Medications for Heart Failure

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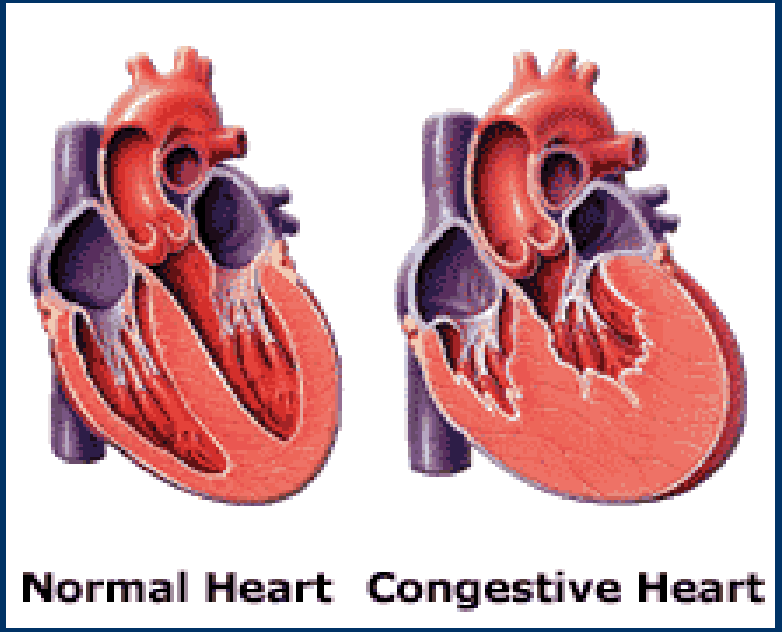
Causes of Heart Failure:
Multifactorial

- Hypertension
- Coronary artery disease (CAD)
- Diabetes
- Mitral valve disease
- Alcohol



NYHA Classification of HF

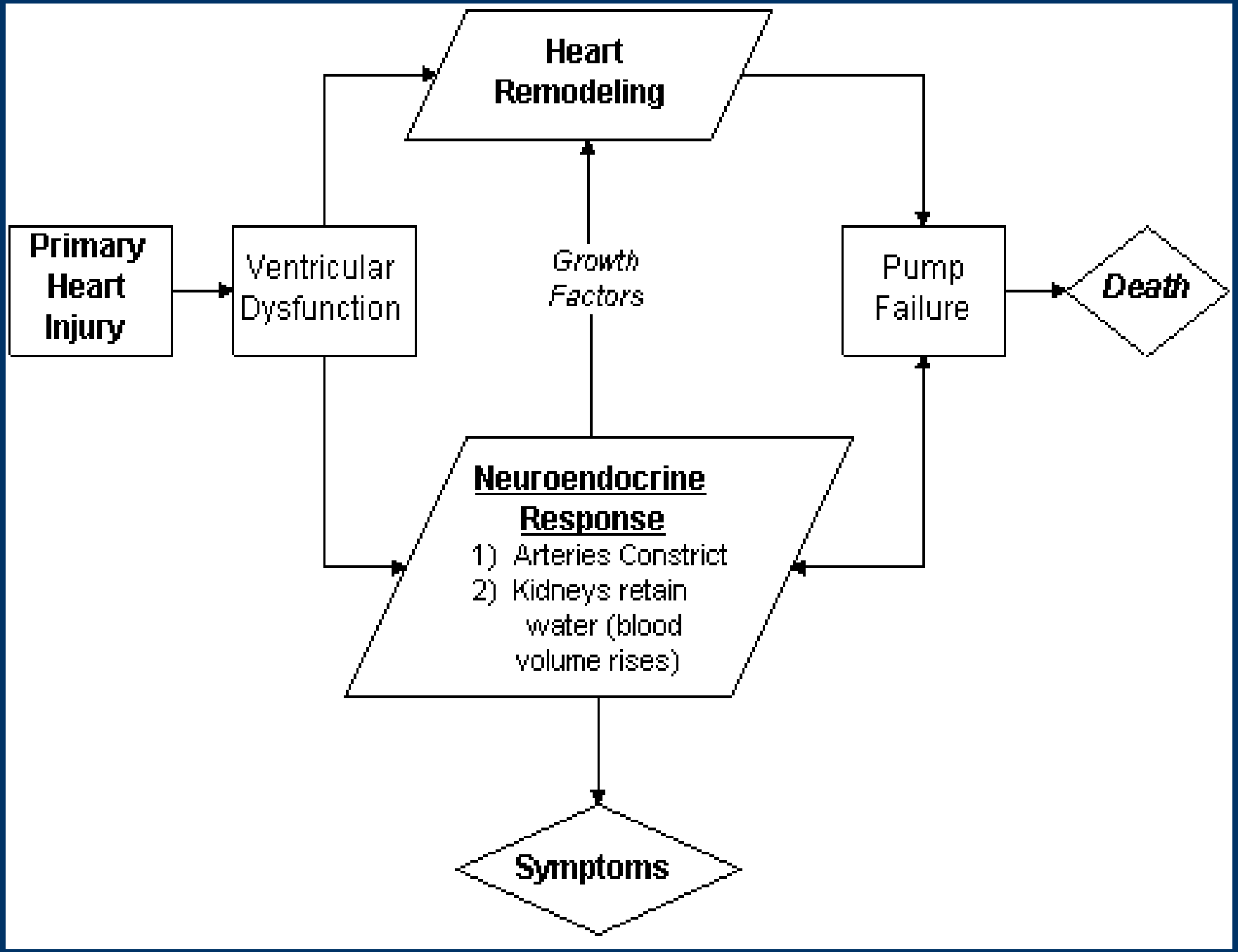
Class	Description
I	No limitations in physical activity by HF symptoms
II	Symptoms of HF with normal level of activity
III	Marked limitations in physical activity because of HF symptoms
IV	Symptoms of HF at rest

