics for Easy Recall

1. Anticoagulants: "Help Prevent Fatal Clots" (HPFC)

H = Heparins (UFH, LMWH, Fondaparinux)

P = Parenteral Direct Thrombin Inhibitor (Bivalirudin, Argatroban)

F = Factor Xa Inhibitors (Apixaban, Rivaroxaban)

C = Coumadin (Warfarin - Vitamin K antagonist)

2. Antiplatelets: "Always Cut The Thrombus" (ACTT)

A = Aspirin (COX-1 Inhibitor)

C = Clopidogrel, Prasugrel, Ticagrelor (P2Y₁₂ inhibitors)

T = Tirofiban, Eptifibatide, Abciximab (GP IIb/IIIa inhibitors)

T = tPA (Fibrinolytics - Alteplase, Tenecteplase)

Summary Table

Class	Example Drugs	Key Notes
Parenteral Anticoagulants	Heparin, LMWH, Fondaparinux	UFH requires aPTT monitoring , HIT risk
Oral Anticoagulants (Warfarin)	Warfarin	INR monitoring , Vitamin K antidote
DOACs (Factor Xa Inhibitors)	Apixaban, Rivaroxaban	No monitoring , Andexanet antidote
DOACs (Direct Thrombin Inhibitor)	Dabigatran	Idarucizumab antidote
COX-1 Inhibitor	Aspirin	Irreversible COX-1 inhibitor , Reye's syndrome risk
P2Y12 Inhibitors	Clopidogrel, Ticagrelor	Clopidogrel requires CYP2C19 activation
Glycoprotein IIb/IIIa Inhibitors	Abciximab, Tirofiban	Most potent antiplatelets , used in PCI
Phosphodiesterase Inhibitors	Cilostazol, Dipyridamole	Used in PAD & stroke prevention
Fibrinolytics (tPA)	Alteplase, Tenecteplase	STEMI, Stroke (<4.5h window) , PE

Which One to Use?

- **Atrial Fibrillation (AFib)? → DOACs (Apixaban, Rivaroxaban) preferred over Warfarin**
- **DVT/PE Treatment? → LMWH or DOACs (Rivaroxaban, Apixaban)**
- **Post-MI or Stroke Prevention? → Aspirin + Clopidogrel (Dual Antiplatelet Therapy - DAPT)**
- **STEMI or Ischemic Stroke? → tPA if within 4.5-hour window**

7. Lipid Lowering Agents

1. HMG-CoA Reductase Inhibitors ("Statins")

- Most effective for lowering LDL (bad cholesterol) and reducing cardiovascular events.
 - **Drugs:** Atorvastatin, Rosuvastatin, Simvastatin, Pravastatin, Lovastatin, Fluvastatin, Pitavastatin
 - **Key Notes:**
 - First-line for hypercholesterolemia (LDL lowering)
 - Reduce cardiovascular risk (MI, stroke prevention)
 - Risk of myopathy & rhabdomyolysis (especially with fibrates or CYP3A4 inhibitors like macrolides)
 - Hepatotoxicity → Monitor liver enzymes (ALT, AST)
 - Contraindicated in pregnancy
 - Atorvastatin & Rosuvastatin are high-intensity statins
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2. Cholesterol Absorption Inhibitors

- **Drug: Ezetimibe**
 - **Key Notes:**
 - Blocks NPC1L1 transporter in intestines → decreases cholesterol absorption
 - Lowers LDL, often added to statins if LDL remains high
 - Minimal side effects, but can cause diarrhea
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3. PCSK9 Inhibitors (Monoclonal Antibodies)

- **Drugs: Alirocumab, Evolocumab**
 - **Key Notes:**
 - Powerful LDL-lowering (↓ 50-60%)
 - Used in familial hypercholesterolemia (FH) or statin intolerance
 - Expensive (injectable biologic drug)
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4. Bile Acid Sequestrants (Resins)

- **Drugs:** Cholestyramine, Colesevelam, Colestipol
- **Key Notes:**
 - Binds bile acids in gut → forces liver to use cholesterol to make more bile
 - Lowers LDL
 - Causes GI issues (constipation, bloating, flatulence)
 - Can interfere with absorption of fat-soluble vitamins (A, D, E, K) and warfarin

