Heart Disease Community of Practice Series 2

Diuretic management in the community: Lasix, Metolazone and Bumetanide

Project ECHO
Palliative Care - Canada
BY Pallium Canada

Facilitator: Diana Vincze, Pallium Canada
Presenter: Morgan Krauter, NP
Date: May 17, 2023

Territorial Honouring

The Palliative Care ECHO Project

The Palliative Care ECHO Project is a 5-year national initiative to cultivate communities of practice and establish continuous professional development among health care providers across Canada who care for patients with life-limiting illness.

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The Palliative Care ECHO Project is supported by a financial contribution from Health Canada. The views expressed herein do not necessarily represent the views of Health Canada.

Health Canada Santé Canada

Project ECHO Palliative Care - Canada BY Pallium Canada

Introductions

Facilitator

Diana Vincze
Palliative Care ECHO Project Manager,
Pallium Canada

Presenter

Morgan Krauter, NP, CCN(C)
Nurse Practitioner, Heart Function

ECHO Support

Aliya Mamdeen
Program Delivery Officer, Pallium Canada

Introductions

Panelists

Dr. Lynn Straatman, MD FRCPC
Clinical Assistant Professor, UBC
Department of Medicine (Cardiology and Palliative Care)
Department of Pediatrics (Adolescent Health)
Medical Director, Cardiac Function Clinic
Co-chair Physician Diversity, Equity and Inclusion Committee, VCH

Dr. Leah Steinberg, MD, CFPC, FCFP, MA
Palliative Care Clinician, Sinai Health System
Assistant Professor, Division of Palliative Care, University of Toronto

Dr. Michael Slawnych, MD FRCPC
Clinical Assistant Professor
Department of Cardiology, St Paul's Hospital
University of British Columbia

Dr. Caroline McGuinty, MD FRCPC
Cardiologist, Advanced Heart Failure and Transplantation, Cardiac Palliative Care
University of Ottawa Heart Institute
Assistant Professor, University of Ottawa

Shannon Poyntz, NP-PHC, MN
Nurse Practitioner, Supportive Care

Drew Stumborg, RN
Saskatchewan Health Authority

Disclosure

Relationship with Financial Sponsors:

Pallium Canada

- Not-for-profit
- Funded by Health Canada
- Boehringer Ingelheim supports Pallium Canada through an in-kind grant to expand interprofessional education in palliative care.

Disclosure

This program has received financial support from:

- Health Canada in the form of a contribution program
- Pallium Canada generates funds to support operations and R&D from Pallium Pocketbook sales and course registration fees
- An educational grant or in-kind resources from Boehringer Ingelheim.

Facilitator/ Presenter/Panelists:

- Diana Vincze: Palliative Care ECHO Project Manager at Pallium Canada.
- Morgan Krauter: None to disclose.
- Dr. Michael Slawnych: Novartis.
- Dr. Leah Steinberg: Pallium Canada (education material), HPCO (clinical advisory committee, educator).
- Dr. Caroline McGuinty: Servier (consulting fees), Novartis (speaker fees).
- Dr. Lynn Straatman: Servier, Novartis, Astra Zeneca, BI, Medtronic, Pfizer, Eli Lilly, Bayer, Merck (clinical trials).
- Shannon Poyntz: None to disclose.
- Drew Stumborg: None to disclose.

Disclosure

Mitigating Potential Biases:

- The scientific planning committee had complete independent control over the development of program content

Welcome and Reminders

- Please introduce yourself in the chat!
- Your microphones are muted. There will be time during this session for questions and discussion.
- You are also welcome to use chat function to ask questions, add comments or to let us know if you are having technical difficulties, but also feel free to raise your hand!
- This session is being recorded and will be emailed to registrants within the next week.
- Remember not to disclose any Personal Health Information (PHI) during the session.
- This 1-credit-per hour Group Learning program has been certified by the College of Family Physicians of Canada for up to **6 Mainpro+** credits.
- This event is also an Accredited Group Learning Activity through the Royal College of Physicians and Surgeons of Canada. You may claim a maximum of **6.00 hours.**

Objectives of this Series

After participating in this program, participants will be able to:

- Describe what others have done to integrate palliative care services into their practice.
- Share knowledge and experience with their peers.
- Increase their knowledge and comfort around integrating a palliative care approach for their patients with advanced heart failure.

Overview of Topics

Session #	Session title	Date/ Time
Session 1	Update to medical management of HF decompensations in the community, including Cardiorenal dysfunction: how to manage with a palliative approach to care	November 16, 2022 from 12-1pm ET
Session 2	Demystifying ICDs – do you always need to deactivate?	January 18, 2023 from 12-1pm ET
Session 3	Complex case management/ Patients with complex goals of care	March 15, 2023 from 12-1pm ET
Session 4	Diuretic management in the community: Lasix, Metolazone and Bumetanide	May 17, 2023 from 12-1pm ET
Session 5	Multi-morbidity and Heart Failure- Managing Patients with Multiple Illnesses	September 20, 2023 from 12-1pm ET
Session 6	De-prescribing cardiac and other medications: palliative care in people with advanced heart failure	November 15, 2023 from 12-1pm ET

