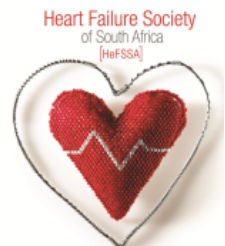


HeFSSA Practitioners Program 2016

“What is NEW in Heart Failure treatment?”

08:00	Registration
08:25	Welcome and Thank You to Sponsors
08:30	The new kid on the block – “ ARNI”
09:15	How do I effectively diurese my patient? Anything new?
10:00	Tea Break
10:30	Drugs, devices and procedures to offer the atrial fibrillation patient- new and exciting
11:15	The NEW heart failure guidelines from Europe
11:45	Questionnaire
12:00	Departure



CASE STUDY:

How do I effectively diurese my patient?

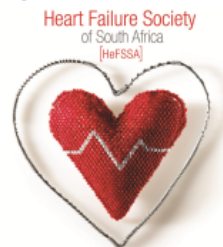
Anything new?



Case Study

Mrs HM, 54 years, 4 children, nursing sister, widow

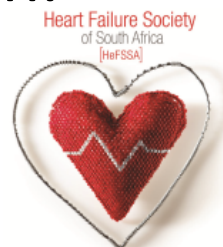
- Known heart failure patient since 2001 (age 39), was diagnosed as a peri-partum cardiomyopathy (EF 33%) and secondary mitral regurgitation. LV internal diastolic diameter (LVIDD) 58 mm
- Seen by a different cardiologist in June 2013, diagnosed as Rheumatic Mitral Valve Disease, EF 40%, atrial fibrillation and failed electrical cardioversion, LVIDD = 67 mm
- Confirmed RHD by another cardiologist in September 2013, had a mitral valve mechanical replacement, tricuspid valve repair and excision of the left atrial appendage



