



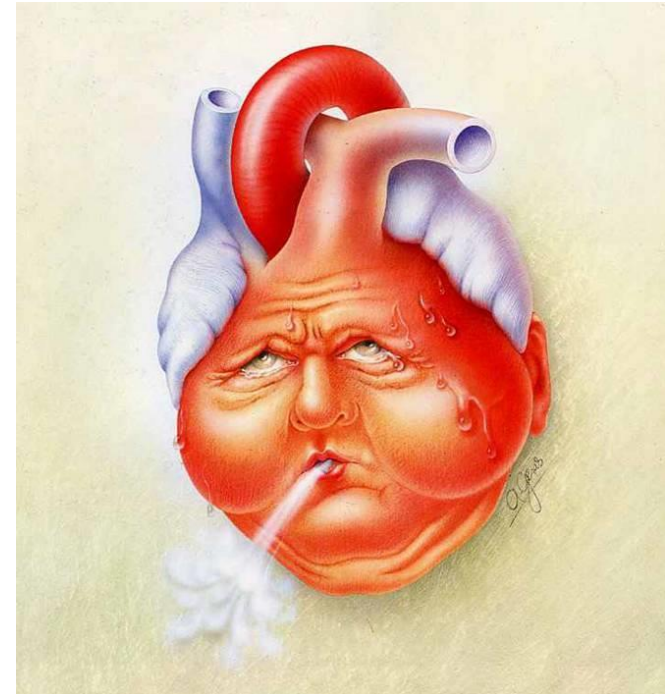
Drug therapy of congestive heart failure (Part I)

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Objectives

- 1- List major drug groups used in treatment of heart failure
- 2- Describe the clinical implications of diuretics, vasodilators, ACE inhibitors and other drugs that lack positive inotropic effects in heart failure
- 3- Explain mechanism of action of digitalis and its major effects
- 4- Explain the nature and mechanism of digitalis toxic effects
- 5- Ivabredine and ARNIs
- 6- Describe the strategies used in the treatment of heart failure

→ In hyperdynamic circulation → ↑COP
 as in pregnant, thyrotoxicosis

Causes of HF (classification)

Congestive Heart Failure.

ملاؤدي لا left

Etiology	Left-sided HF يمكن تكونه لحالها وتؤدي إلى الارتفاع Right	Right-sided HF ما بتصير لحالها on top of left HF.
<p>زيادة في حجم الدم = volume overload. Increased preload means precontraction = Filling بلا ventricles</p>	<p>Aortic regurg, Mitral AR, MR, VSD, ventricular septal defect. hyperdynamic circulation</p>	<p>TR, PR, VSD, hyperdynamic circulation</p>
<p>زيادة المقاومة في العضلات = Increased afterload after contraction. eject against pressure. مقاومة في العضلات</p>	<p>Aortic stenosis AS, Aortic cortication, systemic hypertension</p>	<p>PS, Pulmonary hypertension, COPD</p>
<p>Decreased contractility which caused by organic disease.</p>	<p>Coronary ischemia, cardiomyopathy, myocarditis Proper Contraction . لا سببه ما بتخلي دجيلة القلب تعمل</p>	

Structural → Stenosis
Functional → regurg.

→ Iatrogenic (physician-induced)

Drug-induced HF

cause cardiomyopathy
Alcoholism and drug abuse

Calcium channel blockers
Antihypertensive Drugs
bc it cause systolic dysfunction.

Potassium supplements and other drugs associated with hyperkalemia → Arrhythmia → HF

Antiarrhythmic agents
as digitalis

Androgens
Anabolic Steroids (Gym)
with time cause atherosclerosis → HF.

Sodium-containing preparations
cause Na-water retention → ↑ BV
↓
↑ preload.

TNF-alpha inhibitors
Toxicity on Myocytes

Pathological insult to myocardium

Fall in mean arterial pressure secondary to reduced cardiac output

sensor to BP:

Carotid and aortic baroreceptor response

by Brain

Sympathetic nervous system

Neurohormonal activation

By Kidney

Renin-angiotensin-aldosterone system

β_1 in Juxtaglomerular apparatus with release Renin.

