Beta-Blockers

A Drug Class Review | Follow-Along & Study Notes

Anthony Busti, MD, PharmD, MSc, FAHA, FNLA

A slower pulse is an effect, not a complete treatment goal. Studying this class means connecting the indication, receptor profile, formulation and drug exposure to the benefit we want—and the problems we need to anticipate.

Start With the Clinical Job

Clinical Goal	What Guides the Choice
Stable HFrEF	Choose an outcome-supported agent and formulation; initiate and titrate when clinically stable. [1]
Uncomplicated hypertension	Other classes are usually first-line. A separate cardiac indication may favor a beta-blocker. [2]
AF ventricular-rate control	Slow AV nodal conduction. Rate control does not restore sinus rhythm or replace stroke-risk assessment. [3]
Angina / after MI	Consider myocardial demand, ventricular function, symptoms and the continuing indication.
Selected noncardiac uses	Match the agent to the specific goal: tremor, migraine prevention or selected physical anxiety symptoms.

Follow along: class properties and receptors (pp. 2–4); mechanisms (pp. 5–9); exposure, benefit and safety (pp. 10–14). Then use the review prompts (p. 15) and reference tables (pp. 17–18).

Watch or Listen to the Full Lecture
YouTube channel · Spotify show · Apple Podcasts show

Learn the Family, Then the Agent

The family provides a starting point. The individual agent, release formulation and clinical evidence determine whether it fits the intended use.

Family	Agents in This Lecture
Relative β_1 preference	Acebutolol, atenolol, bisoprolol, esmolol, landiolol, metoprolol succinate ER, metoprolol tartrate, nebivolol
Nonselective β blockade	Nadolol, pindolol, propranolol, sotalol
β + α_1 blockade	Carvedilol, labetalol

The Formulation Belongs in the Name

Metoprolol succinate extended release (ER) is the HFrEF-supported formulation. Metoprolol tartrate is not an equivalent evidence-based substitution. Likewise, immediate- and extended-release carvedilol products have product-specific schedules and conversion instructions. [1,4,5]

Recognize the Distinguishing Property

- Esmolol and landiolol: rapid offset supports closely monitored IV use. A short offset still requires attention to perfusion.
- Sotalol: beta blockade plus a class III effect introduces QT prolongation and torsades risk; renal function and ECG monitoring matter.
- Acebutolol and pindolol: intrinsic sympathomimetic activity (ISA) means partial agonism. The next page explains why the background signal matters.

> READ PRODUCT STATUS PRECISELY
>
> A discontinued brand, a discontinued formulation, a safety withdrawal and a drug that is no longer preferred are different facts. The larger agent table is on p. 17.

ISA Depends on the Background Signal

A partial agonist can activate a receptor, but less strongly than a full agonist under comparable conditions. Its net effect therefore depends on the sympathetic activity already present.

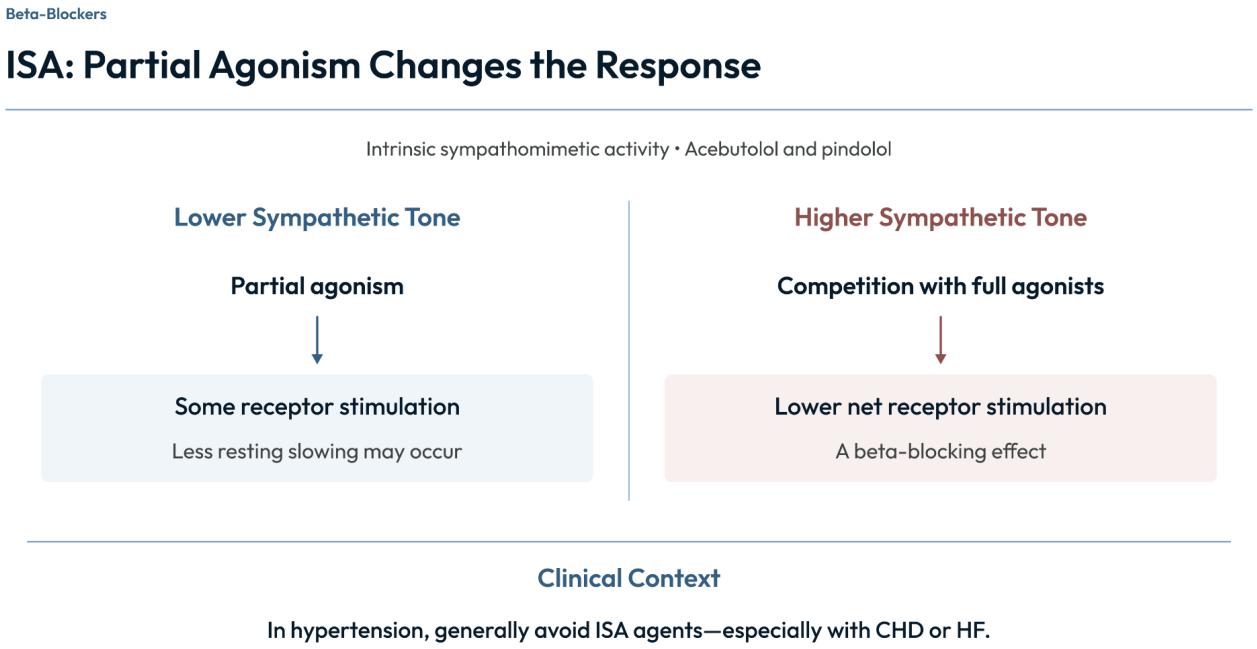


Figure 1. Partial agonism depends on the background catecholamine signal.

Read the Two Conditions Together

With lower sympathetic tone, residual activity can mean less slowing of the resting heart rate. With higher tone, receptor occupancy limits the effects of full agonists, producing a beta-blocking effect relative to that stronger signal.

