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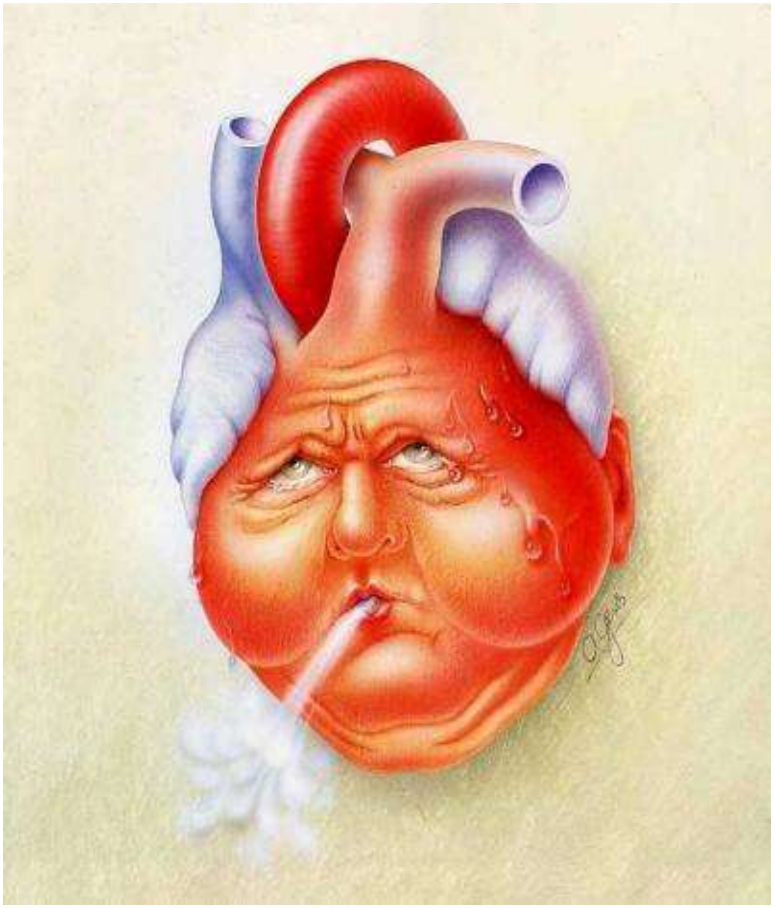
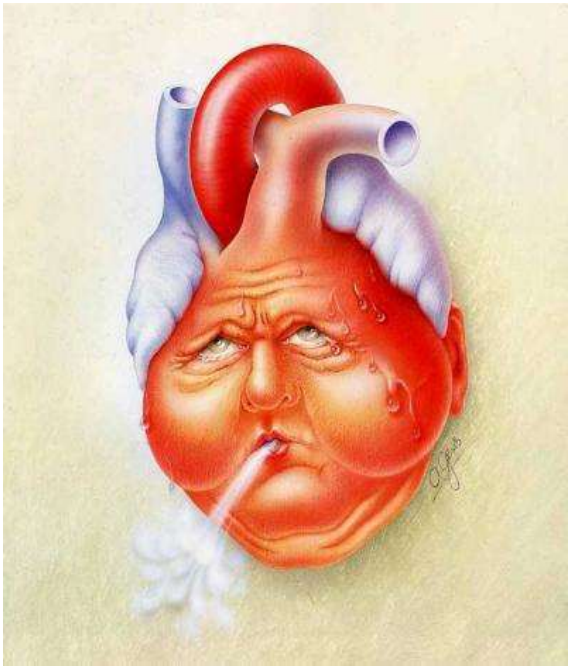
Part 4: Chronic Heart Failure Continued

Karen Kopacek, M.S., R.Ph.
Associate Professor (CHS)
Spring 2021



HF Part 4

- Medication therapies for stages in the development and progression of HF
  - Stage A meds (RAAS)
  - Stage B meds (SNS)



Objectives for Part 4

- Use the ACC/AHA HF Treatment Guidelines to recommend appropriate drug therapy for patients with various stages and phenotypes of HF.

- Review the mechanism of action, target doses, monitoring parameters, and side effects for each drug class.

Medication Approach to HF*r*EF

- **Prevent HF Progression and Death**
  - **Vasodilators**
    - ARNI, ACEI/ARB, or hydralazine/isosorbide
  - **Beta Blockers**
  - **Aldosterone Antagonists**
  - **SGLT-2 inh (CV death)**
  - **Vericiguat (CV death)**