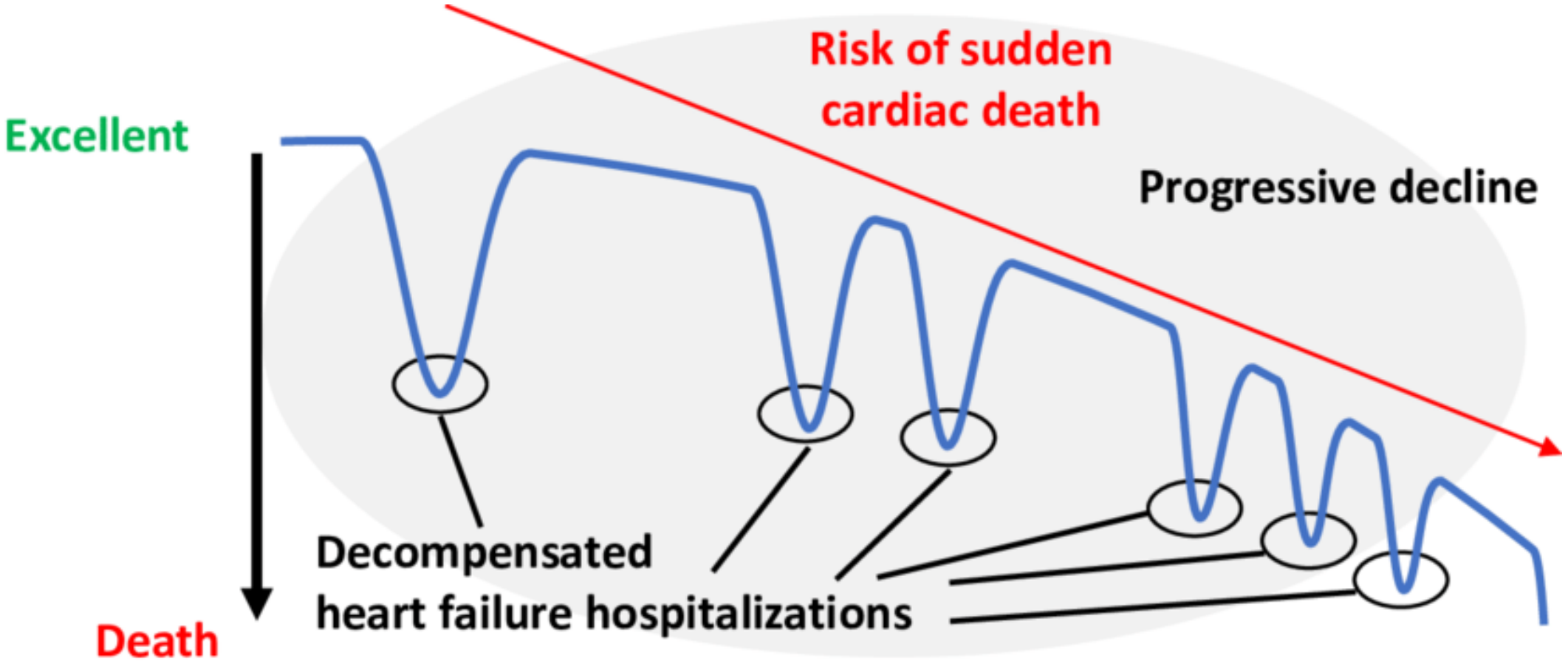
Objectives of this Session

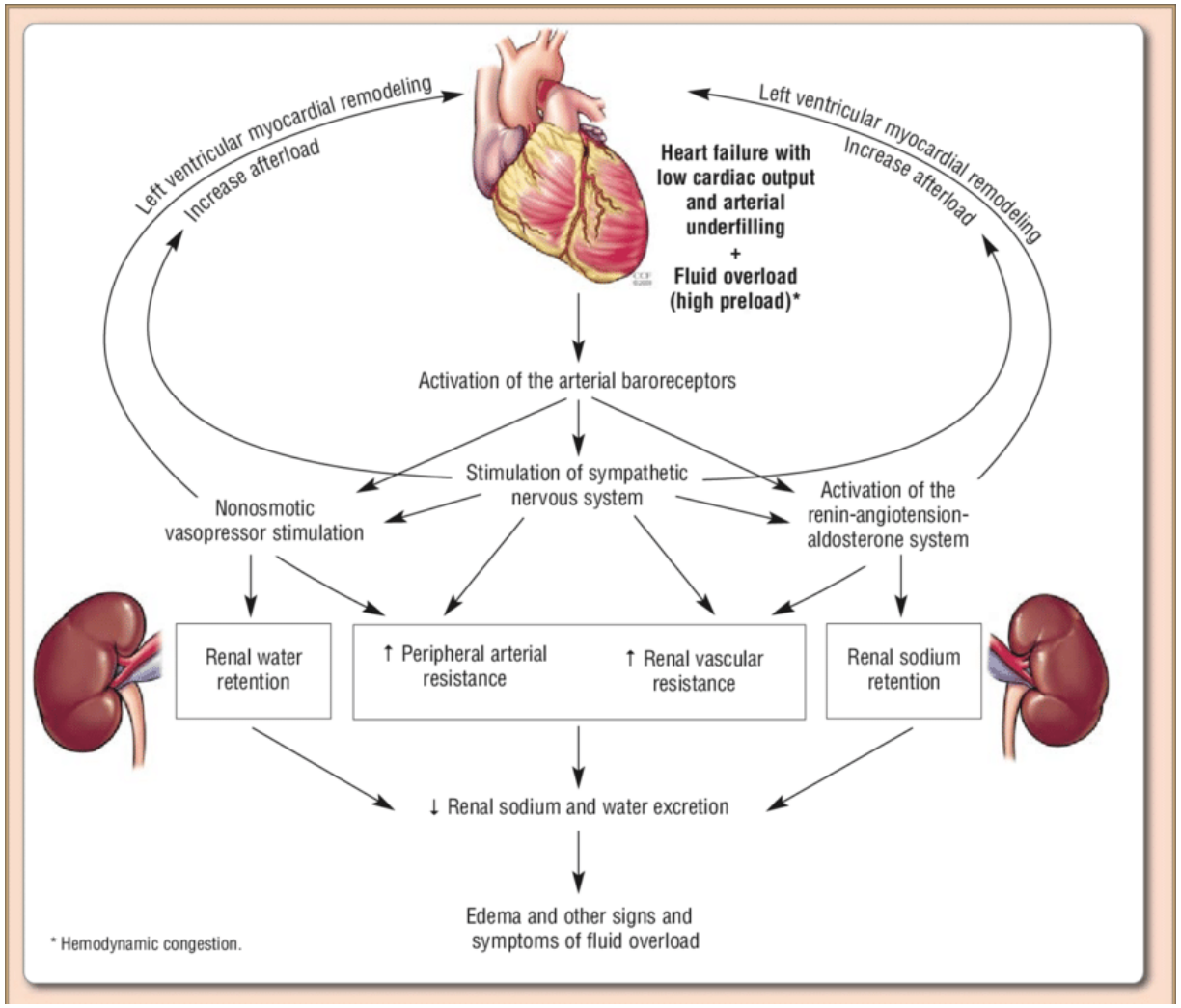
After participating in this session, participants will be able to:

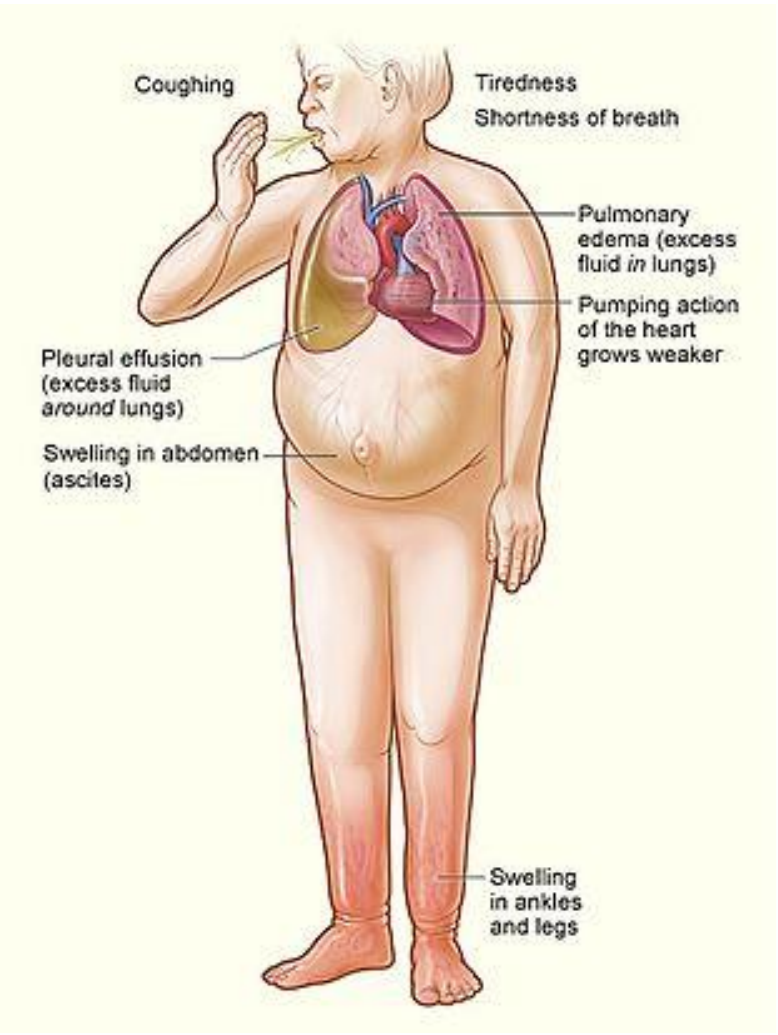
- Increase their knowledge and skill in using diuretics in the community.
- Appreciate the challenges and benefits of parenteral diuretic use.
- Apply diuretic protocols in their practice.

Ambulatory management of heart failure exacerbations

Natural HF History




Left ventricular myocardial remodeling
Increase afterload
Left ventricular myocardial remodeling
Increase afterload
Heart failure with low cardiac output and arterial underfilling
+
Fluid overload (high preload)*
Activation of the arterial baroreceptors
Stimulation of sympathetic nervous system
Nonosmotic vasopressor stimulation
Activation of the renin-angiotension-aldosterone system
Renal water retention
↑ Peripheral arterial resistance
↑ Renal vascular resistance
Renal sodium retention
↓ Renal sodium and water excretion
Edema and other signs and symptoms of fluid overload
* Hemodynamic congestion.