> CLINICAL PEARL
>
> Less resting bradycardia does not establish better outcomes. ISA agents have a limited current role; hypertension guidance generally advises avoiding them, especially with coronary heart disease or heart failure. [2]

“Cardioselective” Is Not “Heart-Only”

Receptor names describe a preference, not an organ boundary. This map highlights useful connections; an organ can contain more than one subtype. [8]

Location / Receptor	Clinical Connection
Heart: β_1 and β_2	Rate, conduction and contractility; β_1 is central to the familiar cardiac effects.
Kidney JG granular cells: β_1	Renin release from cells in the afferent arteriolar wall near the glomerulus.
Airway smooth muscle: β_2	Activation promotes relaxation; blockade can provoke bronchospasm.
Liver / skeletal muscle / vessels: β_2	Glucose mobilization, tremor and vascular relaxation.
Brain / CNS: β_1 and β_2	CNS entry varies by drug; receptor presence alone does not predict the clinical effect.
Eye: ciliary body, mainly β_2	Beta-blocker drops reduce aqueous formation and intraocular pressure; systemic effects remain possible.
Bladder: β_3	Activation relaxes detrusor during filling; a contrast rather than the usual target of this class.
Vascular smooth muscle: α_1	Carvedilol and labetalol also block α_1, reducing vascular resistance.

CORE CONCEPT

Higher exposure can increase clinically meaningful β_2 blockade. A higher dose, impaired clearance or an interacting drug can change the practical meaning of “β_1 selective.” [4]

Follow the Impulse

In the SA node, reduced adrenergic support slows the approach to threshold. The next impulse occurs later. In atrial fibrillation (AF), ventricular-rate control instead depends on conduction through the AV node. [3,8]

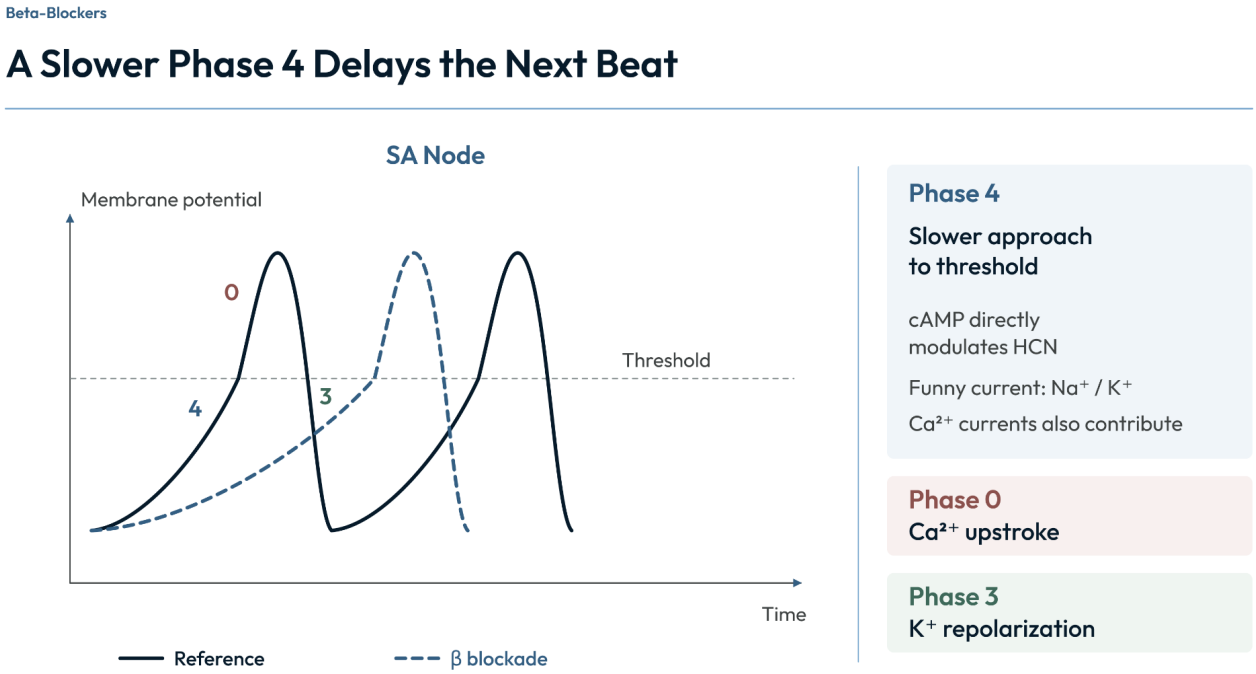


Figure 2. Reduced adrenergic support delays the next sinus impulse.

Structure	Effect of β Blockade	Clinical Meaning
SA node	↓ Automaticity	Slower sinus rate
AV node	↓ Conduction; increased refractoriness	Slower ventricular response in AF

AF can persist despite a lower ventricular rate. Diltiazem/verapamil block L-type Ca^{2+} channels; digoxin adds vagal AV nodal slowing. Ivabradine inhibits the HCN funny current and is not a substitute for AV nodal rate control in AF. [3]

Calcium Links Signaling to Force

In a working cardiomyocyte, β1 signaling increases adrenergic support for calcium handling. The figure shows stimulation of the pathway; a beta-blocker reduces that amplification upstream at the receptor.