5. Fibrates (Fibric Acid Derivatives)

- **Drugs:** Fenofibrate, Gemfibrozil
- **Key Notes:**
 - Best for lowering triglycerides (TG)
 - Activates PPAR- α → increases lipoprotein lipase (LPL) activity
 - Can cause myopathy (especially with statins, highest risk with Gemfibrozil + statin)
 - Can cause gallstones

6. Omega-3 Fatty Acids (Fish Oil Derivatives)

- **Drugs:** Lovaza (EPA + DHA), Vascepa (Pure EPA - Icosapent Ethyl)
- **Key Notes:**
 - Used for hypertriglyceridemia
 - Reduces inflammation & TGs
 - May increase bleeding risk (caution with anticoagulants)

7. Niacin (Vitamin B3)

- **Drugs:** Nicotinic acid (Niacin)
- **Key Notes:**
 - Increases HDL (good cholesterol)

- Lowers LDL & TGs
 - Causes flushing & itching (can be reduced with aspirin)
 - Risk of hepatotoxicity, hyperglycemia (caution in diabetics)
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8. CETP Inhibitors (Experimental - Not Commonly Used)

- **Drugs: Anacetrapib, Evacetrapib** (Investigational drugs, not widely available)
 - Key Notes:
 - Increase HDL significantly, lower LDL
 - Some failed in clinical trials due to side effects
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Quick Mnemonics for Easy Recall

1. LDL Lowering: "SPEB" (Statins Protect Every Blood Vessel)

S = Statins (First-line)

P = PCSK9 Inhibitors (Alirocumab, Evolocumab)

E = Ezetimibe (Cholesterol absorption inhibitor)

B = Bile acid sequestrants (Cholestyramine, Colesevelam)

2. TG Lowering: "FOF" (Fish, Oils, and Fibrates)

F = Fibrates (Fenofibrate, Gemfibrozil)

O = Omega-3 Fatty Acids (Fish Oil)

F = Fish-derived Icosapent Ethyl (Vascepa)

3. HDL Raising: "Niacin Helps"

Niacin (B3) is the best for raising HDL, but it's rarely used due to flushing & side effects.

Summary Table

Class	Example Drugs	Primary Effect	Key Notes
Statins (HMG-CoA Reductase Inhibitors)	Atorvastatin, Rosuvastatin	↓↓↓ LDL	First-line, myopathy, hepatotoxicity
Cholesterol Absorption Inhibitor	Ezetimibe	↓ LDL	Add-on to statins
PCSK9 Inhibitors	Alirocumab, Evolocumab	↓↓↓ LDL	Expensive, injection
Bile Acid Sequestrants	Cholestyramine, Colesevelam	↓ LDL	GI side effects, ↓ fat-soluble vitamin absorption
Fibrates (PPAR-α Activators)	Fenofibrate, Gemfibrozil	↓↓↓ TG	Best for TG, risk of gallstones
Omega-3 Fatty Acids	Vascepa (Icosapent Ethyl), Lovaza	↓ TG	Anti-inflammatory, bleeding risk
Niacin (Vitamin B3)	Nicotinic Acid	↑ HDL	Flushing, hepatotoxicity
CETP Inhibitors (Experimental)	Anacetrapib	↑ HDL	Research stage

Which One to Use?

- High LDL? → Statins first, then add Ezetimibe or PCSK9 inhibitors if needed
 - High TG? → Fibrates or Omega-3 fatty acids
 - Low HDL? → Niacin (rarely used due to side effects)
 - Statin intolerance? → PCSK9 inhibitors, Ezetimibe, or Bile Acid Sequestrants
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1. Insulin Therapy (Injectable)

- **Examples:** Regular Insulin, Lispro, Aspart, Glulisine, NPH, Glargine, Detemir, Degludec
 - **Mechanism of Action:**
 - Lowers blood glucose levels by **promoting glucose uptake** into muscle and fat cells.
 - Suppresses **hepatic glucose production** (gluconeogenesis).
 - Inhibits **lipolysis and proteolysis**, reducing free fatty acids and amino acids in circulation.
 - Enhances **glycogen synthesis** for storage.
 - **Key Notes:**
 - First-line for **type 1 diabetes mellitus (T1DM)** and **insulin-dependent type 2 diabetes mellitus (T2DM)**.
 - Safe for use in **pregnancy** (NPH, regular insulin, rapid-acting insulins).
 - Risk of **hypoglycemia**, particularly with **short-acting and intermediate-acting insulins**.
 - Can cause **lipodystrophy**, requiring **rotation of injection sites**.
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2. Biguanides