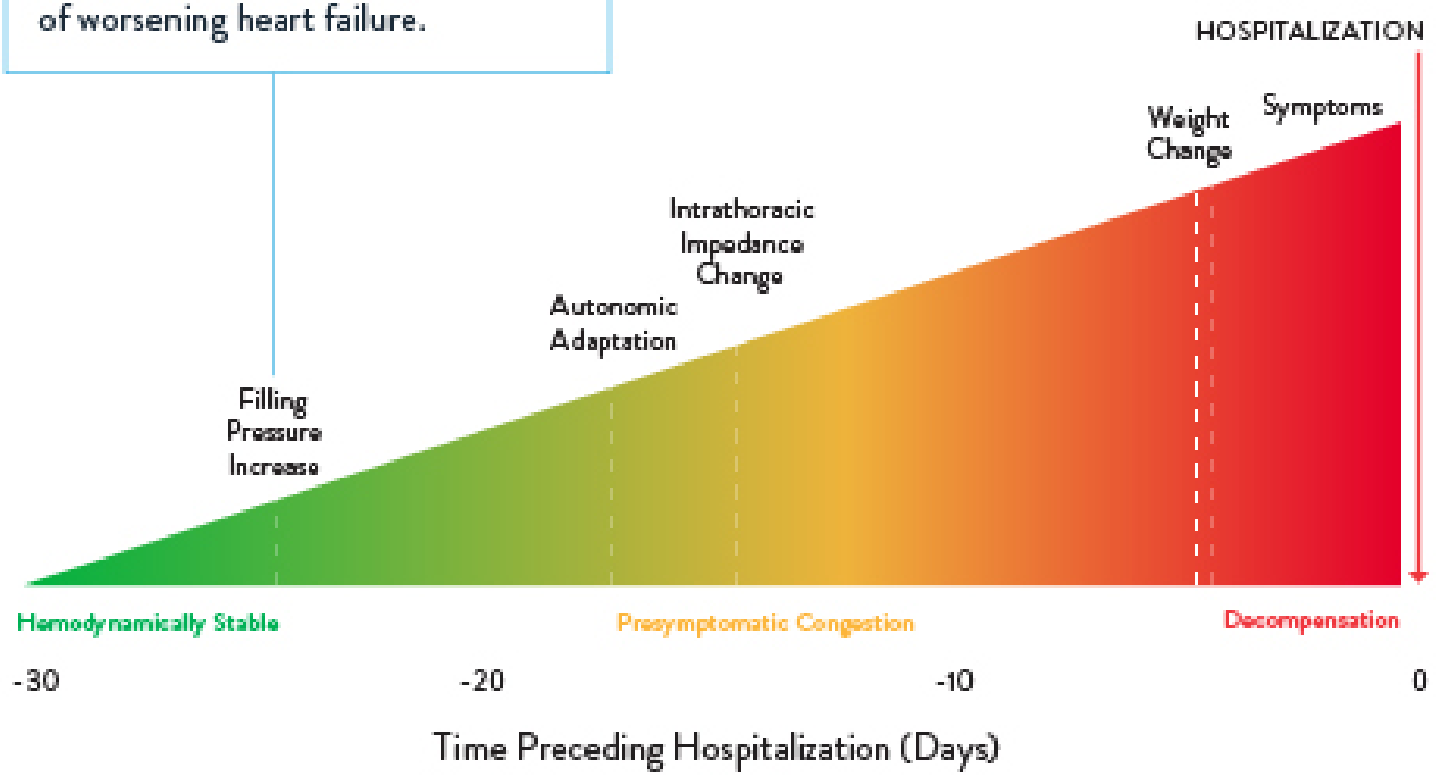

Coughing
Tiredness
Shortness of breath
Pulmonary edema (excess fluid *in* lungs)
Pumping action of the heart grows weaker
Pleural effusion (excess fluid *around* lungs)
Swelling in abdomen (ascites)
Swelling in ankles and legs

Proactive and Actionable

Real-time remote monitoring shows changes in pulmonary artery (PA) pressure, an early indicator of worsening heart failure.

Reactive and Inexact

Care teams have traditionally had to rely on physical markers, such as weight, blood pressure and symptoms.



Graph adapted from Adamson PB. Pathophysiology of the transition from chronic compensated and acute decompensated heart failure: new insights from continuous monitoring devices. Current Heart Failure Reports. 2009;6:287-292.

Diuretics

- Primary symptomatic management of acute decompensated heart failure (HF) but practice varies widely re. dose and administration.
- Not shown to provide mortality benefit.
- Loop diuretics are mainstay therapy.
- Adjunct therapy for synergistic effect in setting of diuretic resistance.

Goals of diuretic therapy

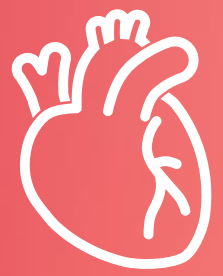
According to Guidelines

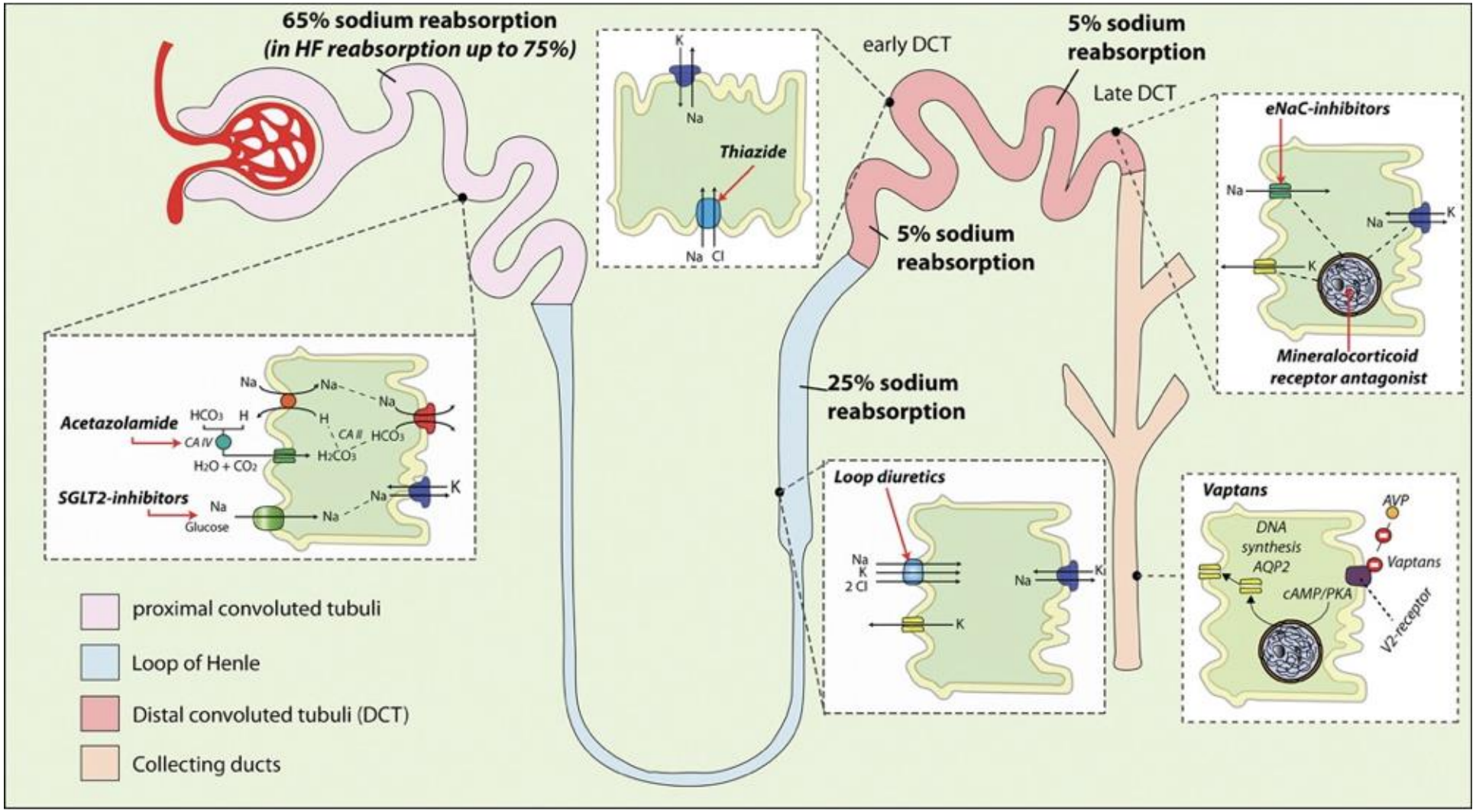
1. Achieve thorough decongestion without residual volume overload
2. Ensure adequate perfusion pressure to guarantee organ perfusion
3. Maintain guide-directed medical therapies as they can increase diuretic response and improve long-term survival