Angiotensinogen

Renin

Angiotensin I

ACE

Angiotensin II

Powerful Vasoconstriction

Aldosterone

Vasopressin

Sodium and fluid retention

Fluid retention

caused by brain, Kidney

to adapt... death of Cardiac Muscles

Catecholamin, Angio. II, Aldosterone

β -blocker

ACE inhibitors

Aldosterone Antagonist

by β_1 -receptors

Increased heart rate and contractility

$CO = SV \times HR$
زيادة حاد في HR
زيادة الـ CO
يكون الـ SV يتغير
لهيكل المشكل للـ CO

Peripheral vasoconstriction $\alpha 1$

حتى اوجه الـ blood supply for vital Organs.

Vicious cycle of maladaptive remodelling of left ventricular function leading to Apoptosis

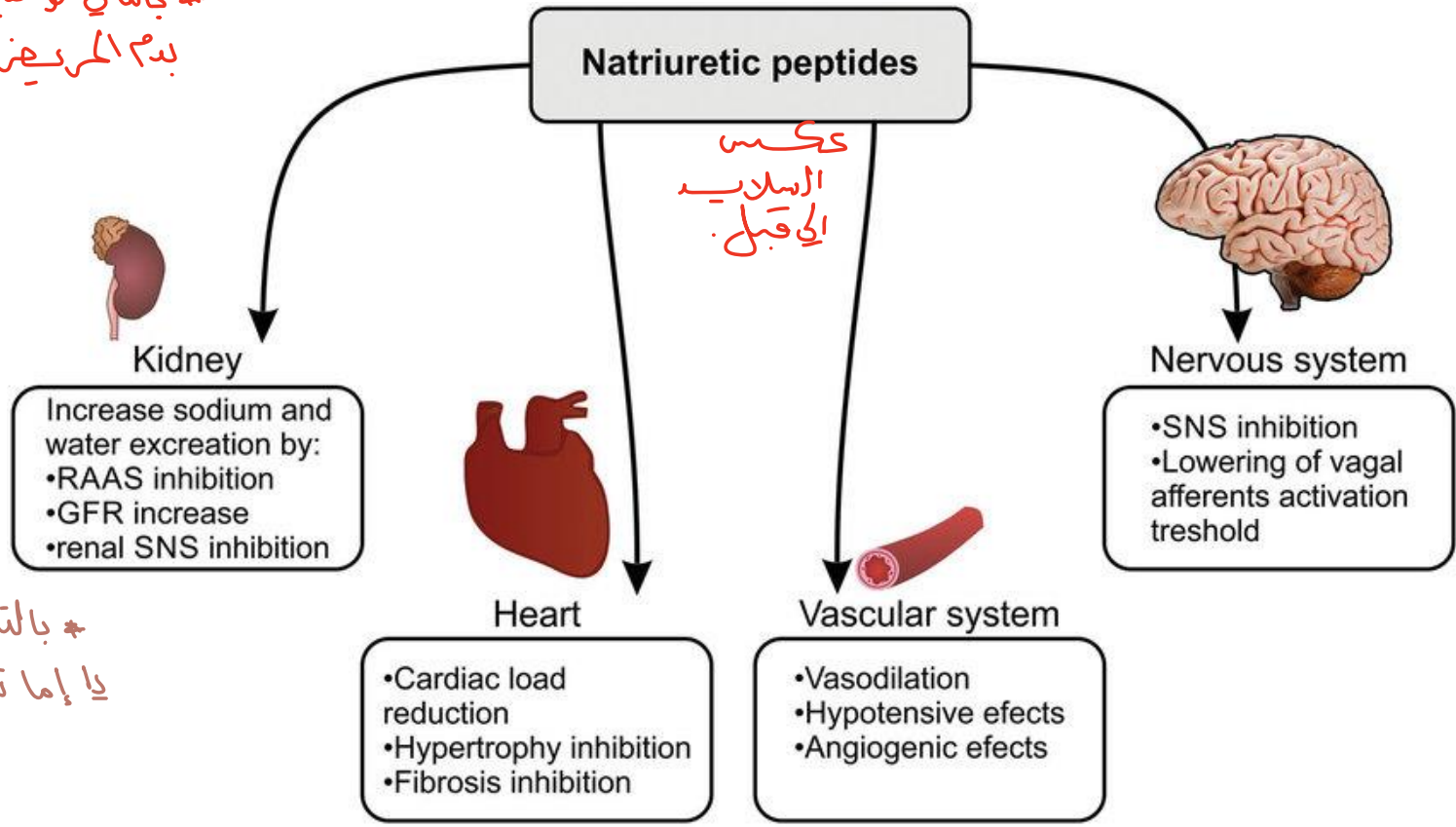
HF يعانوا من Tachycardia bc of sympathetic stimulation