NYHA = New York Heart Association
HF = Heart failure

ACCF/AHA Staging

Stage	Description
A	At high risk for HF but without structural heart disease or symptoms
B	Structural heart disease but without symptoms
C	Structural heart disease with prior or current symptoms
D	Refractory HF requiring specialized interventions

ACCF = American College of Cardiology Foundation
AHA= American Heart Association



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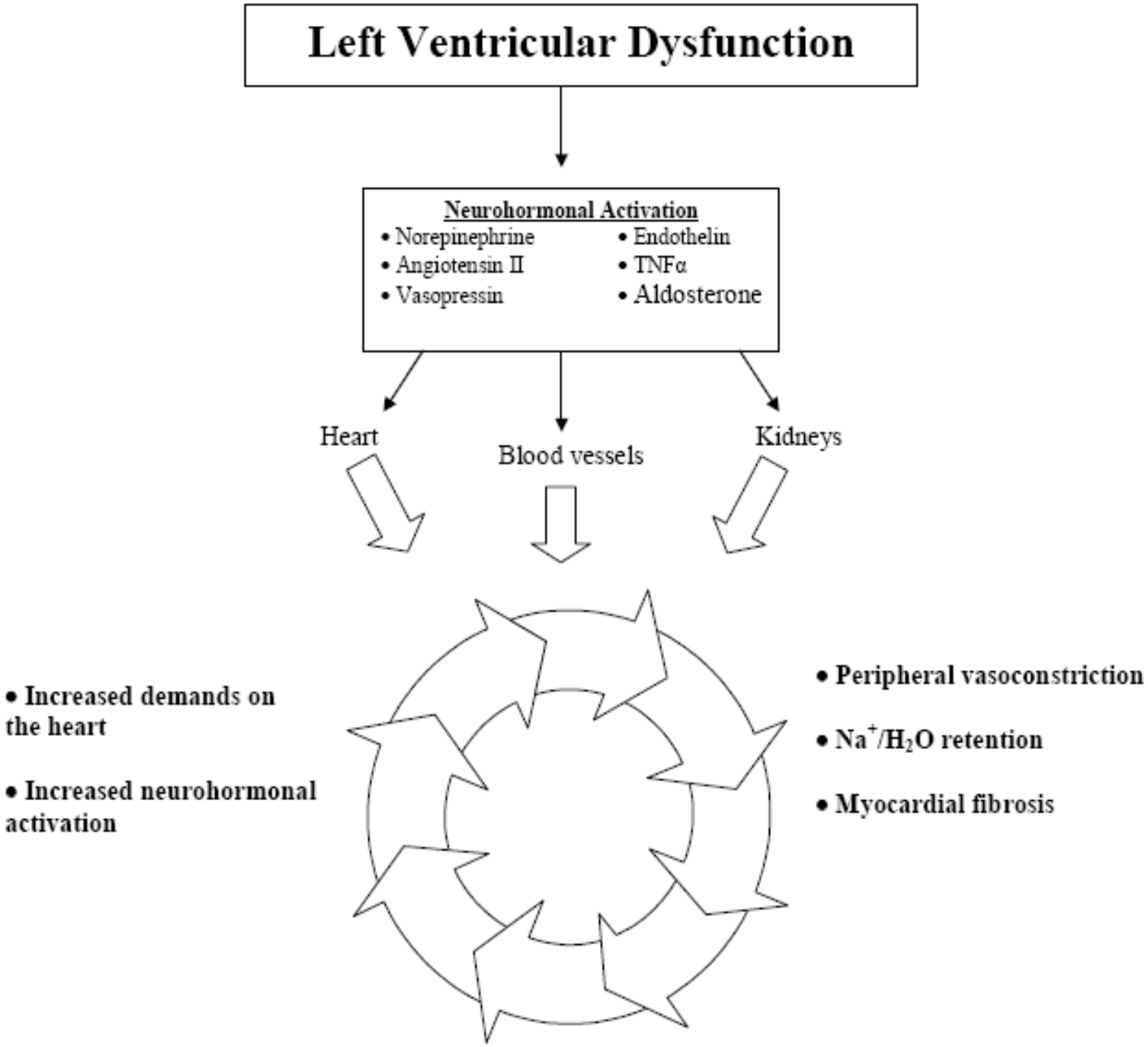