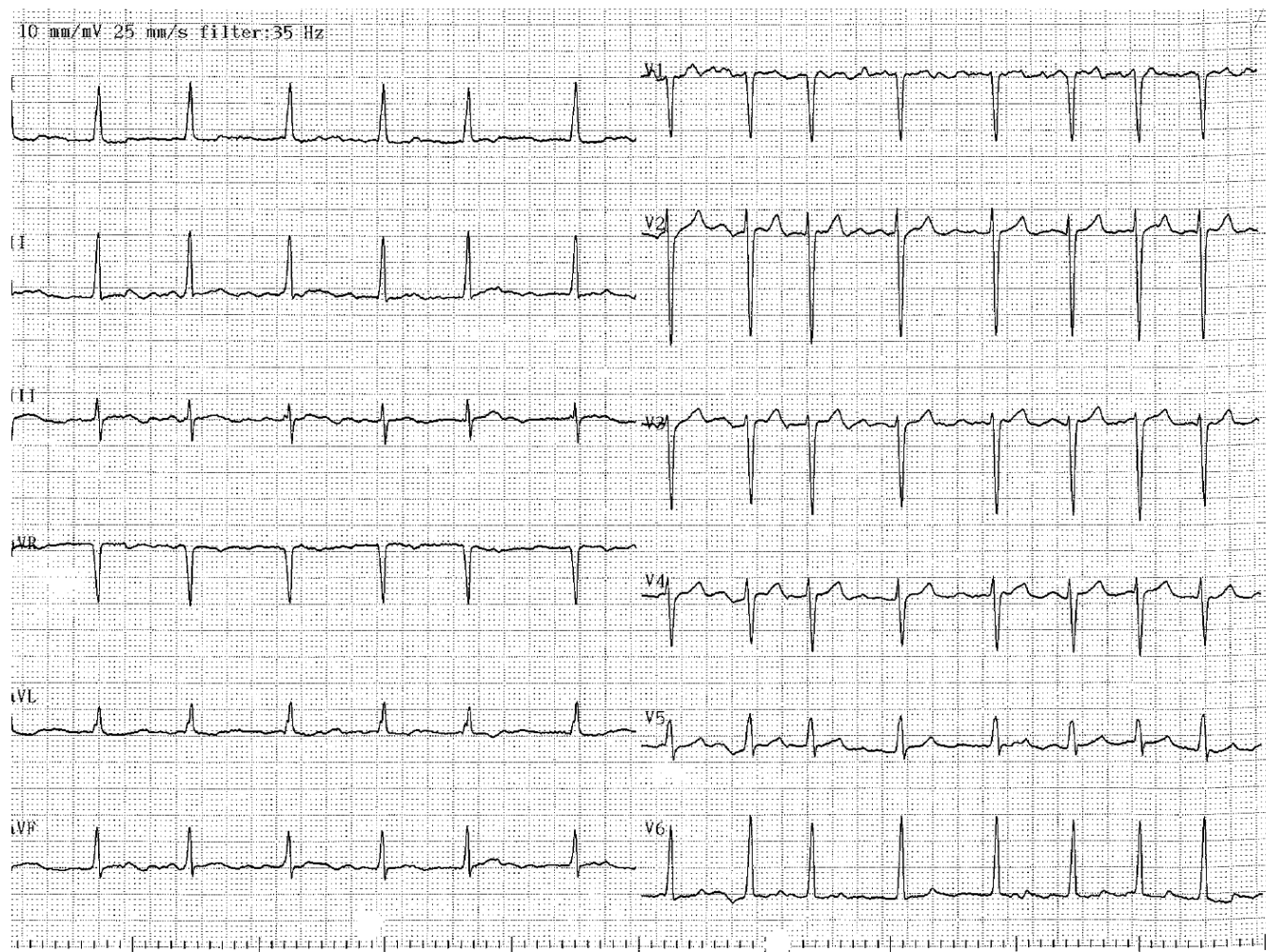
Case Study

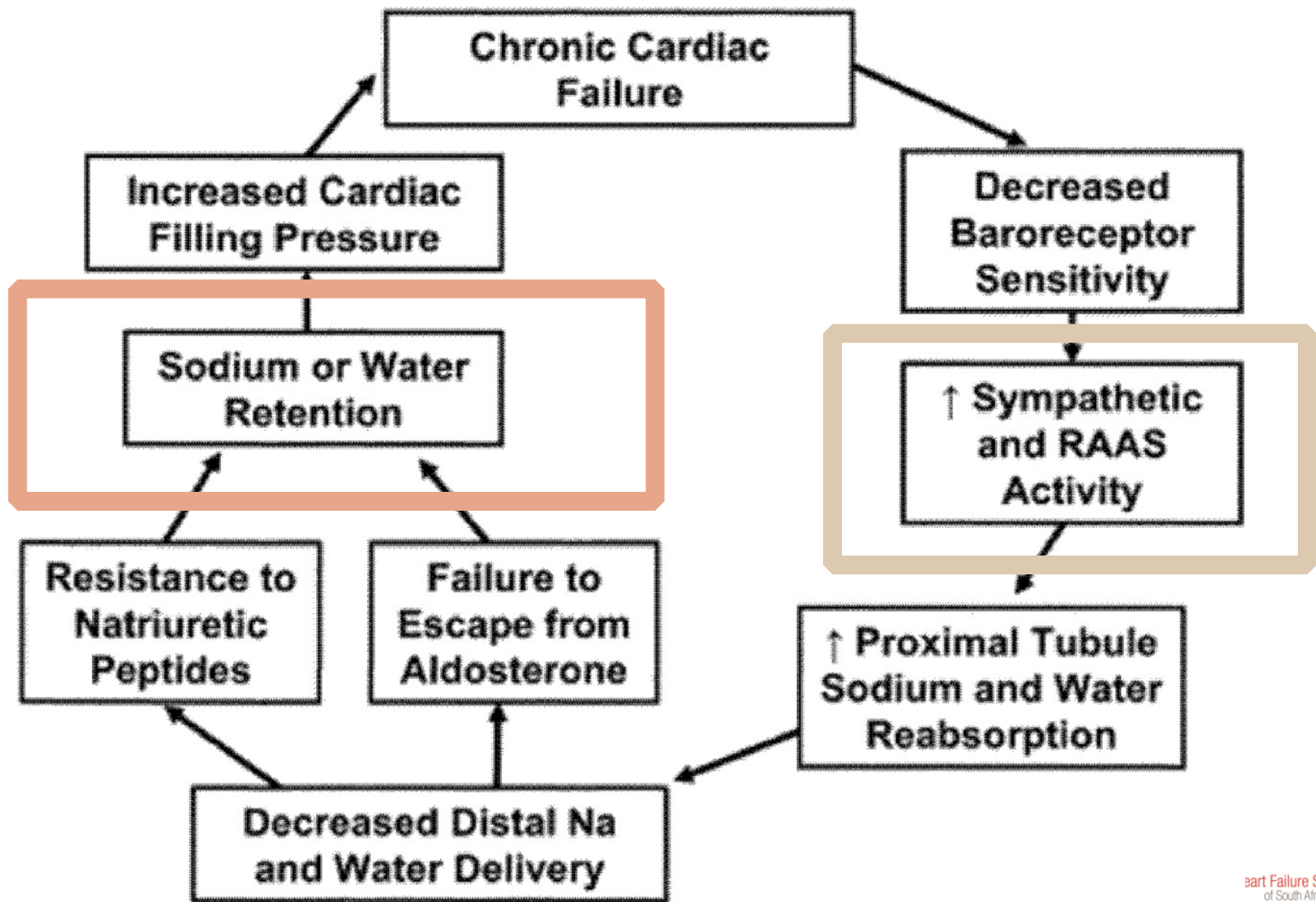
Mrs HM

- Seen on **6 March 2016** by a fourth cardiologist, having had recurrent admissions for deteriorating heart failure since late 2015.
- Cold peripheries, severely congested, cachectic, rapid and irregular pulse 90 beats/minute, BP 90/60
- EF = 16%, LVIDD = 73mm, Pulmonary artery peak pressure = 60 mmHg, IVC = 34 mm and non collapsing in inspiration, functioning mitral valve prosthesis (including valve X-Ray screening)
- Admission (mmol/l) :Na =129, potassium 5.4, urea 8.6 and Creat 99umol/l- eGFR=56 ml/min. INR = 4.1. proBNP=4425pg/ml

