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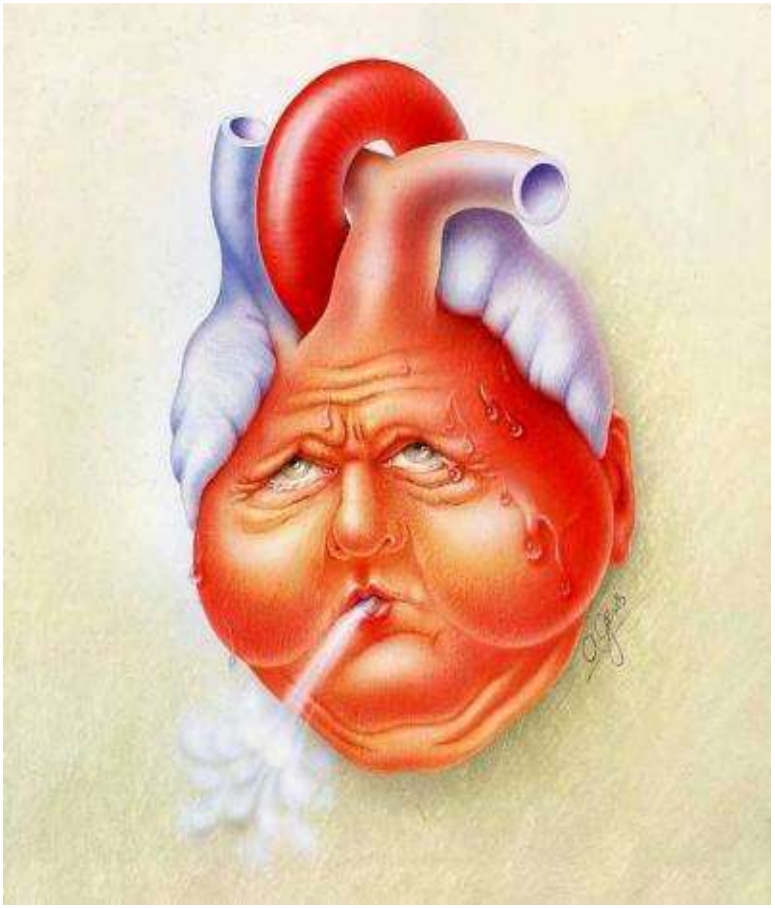
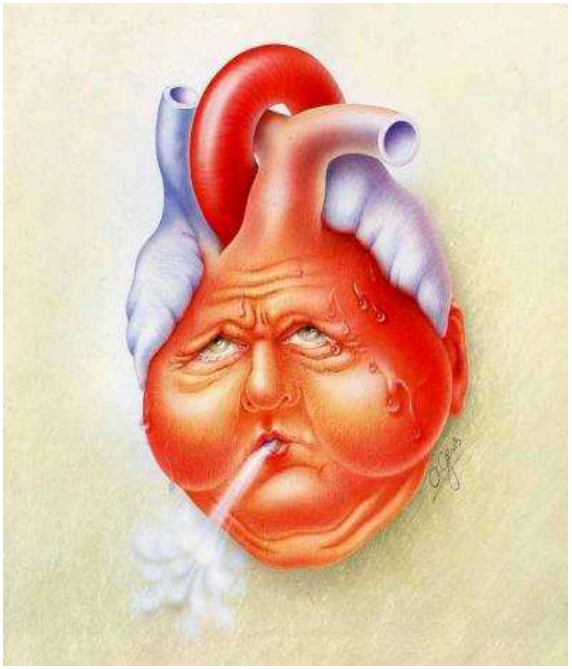
Part 5: Chronic Heart Failure Continued