Figure 1.
H_2O = water; Na = sodium; TNFα = tumor necrosis factor alpha.

Goals of Pharmacological Treatment of Heart Failure

- Improve symptoms
- Slow and reverse deterioration of heart function
- Prolong survival

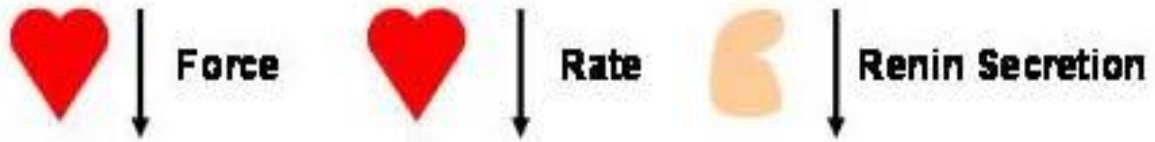
Classes of Heart Failure Medications

- Beta blockers
- ACE-Inhibitors
- ARBs
- Hydralazine and nitrates
- Aldosterone antagonists
- Diuretics
- Digoxin

BETA BLOCKERS: 1st line (↓M/M)

How do beta blockers work?

Blockade of the Beta$_1$ Receptor Blockers



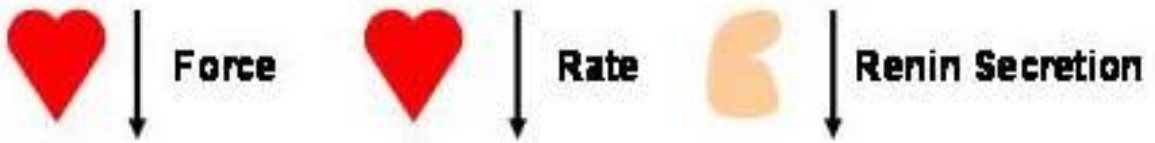
Blockade of the Beta$_2$ Receptor Blockers

***Piascik, University of Kentucky lecture: The Pharmacology of Adrenergic Receptors**

BETA BLOCKERS: 1st line (↓M/M)

- How do beta blockers work?
  - **Slow heart rate (allow more filling of the ventricles)**
  - **Improve cardiac output**
- Who should take them?
  - Heart failure (EF ≤ 40%) - *symptomatic*
  - Prior myocardial infarct (MI)
- Preferred (**β1 > β2**)
  - Carvedilol (has α-1 inhibition)
  - Metoprolol succinate
  - Bisoprolol

Blockade of the
Beta$_1$ Receptor Blockers



β1 >> β2

Blockade of the
Beta$_2$ Receptor Blockers → **Worsens asthma**

*Piascik, University of Kentucky lecture: The Pharmacology of Adrenergic Receptors

BETA BLOCKERS: 1st line (↓M/M)

- Dosing
  - Start **LOW** and titrate to target doses

Drug	Initial	Target
Carvedilol	**3.125mg BID**	**25mg BID**
Metoprolol succ.	**12.5mg daily**	**200mg daily**
Bisoprolol	**1.25mg daily**	**10mg daily**

- Side effects
  - Bradycardia, dizziness, bronchospasm, fatigue
- Contraindications
  - Acute cardiac failure, significant bradycardia, shock, active bronchospasm, sick sinus syndrome

CLINICAL QUESTION

- Q: Mr. Mouse has a history of heart failure and has been taking metoprolol succinate 100mg po daily. He has recently been diagnosed with type II diabetes. What other medication should he be taking?