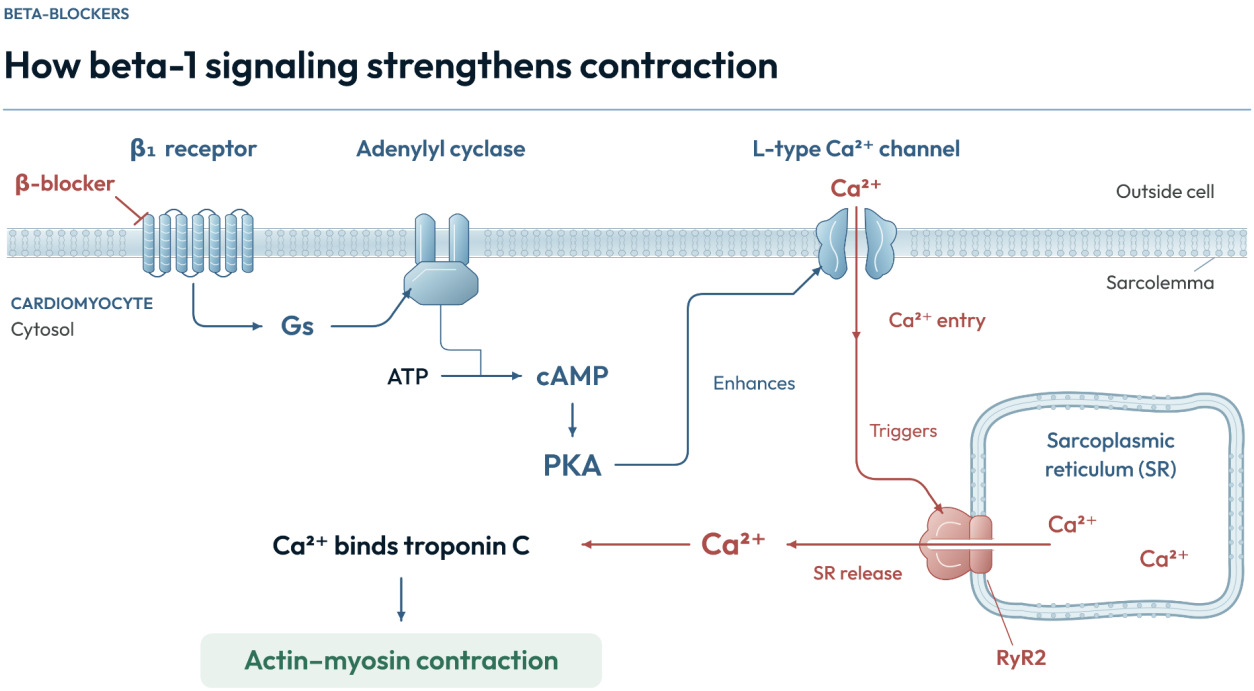


Figure 3. β1 signaling amplifies calcium entry and SR release. [7,8]

From a Small Entry to a Larger Release

Calcium entering through L-type channels helps open RyR2 channels in the SR. The released calcium binds troponin C, allowing actin and myosin to generate force. This is calcium-induced calcium release.

> CONNECT THE TARGET TO THE EFFECT
>
> Beta-blockers act at adrenergic receptors. Diltiazem and verapamil act directly on L-type calcium channels. Some downstream effects overlap, but their molecular targets differ.

Relaxation Requires Calcium Removal

A heartbeat requires cytosolic calcium to rise and then fall. SERCA uses ATP to return calcium to the SR. The figure isolates this connection; other calcium-removal pathways also contribute.

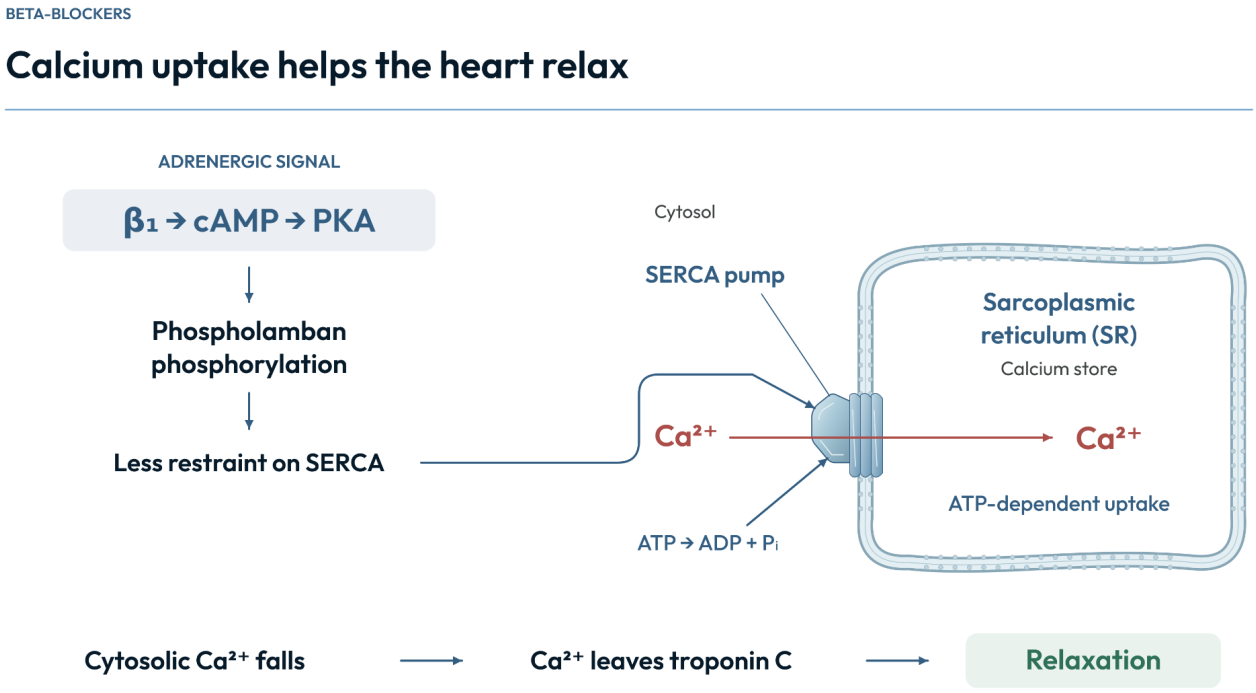


Figure 4. SERCA returns calcium to the sarcoplasmic reticulum (SR). [7,8]

Why Stronger Contraction Can Accompany Faster Relaxation

PKA phosphorylates phospholamban, relieving its restraint on SERCA. As calcium falls, it leaves troponin C and the cell relaxes. Adrenergic stimulation supports both contraction and relaxation; beta blockade reduces that stimulation, while a slower rate allows more time between beats.