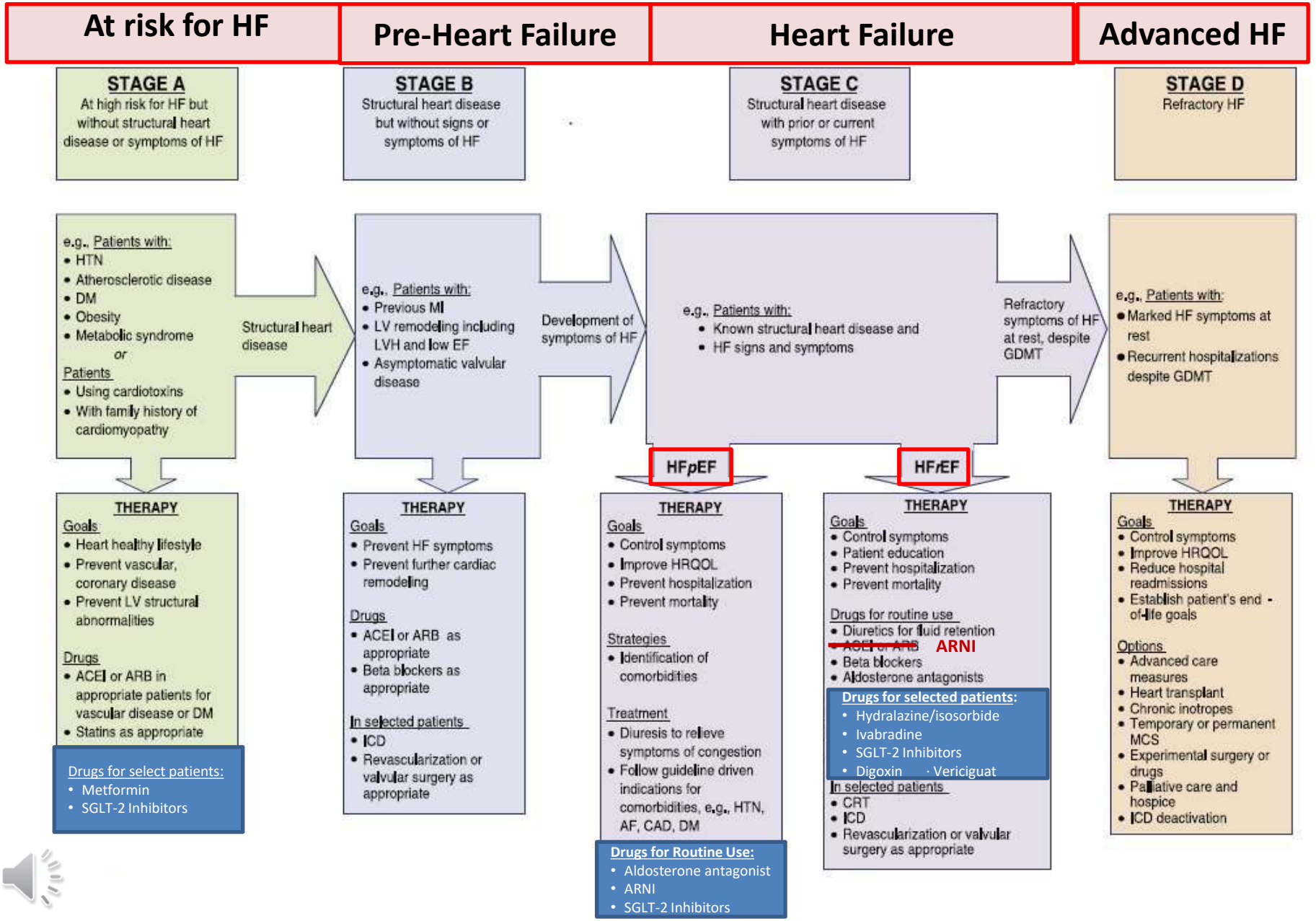
Medical Therapy	Relative Risk Reduction in Mortality	Number Needed to Treat for Mortality Reduction	Relative Risk Reduction In Heart Failure Hospitalizations (%)
ACE inhibitors or ARBs	17	26	31
Beta-blocker	39	4	41
Aldosterone antagonist	30	6	35
Hydralazine/nitrate	43	7	33

ACE, *Angiotensin-converting enzyme;* ARBs, *angiotensin II receptor blockers.*

- **Reduce Hospitalizations**
  - **Digoxin - SGLT-2 inh**
  - **Ivabradine - Vericiguat**

- **Symptom Management**
  - **Diuretics (Both HF phenotypes)**
    - Loop diuretics preferred
    - Combo loop/thiazide in special circumstances
    - SGLT-2 inhibitors
  - **Digoxin**
    - Helps patients feel better
    - Used in addition to and after starting ACEI, BB, and AA

2013, 2016, 2021 ACC/AHA HF Guidelines



Yancy et al. 2013 ACCF/AHA HF Guidelines. JACC 2013;62;e147-239; Bozukurt et al. J Card Fail. 2021 Mar 1;S1071-91. Online ahead of print; Bozkurt et al. 2021 ACC/AHA Definitions for Heart Failure. JACC 2021;Online ahead of print.

New HF Definition and Classification

New definition of HF: A clinical syndrome with current or prior s/sx caused by structural and/or functional cardiac abnormality and corroborated by at least one of the following:

- Elevated natriuretic peptide levels:

	Ambulatory	Hospitalized/ Decompensated
BNP	**≥ 35 pg/ml**	**≥ 100 pg/ml**
NT-proBNP	**≥ 125**	**≥ 300**

- Objective evidence of cardiogenic pulmonary or systemic congestion by diagnostic modalities

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Bozukurt et al. J Card Fail. 2021 Mar 1;S1071-9164(21)00050-6. doi: 10.1016/j.cardfail.2021.01.022. Online ahead of print.

New HF Definition and Classification Continued

New classifications of HF based on EF:

Phenotype	Definition
HFrEF (reduced)	HF with LVEF ≤ 40%
HFmrEF (mildly reduced- HFSA) (mid-range- ACC/AHA)	HF with LVEF 41-49%
HFpEF (preserved)	HF with LVEF ≥ 50%
HFimpEF (improved- HFSA) (with recovered- ACC/AHA)	HF with a baseline LVEF ≤ 40%, a ≥ 10-point increase from baseline LVEF, and a second measurement of LVEF > 40%