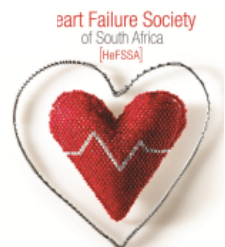


Resting ECG – on admission





Mohammad Sarraf et al. CJASN 2009;4:2013-2026



Case Study

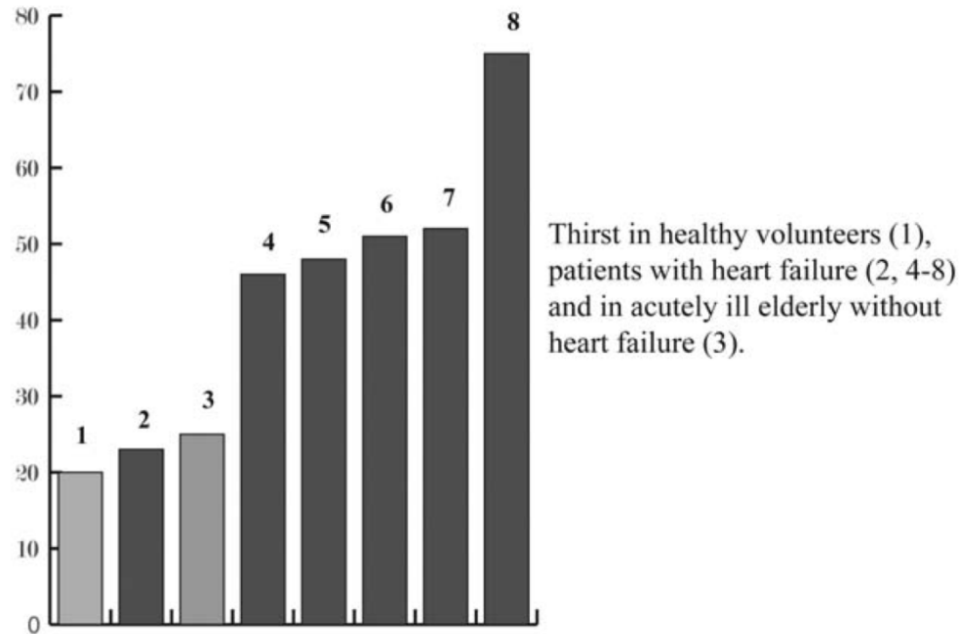
Mrs HM

- She had been on Furosemide 80 mg daily, Plenish K 3 daily, Perindopril 4 mg daily, Spironolactone 25 mg daily, Carvedilol 12.5 mg bd and Warfarin.
- Because of a sore big toe she had been taking Diclofenac 100 mg daily.
- She had noticed that the furosemide was not having its desired effect although she was drinking > 3 l water / day!

Thirst

Thirst Intensity (visual analogue scale, VAS 0-100 mm)

VAS scale



1 Healthy volunteers; Hahn & Waldréus (2012) submitted.

2 Stable heart failure with liberal fluid intake; Holst et al. (2008).

3 Acutely ill elderly without heart failure; Waldréus et al. (2011).

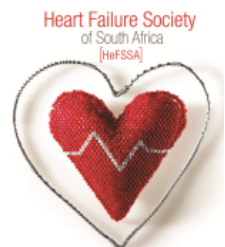
4 Stable heart failure with fluid and salt restriction; Philipson et al. (2010).