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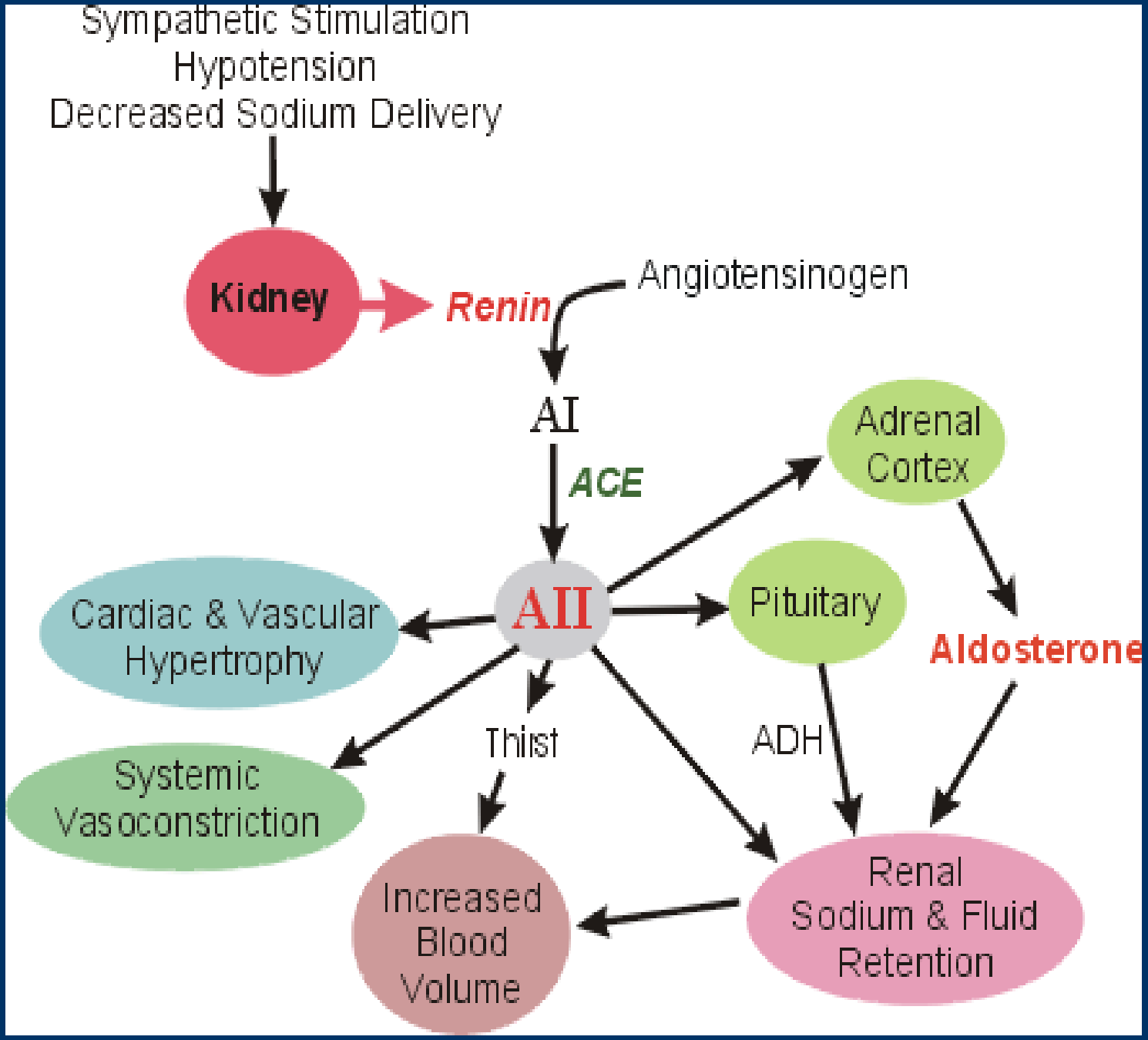
ACE-Inhibitor