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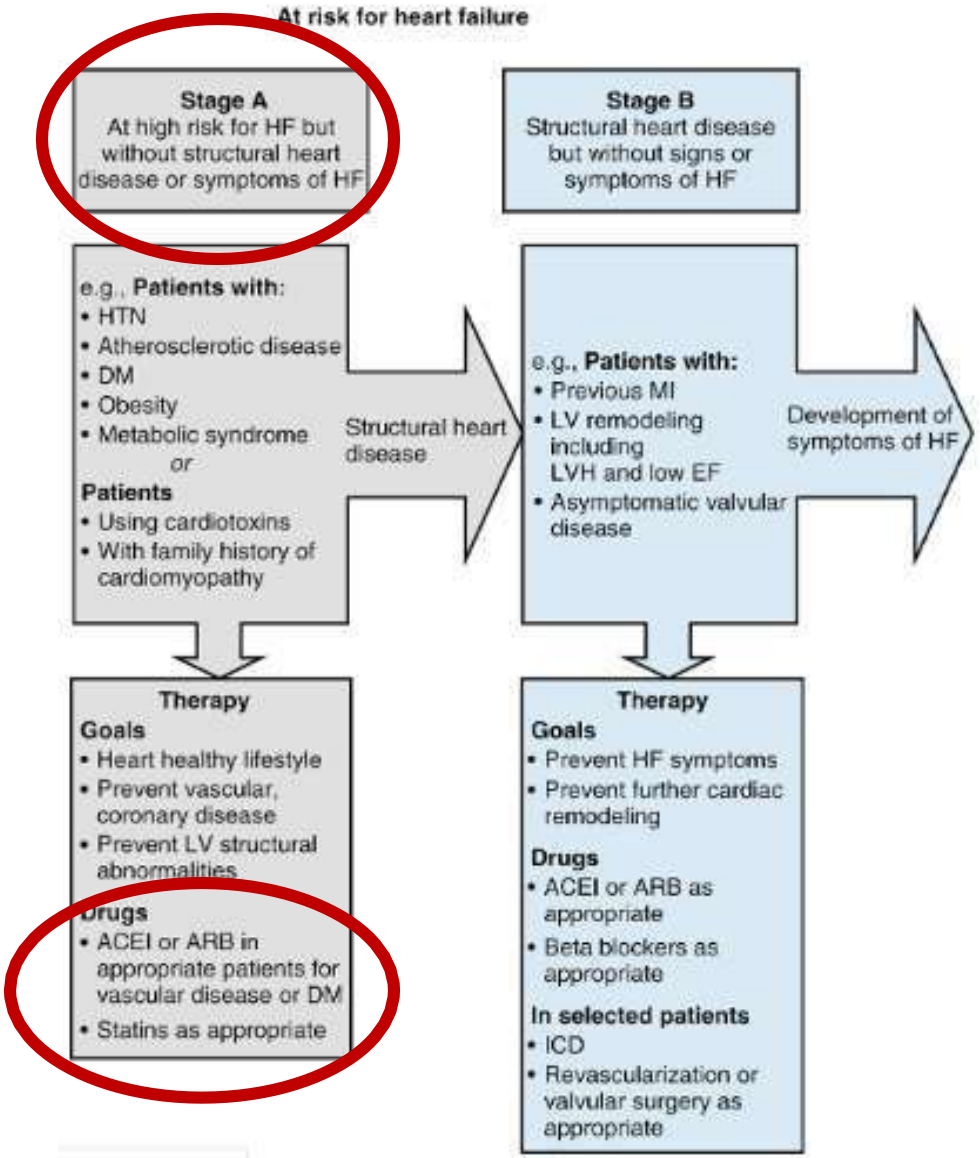
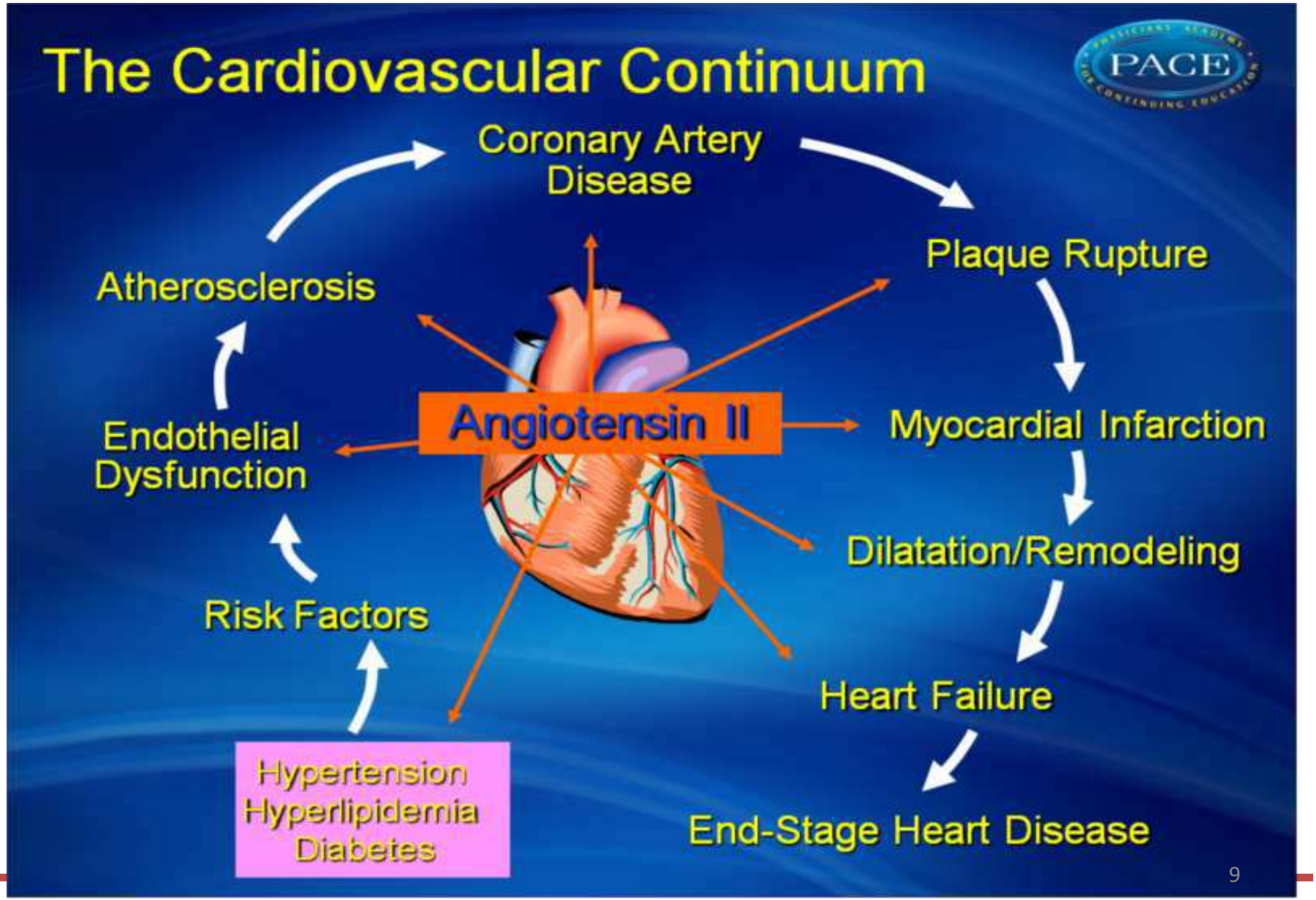
Bozukurt et al. J Card Fail. 2021 Mar 1;S1071-9164(21)00050-6. Online ahead of print.;
Bozkurt et al. 2021 ACC/AHA Definitions for Heart Failure. JACC 2021;Online ahead of print.