- **Example:** Metformin
- **Mechanism of Action:**
 - Decreases blood glucose levels by **decreasing hepatic glucose production (gluconeogenesis)**.
 - Decreases **intestinal glucose absorption**.
 - Increases **insulin sensitivity** by **enhancing peripheral glucose uptake and utilization**.
- **Key Notes:**
 - First-line therapy for **T2DM** due to **efficacy and cardiovascular benefits**.
 - Does **not** cause **hypoglycemia**.
 - Promotes **weight loss** or is **weight neutral**.

- Contraindicated in **renal failure (eGFR <30 mL/min)** due to the risk of **lactic acidosis**.
 - Can cause **gastrointestinal side effects** (diarrhea, nausea), which can be **minimized by taking with food**.
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3. Sulfonylureas (Insulin Secretagogues)

- **Examples:** Glimepiride, Glipizide, Glyburide (Glibenclamide)
 - **Mechanism of Action:**
 - Increases **insulin secretion** from pancreatic **β -cells** by:
 - **Binding to sulfonylurea receptors (SUR1) on pancreatic β -cells.**
 - **Closing ATP-sensitive potassium (K^+) channels**, leading to **cell depolarization**.
 - **Opening voltage-gated calcium (Ca^{2+}) channels**, allowing **calcium influx**.
 - **Triggering insulin granule exocytosis**.
 - **Key Notes:**
 - Effective in **early-stage T2DM** when β -cell function is preserved.
 - Risk of **hypoglycemia**, especially with **Glyburide**.
 - Causes **weight gain**.
 - May lead to **β -cell exhaustion**, reducing long-term efficacy.
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4. Meglitinides (Short-Acting Insulin Secretagogues)

- **Examples:** Repaglinide, Nateglinide
- **Mechanism of Action:**
 - Stimulates **rapid and short-lived insulin secretion** by **closing ATP-sensitive potassium channels** on β -cells, similar to sulfonylureas but with a **shorter duration of action**.
- **Key Notes:**
 - Used for **postprandial glucose control**.

- Risk of **hypoglycemia**, though lower than sulfonylureas.
 - Causes **weight gain**.
 - Short half-life, requiring **frequent dosing before meals**.
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5. Thiazolidinediones (TZDs, “Glitazones”)

- **Examples:** Pioglitazone, Rosiglitazone
 - **Mechanism of Action:**
 - Activates **peroxisome proliferator-activated receptor gamma (PPAR-γ)**, leading to:
 - **Increased insulin sensitivity** in muscle, liver, and adipose tissue.
 - **Enhanced glucose uptake** and **reduced hepatic glucose output**.
 - **Key Notes:**
 - Does **not** cause **hypoglycemia**.
 - Causes **weight gain and fluid retention**, leading to **edema**.
 - Contraindicated in **heart failure** due to risk of **fluid overload**.
 - Pioglitazone may increase the risk of **bladder cancer**.
 - Can reduce **bone mineral density**, increasing **fracture risk**.
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6. DPP-4 Inhibitors (“Gliptins”)

- **Examples:** Sitagliptin, Linagliptin, Saxagliptin, Alogliptin
 - **Mechanism of Action:**
 - Inhibits **dipeptidyl peptidase-4 (DPP-4)**, preventing the breakdown of **incretins (GLP-1 and GIP)**, leading to:
 - **Increased insulin secretion** in response to meals.
 - **Reduced glucagon release**, lowering **hepatic glucose production**.
 - **Key Notes:**
 - **Weight neutral**.
 - Low risk of **hypoglycemia**.
 - May increase risk of **pancreatitis**.
 - Saxagliptin may **worsen heart failure**.
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7. GLP-1 Receptor Agonists (“Incretin Mimetics”)