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

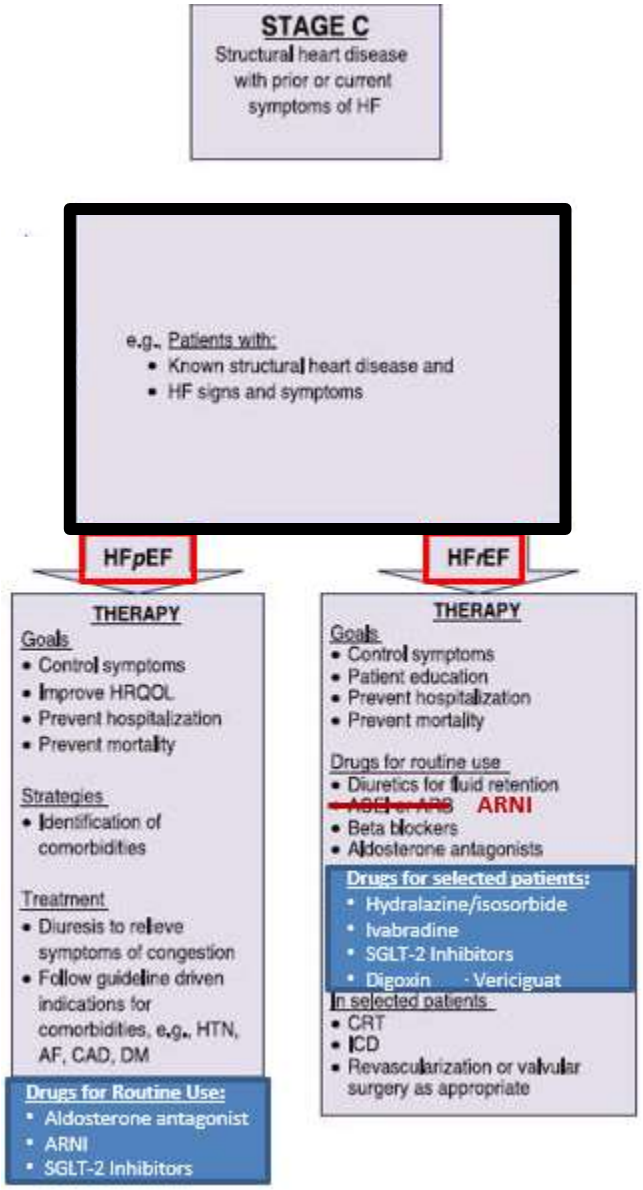
HF Part 5



- Medication therapies for stages in the development and progression of HF
  - Stage C meds- natriuresis and diuresis
- Patient case continued

Stages C – Has/Had HF Symptoms

- **Diuretics**
- **SGLT-2 inhibitors**
- ARNI
- Hydralazine/isosorbide
- Aldosterone Antagonists
- Ivabradine
- Digoxin
- Vericiguat
- Device therapy



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Diuretic Therapy for HF

- Diuretics are recommended in **patients with any phenotype who have evidence of fluid retention** to improve symptoms *Class IC rec*
- Enhance excretion of sodium (natriuresis) and water (diuresis) to decrease pulmonary congestion and edema
- Only drugs used in HF that can effectively control fluid retention
- Effectiveness depends on diuretic's site of action and patient's renal function
- Used initially as needed (PRN) until patient has persistent fluid overload, then becomes daily therapy
- Always use in combination with vasodilator! Why?