Stage A - At Risk for HF



- **ACE inhibitors (ACEI)**
- Or ARBs
- Statins
- Other meds in select patients:
  - Meformin
  - SGLT-2 inh

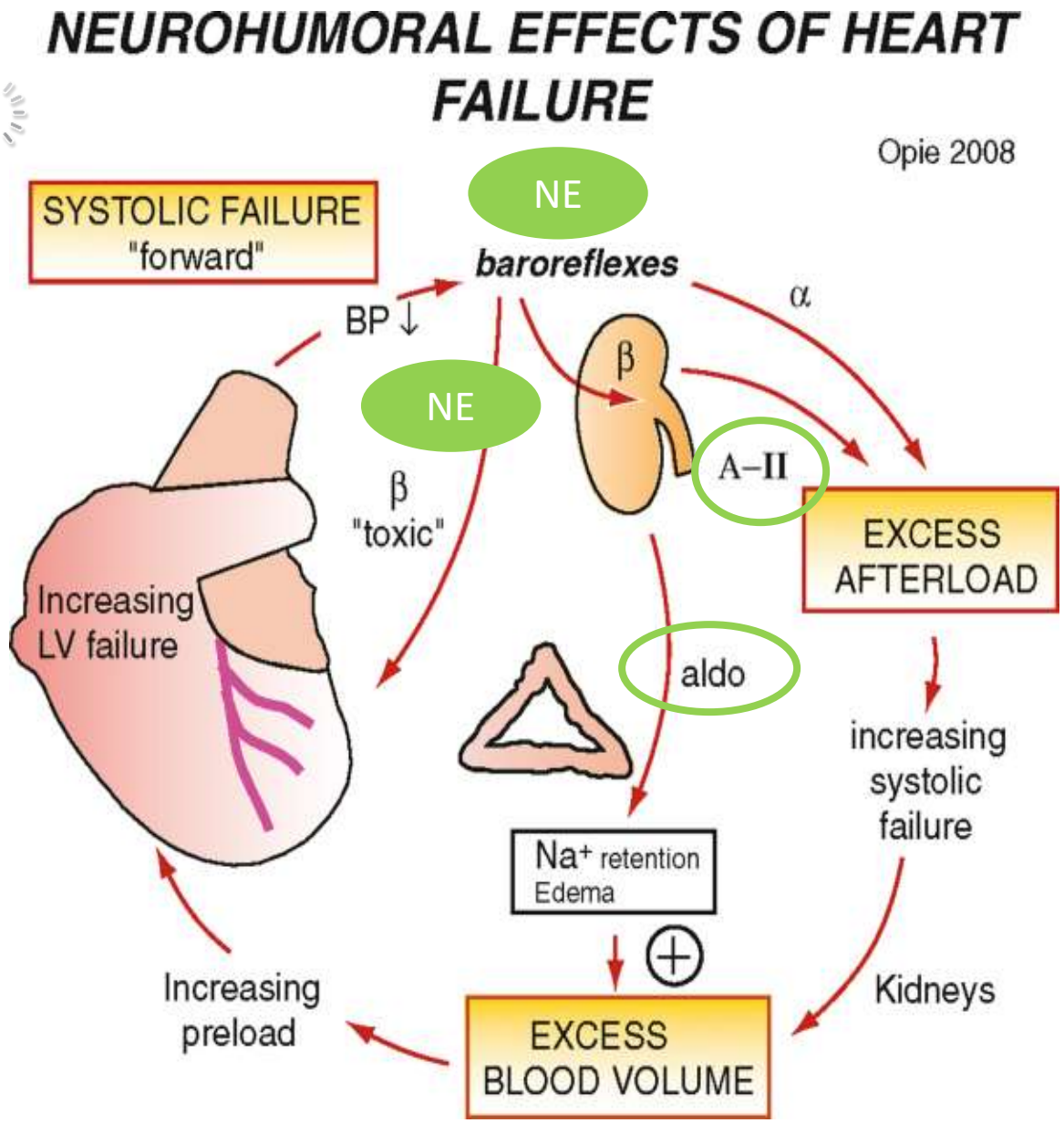
Deleterious Effects of AT II



ACEI or ARB Therapy in HF

- **ACEI should be used in <u>all patients at risk for developing HF (Stage A and B)</u>** *Class IA rec*
- Proven to delay HF progression and prevent mortality in all stages (esp. HFrEF)
  - Decreases resistance to left ventricular ejection (afterload), increases stroke volume, and decreases ventricular filling pressure (preload) to ultimately increase CO
  - Stabilize LV remodeling, improve symptoms, prevent hospitalizations, and prolong life
  - All ACEI equally effective in treating HFrEF

2013 ACCF/AHA Guideline for Management of HF; 2016 Update



Adapted from Drugs for the Heart, 7th Edition. Figure 5.8

BP = CO x PVR

CO = HR X SV

SV determined by preload, afterload, and contractility

ACEI/ARBs target the negative effects of ATII (afterload) and aldosterone (preload) to improve SV and CO.