- **Examples:** Exenatide, Liraglutide, Semaglutide, Dulaglutide
 - **Mechanism of Action:**
 - Mimics **glucagon-like peptide-1 (GLP-1)**, leading to:
 - **Increased glucose-dependent insulin secretion.**
 - **Slowed gastric emptying**, reducing postprandial spikes.
 - **Reduced appetite and food intake.**
 - **Decreased glucagon secretion**, reducing hepatic glucose production.
 - **Key Notes:**
 - Promotes **weight loss**.
 - Cardioprotective (Liraglutide, Semaglutide).
 - Risk of **pancreatitis**.
 - Causes **gastrointestinal side effects** (nausea, vomiting).
 - Contraindicated in patients with **medullary thyroid cancer or MEN-2 syndrome**.
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8. SGLT2 Inhibitors (“Gliflozins”)

- **Examples:** Empagliflozin, Canagliflozin, Dapagliflozin
 - **Mechanism of Action:**
 - Inhibits **sodium-glucose cotransporter-2 (SGLT2)** in the **proximal renal tubule**, leading to:
 - **Increased urinary glucose excretion.**
 - **Reduced blood glucose levels** independent of insulin.
 - **Key Notes:**
 - Promotes **weight loss** and lowers **blood pressure**.
 - Cardioprotective and **renal protective** (Empagliflozin, Canagliflozin).
 - Risk of **genital infections (UTIs, yeast infections)** due to glycosuria.
 - Canagliflozin may increase the risk of **amputations**.
 - Risk of **euglycemic diabetic ketoacidosis (DKA)**.
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9. Alpha-Glucosidase Inhibitors

- **Examples:** Acarbose, Miglitol
 - **Mechanism of Action:**
 - Inhibits **alpha-glucosidase enzymes** in the **small intestine**, leading to:
 - **Delayed carbohydrate digestion and absorption.**
 - **Reduced postprandial glucose spikes.**
 - **Key Notes:**
 - Used for **postprandial glucose control.**
 - Causes **gastrointestinal side effects** (flatulence, bloating, diarrhea).
 - Not commonly used due to **poor tolerability.**
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Quick Mnemonics for Easy Recall

1. First-Line T2DM Treatment: "Metformin First"

- **Metformin** is always first-line unless contraindicated.

2. Weight Loss Benefits: "SGLT-GLP Slim"

- **SGLT2 inhibitors** (Empagliflozin, Canagliflozin)
- **GLP-1 receptor agonists** (Liraglutide, Semaglutide)

3. Weight Gain Risks: "Secretagogues & Glitazones Make You Fat"

- **Sulfonylureas** (Glipizide, Glyburide, Glimepiride)
- **Meglitinides** (Repaglinide, Nateglinide)
- **Glitazones** (Pioglitazone, Rosiglitazone)

4. Hypoglycemia Risk: "Secretagogues Scare"

- **Sulfonylureas & Meglitinides** cause **hypoglycemia.**
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Summary Table

Class	Example Drugs	Key Effects	Warnings
Biguanide	Metformin	First-line, weight loss	Lactic acidosis risk
Sulfonylureas	Glipizide, Glyburide	Hypoglycemia risk	Weight gain
Meglitinides	Repaglinide	Short-acting	Hypoglycemia
TZDs	Pioglitazone	Insulin sensitizer	Heart failure risk
DPP-4 Inhibitors	Sitagliptin	Weight neutral	Pancreatitis risk
GLP-1 Agonists	Liraglutide	Weight loss	GI side effects
SGLT2 Inhibitors	Empagliflozin	Weight loss, cardioprotective	UTI risk
Alpha-Glucosidase Inhibitors	Acarbose	Delays carb absorption	GI issues

Types of Insulin

Type	Example Drugs	Onset	Peak	Duration
Ultra-Rapid Acting	Afrezza (inhaled insulin)	5-15 min	30 min	2-3 hrs
Rapid-Acting (Bolus)	Lispro, Aspart, Glulisine	10-30 min	30-90 min	3-5 hrs
Short-Acting (Bolus)	Regular Insulin (Humulin R, Novolin R)	30-60 min	2-4 hrs	6-8 hrs
Intermediate-Acting (Basal)	NPH (Humulin N, Novolin N)	2-4 hrs	4-12 hrs	12-18 hrs
Long-Acting (Basal)	Glargine (Lantus), Detemir (Levemir)	2-4 hrs	No peak	18-24 hrs
Ultra-Long Acting (Basal)	Degludec (Tresiba)	1 hr	No peak	42 hrs

Risk: Hypoglycemia (especially with short-acting and intermediate-acting insulins).

Lipodystrophy (Rotate injection sites to prevent fat hypertrophy).