> KEEP PHYSIOLOGY AND OUTCOMES DISTINCT
>
> An immediate reduction in force explains an initiation risk. It does not establish the long-term result in stable HFrEF; clinical trials answer the questions about hospitalization and survival. [1]

Place the Effect in the Circulation

Cardiac output equals heart rate multiplied by stroke volume. Pressure also depends on vascular resistance. Because these variables interact, the same rate change can have different effects on perfusion. [8]

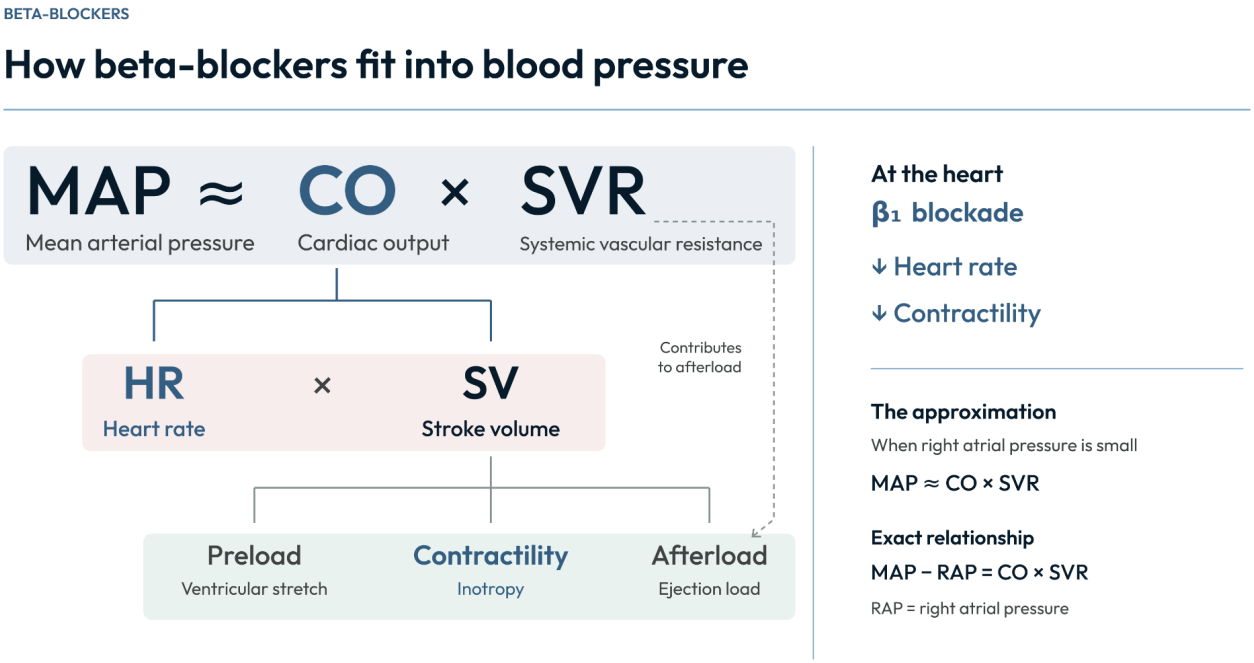


Figure 5. Connect pressure, cardiac output and the determinants of stroke volume.

Use the Relationships, Not Just the Abbreviations

Preload is filling-related stretch before contraction. Contractility is force generation at a given loading condition. Afterload is the load against which the ventricle ejects; systemic vascular resistance contributes to it.

> CLINICAL PEARL
>
> Slowing a very rapid rate may improve filling and stroke volume. Suppressing a compensatory tachycardia may reduce output. Interpret the rate together with the cause, symptoms and perfusion.

The Kidney Adds a Second Connection

Juxtaglomerular (JG) granular cells lie in the afferent arteriolar wall. β_1 signaling supports cAMP and renin release. The nearby macula densa is tubular epithelium; it is not the renin-secreting cell. [8]