Neurohumoral Activation in Setting of Hypotension/Heart Failure

BP = CO X PVR CO = HR X SV

SV determined by preload, afterload, and contractility

↑ diuresis will ↓ preload

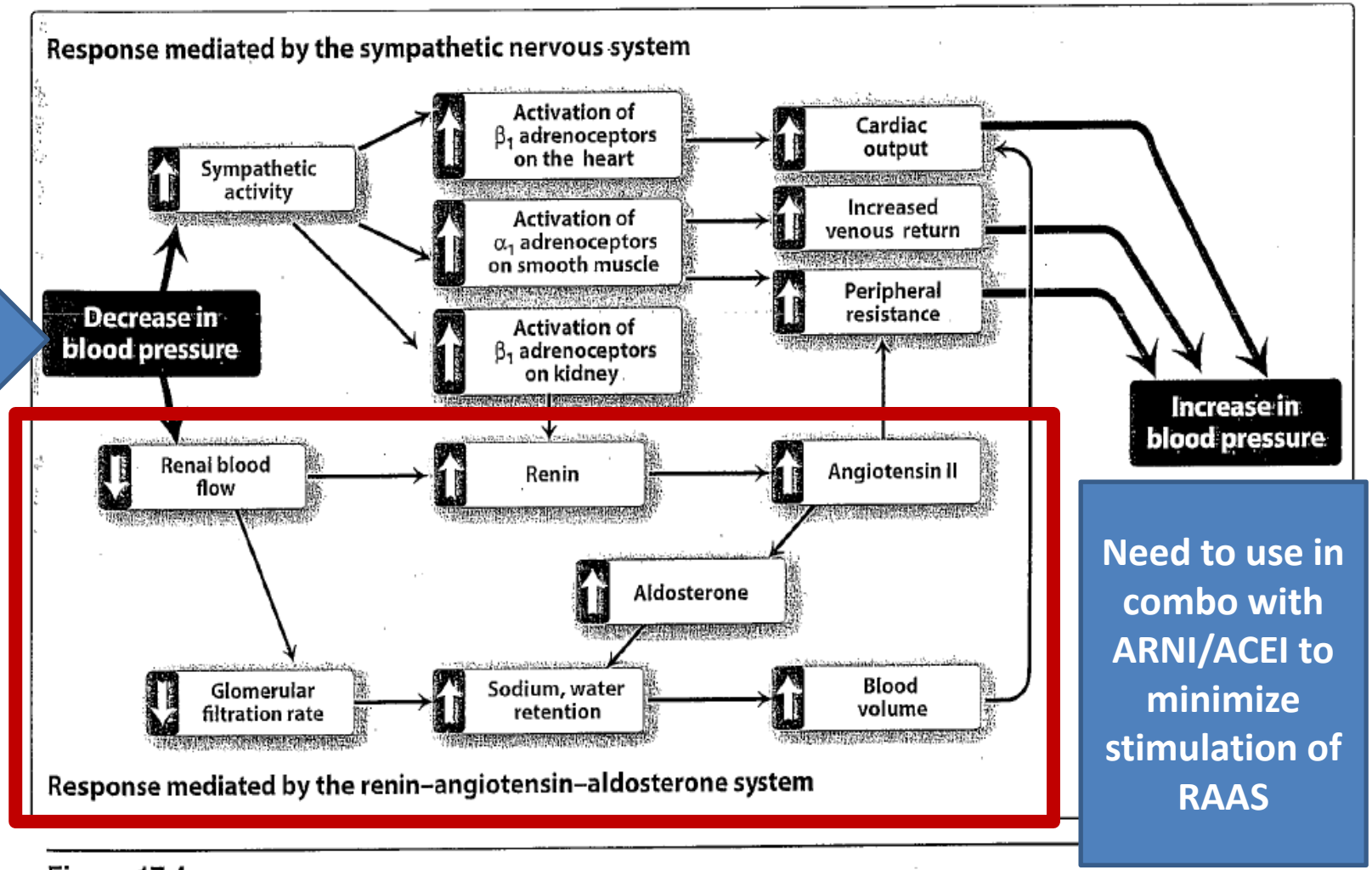
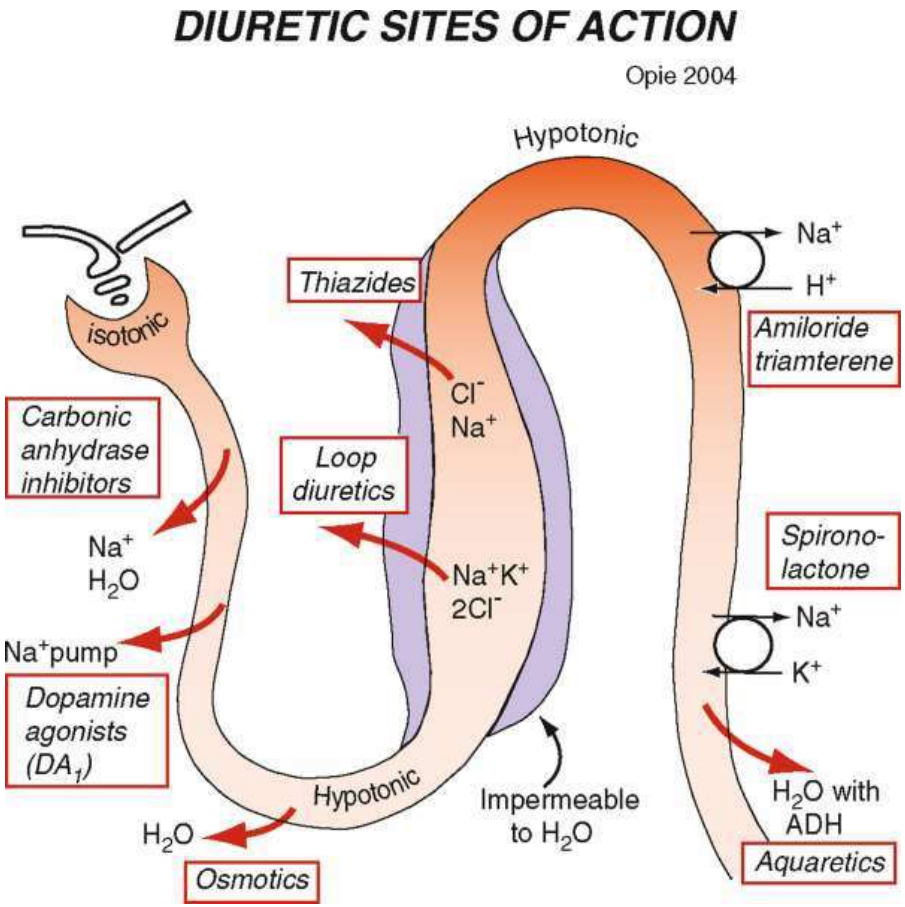


Figure 17.4

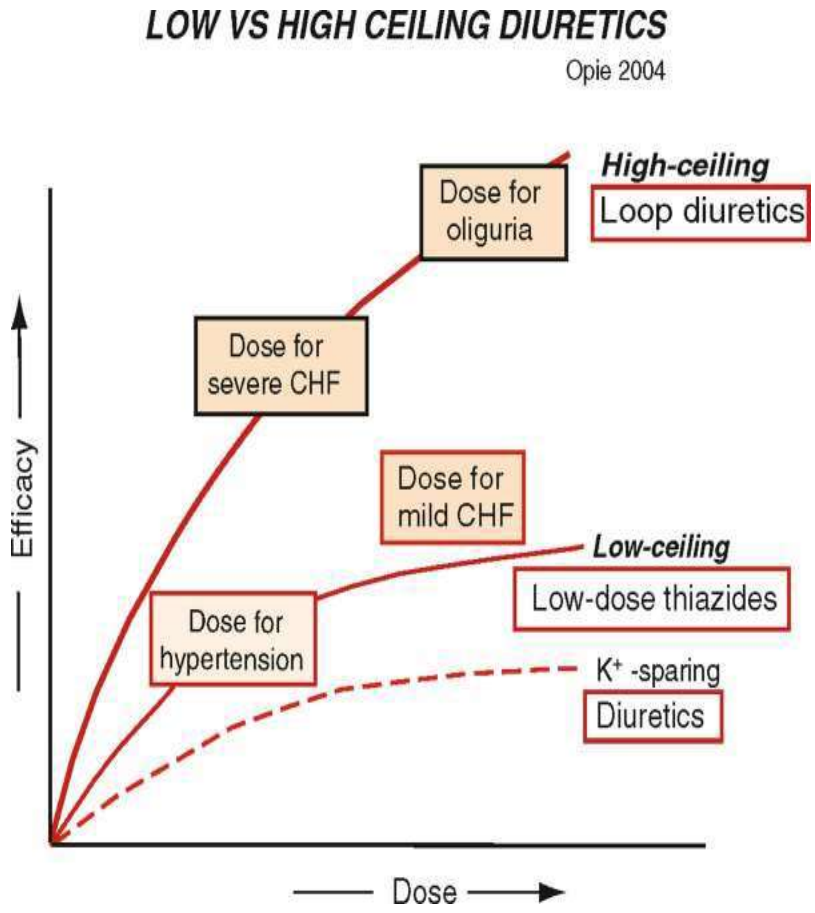
Need to use in combo with ARNI/ACEI to minimize stimulation of RAAS