Palliative Approach to Care

1. Symptom relief
2. Euvolemia
3. Minimize side effects:
   - Presyncope
   - Electrolyte dysfunction
   - Renal impairment
   - Functional decline
   - Incontinence

Diuretics in HF

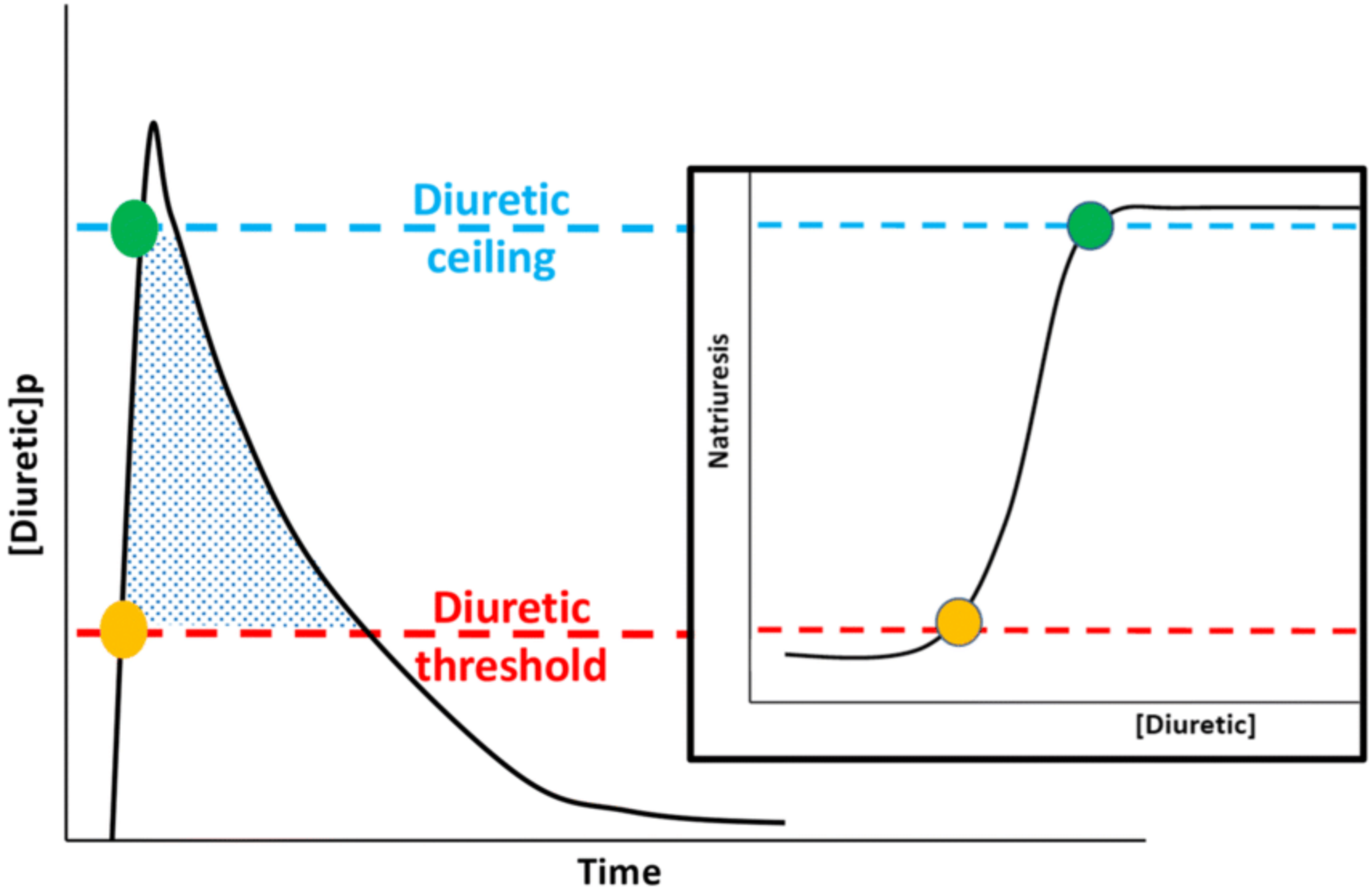




European J of Heart Fail, Volume: 21, Issue: 2, Pages: 137-155, First published: 01 January 2019, DOI: (10.1002/ejhf.1369)

Loop Diuretics

- Furosemide (Lasix), Bumetanide (Bumex)
- Highly protein-bound organic anions secreted across the proximal convoluted tubule where they act on sodium-potassium chloride channel in thick ascending loop of Henle to inhibit Na+ reabsorption to promote delivery of Na+ to distal tubule
- Steep dose-response curve and threshold dose below which they do not produce natriuresis
- “High ceiling” diuretics: progressive increase in their dose promotes more natriuresis but after certain maximal dose the effect plateaus