COP... زيادة في الـ CO

هدفها التخلص من ال Na وال Water الزيادة. (Protective)

Activation of natriuretic peptide system in HF

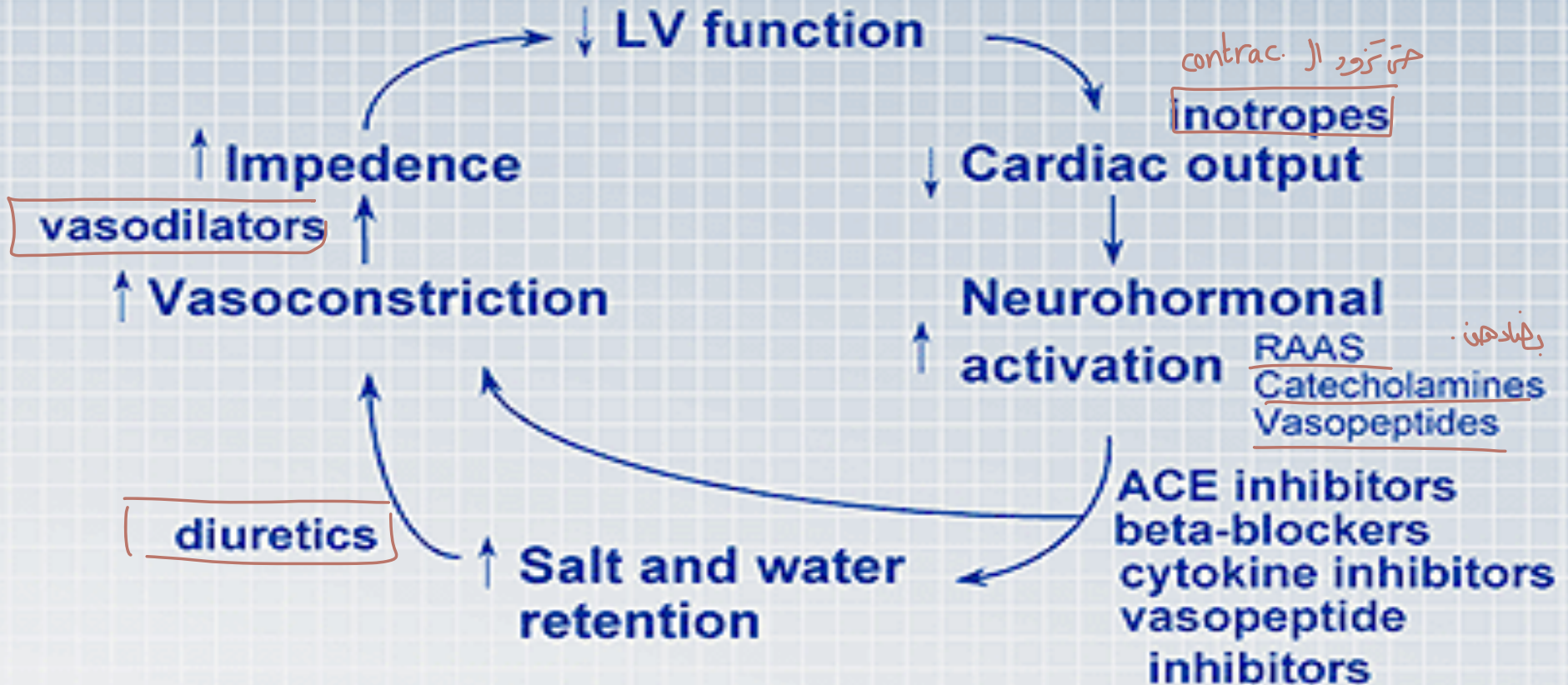
* بالتالي لو لقيت نسبتها عالية
بدء المريض HF.