5 Stable heart failure with liberal fluid and salt intake; Philipson et al. (2010).

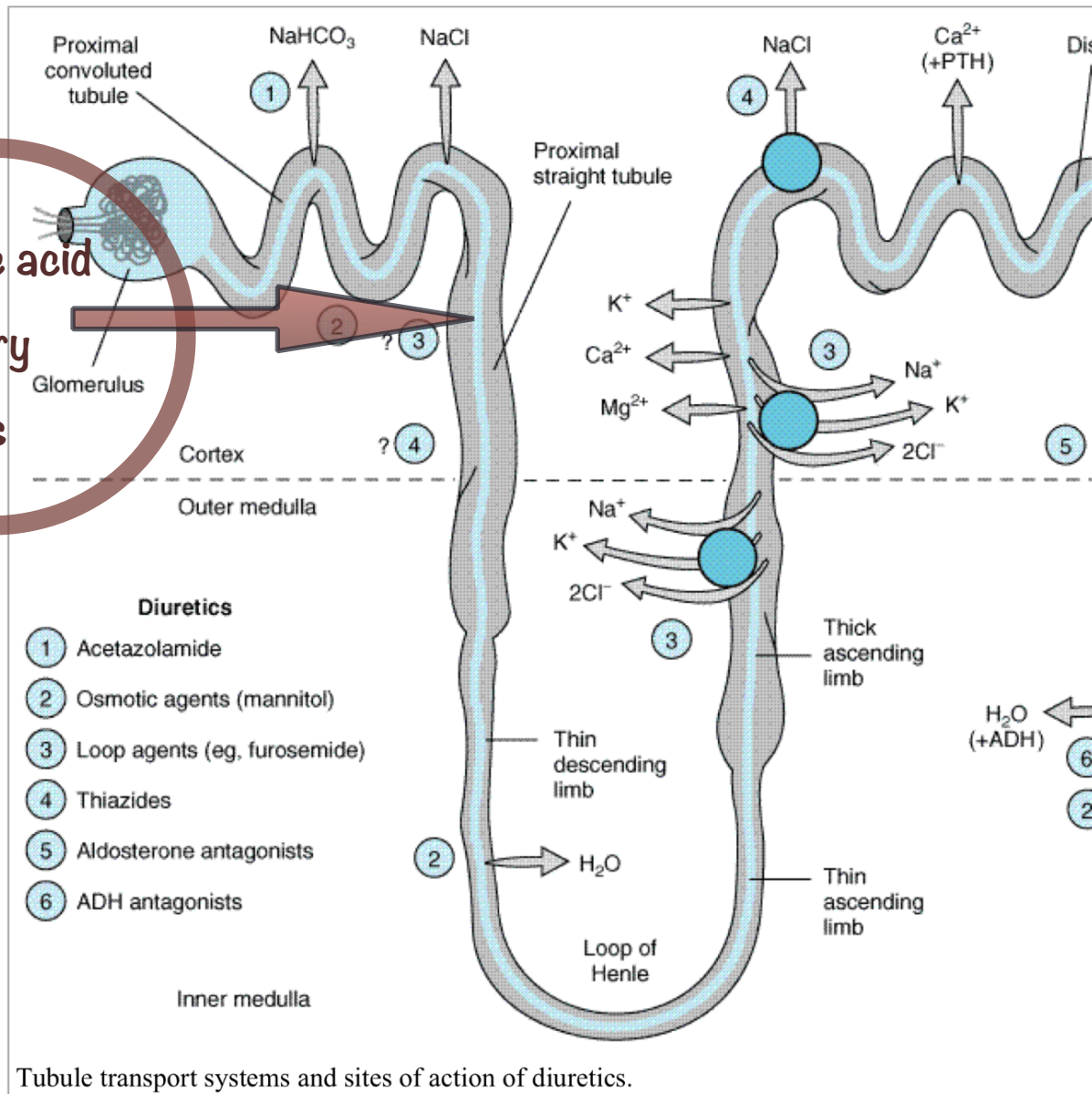
6 Stable heart failure with fluid restriction; Holst et al. (2008).

7 Stable heart failure; Philipson et al. (2010).

8 Worsening heart failure; Waldréus et al. (2011).



Organic acid
secretory
systems



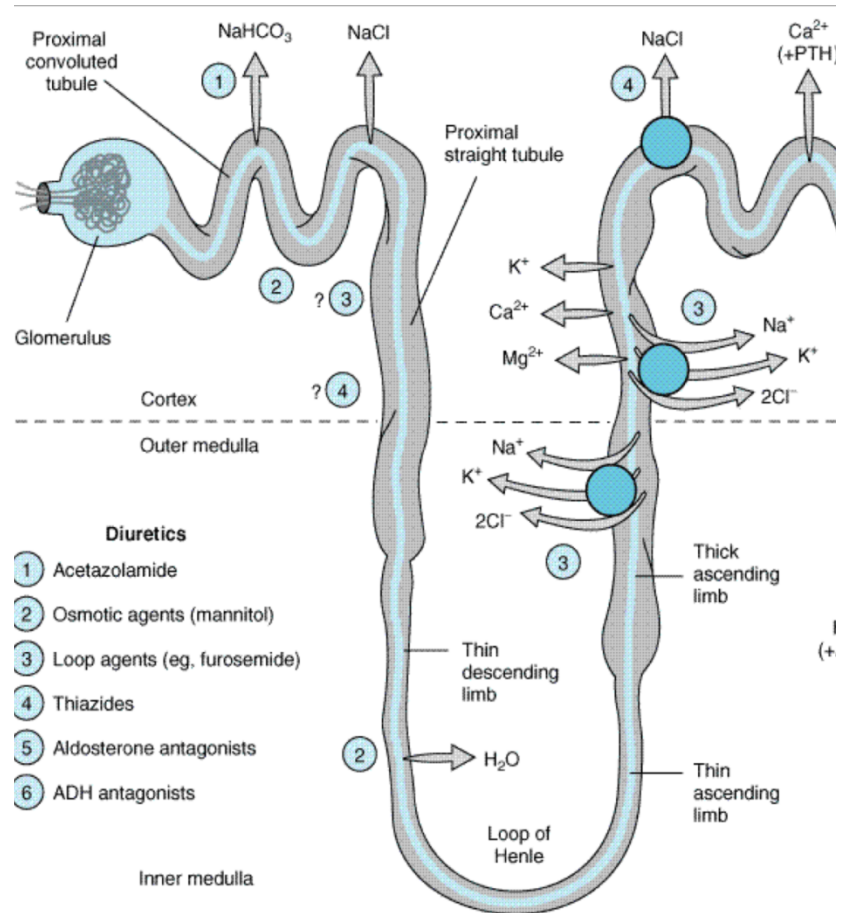
HF patients less responsive to diuretics