Which Diuretics Should Be Used in HF?

Potency



Ceiling Effect



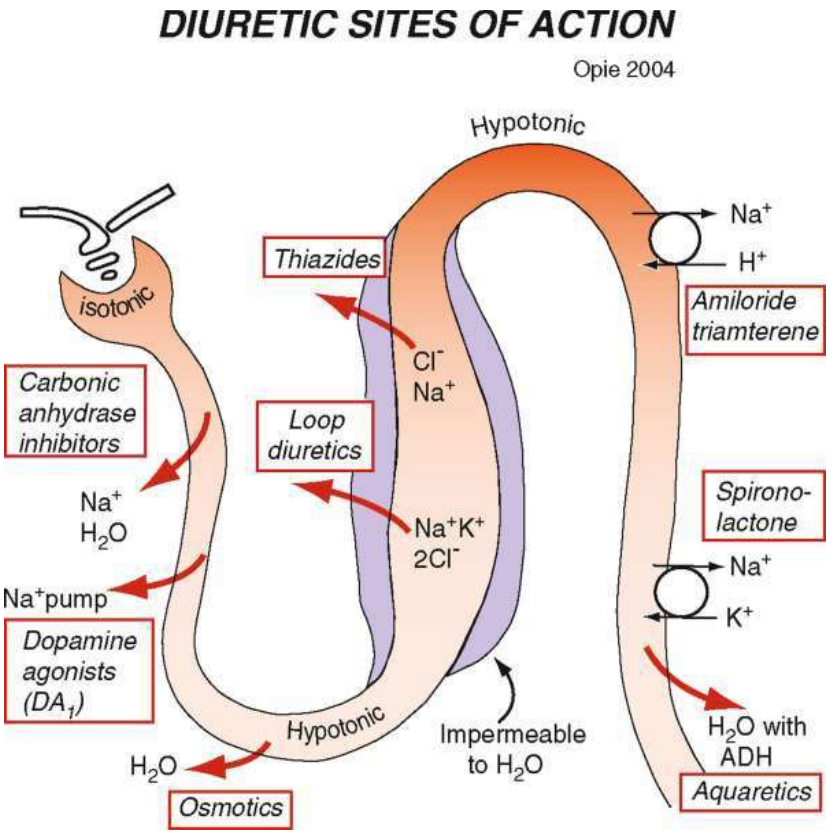
Adapted from Drugs for the Heart, 7th Edition. Figures 4-2 and 4-3.

Thiazide Diuretics Used in HF
(Mild Edema Only!)

- Chlorthalidone
  - Dose: 12.5-25 mg QD (max dose 100 mg/day)
- Hydrochlorothiazide
  - Dose: 12.5-25 mg QD-BID (max dose 200 mg/day)
- Key Points:
  - Use for mild sodium retention/symptoms only
  - Less effective than loop diuretics due to site of action
  - Use only if CrCL > 30 ml/min

Thiazide Diuretics Continued

- **Metolazone**
  - Dose: 2.5-5 mg PRN or QD (max dose 20 mg/day)
  - Potent diuretic that is effective when CrCL < 30mL/min
  - Most commonly used with a loop diuretic for refractory edema
  - Requires aggressive electrolyte monitoring!



Loop Diuretics

- Preferred in HF:
  - Superior fluid clearance (potency)
  - Work despite renal impairment
  - Increasing the dose increases diuretic response

	Initial Dose	Max Daily Dose
Furosemide (Lasix)	20-40mg QD or BID	600mg/day
Bumetanide (Bumex)	0.5-1mg QD or BID	10mg/day
Torsemide (Demadex)	10-20mg QD	200mg/day

2013 ACCF/AHA Guideline for Management of HF

Loop Diuretics Key Points

- Initiate at low doses and titrate upward to relieve S/Sx of fluid overload
- Use IV for acute decompensation
- Conversions:
  - Furosemide 40mg PO = furosemide (Lasix) 20mg IV
  - Furosemide 40mg PO = bumetanide 1mg IV/PO
  - Furosemide 40mg PO = torsemide 10-20mg PO (IV)
- F and B have short durations of action (~3-5 hrs) so BID dosing may be preferable
  - First dose: take upon awakening
  - Second dose: take no later than 2-3pm to avoid nocturia