* بالتالي ادوية حج تكون
دا إما تثبط الي قبل او تزود هاز.

Pathogenesis and Therapeutic Approaches

✳️ التدخل الدوائي عند كل مرحلة من الـ pathogenesis



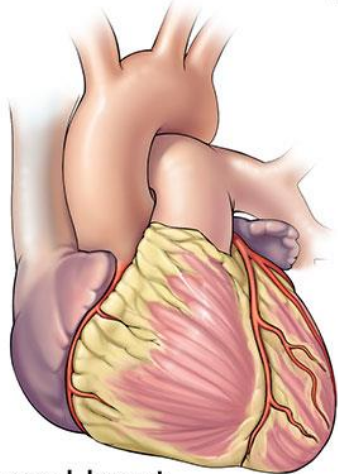
Diagnostic Criteria Of HF

• Triade of:

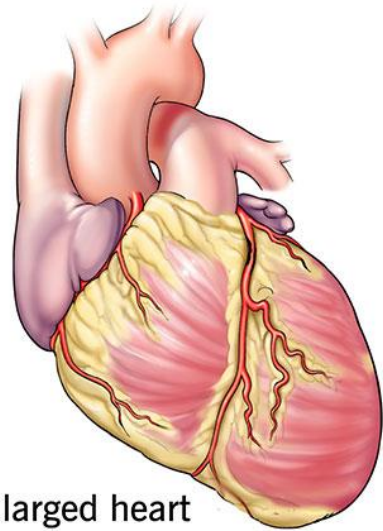
- **Symptoms:** shortness of breath, physical fatigue
كونه غير blood كافي.
- **Signs:** tachycardia, tachypnea, edema
كونه في fluid على lung، وتبهر عن تبادل نفوسه نفس الهم.
- **Evidence of structural or functional abnormality of heart,**
example: cardiomegaly