- As compared with normal subjects, patients with NYHA FC II - III HF have up to a third of the natriuretic response to maximally effective doses of loop diuretics, and the response is even smaller in patients with more severe heart failure
- An ominous sign



Clinical Pharmacology

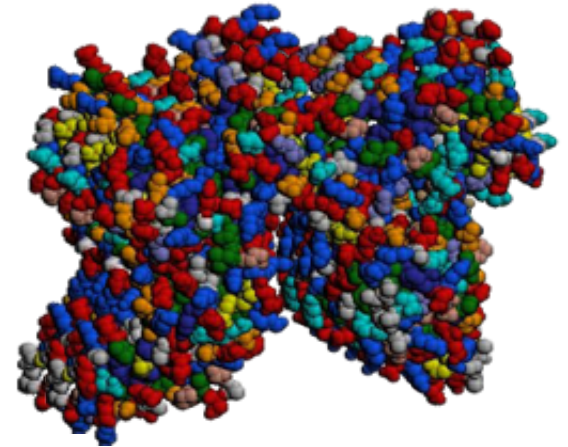
- **Pharmacokinetics**
- **Getting drug to the target**
- **Delivery**
- **Pharmacodynamics**
- **Getting target to respond**
- **Response**



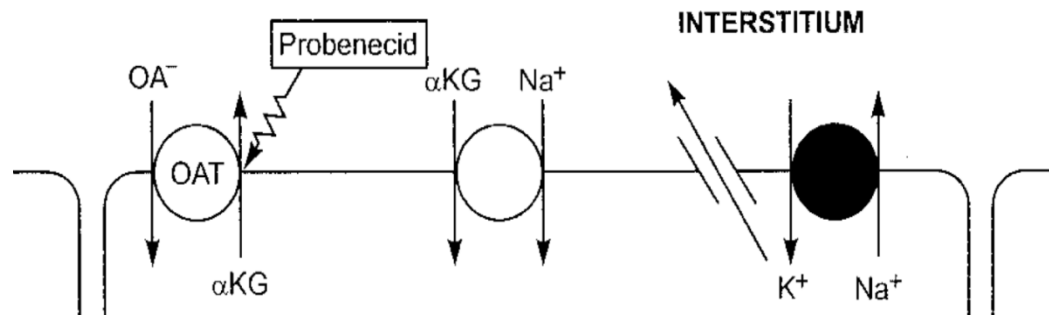
Pharmacokinetics



Human Serum Albumin
Human Serum Albumin

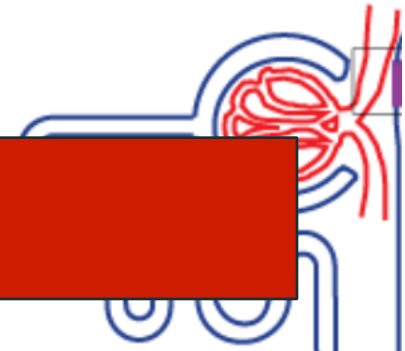
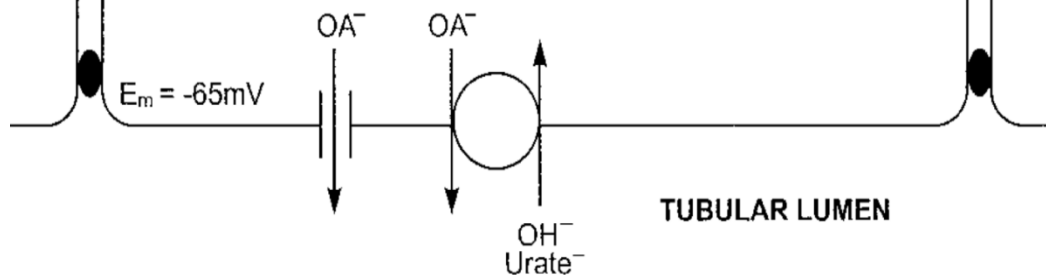