Diuretic ceiling
Diuretic threshold
[Diuretic]p
Time
Natriuresis
[Diuretic]

Loop diuretic resistance in HF

- Heavily protein-bound (> 90%) and requires sufficient plasma levels as renal perfusion is often reduced in HF, resulting in decreased secretion of loop diuretics.
  - Also impacted by decreased plasma protein content in cachexia / malnutrition.
- Bioavailability is highly variable for oral furosemide and determined by gastrointestinal tract absorption, which is impaired by reduced cardiac output and bowel edema.
- Chronic use of loop diuretics induces compensatory distal tubular sodium reabsorption through tubular cell hypertrophy, leading to reduced natriuresis and need for progressive dose increase over disease course.

Furosemide vs. Bumetanide

Characteristics	Furosemide (Lasix)	Bumetanide (Bumex)
Half-life (hours)	1.5-2	1-1.5
Bioavailability	10-100	80-100
Initial oral dosing (mg)	20 - 40	0.5 – 1
Relative potency	40	1
IV to oral dosing	1:2	1:1 (IV not available in Canada)
Maximum dosing in 24 hours (mg)	600	10
Duration of effect (hours)	~ 6	4-6

DOSE-HF (2008)

- RCT comparing bolus doses vs. infusion and low (equivalent to baseline dose) vs. high (2.5x baseline oral dosage) dose of loop diuretics.
- Mode of administration (bolus vs. continuous infusion) and dose (low vs. high) of loop diuretics had no significant effect on primary endpoint of overall effectiveness or safety of therapy.
- Higher doses of loop diuretics led to significantly greater diuresis, improved dyspnea, and fewer adverse events than lower doses.

Oral (PO) vs. Intravenous (IV) furosemide

- In the setting of acute decompensated HF, gastrointestinal absorption of oral diuretics is decreased due to gut edema and duodenal blood flow contributing to oral therapy resistance.
- IV administration bypasses gut edema and is more efficacious in setting where there is decreased absorption of oral medications.
- Guideline-directed care recommends IV furosemide administration in the hospital setting, but novel administration in ambulatory clinic and home settings are emerging.

Practical Considerations

- Bumetanide (Bumex) PO 1mg = Furosemide (Lasix) PO 40mg / IV 20mg
- Bumex is expensive compared to Lasix
  - Bumex 1mg x 30 tabs = $43.99 ($1.46 / tab)
  - Lasix 40mg x 100 tabs = $27.99 ($0.28 / tab)
- Bumex not covered by Ontario Drug Benefit (ODB) program but available through Exceptional Access Program (EAP)
  - Pre-pandemic, process could take 4-6 weeks; now, 2-3 days due to Priority 1 status.
  - Requires evidence of failed diuretic escalation with covered drugs like furosemide, metolazone., acetazolamide

Thiazide Diuretics

- Hydrochlorothiazide or Metolazone (Zaroxolyn)
- Act on distal convoluted tubule by blocking NaCl co-transporter, where 3-5% of Na+ reabsorption occurs
- Sequential nephron blockade as adjunct therapy to augment diuresis and alleviate diuretic resistance
- Combination therapy associated with increased risk of adverse events: hypokalemia, hyponatremia, hypomagnesemia, hypochloremia, metabolic acidosis, worsening renal dysfunction, hypotension, cardiac arrhythmias

Potassium-Sparing Diuretics

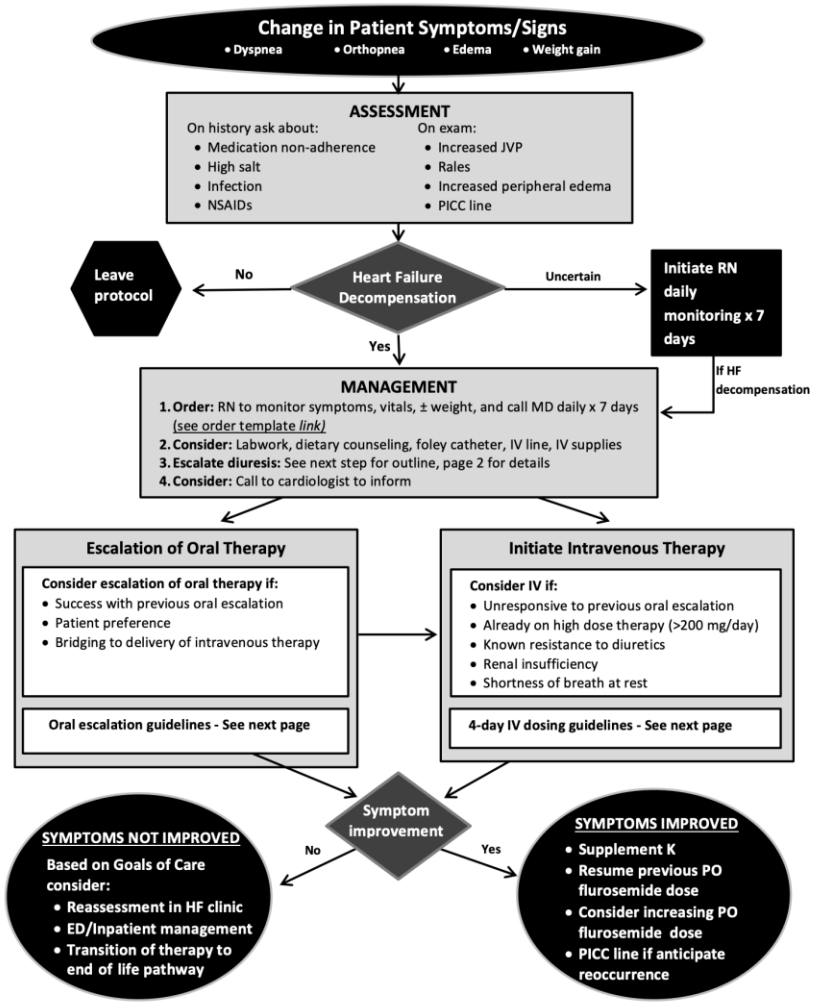
- Spironolactone (Aldactone), eplerenone (Inspra)
- “weak diuretics”: acts at collecting duct where only 3% of Na+ reabsorption occurs; aldosterone receptor blockers down-regulate Na+/K+ pump and epithelial Na+ channels leading to decreased Na+ reabsorption and secretion of H+ and K+ cations.
- Disease modifying therapeutic agent in symptomatic patients with chronic HFrEF.
- Useful in offsetting hypokalemic effect of potassium-wasting loop and thiazide diuretics.