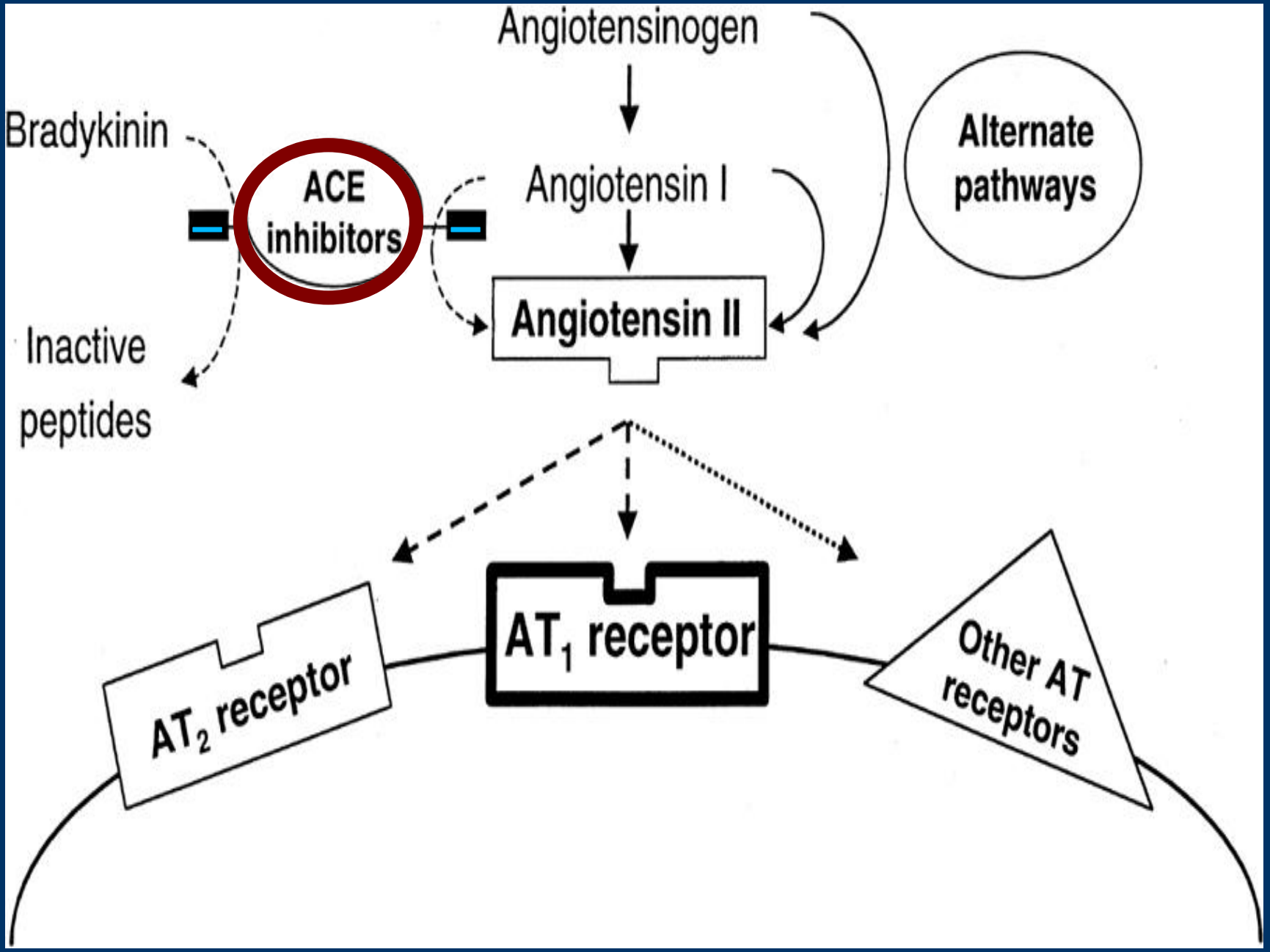
ACE-I: 1st line (↓M/M)

Angiotensin converting enzyme inhibitors

How do ACE-I work?



*CV pharmacology.org



***Weir, American Journal of Hypertension 2011, *Nature*: Diabetes and Hypertension**

ACE-I: 1st line (↓M/M)
Angiotensin converting enzyme inhibitors

- How do ACE-I work?
  - Block the enzyme that converts angiotensin I to II
  - **Lower blood pressure, block harmful neurohormones**

- Who should take them?
  - Heart failure (EF ≤ 40%) - *symptomatic OR asymptomatic*
  - High risk for HF:
    - CAD
    - Peripheral vascular disease
    - Prior stroke
    - Diabetes (with another risk factor or who also smoke)

ACE-I: 1st line (↓M/M)

- Dosing
  - Start LOW and titrate to target doses
- Preferred: ACE-I over ARBs

Drug	Initial	Target
Captopril	**6.25mg TID**	**50mg TID**
Enalapril	**2.5mg BID**	**10-20mg BID**
Lisinopril	**2.5-5mg daily**	**20-40mg daily**

*Captopril: can be given sublingually

ACE-I: 1st line (↓M/M)

- Side effects
  - Hypotension, dizziness, renal insufficiency, angioedema, hyperK+, dry cough
  - **LABS: Scr, K+**
- Contraindications
  - Acute renal failure, hyperK+, pregnancy, bilateral renal stenosis, angioedema (caused by ACE-I)

CLINICAL QUESTION

- Mrs. Mouse comes to clinic complaining of an irritating dry cough since starting her lisinopril several months ago and refuses to keep taking it. What other medication can she take?