Key Points Continued

- Usually requires 2-3 days of therapy before weight returns to baseline
- **Patient should not lose > 1 kg/day! (as outpatient)**
- Once fluid retention resolved, maintenance dose should be continued with dose reassessed and adjusted periodically
- Patients should be educated on self-adjustment based on weight and symptoms
  - Weight gain NMT $\geq$ 3 pounds in 24 hours or $\geq$ 5 pounds over 5 days
- May need to use 2 or more diuretics (thiazide + loop) for enhanced effect due to tolerance

Key Points Continued

- Side effects: hypotension, electrolyte imbalance, alkalosis, dehydration, gout, ototoxicity (IV form only)
- Side effect management:
  - Maintain potassium level >/= 4 mEq/L by supplementing with KCL if level < 4
    - **Usual dose is 50% of diuretic dose**
    - **If also starting ACEI/ARNI or AA** at the same time, **wait to initiate KCL therapy** until follow-up labs assessed
  - Maintain magnesium level >/= 2 mg/dL by supplementing with Mg++ if level < 2
    - Magnesium oxide 400mg BID-TID
  - Hypotensive symptoms in volume depleted patients can be relieved by decreasing diuretic dose or frequency of dosing

Key Points Continued

- Monitoring parameters:
  - Weight
    - Counsel patients to weigh themselves daily after voiding and wearing the same amount of clothing
    - Record readings and bring to appointments
    - Determine when patient should contact provider due to weight gain
  - BP/HR
    - Record and bring to appointments
  - Labs: electrolytes and SCr/BUN
    - Monitor and replace electrolytes
  - S/Sx of HF
  - I/O (hospitalized patients)

Refractory Edema

- Patients may become refractory (tolerant) to diuretic therapy due to:
  - changes in renal tubules (sodium reabsorption due to hypertrophy of distal nephron segment)
  - gut wall edema (decreases absorption up to 50%)

- If reaching high doses of loop diuretic (equivalent to furosemide 80mg BID), consider the following strategies to overcome resistance:
  - change to different loop diuretic or
  - add metolazone to loop diuretic or
  - give by IV instead of oral (acute care setting)

SGLT-2 Inhibitors for Stage C HF

- FDA approved indications:

	Canagliflozin (Invokana)	**Dapagliflozin (Farxiga)**	**Emplagliflozin (Jardiance)**	Ertugliflozin (Steglatro)
T2 DM	**X**	**X**	**X**	**X**
Reduce risk of CV death in adults with T2DM & established CV disease	**X**	**X**	**X**	

- HFrEF guidelines recommend addition of SGLT-2 inhibitor to GDMT:
  - Reduce risk of CV death and hospitalization for heart failure in adults with HFrEF **with or without DM**
    - Dapagliflozin FDA approved, empagliflozin pending

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2021 Update to the 2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment

CV Disease Benefits of SGLT-2 Inhibitors

Potential cardioprotective mechanisms:

- BP lowering (decrease afterload)
- Increasing diuresis/ natriuresis (decrease preload)
- Improving cardiac energy metabolism
- Preventing inflammation
- Weight loss
- Improving glucose control
- Inhibiting SNS
- Preventing ischemia/ reperfusion injury and fibrosis
- Improving vascular function