Carbonic Anhydrase Inhibitor

- Acetazolamide (Diamox)
- Acts on proximal convoluted tubule to inhibit sodium reabsorption.
- According to ADVOR (2022) trial, addition of acetazolamide (500mg IV daily) to standardized IV loop-diuretic therapy associated with higher incidence of successful decongestion within 3 days after randomization.
- Practical dosing: acetazolamide 250-500mg PO BID in combination with PO or IV loop diuretic therapy.

Sodium-Glucose Linked Transporter-2 Inhibitors (SGLT2)

- Empagliflozin (Jardiance), dapagliflozin (Farxiga), canagliflozin (Invokana).
- Inhibit proximal sodium absorption.
- Modest natriuretic effect of SGLT2 in addition to loop diuretics from glucosuric effect.
- Disease modifying therapeutic agent in symptomatic patients with chronic HFrEF.
- Decreases magnesium excretion and increased uric acid excretion and not known to worsen renal potassium excretion like loop diuretics.



Escalation of Oral Therapy

Suggested dose increases	
Current Daily Dose	**Suggested New Dose**
<40 mg/d	40 mg BID
40 to 120 mg/d	80 mg qAM/40 mg qPM OR 80 mg BID
120 to 240 mg/d	120-160 mg BID Consider add on therapy
>240 mg/d	160 mg BID Consider add on therapy
Day 3 5 Reassessment	
Weight Decreasing Patient improving	Continue current dose Administer kdur May resume previous oral therapy dose
Weight Unchanged or Increasing	Continue current dose Consider add on therapy
Day 7 Reassessment	
Weight Decreasing Patient improving	Continue current dose Administer kdur May resume previous oral therapy dose
Weight Unchanged or Increasing	Increase current dose Consider add on therapy Consider IV diuresis

Add on therapies to consider	
Metolazone	2.5-5mg/d x 3 days 2.5-5mg/d, M, W, F Metolazone can be very effective Limit to short, 3 dose trials and reassess
Hydrochlorthiazide	12.5-50 mg/d

Initiate Intravenous Therapy

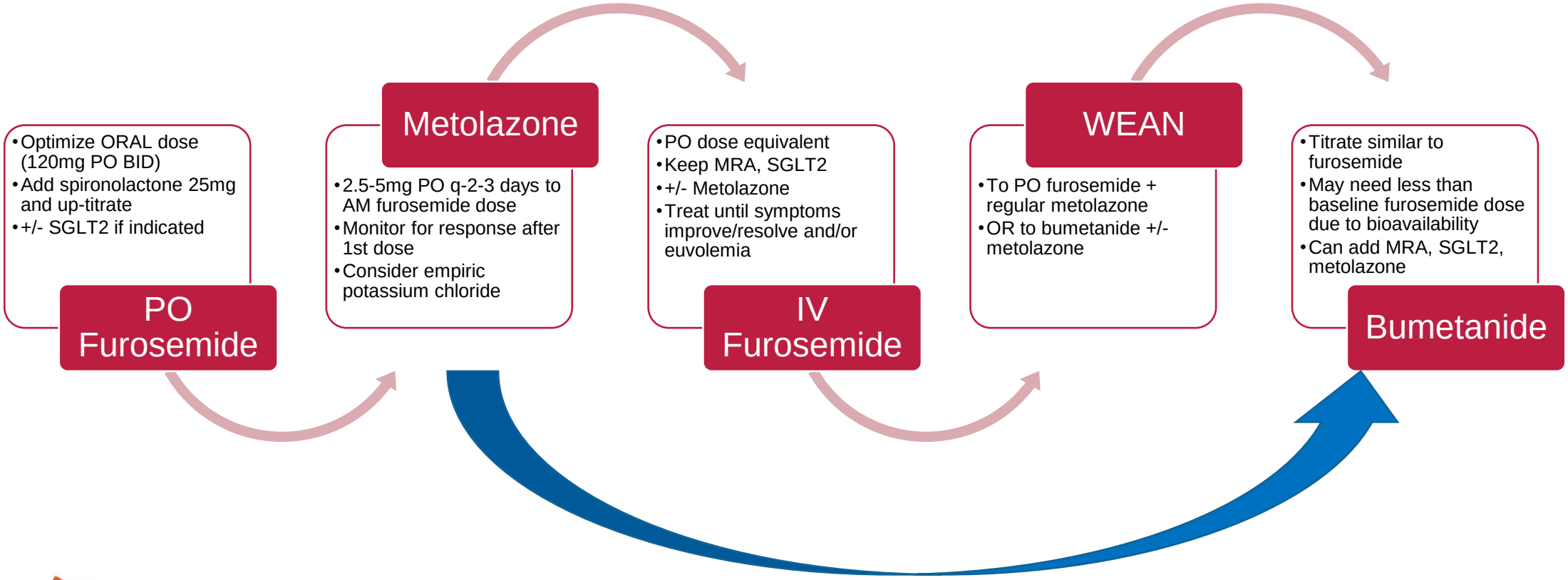
Day 1	
Current Daily Dose	**Suggested New Dose**
≤120 mg/day >120 mg/day	40 mg IV BID 80 mg IV BID Consider add on therapy
Day 2 Reassessment	
Weight Decreasing Patient improving	Continue current dose Administer kdur
Weight Unchanged or Increasing	Continue current dose Consider add on therapy
Day 3 Reassessment	
Weight Decreasing Patient improving	Continue current dose Administer kdur Can consider stepping down to PO
Weight Unchanged or Increasing	Increase 40 BID to 80 IV BID Increase 80 BID to 120 IV BID Consider add on therapy
Day 4 Reassessment	
Weight Decreasing Patient improving	Continue current dose Administer kdur Can consider stepping down to PO
Weight Unchanged or Increasing	Increase 40 BID to 80 BID Increase 80 BID to 120 BID Consider add on therapy Can continue beyond 4 days