ACEI or ARB Therapy in HF

- Use ARB in patients who are intolerant to ACE inhibitors (cough, angioedema)

- **Replace ACEI/ARB with ARNI for patient in Stage C to further reduce morbidity and mortality**
  - ARNI: angiotensin receptor and neprilysin inhibitor
  - Switch in patients with HFrEF; start in patients with chronic HF (other phenotypes)

2013 ACCF/AHA Guideline for Management of HF; 2017 Update; 2021 Update to 2017 Expert Consensus Decision Pathway

ACEI/ARB Key Points

- Initiate at low doses, titrate every 2 weeks until maximum tolerated or target dose achieved
  - Higher doses more effective at preventing hospitalizations
  - May need to hold upward dose titration when beta-blocker therapy initiated (too many drug changes can lead to symptomatic hypotension)
- Optimize dose of diuretic first as fluid overload can attenuate effects of ACEI/ARB
  - Diuretic dose may require reduction (cut dose by 50%) with start of therapy to prevent symptomatic hypotension

Yancy et al. Pathway for Optimization of HF Treatments JACC 2017; 2021 Update to the 2017 ACC Expert Consensus Decision Pathway for Optimization of HF Treatment

ACEI and ARB Dosing in HF

	Initial Dose	Target Dose
Captopril	6.25 mg TID	50 mg TID
Enalapril	2.5 mg BID	10-20 mg BID
Lisinopril	2.5-5 mg QD	**20-40 mg QD**
Ramipril	1.25 mg QD	10 mg QD

	Initial Dose	Target Dose
Losartan	25-50 mg QD	150 mg QD
Valsartan	40 mg BID	160 mg BID
Candesartan	4-8 mg QD	32 mg QD

2013 ACCF/AHA Guideline for Management of HF; 2021 Update

ACEI/ARB Key Points

- Close follow-up required with initiation and each dosage titration:
  - Check BP (including postural changes), renal function, and potassium level within 1-2 weeks after initiation/dose change
  - Use caution if SBP < 90 mmHg, K+ > 5 mmol/L, or SCr > 3 mg/dL
    - Consider holding diuretic for 1-2 day if SCr elevated
  - **Avoid abrupt discontinuation** unless life threatening side effects occur
    - Therapy withdrawal may lead to clinical deterioration

Monitoring Renal Function with ACEI/ARB/ARNI

Table 137. Changes in Management Based on Magnitude of Early Decrease in GFR

	Early decrease in estimated GFR (%)			
	0-15%	15-30%	30-50%	>50%
Dosage adjustment for ACEI and ARB	None	None	Reduce	Discontinue
Recommended interval for monitoring GFR	As per GFR (previous table)	Once after 10-14 days. If repeat GFR remains within 15-30% of baseline value, resume monitoring schedule as per GFR (previous table)	Every 5-7 days until GFR is within 30% of baseline value	Every 5-7 days until GFR is within 15% of baseline value
Evaluate for causes of decreased GFR (including consideration of RAD, see Guideline 4)	No	No	Yes	Yes

National Kidney Foundation. K/DOQI Clinical Practice Guidelines on Hypertension and Antihypertensive Agents in Chronic Kidney Disease. Am J Kidney Dis 43:S1-S290, 2004 (suppl 1).

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Monitoring Serum Potassium: Before initiating ACEI/ARB/ARNI and with dose increases

FYI!

Table 142. Recommendations for Prevention and Management of Hyperkalemia, According to Baseline Serum Potassium

	Baseline Serum Potassium (mEq/L)			
	≤4.5	4.6-5.0	5.1-5.5	>5.5
Education to avoid high potassium foods	No	Yes	Yes	Yes
Measures to lower serum potassium	No	No	Simultaneous with initiation	Prior to initiation
Recommended interval for monitoring serum potassium after initiation or change in dose of antihypertensive therapy	4-12 weeks	2-4 weeks	≤2 weeks	≤2 weeks

National Kidney Foundation. K/DOQI Clinical Practice Guidelines on Hypertension and Antihypertensive Agents in Chronic Kidney Disease. Am J Kidney Dis 43:S1-S290, 2004 (suppl 1).

