Antihypertensive Drugs

A Comprehensive Overview: Pharmacology and Clinical Use

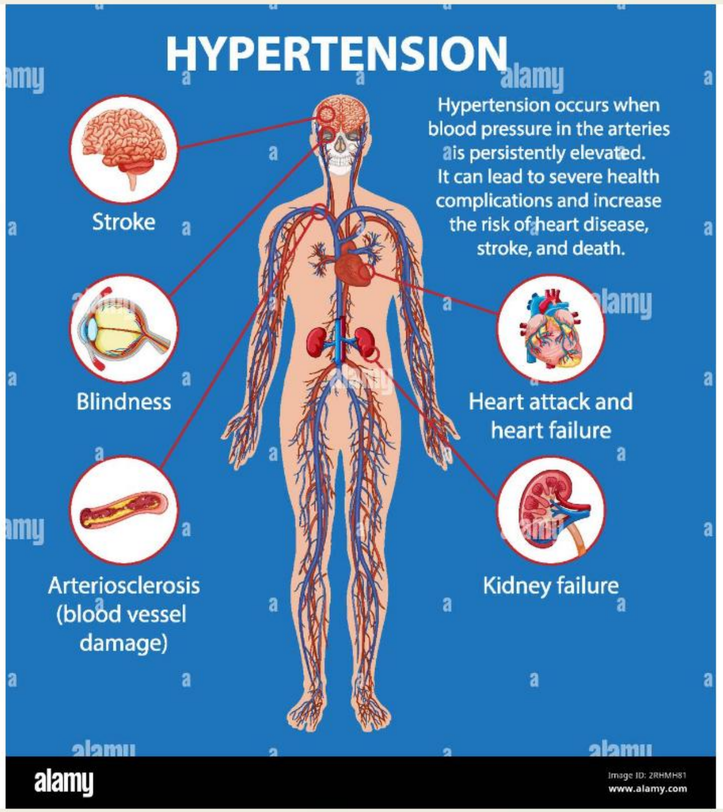
What is Hypertension?

Definition & Risks

Hypertension, or High Blood Pressure, is a chronic medical condition where the pressure in the arteries of the circulatory system is persistently elevated (typically ≥ 130/80 mmHg).

It is often called the **"silent killer"** as it typically has no symptoms, but if untreated, it directly damages major organs:

- **Cardiovascular:** Myocardial Infarction, Heart Failure.
- **Cerebrovascular:** Stroke (Ischemic and Hemorrhagic).
- **Renal:** Chronic Kidney Disease (CKD).
- **Ocular:** Retinopathy.



Classification of Antihypertensives

- **Thiazide Diuretics:** Promote salt and water excretion.
- **ACE Inhibitors (ACE-I):** Block the production of angiotensin II.
- **Angiotensin II Receptor Blockers (ARBs):** Block the action of angiotensin II.
- **Calcium Channel Blockers (CCBs):** Relax blood vessels by blocking calcium entry.
- **Beta-Blockers:** Reduce heart rate and cardiac output.
- **Other Classes:** Include Alpha-blockers, Central Agonists, and Direct Renin Inhibitors.

Class 1: Thiazide Diuretics

Mechanism of Action

Inhibits the Na^+/Cl^- symporter in the distal convoluted tubule (DCT) of the kidney. This prevents reabsorption of sodium and chloride, leading to increased water excretion (diuresis) and decreased blood volume.

Example & Dosing

Drug: Hydrochlorothiazide (HCTZ)
Brand: Microzide
Dosage: 12.5 - 25 mg once daily.

Often used in combination with other agents.