Congestive Heart Failure

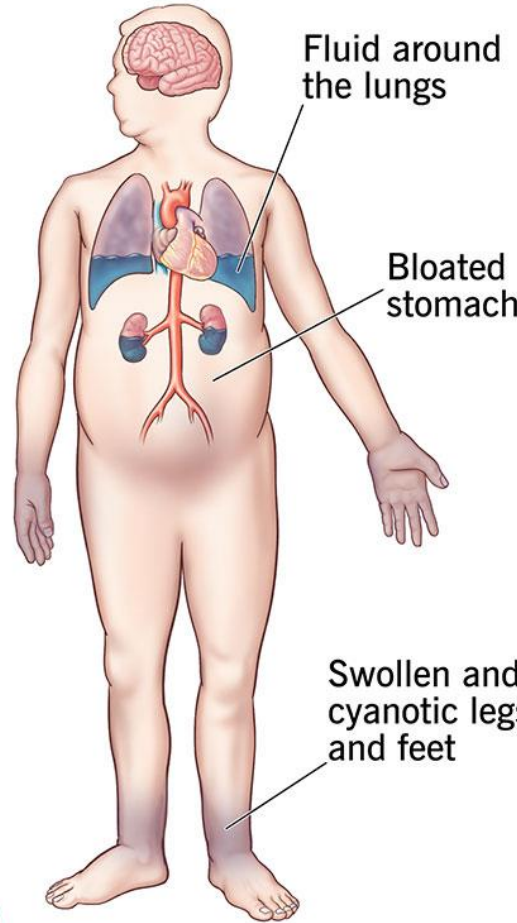
Heart Failure



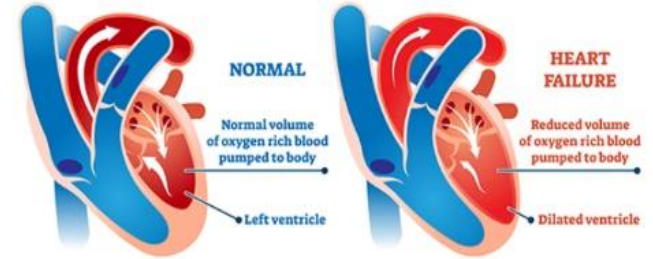
Normal heart



Enlarged heart



CONGESTIVE HEART FAILURE



Enlarged heart
Chest congestion



Excess fluid around lungs
Shortness of breath



Swelling in legs and feet
Edema

Factors Affecting Cardiac Output And Heart Failure

ما لا يكون في HF بسببه زيادة ال preload .
 - تخيل عندك جالون وعينته كثير بالتالي حيصفو على
 جدرانها هذا جوا لبرا ، نري هيك حيصر بعضلات القلب
 مع تراكم الدم ، حسب starting انه بزيادة ال stretch حتى يرد ال
 لكن within limit ، لما اتعداه رح تترهل هاي الوضلات .
 - حيصر عننا dilatation لبرا ، فبالتالي ال lumen زاد .

- Cardiac contractility

- Preload: volume overload: cardiac dilatation

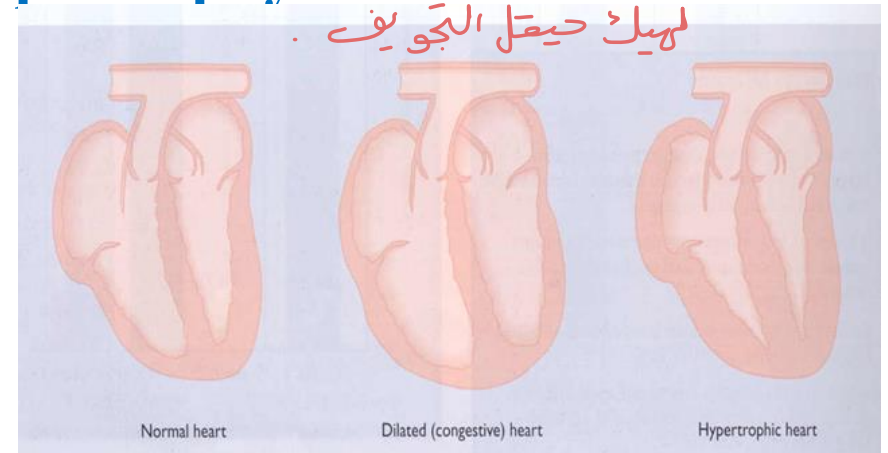
- Afterload: tension overload: cardiac hypertrophy

ما ازود الضيف حيعل Hypertrophy

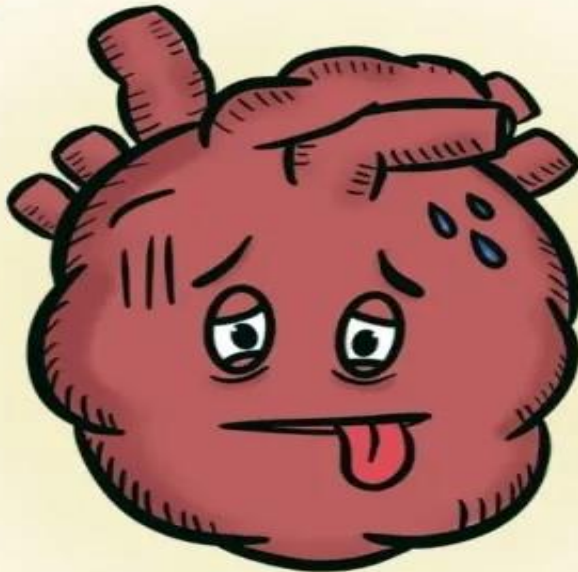
causing ischemia

↑ Thickness of wall
 لهيك حيعل الجوف

- Heart rate: tachycardia



HEART FAILURE



DRUGS

Drugs that decrease preload & afterload

- ACEIs & ARBs

Inotropics

- Cardiac glycosides
- Phosphodiesterase inhibitors
- Sympathomimetics

Drugs that decrease preload

- Duretics
- venodilators

Drugs Used in Heart Failure

Drugs that decrease after load

- arteriodilators

Drugs that decrease heart rate

β - adrenoceptor agonists

Drug therapy of HF

- First line drugs for HF with reduced ejection fraction (HFrEF):
ACEIs (ARBs), ARNI and B-blockers
- First line drugs for HF with volume overload (edema and congestion):
• Diuretics and positive inotropic drugs

ACE Inhibitors & Angiotensin Receptor Blockers

- Are now considered as first –line drugs for heart failure therapy

الشين على
RAS

- ACEIs: Captopril, enalapril, ramipril, lisinopril

- AT1 receptor blockers: Losartan, candesartan, valsartan, telmisartan

- **Effects of converting enzyme inhibitors (ACEIs)** → Decrease mortality by decrease remodeling.