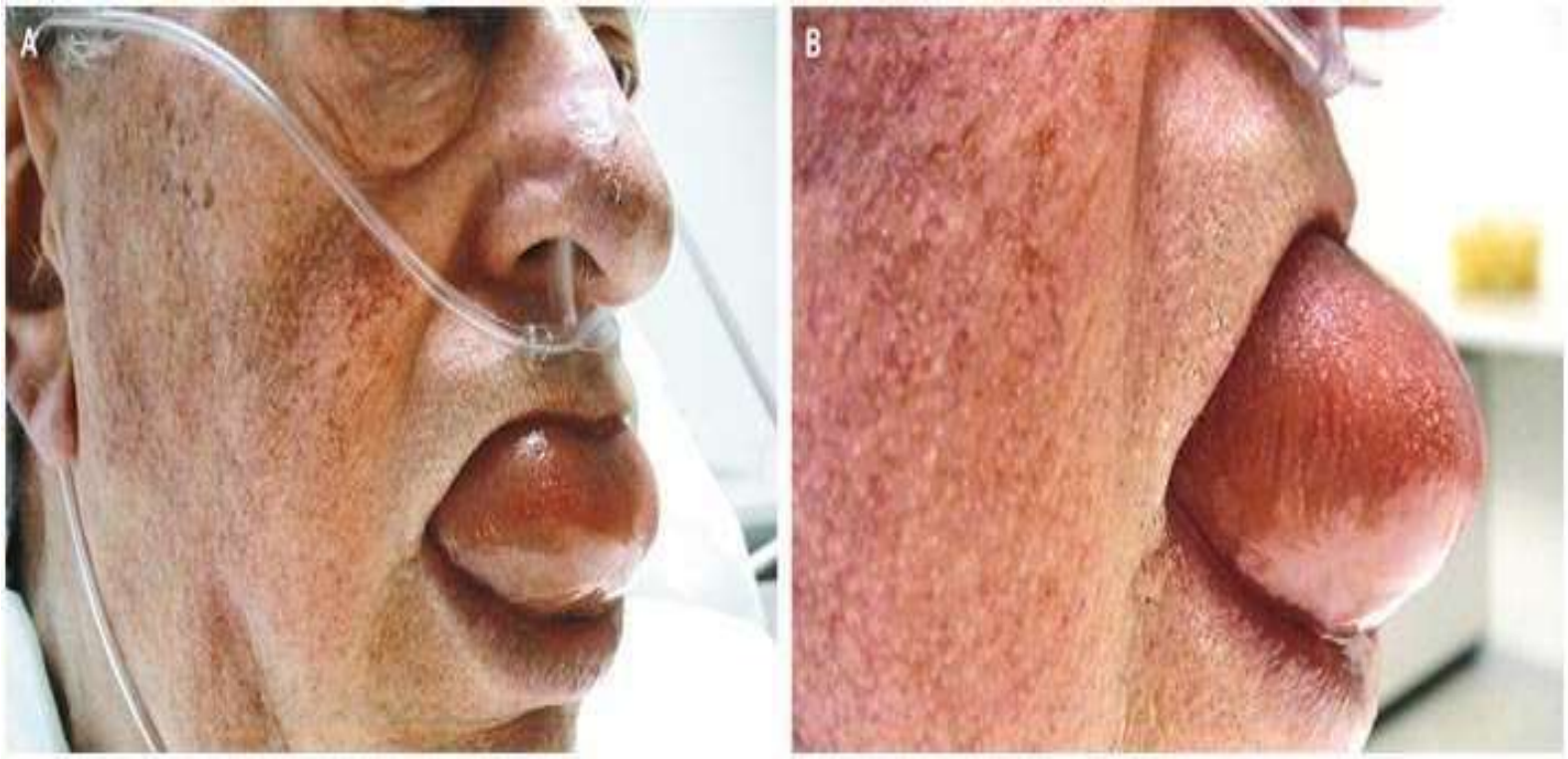
ACEI/ARB Key Points

- Side effect management:
  - Do not stop ACEI if patient c/o cough until fluid status assessed (see slide 20)
  - Hypotension is common during titration and often improves over time
    - Reassure patient
    - Slow down titration
    - Consider decreasing diuretic dose if patient dry
  - Angioedema has been documented with ARB therapy, not just ACEI (see slide 21)

Cough due to ACEI or HF?

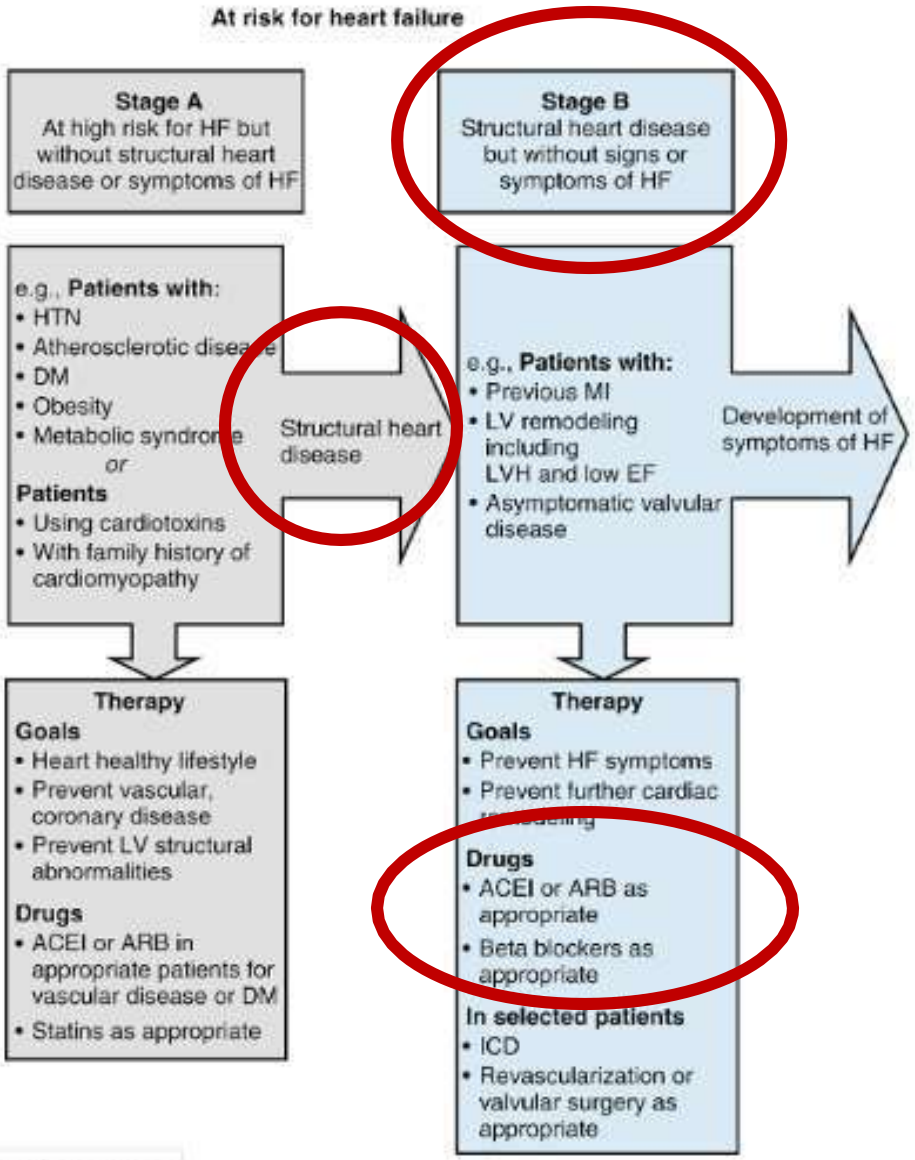
- Cough due to ACEI usually develops within first few months of therapy and disappears within 1-2 weeks of discontinuation
- In patients with HF, retry therapy with a different ACEI
  - If cough returns with drug challenge, cough was due to ACEI and NOT a symptom of HF
  - Switch ACEI to ARB