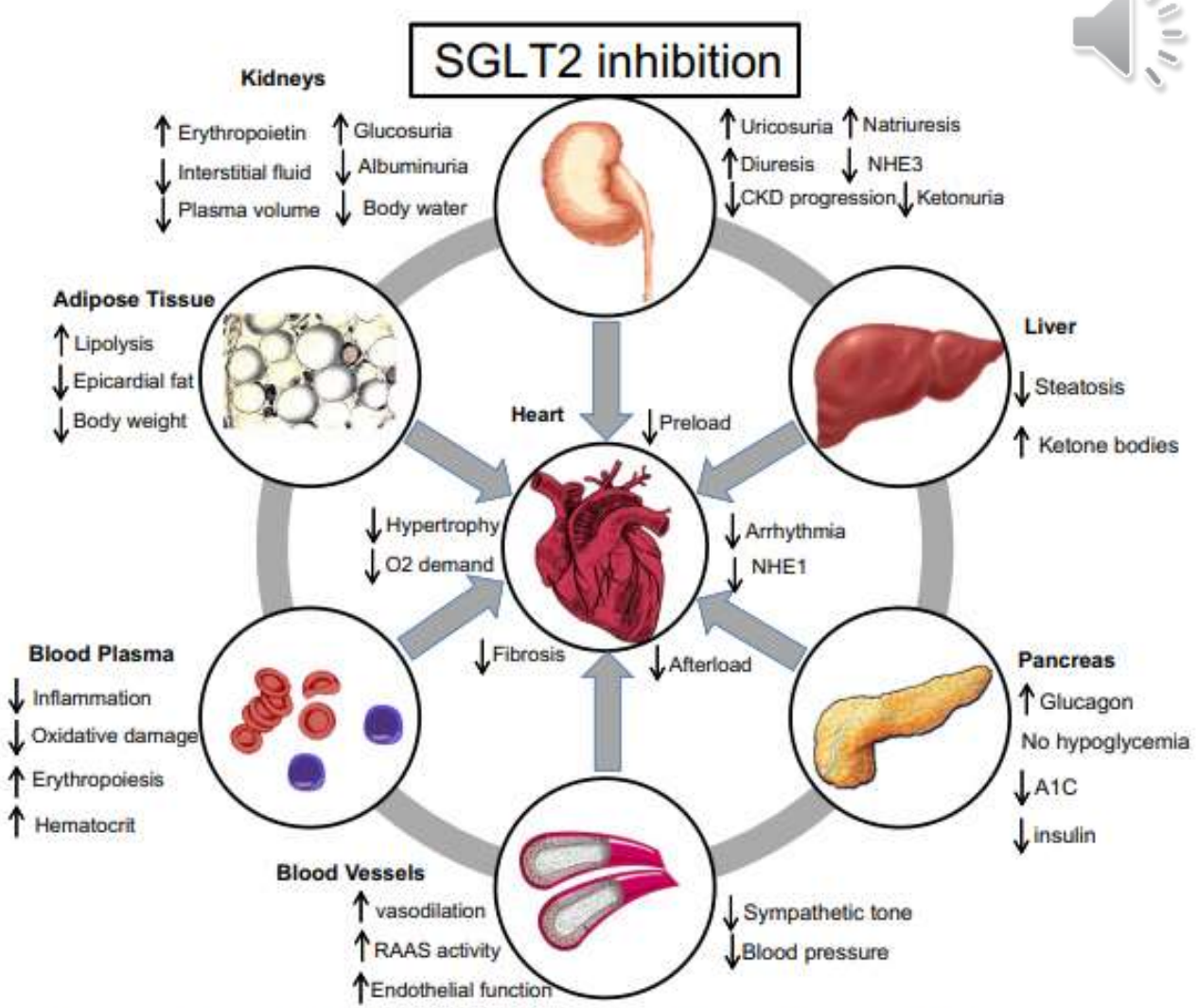

Fig. 1 A schematic representation of the different mechanisms implicated in the cardiovascular benefits of SGLT2 inhibitors

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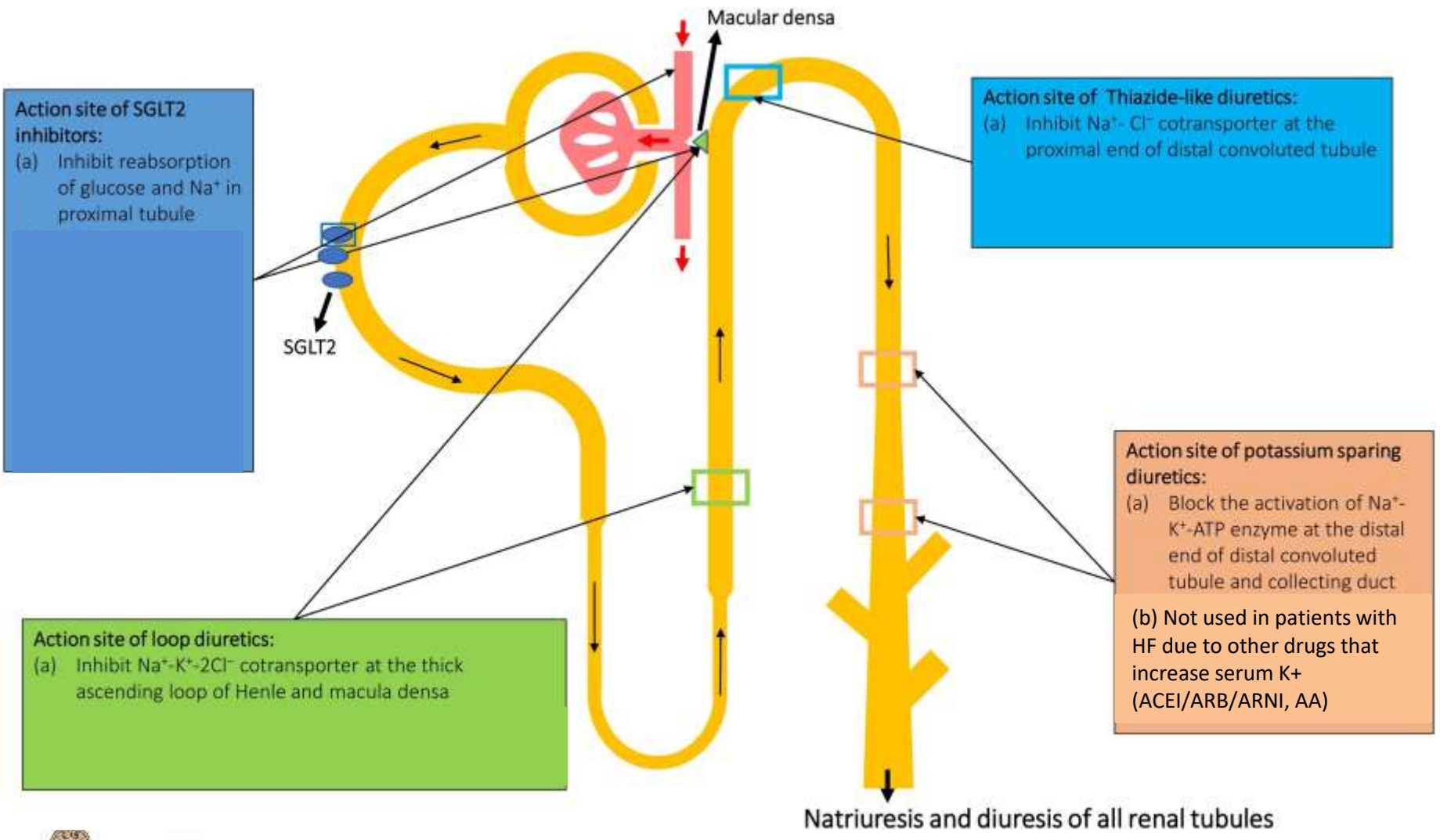
Wojcik and Warden. Curr Card Reports 2019;21:130; Lopaschuk and Verma. JACC: Basic to Translational Science 2020;5:632-44