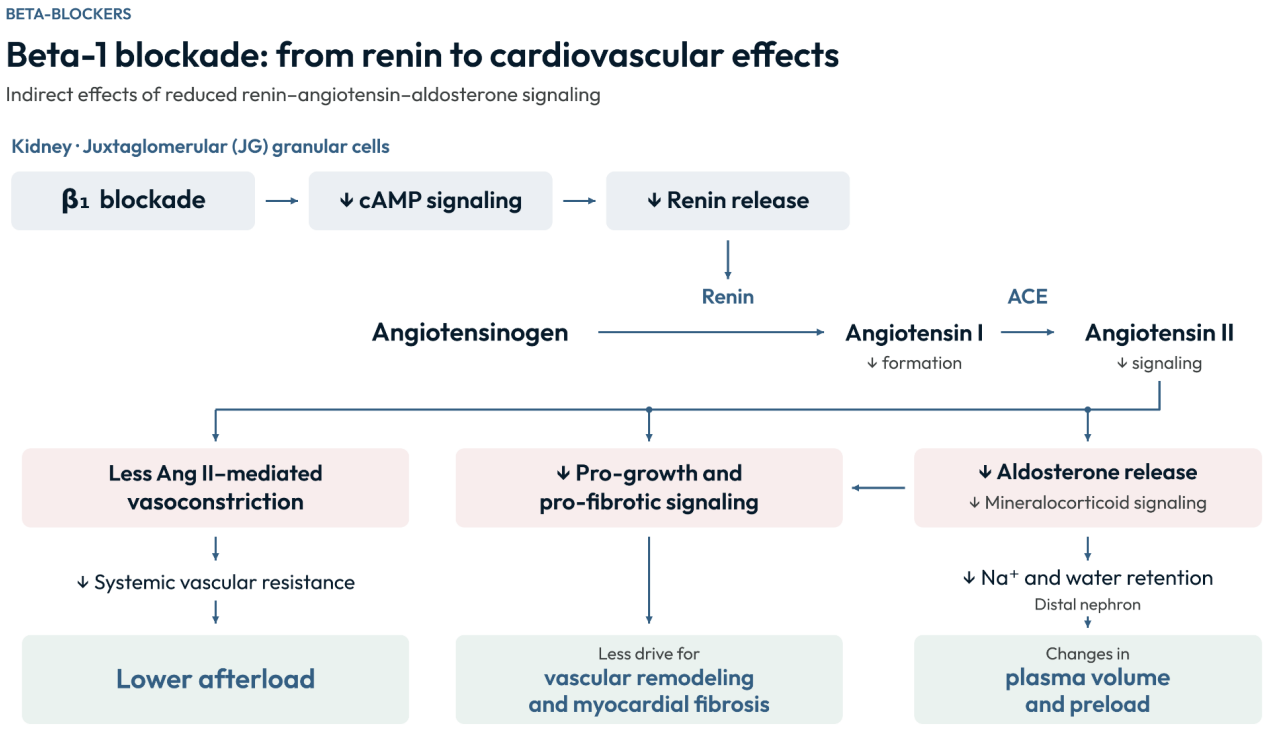


Figure 6. Reduced renin input influences vascular resistance, remodeling and volume.

Follow the Three Consequences

- Less angiotensin II–mediated vasoconstriction can reduce vascular resistance and afterload.
- Reduced pro-growth and pro-fibrotic signaling provides a connection to cardiovascular remodeling.
- Less aldosterone signaling reduces sodium and water retention, influencing plasma volume and preload.

Clinical connection: renin suppression is not direct ACE inhibition, angiotensin-receptor blockade or mineralocorticoid-receptor blockade. A beta-blocker does not rapidly treat substantial fluid overload or replace other indicated HF therapy.

The Same Dose Can Act Differently

Clearance affects exposure: atenolol, nadolol and sotalol rely substantially on renal elimination; bisoprolol has mixed renal and metabolic elimination; esmolol is hydrolyzed by red-cell esterases.

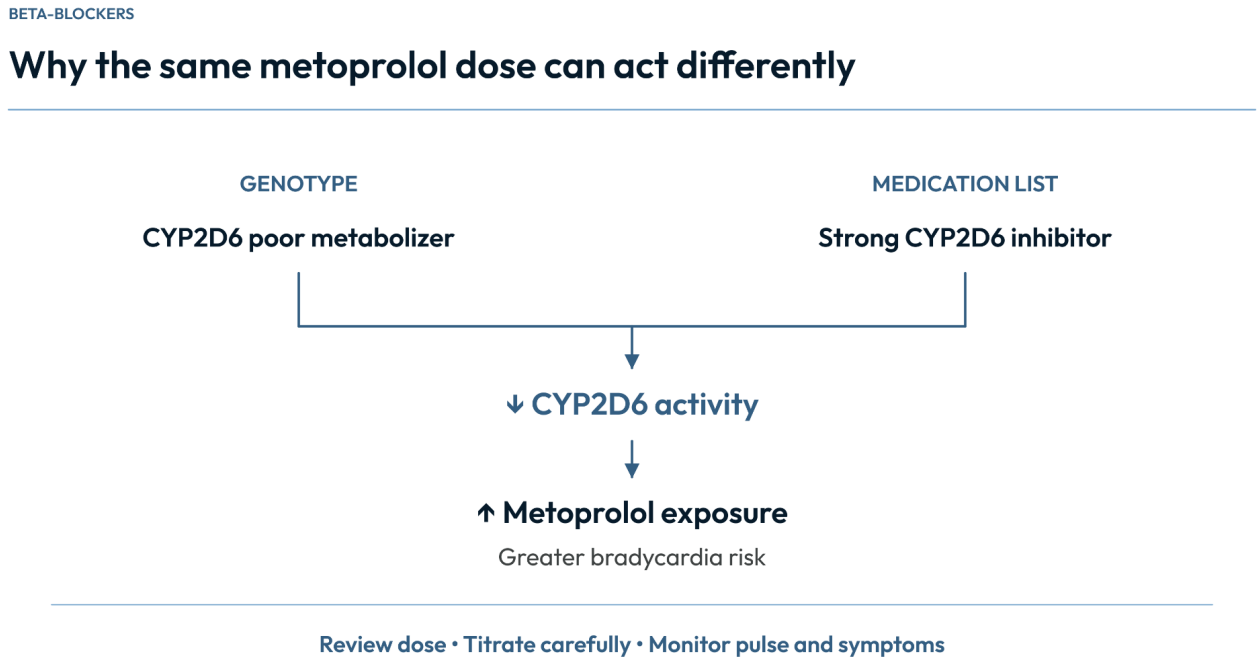


Figure 7. Genotype and enzyme inhibitors can increase metoprolol exposure. [4,6]

Review the Medication List as Part of the Mechanism

CYP2D6 inhibitors such as fluoxetine, paroxetine and bupropion can increase metoprolol exposure. This change in metabolic activity is called phenoconversion. Separately, verapamil, diltiazem and digoxin can add nodal slowing. [3,4,6]