Angioedema of the Tongue



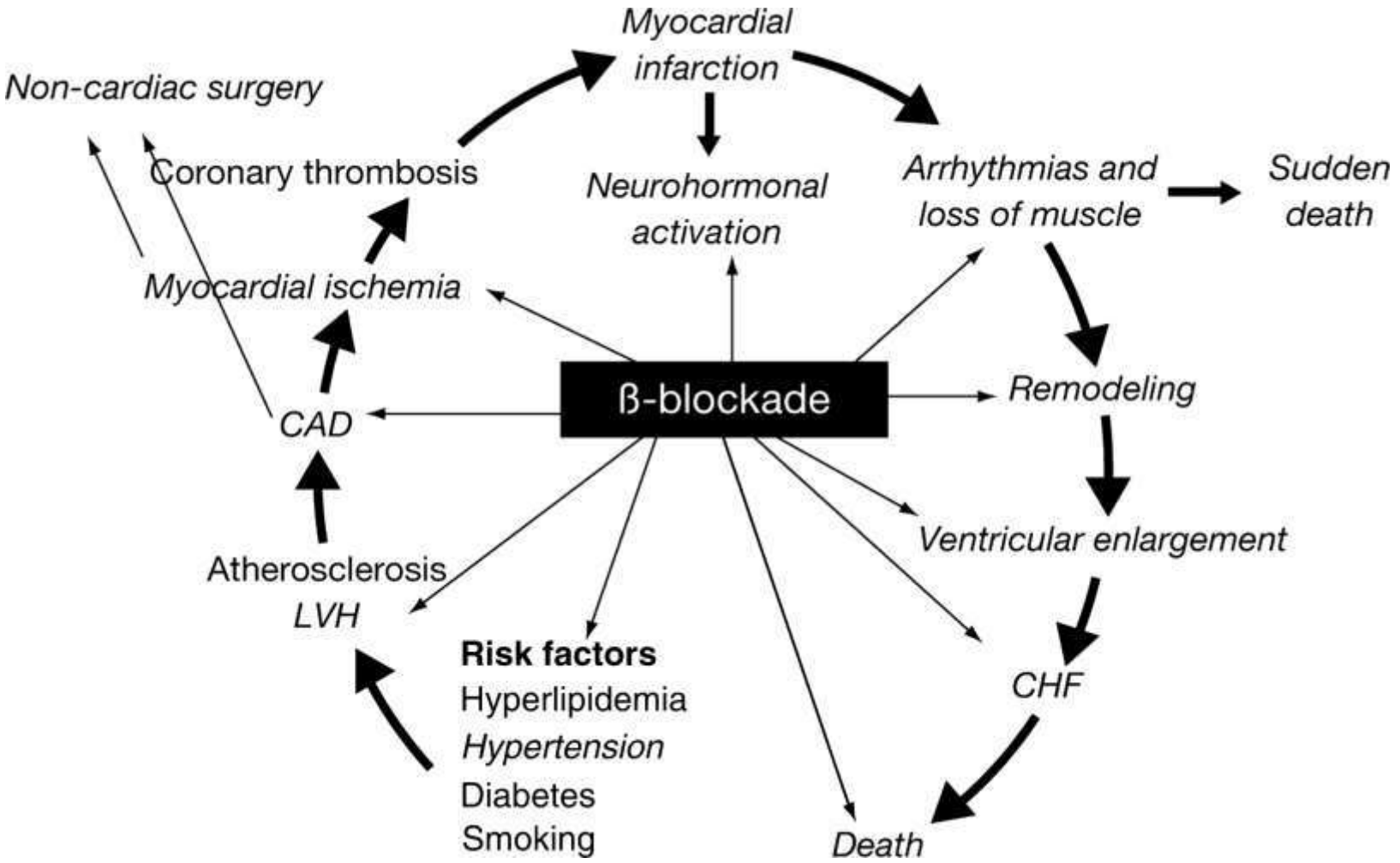
Westra SW, de Jager CP. N Engl J Med 2006;355:295-295.