- ↓angiotensin II and aldosterone leading to (inhibition of RAAS):

II كونه ال
VC بعمل

- 1- ↓Peripheral resistance (↓**Afterload**)

ald. كونه ال
عمل retention

- 2- ↓Venous return (↓**Preload**)

- 3- ↓cardiac remodeling → ↓mortality rate

Adverse effects of ACEIs

- 1- Dry cough: 10% *أكثر شيئا بضيق المريض.*
- 2- Headach *بجول العلاج من ACEI لا ARBs*

bradykinin cause irritation of RS.
 كونه لما ثبتت تحويل الـ Ang I لا II
 مما عني collateral damage
 ويحل بصير تحطيم لا Bradykinin

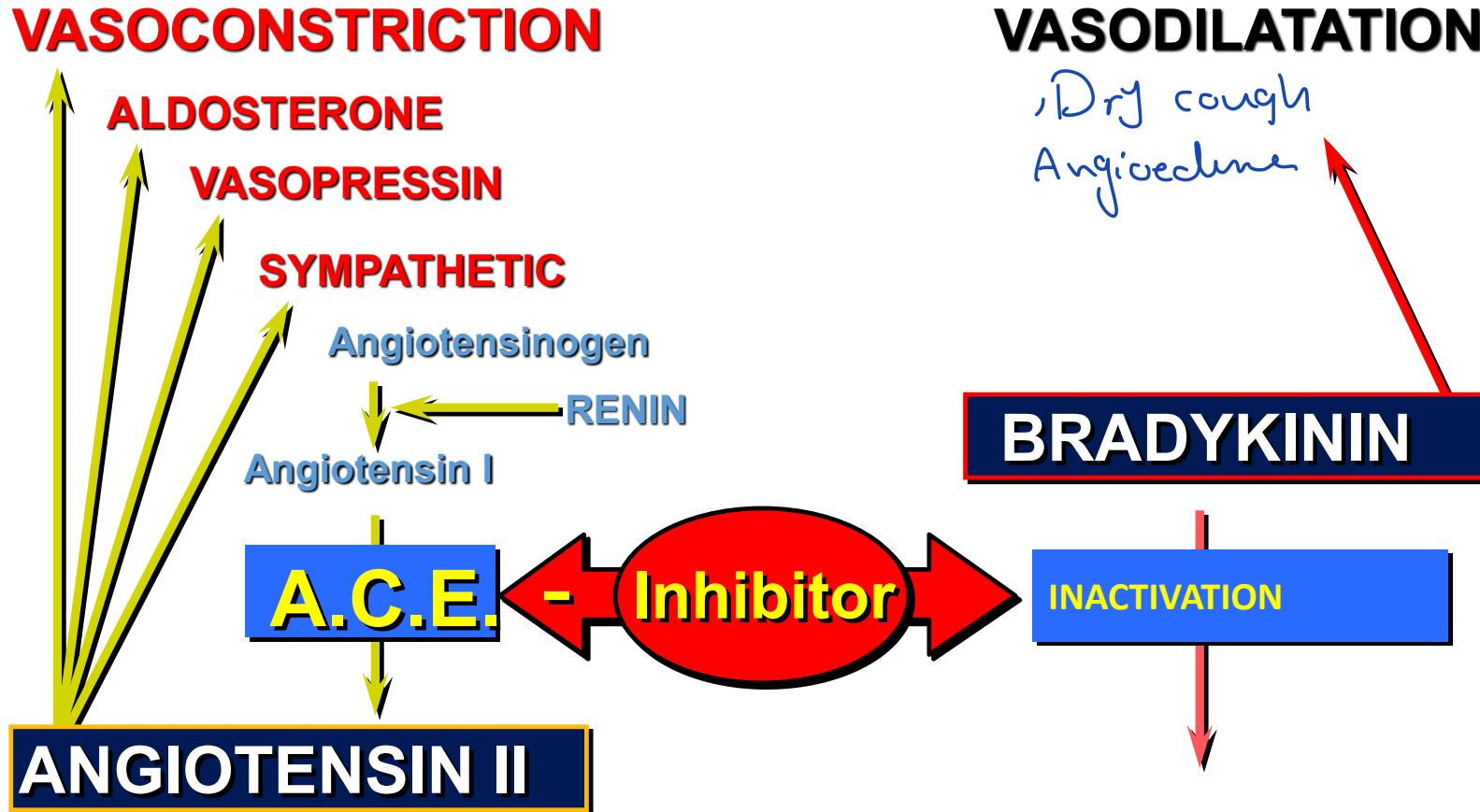


*طبعًا تختلف آليات
 حيث يوجد other mechanisms
 for degradation of bradykinin.*

- 3- Hypotension *و.V.D.*
- 4- Angioedema: rare
- **Dry cough and angioedema are due to elevated plasma bradykinins.**
- **ARBs:** less effective and typically used in patients who can not tolerate ACEIs.

Angiotensin converting enzyme inhibitors

MECHANISM OF ACTION



B-adrenoceptor Blockers In Heart Failure

• Benefits in HF:

- Reduce catecholamine myocyte toxicity (**remodeling**)
- Inhibit renin release
- Decrease heart rate
- **Decrease mortality rate**

• **Adverse effects:**

- 1- Hypotension 2- Rare but severe: bradycardia, A-V block

• Contraindications in HF:

- 1- Beta blockers in large dose
- 2- Acute HF

not in Acute

• Beta blockers approved in HF (stable cases, in small doses):

1- Bisoprolol

MBC

2- Metoprolol

3- **Carvedilol (additional VD)**

↓ Preload.

Vasodilators

dilation of Arteries → ↓ afterload (Resistance)

dilatation of veins → ↓ Preload.

• Indications of vasodilators in HF:

• **patients who can not tolerate ACEIs, ARBs**

• Arterioldilators: hydralazine, minoxidil, nicorandil

• **Hydralazine:**

• Direct acting vasodilator

• Reduces both right and left ventricular **afterload** by reducing

on Right

pulmonary and systemic vascular resistance

on left

* Patient with HF and renal impairment