> WHEN A POOR-METABOLIZER RESULT IS KNOWN
>
> CPIC advises the lowest recommended metoprolol starting dose, careful titration and closer bradycardia monitoring, or consideration of an alternative. This does not recommend testing every beta-blocker recipient. [6]

HFrEF: Effect Today, Benefit Over Time

How can reduced contractility accompany long-term benefit? β blockade can initially reduce rate and force. In chronic, stable heart failure with reduced ejection fraction (HFrEF), selected agents improve outcomes. These are different time scales and questions. [1]

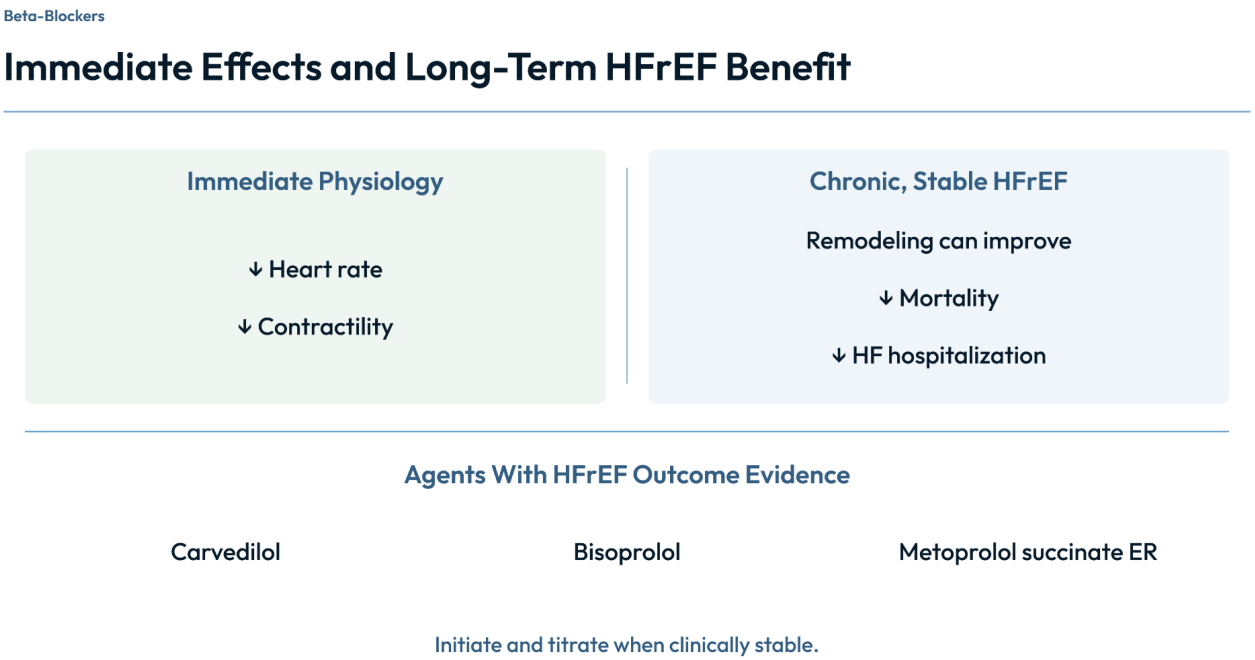


Figure 8. Immediate physiology and long-term HFrEF benefit differ. [1]

Separate Three Types of Benefit

- Physiologic: a change such as a lower pulse or reduced contractile drive.
- Symptomatic: an improvement such as less angina or fewer palpitations.
- Clinical outcome: fewer heart-failure hospitalizations or deaths in the studied population.

The treatment goal depends on the indication. A mechanism helps explain the effect; it cannot substitute for the clinical evidence supporting the specific drug and regimen.

Initiate Low, Reassess, Then Titrate

Starting doses allow assessment of tolerability before approaching the target. Begin when clinically stable; reassess symptoms and perfusion before each increase. [1,4,5]

Agent / Formulation	Starting Dose	Target if Tolerated
Bisoprolol	1.25 mg once daily	10 mg once daily
Carvedilol immediate release	3.125 mg twice daily	25 mg twice daily*
Metoprolol succinate ER	12.5–25 mg once daily	200 mg once daily

All doses above are oral and specific to stable adult HFrEF. *The guideline target range for carvedilol extends to 50 mg twice daily; labeling describes that higher dose in selected patients with mild-to-moderate HF weighing >85 kg. [1,4,5]

Before the Next Increase

- Ask about dizziness, presyncope, fatigue, exercise tolerance, breathlessness, swelling and weight change.
- Interpret heart rate and blood pressure with symptoms, perfusion and fluid status.
- Recheck the formulation, adherence and other drugs that affect exposure, rate or conduction.

Metoprolol succinate labeling describes doubling at two-week intervals as tolerated; carvedilol labeling uses intervals of at least two weeks. Clinical stability and tolerability determine the actual pace. Carvedilol immediate release is taken with food. [4,5]

> WHEN THE PATIENT WORSENS
>
> Treat heart failure exacerbation due to fluid overload. Reconsider titration with symptomatic bradycardia or poor perfusion. Admission alone does not automatically require stopping established therapy. [1,4,5]

Hypoglycemia: Why Sweating Can Persist

Beta blockade may blunt the tachycardic warning of hypoglycemia. Sweating can persist because the sympathetic pathway to eccrine glands uses a different postganglionic transmitter and receptor. [4,8]