Sites of Action for HF Drugs that Cause Natriuresis and Diuresis



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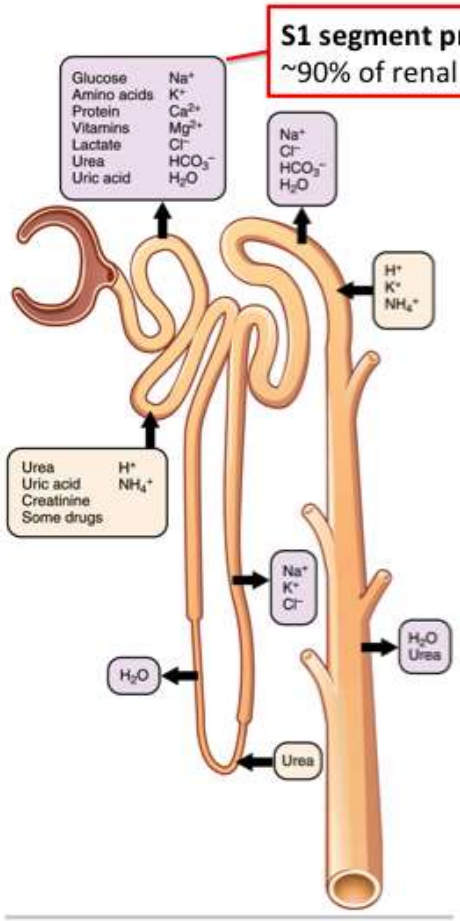
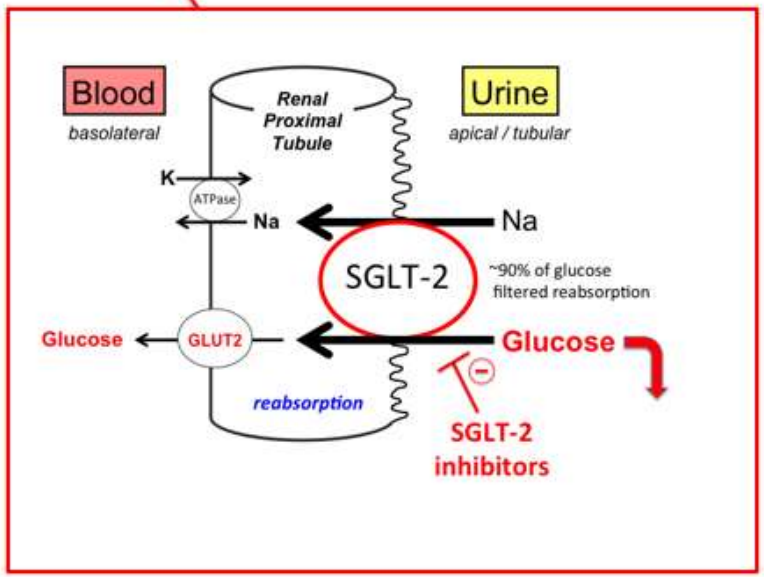
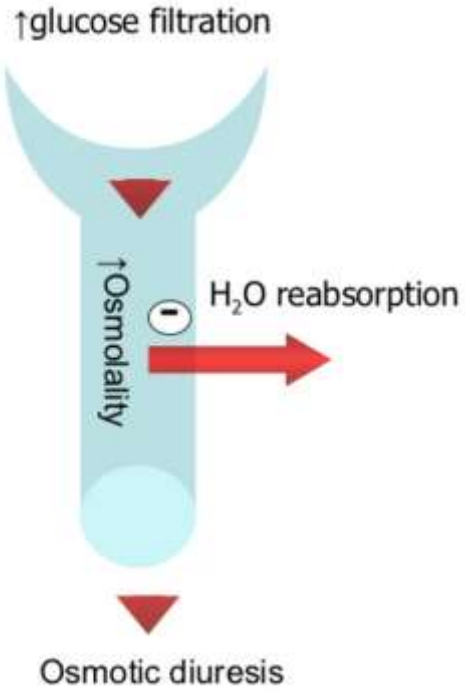
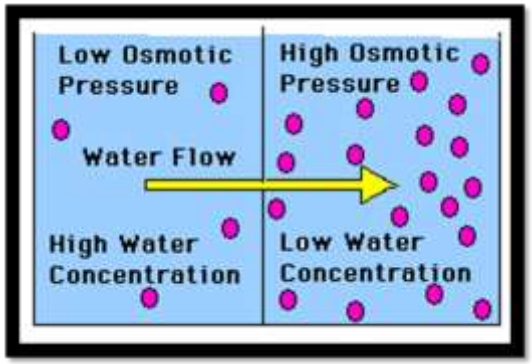
Cai et al. Biomedicine & Pharmacotherapy 2020;127:110192