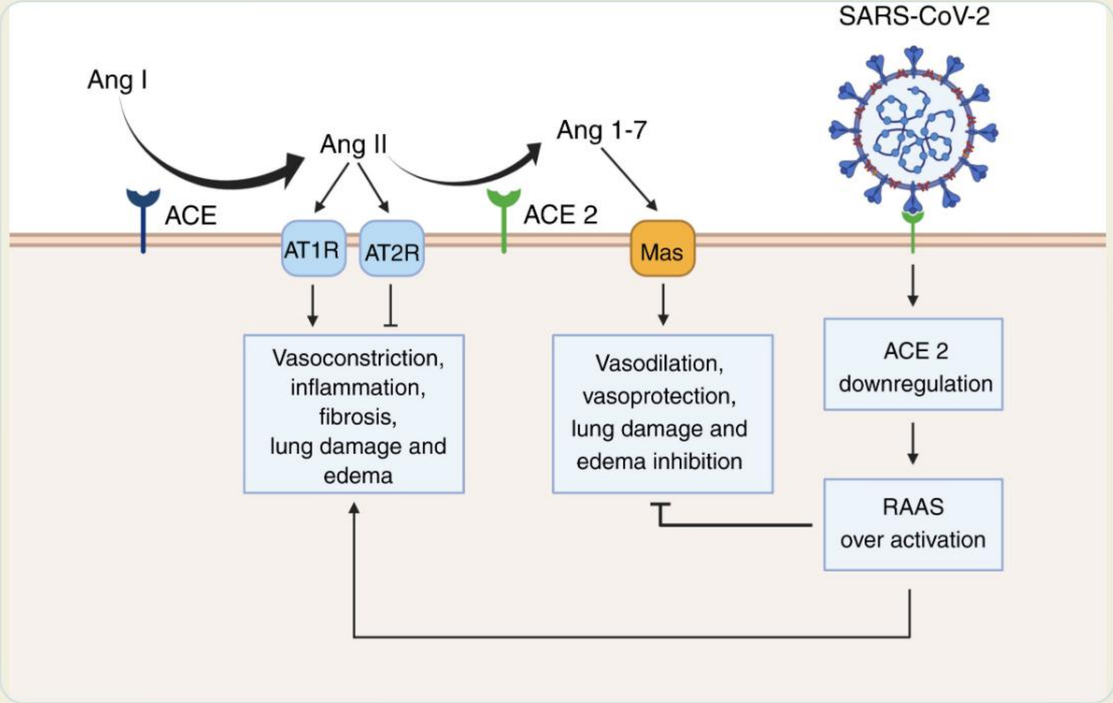
Adverse Effects

Key side effects are related to electrolyte imbalances:

- **Hypokalemia** (low potassium)
- Hyponatremia (low sodium)
- **Hyperuricemia** (can trigger gout)
- Hyperglycemia

Mechanism of Action (Flowchart)

- Angiotensin I (Inactive)
  ↓
- *Angiotensin-Converting Enzyme (ACE)*
- ⛔ **ACE Inhibitor BLOCKS here**
- ~~Angiotensin II (Potent Vasoconstrictor)~~
  ↓
- **Leads to Vasodilation & Reduced BP**



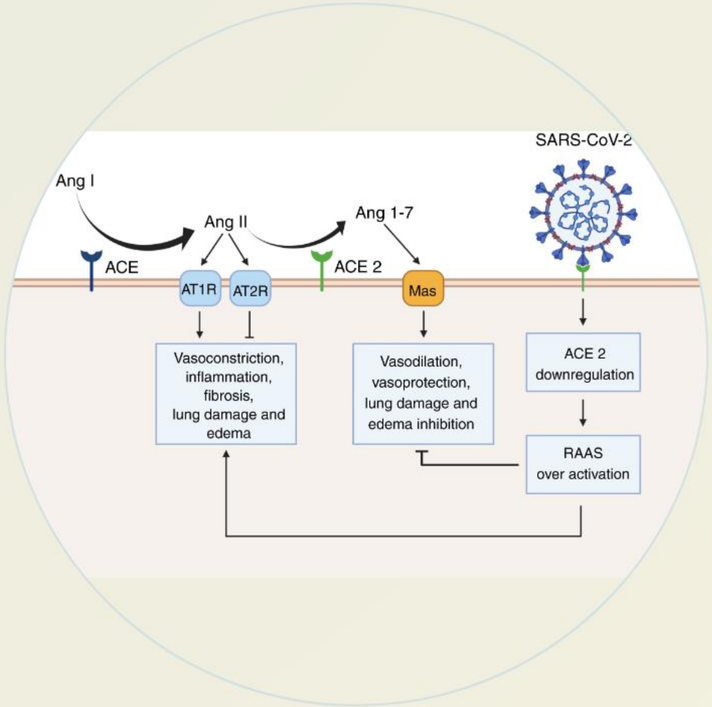
Example & Dosing

Drug: Lisinopril
Brands: Zestril, Prinivil
Dosage: 10 - 40 mg once daily.

Adverse Effects & Contraindications

- **Dry, persistent cough** (due to increased bradykinin)
- Hyperkalemia (high potassium)
- Angioedema (rare, but serious swelling)

Class 3: ARBs (The "-sartans")



Mechanism of Action

Selectively blocks Angiotensin II from binding to its primary receptor (AT_1). This produces similar effects to ACE inhibitors (vasodilation) but works one step further down the pathway.

Example & Dosing

Drug: Losartan
Brand: Cozaar
Dosage: 50 - 100 mg once daily.