OAT and the PCT



RBF

Increase Dose



Heart Failure Society
of South Africa
[HfSSA]

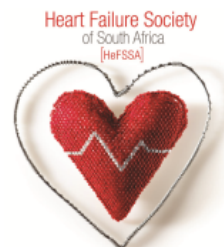


Case Study

Mrs HM

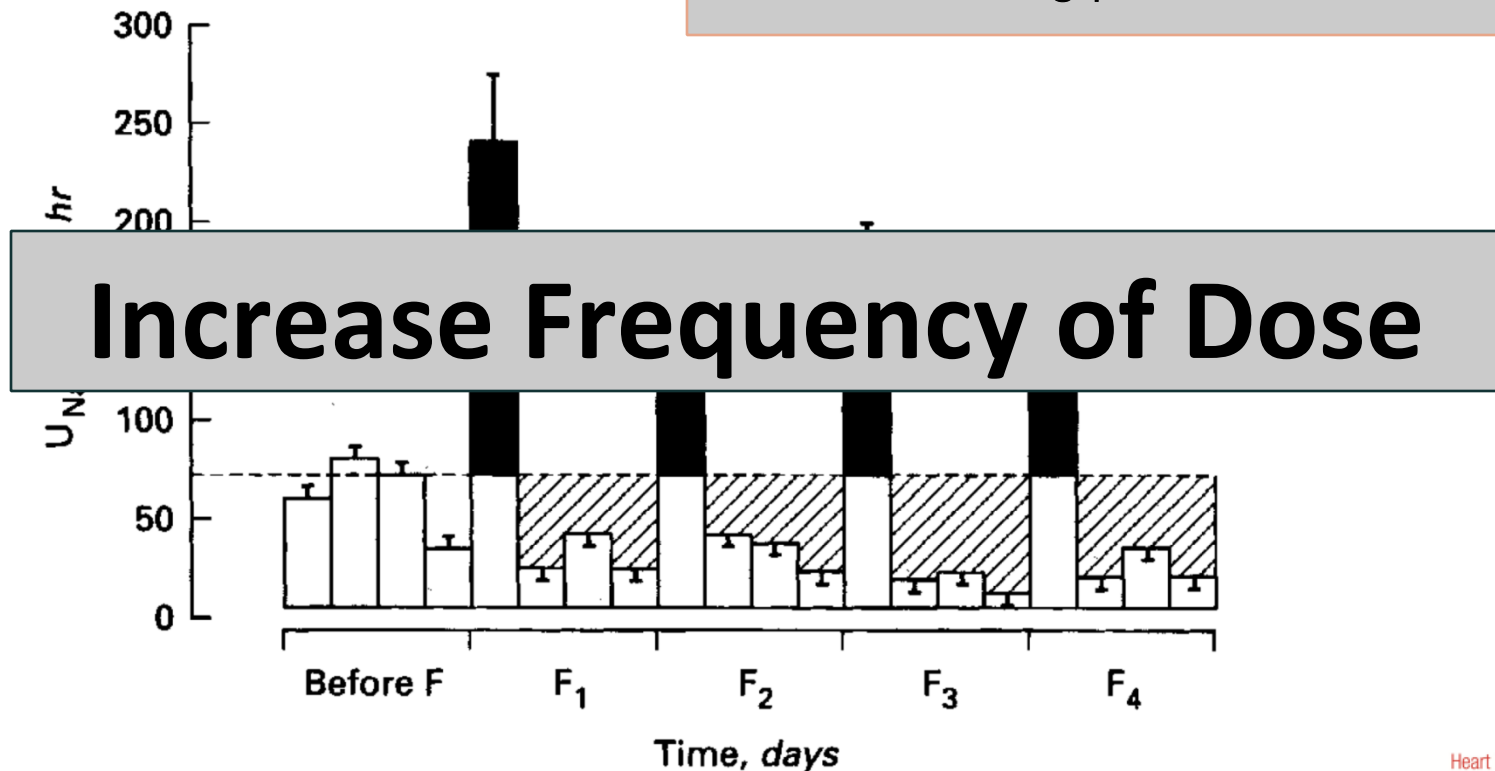
- This patient was assessed as being cold and wet and resistant to the current diuretic regimen, drinking excess fluid orally and taking NSAID.