Add on therapies to consider	
Metolazone	2.5-5mg/d x 3 days 2.5-5mg/d, M, W, F Metolazone can be very effective Limit to short, 3 dose trials and reassess

STOP THERAPY AT ANY TIME IF:

- Unacceptable biochemical derangement
- Symptomatic Hypotension
- Total of 6 days of therapy without symptomatic response

Morgan's Step Wise Approach (with labs)

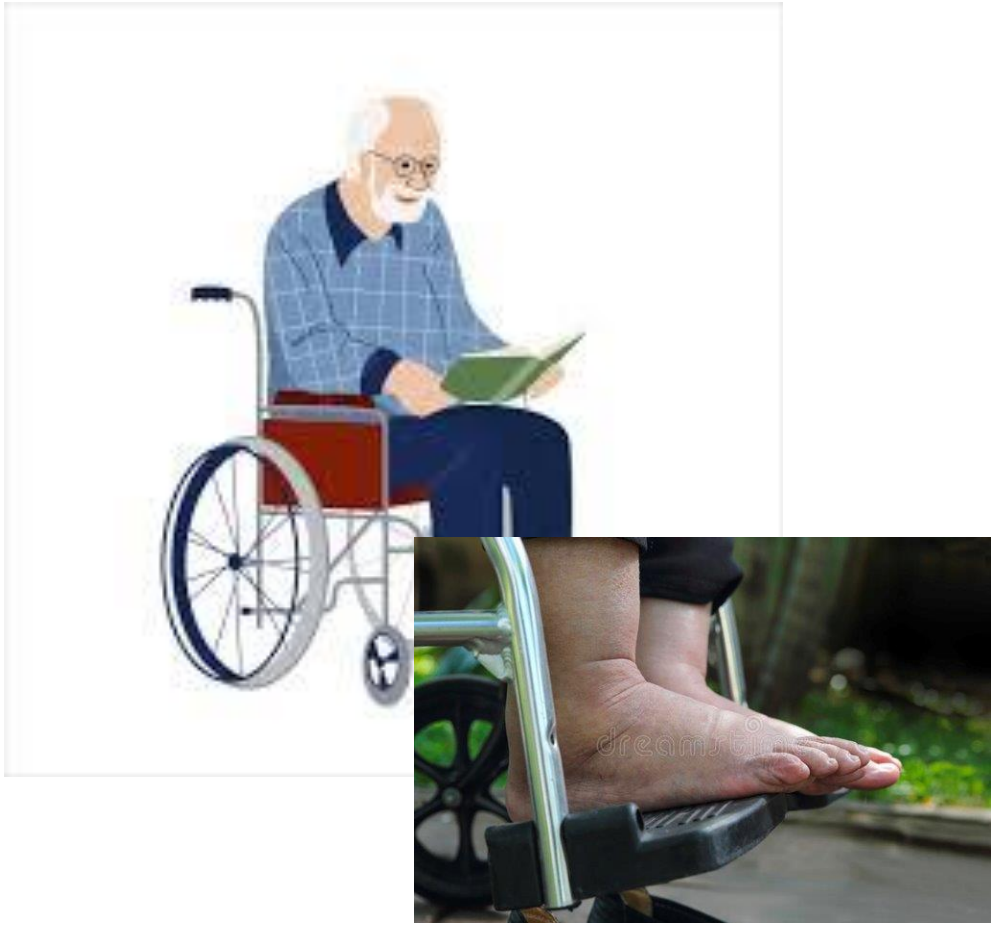


Practical Considerations of Diuretic Therapy

- Step-wise approach for escalation / de-escalation
- What's your wean plan?
- Intravenous access: IV vs. PICC vs. Midline
  - According to patient treatment preference, risk of infection, and need for / accessibility to labs
- Simple vs. Complex regimens
  - Patient / caregiver ability to recognize symptoms and self-manage
  - Patient desire for control / autonomy over diuretic treatment
  - Risk of side effects, hemodynamic instability

Case-Based Discussion

CASE



Details: 85-year-old man with history of MI, LVEF 42%, CKD (creatinine 160-180), T2DM, HTN, dyslipidemia. Fourth admission to hospital last month for HF at which time goals changed to active management with palliative approach. Wants to avoid return to hospital.

Social situation: retired from the navy, lives at home with his wife as primary caregiver

Medications: Furosemide 80mg PO BID, Spironolactone 25mg daily, Bisoprolol 5mg daily, Hydralazine 75mg TID, Nitro patch 0.4mg/hr TD, Atorvastatin 40mg daily, Allopurinol 200mg daily

- **Where do you start?**
- **What are the challenges you currently face?**
- **What can we strive to do differently?**

Questions

Wrap Up

- Please fill out the feedback survey following the session! Link has been added into the chat.
- A recording of this session will be e-mailed to registrants within the next week.
- Please join us for the next session in this series on **Multi-morbidity and Heart Failure-Managing Patients with Multiple Illnesses** **September 20, 2023 from 12–1:00 p.m. ET.**

Thank You

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