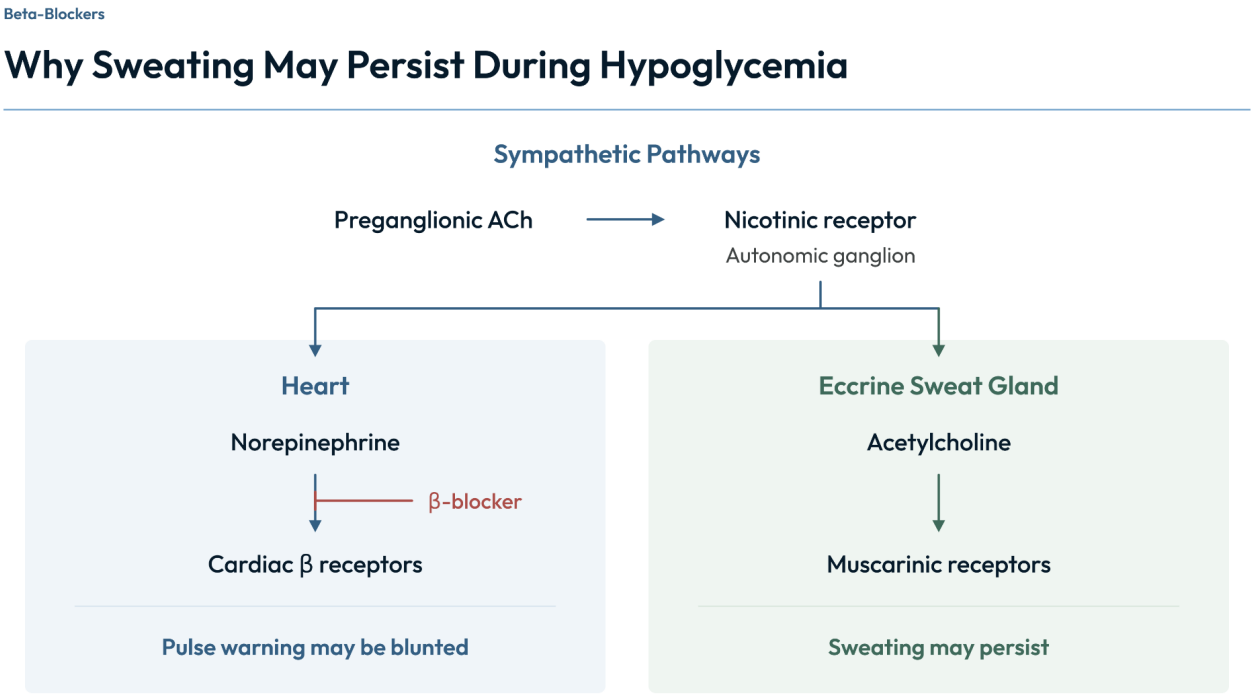


Figure 9. The cardiac and sweat-gland sympathetic pathways diverge.

Trace the Transmitter Before Naming the Effect

Cardiac postganglionic signaling uses norepinephrine at adrenergic receptors. Eccrine sweat glands receive acetylcholine at muscarinic receptors. A beta-blocker does not directly block that muscarinic connection.

> CLINICAL PEARL
>
> Nonselective blockade may also impair glucose recovery. Use glucose monitoring and a response plan; do not rely on pulse or sweating alone. Diabetes does not automatically exclude an otherwise indicated beta-blocker. [4]

Apply the Mechanism at the Bedside

The intended effect can become the reason for intolerance. A low pulse in a comfortable, well-perfused patient differs from the same pulse with syncope or deteriorating circulation.

Check	What the Finding May Mean
Pulse, ECG, perfusion	Excess nodal slowing can cause bradycardia or block. Shock and unstable HF change treatment decisions.
Airway symptoms	β_2 blockade can provoke bronchospasm, especially in asthma. β_1-preferring drugs may be used cautiously for a cardiac indication in COPD; risk is not zero.
BP, dizziness, fluid status	Reduced output or vascular effects may cause intolerance. Review symptoms, perfusion and the complete medication list—including eye drops.

> A DIFFERENT PATHWAY IN AF
>
> Hemodynamic instability attributable to AF calls for urgent electrical cardioversion. In preexcited AF, AV nodal blockers—including beta-blockers—are contraindicated. Diagnose the rhythm before applying routine rate control. [3]

Keep Noncardiac Uses Specific

Propranolol: essential tremor and migraine prevention are different goals from selected performance-related physical symptoms. Anxiety use is off-label; evidence does not establish a comprehensive treatment for anxiety disorders.

Portal hypertension: nonselective blockade reduces portal inflow; carvedilol adds an effect on intrahepatic resistance. A β_1-preferring agent is not an equivalent substitution. Thyrotoxicosis: symptom control does not stop thyroid hormone synthesis.

Explain the Why Without the Slide

Use each prompt before reading the answer. Name the mechanism, then its clinical implication.

1. Why is a slower pulse not enough to choose a beta-blocker?

The indication, receptor profile, formulation, exposure and outcome evidence must fit the goal. The same pulse can arise from different mechanisms.

2. Which node explains ventricular-rate control during AF?

The AV node. Reduced conduction and increased refractoriness limit impulses reaching the ventricles; sinus-node slowing does not explain this effect.

3. Why might an unchanged metoprolol dose cause new bradycardia?

A CYP2D6 inhibitor or reduced metabolic activity can raise exposure. Other nodal drugs may add to the effect; assess symptoms and hemodynamics.

4. Why can sweating persist during hypoglycemia?

Eccrine sweating uses sympathetic acetylcholine–muscarinic signaling, which beta blockade does not directly block.

> THE FIVE-PART CHECK
>
> Indication → Agent + formulation → Mechanism → Exposure → Patient response.
> After MI, reassess ventricular function and ongoing indications. Starting, continuing and withdrawing treatment are different evidence questions.