Perfusion Volume status	Warm	Cold
	Warm	Cold
Wet	Warm/Wet ← A	Cold/Wet
Dry	↓ B Warm/Dry	↑ Cold/Dry

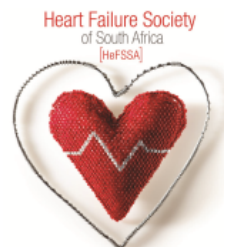


Case Study Mrs HM

Braking phenomenon



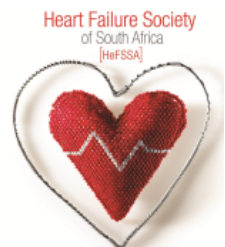
Kidney International 1991: 39:336-352



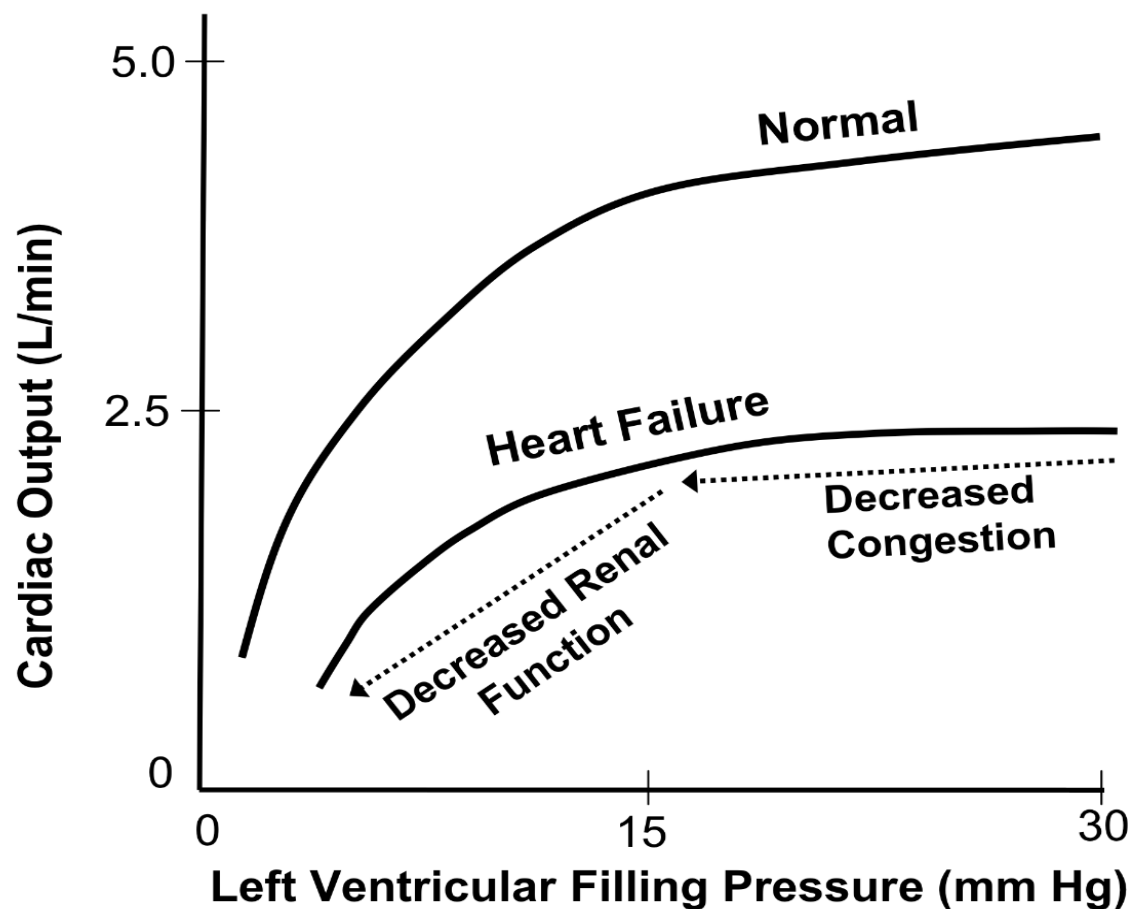
Case Study

Mrs HM

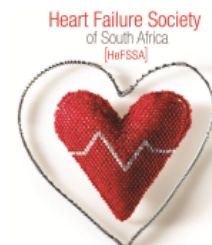
- She received intravenous digitalis, intravenous Lasix at 20 mg IVI 6 hourly to overcome this “braking phenomenon”, oral nitrate at 20 mg bd and fluid restriction.
- Her renal function deteriorated although she improved significantly symptomatically and lost 6 kg in 3 days. 8/3 urea was 9.1 Creat 112 and on 9/3 urea was 11.4 and creat 168.



Potential for worsening renal function



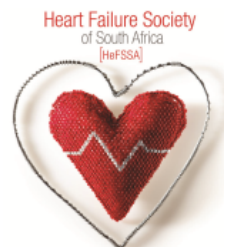
Circ Heart Fail. 2008;1:2-5.



Case Study

Mrs HM

- The intravenous dobutamine and digoxin were continued, the intravenous furosemide reduced to 20 mg IVI 12 hourly and bed rest continued.
- She continued to improve, on **11/3** urea 10.5 and creat 100, INR 2.7
- She was changed to oral furosemide on **11/3** 80 mg mane and 80 mg at 14H00, Isosorbide dinitrate 20 mg bd, Spironolactone built up to 25 mg bd, and digoxin 0.125 mg daily by **14/3**. Dobutamine had stopped on 11/3 and carvedilol started at 3.125 mg bd and built up to 12,5 mg bd by discharge. She became profoundly hypotensive when enalapril 2.5 mg was administered and that was stopped. On **14/3** urea 9.8 and creat 100. Discharged home.