Mechanism of Action









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SGLT-2 Inhibitors Key Points

- Dosing for HFrEF:

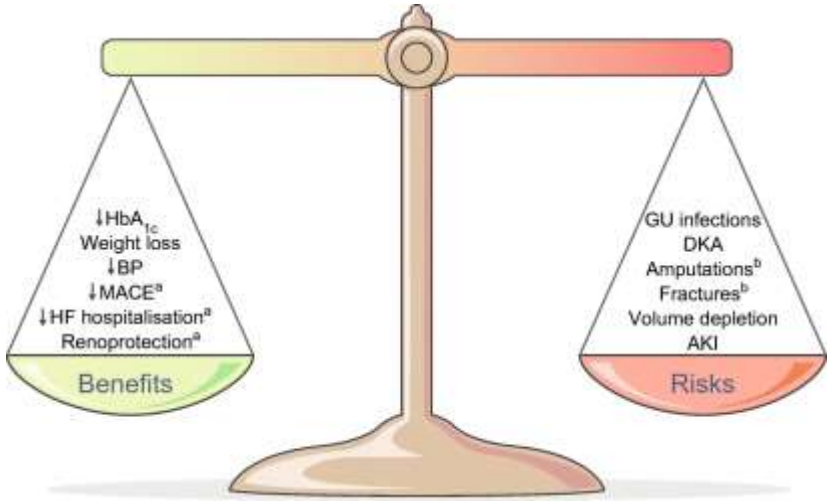
	Initial/Target Dose
Dapagliflozin	10 mg daily
Empagliflozin	10 mg daily

- Precautions:
  - Ensure eGFR $\geq$ 30 ml/min/1.73 m^2 for dapagliflozin and eGFR $\geq$ 20 ml/min/1.73 m^2 for empagliflozin before initiation
- Contraindications: Type 1 DM (increased risk for ketoacidosis), receiving dialysis

SGLT-2 Inhibitors Key Points

Side effects:

- Genitourinary infections (UTI, genital mycotic)
- DKA (euglycemic)
- Lower extremity amputation (canagliflozin)
- Skeletal fractures (canag)
- Volume depletion
- Acute kidney injury



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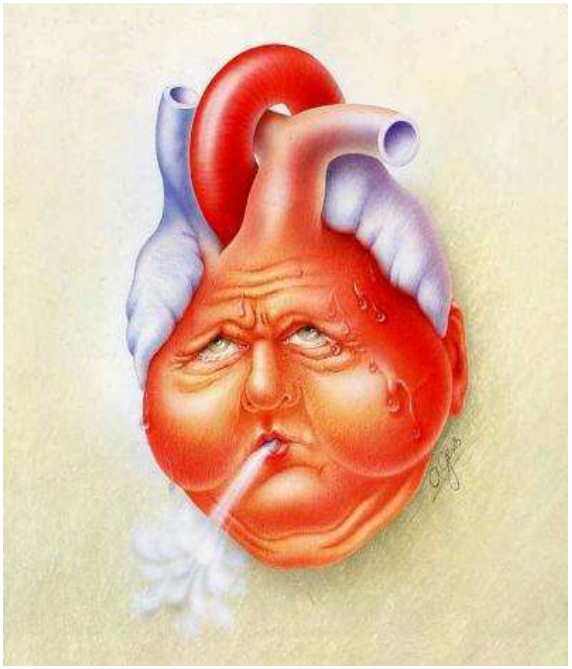
Lupsa and Inzucchi. Diabetologia 2018;61:2118-2125

HF Part 5



- Medication therapies for stages in the development and progression of HF
  - Stage C meds- natriuresis and diuresis

Part 6 Medications for Stage C HF
Stage C: More vasodilators and AA

HF Case: Part 2

- SB is a 64 yo female who presents to clinic complaining of SOB with getting dressed and difficulty sleeping at night due to coughing.
- She notices her ankles are swollen and her socks leave a pronounced mark on her legs.
- She feels nauseous and gets full after eating only half of her meals.
- She can't exercise lately due to fatigue and weakness.

HF Case Continued

- Physical exam:
  - Vitals: BP 108/72 mmHg, HR 92 bpm, RR 16 breaths/min
  - Ht: 66 inches, wt 71 kg ("dry" weight 68kg)
  - HEENT: JVP 10cm water
  - Heart: RRR, S3 present
  - Abd: soft, nontender, normal bowel sounds
  - Ext: 2+ pitting edema bilaterally
  - Lungs: CTA
- Chest X-ray: cardiomegaly
- ECHO: EF 20%

Question #4

- Which of the following medications is most appropriate for treating SB's congestion?
  a. Hydrochlorothiazide 25 mg daily
  b. Furosemide 20mg BID
  c. Spironolactone 25 mg daily
  d. Metolazone 5 mg daily
  e. Eplerenone 50 mg daily

Question #5

- She is currently not receiving any guideline directed medications for HF. What medication(s) should you consider starting once she is (or near) euvolemic?
  a. Carvedilol
  b. Lisinopril
  c. Metoprolol tartrate
  d. Valsartan

Question #6

- What labs would you like to order?

- When would you like the patient to return to clinic for her lab checks?