1 → ACEIs
2 → hydralazine

• **Results in increased cardiac output**

• Reduces renal vascular resistance and increases renal blood flow

• Increases renal blood flow more than any other vasodilator except ACE inhibitors

• **Preferred drug in CHF (ACE intolerant) with renal impairment**

Venodilators: nitrates

- **How nitrates are helpful in CHF?**

- Reduce preload

- Coronary artery dilatation- reperfusion

- **Given alone their efficacy is limited due to:**

- ✓ limited effect on systemic resistance

- ✓ Nitrate tolerance

- **Often combined with other vasodilators for better results:**

- **Hydralazine/isosorbide dinitrate (Bidil)** is a fixed-dose combination:
improve mortality in some cases of HF.

Diuretics

- **Among First-line therapy of heart failure**
- **Role in HF:**
 - 1- Remove the signs and symptoms of volume overload (pulmonary congestion/ peripheral edema).
 - 2- Reduce salt and water retention (Natriuresis) → ↓ ventricular preload and venous pressure.
 - 3- Reduction of cardiac size → improve cardiac performance
- **Loop diuretics – furosemide:** most powerful and used for most patients
- **Thiazide Diuretics- less effective but indicated in patients with hypertension and mild fluid retention:** chlorthiazide, hydrochlorthiazide
- **Side effects of diuretics:** metabolic alkalosis, electrolyte imbalance (hypokalemia) and hypovolemia
- **N.B. Diuretics do not improve the mortality rate in patients**

K⁺ Sparing Diuretics (aldosterone antagonists)

- Spironolactone, triamterene, amiloride are weak diuretics-for achieving volume reduction with minimal K⁺ loss
- **Advantages of spironolactone:**
 - 1- Preserve K: prevents hypokalemia
 - 2- Decreases mortality in cases of sever HF
 - 3- Reverse aldosterone-induced remodeling
- Dose: one tablet lasilactone 50 mg in the morning 5 days a week.

To be continued 