Stage B – Pre-HF



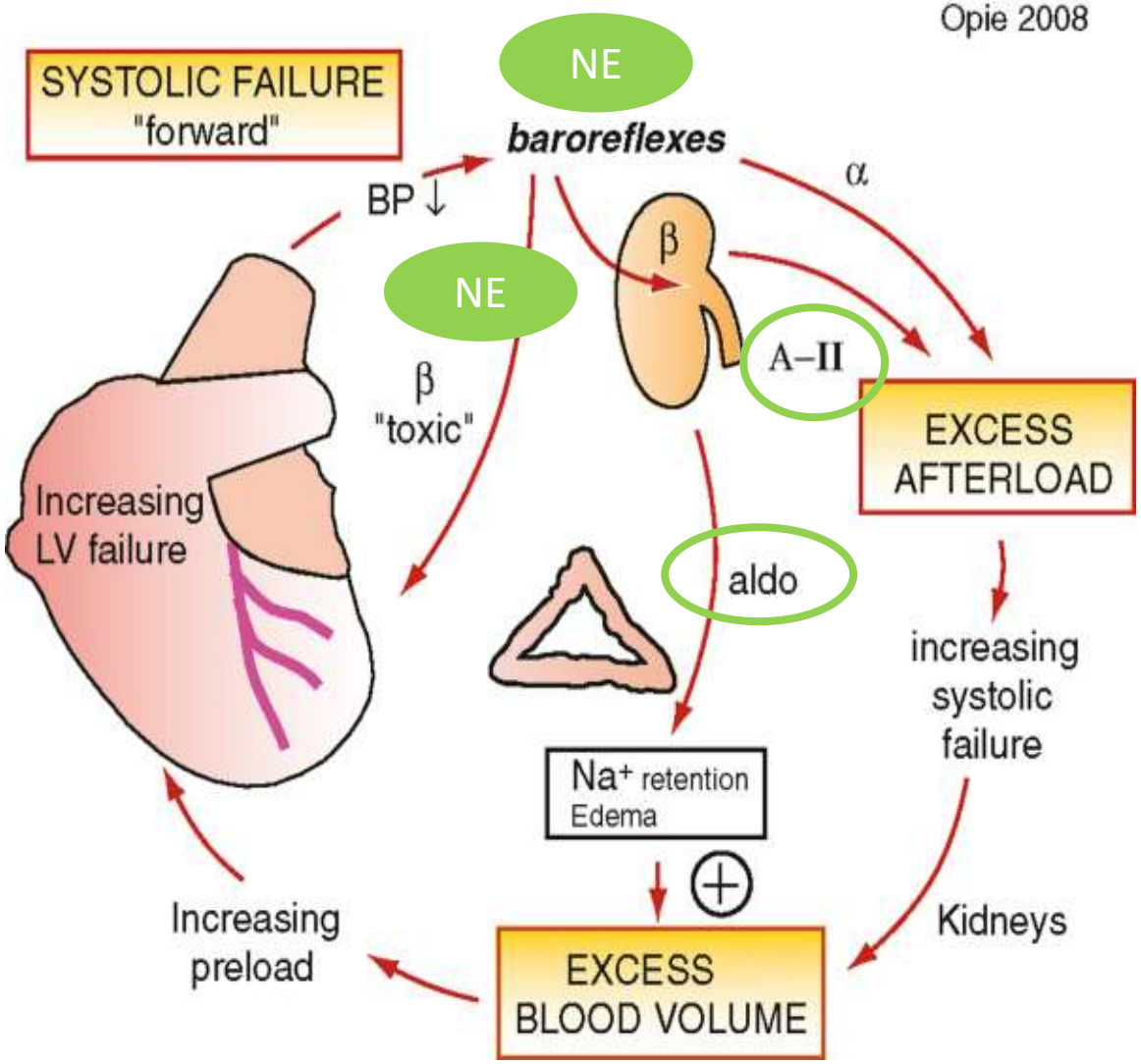
- ACEI/ARB
- **Beta-blockers**

Beta-blockers can intervene at many points in the CV Continuum



Willenheimer R , Erdmann E Eur Heart J Suppl 2009;11:A1-A2

NEUROHUMORAL EFFECTS OF HEART FAILURE



Adapted from Drugs for the Heart, 7th Edition. Figure 5.8

BP = CO x PVR

CO = HR X SV

SV determined by preload, afterload, and contractility

Beta Blockers target the negative effects of NE (indirectly ATII and aldosterone) to decrease afterload and heart rate, while improving SV.

BB Therapy in HF

- BB should be used in all patients (starting at Stage B) with reduced EF (≤ 40%) to prevent symptomatic HF
  Class IC rec
- When given with ACEI, BB reverse LV remodeling, improve symptoms, prevent hospitalization, and prolong life in HFrEF
- Multiple BB available, only 3 have been proven to reduce mortality in HFrEF:
  - **Bisoprolol, carvedilol, metoprolol succinate**
  - Carvedilol preferred in patients who require further BP lowering

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Yancy et al. Pathway for Optimization of HF Treatments JACC 2017; 2021 Update to the 2017 ACC Expert Consensus Decision Pathway for Optimization of HF Treatment

BB Key Points

- Beta-blockade therapy should start low and titrate slowly to minimize worsening HF symptoms
  - Often difficult to initiate due to worsening of HF symptoms; but once stable**, patients feel better and gain significant mortality benefits**
  - Should not be started unless patient is euvolemic; optimize diuretic therapy prior to starting but avoid volume depletion
  - Do not start if patient hospitalized due to HF exacerbation
  - **Initiate at low doses, titrate slowly (every 2 weeks) until maximum tolerated or target dose achieved**

BB Dosing for HF*r*EF

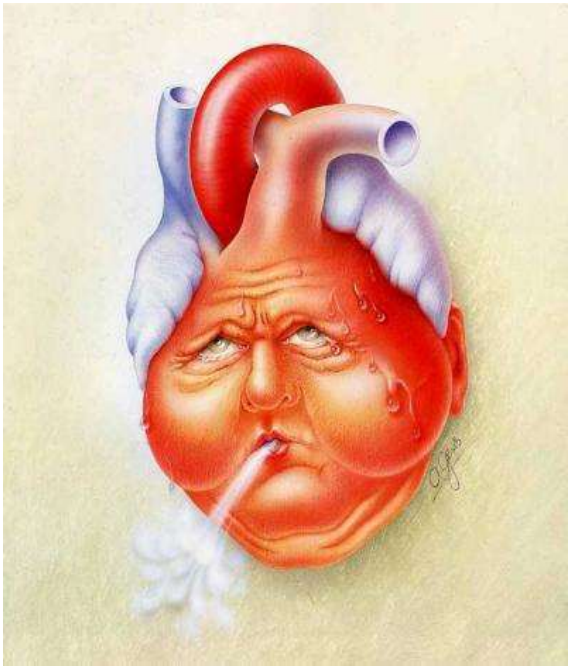
	Initial Dose	Target Dose
Bisoprolol	1.25 mg QD	10 mg QD
Metoprolol succinate	12.5-25 mg QD	**200 mg/day (QD or BID)**
Carvedilol	3.215 mg BID	**25 mg BID (< 85 kg) 50 mg BID (≥ 85 kg)**

Yancy et al. Pathway for Optimization of HF Treatments JACC 2017; 2021 Update to the 2017 ACC Expert Consensus Decision Pathway for Optimization of HF Treatment

BB Key Points

- Side effect management:
  - Many side effects occur within the first several days of therapy and can be minimized by adjusting doses of ACEI and diuretic prior to starting BB
  - Increased fatigue will resolve within several weeks or months; however, may be severe enough to limit BB dose
  - Hypotension during therapy can be managed by decreasing diuretic or vasodilator dose, or by reducing BB dose or stopping temporarily
    - **Metoprolol will lower BP less than carvedilol**
  - Bradycardia (HR < 50 bpm) may require BB dose reduction or discontinuation, or pacemaker placement
  - Fluid retention can be managed with diuretics or by dosage reduction or possible discontinuation of BB

HF Part 4



- Medication therapies for stages in the development and progression of HF
  - Stage A meds
  - Stage B meds

Part 5: Medication Therapies for HF: Stage C