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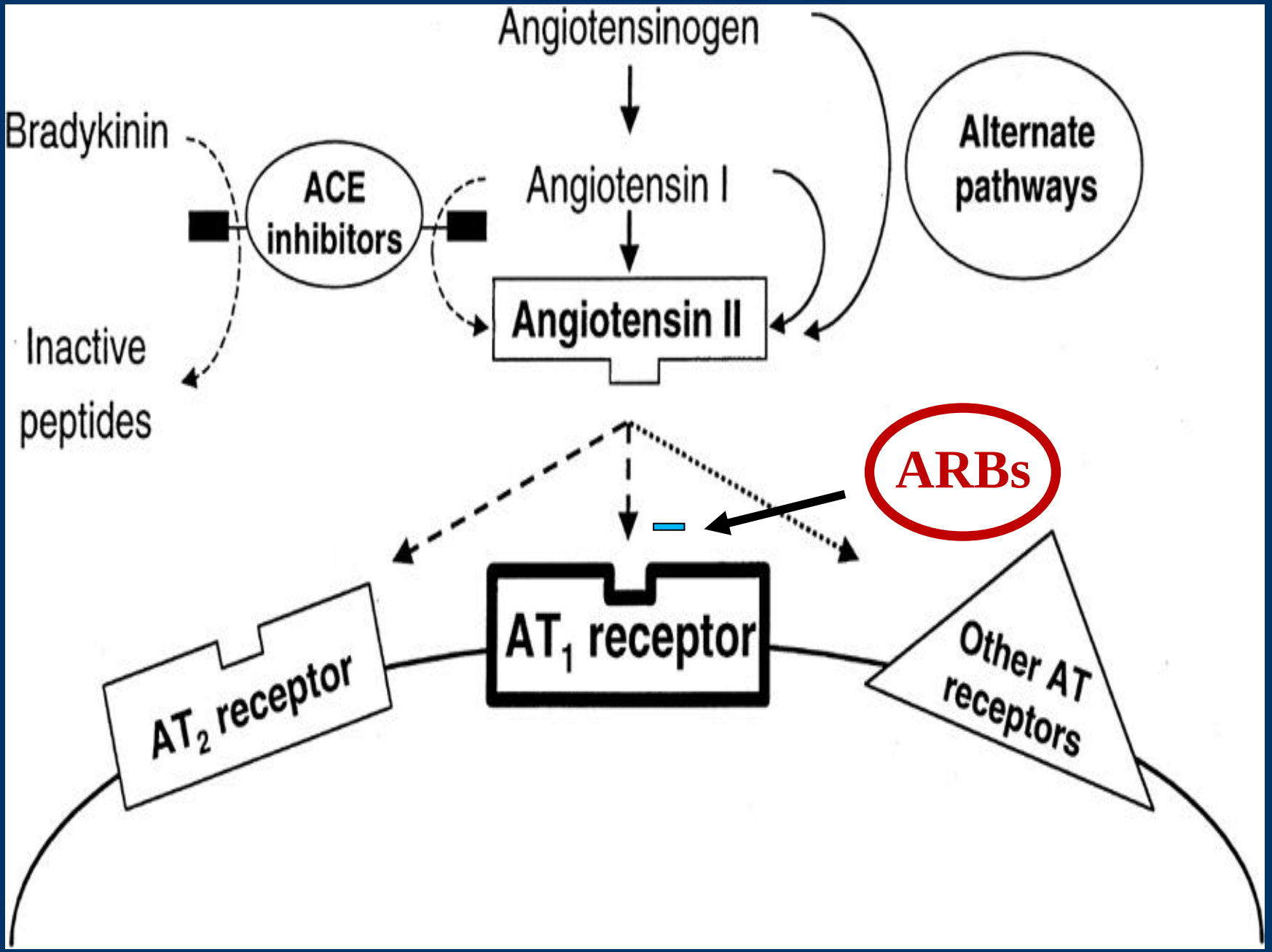
ARBs
(Angiotensin Receptor Blockers)



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ARBs: 1st line (↓M/M)
Angiotensin receptor blockers

- How do ARBs work?
  - Block angiotensin II at the AT1 receptor
- Who should take them?
  - Fail ACE-Inhibitors due to cough
  - ACE-I and ARB combo – generally NO
- Disadvantages: less clinical studies, $$

Drug	Initial	Target
Losartan	12.5-25mg daily	150mg daily
Valsartan	40mg BID	160mg BID

CLINICAL QUESTION

- Mr. Duck is an African American with severe heart failure who still has symptoms (edema, SOB) while on a beta blocker, ACE-I, and high dose furosemide. What medication combination might help Mr. Duck?