Adverse Effects & Contraindications

- Hyperkalemia
- *Much lower* incidence of cough or angioedema compared to ACE-I.
- **Contraindicated in Pregnancy**

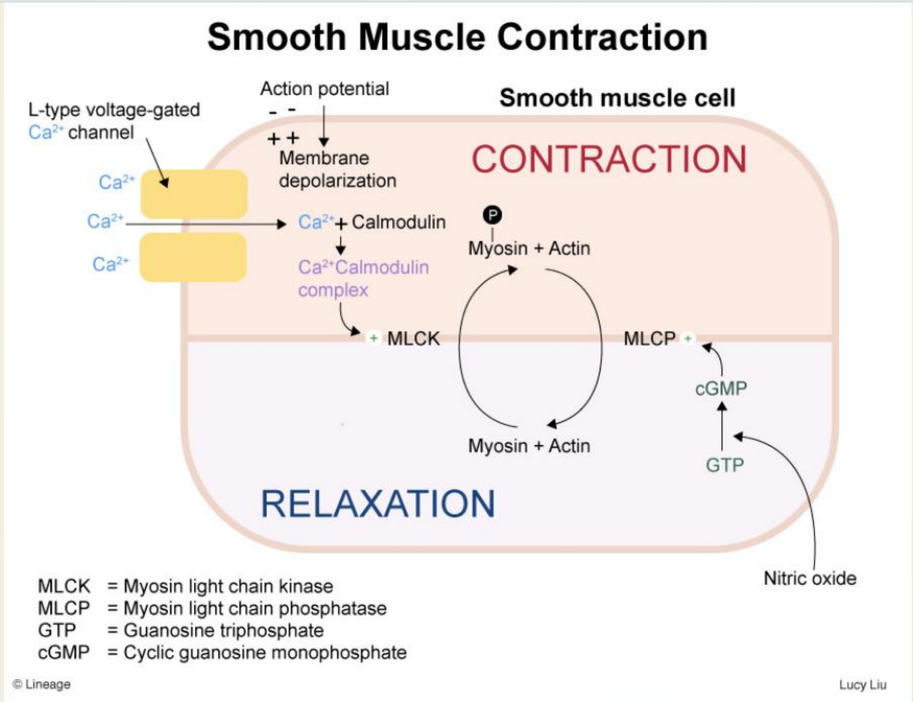
RAAS Blockers: ACE-I vs. ARBs

Feature	ACE Inhibitors (e.g., Lisinopril)	ARBs (e.g., Losartan)
Mechanism	Blocks the **ACE enzyme**	Blocks the **AT_1 receptor**
Effect on Bradykinin	Increases bradykinin levels	No significant effect
Key Side Effect	**Dry Cough**, Angioedema	Lower risk of cough/angioedema
Hyperkalemia Risk	Yes	Yes
Pregnancy	**CONTRAINDICATED**	**CONTRAINDICATED**

Class 4: Calcium Channel Blockers (CCBs)

Mechanism of Action

Blocks L-type calcium channels in vascular smooth muscle, preventing Ca^{2+} influx. This leads to smooth muscle relaxation and systemic vasodilation, lowering peripheral resistance.



Example & Dosing (Dihydropyridine)

Drug: Amlodipine
Brand: Norvasc
Dosage: 5 - 10 mg once daily.

Adverse Effects & Indications

- **Peripheral Edema** (swollen ankles)
- Headache, flushing, dizziness
- Indications: Hypertension, Angina

Primarily block β_1 receptors in the heart. This leads to decreased heart rate (negative chronotropy) and decreased contractility (negative inotropy), which reduces cardiac output and lowers blood pressure.

Example & Dosing

Drug: Metoprolol
Brands: Lopressor (tartrate, BID), Toprol XL (succinate, daily)
Dosage: 50 - 100 mg daily or BID.

Adverse Effects

- **Bradycardia** (slow heart rate)
- Fatigue, dizziness

Pharmacokinetics & Adherence

~80%

of patients may need 2+ drugs

Dosing & Adherence is Key

Pharmacokinetics (PK) determines dosing frequency. Poor adherence is a major cause of treatment failure.

Most first-line drugs are ideal for adherence:

- **Once Daily:** Lisinopril, Losartan, Amlodipine, HCTZ, Metoprolol XL.
- **Twice Daily:** Metoprolol Tartrate (Lopressor).

Once-daily dosing significantly improves patient adherence.

Indications & Contraindications Summary

- **Compelling Indication (Diabetes, CKD):** Start with an **ACE-I or ARB** for their kidney-protective effects.
- **Compelling Indication (Heart Failure):** Must use a combination, typically an **ACE-I/ARB + Beta-Blocker + Diuretic**.
- **Compelling Indication (Post-MI): Beta-Blockers** are essential to reduce mortality.
- **Absolute Contraindication (Pregnancy): AVOID** all RAAS drugs (ACE-I, ARBs, Renin Inhibitors) due to teratogenicity.
- **Absolute Contraindication (Asthma/COPD): AVOID** non-selective Beta-Blockers (e.g., Propranolol) as they can cause bronchospasm.

Questions?

Thank you for your attention.

Image Sources

https://c8.alamy.com/comp/2RHMH81/illustrated-infographic-explaining-how-hypertension-impacts-various-parts-of-the-human-body-2RHMH81.jpg

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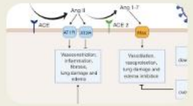

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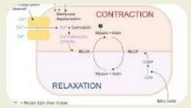

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