When discontinuation is appropriate, plan a supervised, gradual withdrawal rather than abrupt cessation. Use the full lecture for the trial comparisons and specialized treatment contexts.

A Connection to Explain in My Own Words

Selected Sources & Further Reading

The numbered references support the core mechanisms and clinical principles in these notes.

[1] 2022 AHA/ACC/HFSA Heart Failure Guideline. Beta-blocker recommendation, Table 14 and hospitalization guidance.

[2] 2025 AHA/ACC Hypertension Guideline. Initial drug selection and ISA context.

[3] 2023 ACC/AHA/ACCP/HRS Atrial Fibrillation Guideline. Rate control and preexcitation.

[4] TOPROL-XL prescribing information. Dosing, interactions, warnings and pharmacology.

[5] Carvedilol prescribing information. Heart-failure dosing and tolerability.

[6] Duarte et al. CPIC beta-blocker guideline (2024). Metoprolol/CYP2D6 recommendations.

[7] Cardiovascular Research (2014). SERCA/troponin calcium handling during β-adrenergic stimulation.

[8] OpenStax Anatomy and Physiology 2e. Chapters 15, 19, 20 and 25: autonomic pathways, circulation and kidney.

Adapted from the supplied approved lecture script and its evidence record, using the current supplied image revisions. Brief explanations connect the figures to the clinical teaching; they do not reproduce every trial comparison or specialized protocol in the full lecture.

Abbreviations Used in the Notes

AF atrial fibrillation · AV atrioventricular · BP blood pressure · ER / IR extended / immediate release · HF heart failure · HFrEF heart failure with reduced ejection fraction · ISA intrinsic sympathomimetic activity · IV / PO intravenous / oral · MI myocardial infarction · SA sinoatrial · SR sarcoplasmic reticulum

Agent Reference

BETA-BLOCKERS

U.S. Systemic Agents

Common Beta-Blockers in Clinical Practice

Generic Name	Brand Name	Dosage Forms	Notes
Beta-1 Selective Blockers			Selectivity Is Relative
Acebutolol	Sectral (brand discontinued)	PO: capsules	ISA
Atenolol	Tenormin	PO: tablets	
Bisoprolol	Zebeta (brand discontinued)	PO: tablets	
Esmolol	Brevibloc	IV: injection / infusion	Rapid onset (IV)
Landiolol	Rapiblyk	IV: powder for infusion	Rapid onset (IV)
Metoprolol Succinate ER	Toprol-XL; Kapspargo Sprinkle	PO: ER tablets / capsules	
Metoprolol Tartrate	Lopressor (PO)	PO: IR tablets, solution; IV: injection	Rapid onset (IV)
Nebivolol	Bystolic	PO: tablets	Full BP benefit: ~2 weeks
Non-Selective Beta-Blockers			
Nadolol	Corgard (brand discontinued)	PO: tablets	Long duration
Pindolol	Visken (brand discontinued)	PO: tablets	ISA
Propranolol	Inderal LA / XL; InnoPran XL Hemangeol (PO; infantile hemangioma)	PO: tablets, ER capsules, solution IV: injection (generic)	Rapid onset (IV)
Sotalol	Betapace / Betapace AF; Sorine; Sotylize	PO: tablets, solution; IV: infusion	Class III effect
Beta-Blockers With Alpha-1 Blocking Activity			
Carvedilol	Coreg; Coreg CR	PO: IR tablets / ER capsules	
Labetalol	Trandate / Normodyne (brands discontinued)	PO: tablets; IV: injection / infusion	Rapid onset (IV)

Read status precisely: “brand discontinued” does not mean the generic drug has been withdrawn. This is the supplied U.S. lecture inventory, not a live stock or shortage check.

Clearance & Administration Reference

BETA-BLOCKERS

Beta-blocker clearance at a glance

Selected agents • Usual adult schedules

ER = extended release

DRUG	DISTRIBUTION	MAIN CLEARANCE	ROUTE & FREQUENCY	CLINICAL NOTES
Atenolol	Hydrophilic	Renal excretion	Oral: usually once daily	Kidney function
Bisoprolol	Hydrophilic + lipophilic	Renal + hepatic	Oral: once daily	Kidney + liver function
Carvedilol	Lipophilic	Hepatic metabolism CYP2D6 + CYP2C9	Oral: immediate release twice daily Extended release once daily	Take with food; avoid in severe hepatic impairment
Esmolol	Hydrophilic	Red-cell esterases	IV: continuous infusion With or without a loading bolus	Rapid infusion titration
Labetalol	Lipophilic	Hepatic glucuronidation	Oral: usually twice daily; sometimes 3×/day IV: repeat boluses every 10 min or continuous infusion	Orthostatic hypotension
Metoprolol	Lipophilic	Hepatic CYP2D6	Oral: tartrate usually twice daily; succinate extended release once daily IV: every 2 min × 3 boluses (acute MI)	Genotype + inhibitors
Nadolol	Hydrophilic	Renal excretion	Oral: usually once daily	Renal-based dosing interval
Nebivolol	Lipophilic	Hepatic metabolism Glucuronidation + CYP2D6	Oral: once daily	CYP2D6 inhibitors; active metabolites
Propranolol	Lipophilic	Hepatic metabolism CYP2D6 / 1A2 / 2C19	Oral: immediate release 2–4×/day; ER daily IV: slow bolus; may repeat once after 2 min Then wait ≥4 h before further IV doses	Extensive first-pass metabolism
Sotalol	Hydrophilic	Renal excretion	Oral: usually every 12 h IV: loading or oral-substitution infusion	QT monitoring + renal-based dosing interval

Keep the context: these selected adult schedules are not a complete dosing protocol. Distribution is a useful pattern; the actual elimination pathway guides adjustment. Check the current label, indication, organ function and monitoring requirements.