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Hydralazine and Nitrates

Hydralazine/nitrates: 1st line (↓M/M)*
Vasodilators

- How do they work?
  - Nitrates (isosorbide dinitrate): releases nitric oxide, dilates arteries and veins
  - Hydralazine: dilates arteries, prevents nitrate tolerance

- Who should take them?
  - African Americans with NYHA III-IV (AHeFT) already on ACE-I and beta blocker

Drug	Initial	Target
Hydralazine	**10-25mg 3-4 x/day**	**225-300mg/day**
Isosorbide dinitrate	**20mg 3-4x/day**	**240mg/day (max)**

Hydralazine/nitrates: 1st line (↓M/M)*
Vasodilators

- Side effects:
  - Headache, dizziness, hypotension, drug-induced lupus syndrome (hydralazine)
- Contraindications:
  - Concurrent use of phophodiesterase-5 inhibitors (ie Viagra)

CLINICAL QUESTION

- Mrs. Duck has severe heart failure (LVEF<20%) and still has symptoms (edema, dyspnea) while on a beta blocker, ACE-I, and high dose furosemide. What additional medication might help Mrs. Duck?

CLINICAL QUESTION

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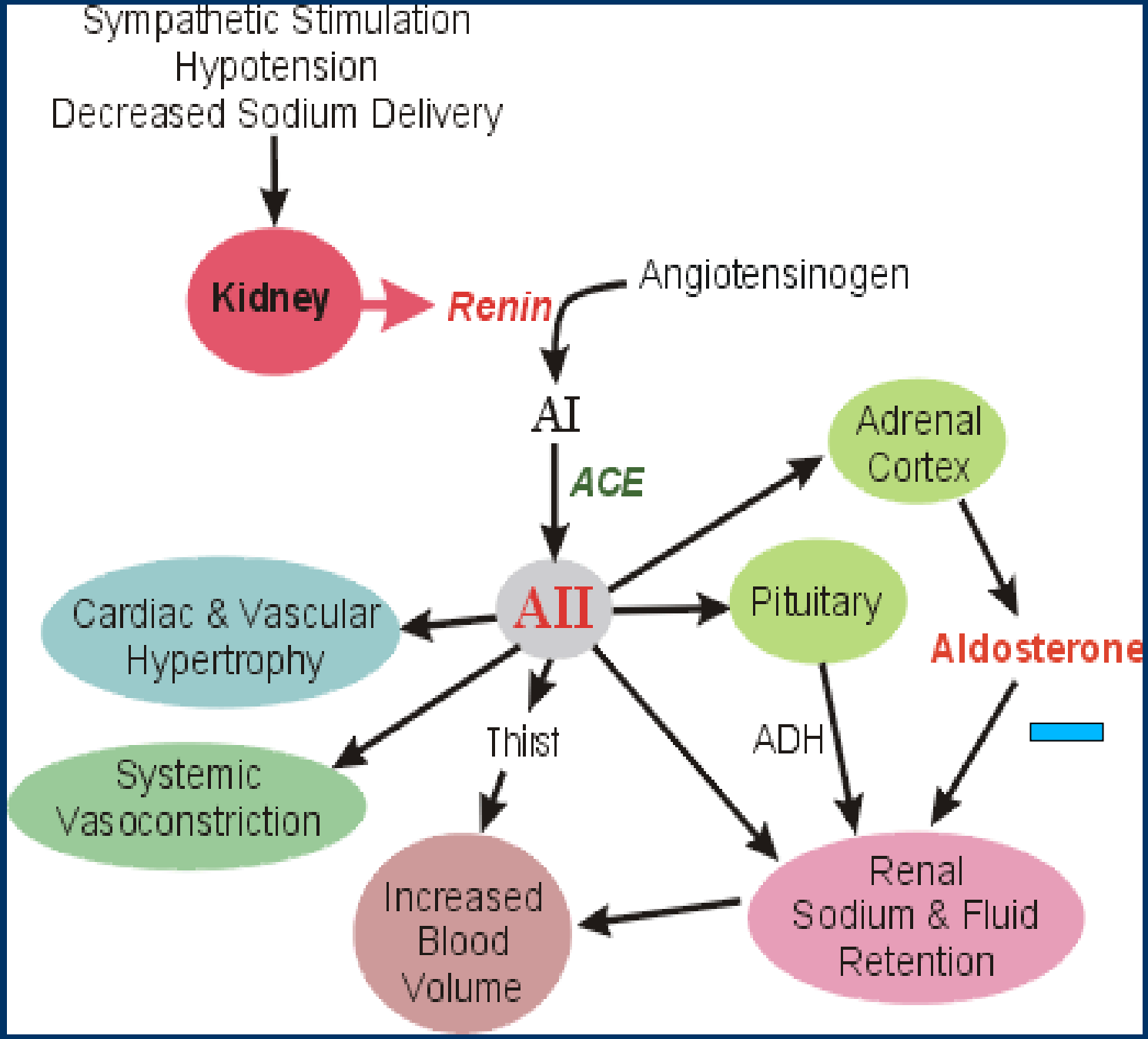
Aldosterone Antagonists



*CV pharmacology.org

Aldosterone Antagonists: 1st line (↓M/M)

- How do they work?
  - Potassium sparing diuretic that blocks aldosterone
- Indications:
  - LVEF ≤ 30% & NYHA II (some symptoms)
  - LVEF < 35% & NYHA III- IV (moderate to severe)
  - LVEF ≤ 40% & Post-MI, on therapeutic ACE-I, and symptomatic HF or diabetes

Drug	Initial	Target
Spironolactone	**12.5-25mg daily**	**50mg daily**
Eplerenone	**25-50mg daily**	**100mg daily**

Aldosterone Antagonists: 1st line (↓M/M)

- Monitoring:
  - Labs: electrolytes (K+) and renal function
- Side effects:
  - HyperK+
  - Hirsutism, gynecomastia (switch to eplerenone)
- Contraindications: K+>5, Scr>2.5 (or GFR<30)

Summary of 1st line medications that ↓M/M

BAAHn

- **Beta-blockers (BB)**
- **ACE-I and ARBs**
- **Aldosterone antagonist (AA)**
- **Hydralazine/nitrates (for African Americans)**

Medications to improve symptoms

- **Symptoms:**
  - Shortness of breath
  - Edema
  - Fatigue

Diuretics (aka 'water pills')

- How do they work?
  - Act at different sections of the kidneys to remove sodium and water, thereby reducing volume overload
- Types:
  - **Loop (1st line)**, thiazides, potassium-sparing
- Dosing:
  - **Furosemide 80mg PO = furosemide 40mg IV**
  - **IV equivalencies:**
    Furosemide 40mg = Torsemide 20mg = Bumetanide 1mg

Diuretics (aka 'water pills')

- Monitoring:
  - Electrolytes (K, Na, Mg), renal function, daily weight
- Side effects:
  - ↓ K, Mg, & Ca, hyperuricemia, dizziness, hypotension, tinnitus
- Precautions:
  - Sulfa allergy, gout
- Loop diuretics are cornerstone for acute HF
  - In diuretic resistance, add thiazide (30 min prior) to augment diuretic effect

TRIVIA QUESTION

- What heart failure medication DOES NOT improve morbidity/mortality and comes from the foxglove plant (seen below)?

TRIVIA QUESTION*

- What heart failure medication DOES NOT improve morbidity/mortality and comes from the foxglove plant (seen below)?

DIGOXIN

Digoxin: Reduces hospitalizations

- How does it work?
  - Cardiac glycoside: inhibits Na+/K+ ATPase pump to increase intracellular sodium concentration, eventually increasing systolic calcium
  - Improves pump filling and improves HF symptoms; first line for HF with atrial fibrillation
- Who should take it?
  - LVEF ≤ 40%, on standard HF therapy, & w/ persistent symptoms
- Target level: 0.5 – 0.8 mcg/mL
- **Does not improve morbidity/mortality**

Digoxin: Reduces hospitalizations

- Monitoring:
  - Electrolytes (K, Mg, Ca), renal function
- Side effects:
  - Nausea, vomiting, bradycardia, visual disturbances, diarrhea, arrhythmias
- Toxicity:
  - Symptomatic control
  - Digibind: antidote made of sheep antibodies
  - Cholestyramine or activated charcoal (2nd line)

Acute vs Chronic Heart Failure

- **Chronic:**
  - Fatigue, fluid retention, dyspnea, exercise intolerance

- **Acute:**
  - Rapid accumulation of fluid within the lungs, pulmonary edema, shortness of breath

Acute Decompensated HF (ADHF)

- **Stabilize**, then rapid correction of hemodynamic and intravascular volume abnormalities

- MEDICATIONS:
  - IV diuretics and vasodilator therapy (nitroglycerin or nitroprusside)
  - Inotropes (dobutamine, milrinone) for advanced HF, decreased LVEF, diminished peripheral perfusion or end-organ function

Medications to Avoid or Use with Caution

- **Anti-arrhythmics (**quinidine, sotalol, ibutilide)
  - Pro-arrhythmic or cardio-depressant
- **Calcium channel blockers** (non-dihydropyridines, i.e. verapamil, diltiazem)
  - Worsening heart failure
- **NSAIDs** (ibuprofen, naproxen, diclofenac)
  - Na+ retention & increases toxicity of diuretics/ACE-I
- **Thiazolidinediones (TZDs)** (pioglitazone, rosiglitazone)
  - Worsening heart failure

SUMMARY

- Beta blockers
- ACE-Inhibitors &ARBs
- Aldosterone antagonists
- Hydralazine and nitrates

BAAHn

1st LINE

- Diuretics-
  - Symptoms

- Digoxin-
  - Symptoms and hospital reduction

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