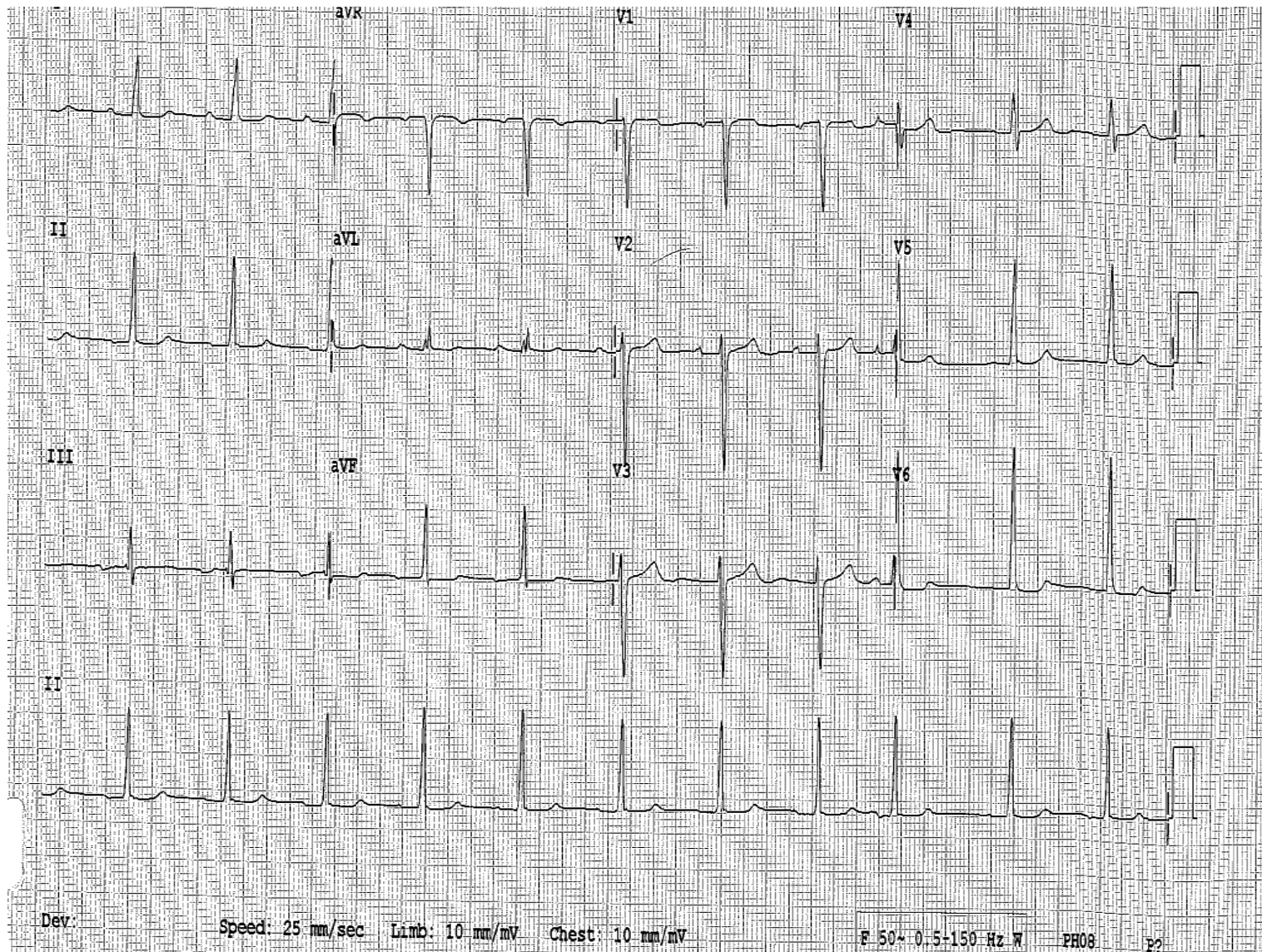
Case Study

Mrs HM

- She was seen again **29/3** as an out-patient - urea 4.5 and creat 71. She had been instructed to keep fluid intake at 1.2 l/day, stay at home and not to return to work
- She was electively cardioverted with 200j on 31/3 into SR
- Furosemide reduced to 40 mg twice daily, carvedilol increased to 25 mg bd, spironolactone 25 mg bd and isosorbide mononitrate at 20 mg bd and digoxin 0.125 mg week days only, by June 2016.
- She was NYHA FC I-II, in SR 67/MIN, BP now 157/74 so enalapril 2.5 mg bd started and increased to 5 mg bd and she was allowed to return to work in July. EF 32%, LVIDD 65 mm, IVC 24 mm/ collapses to 11mm on inspiration.



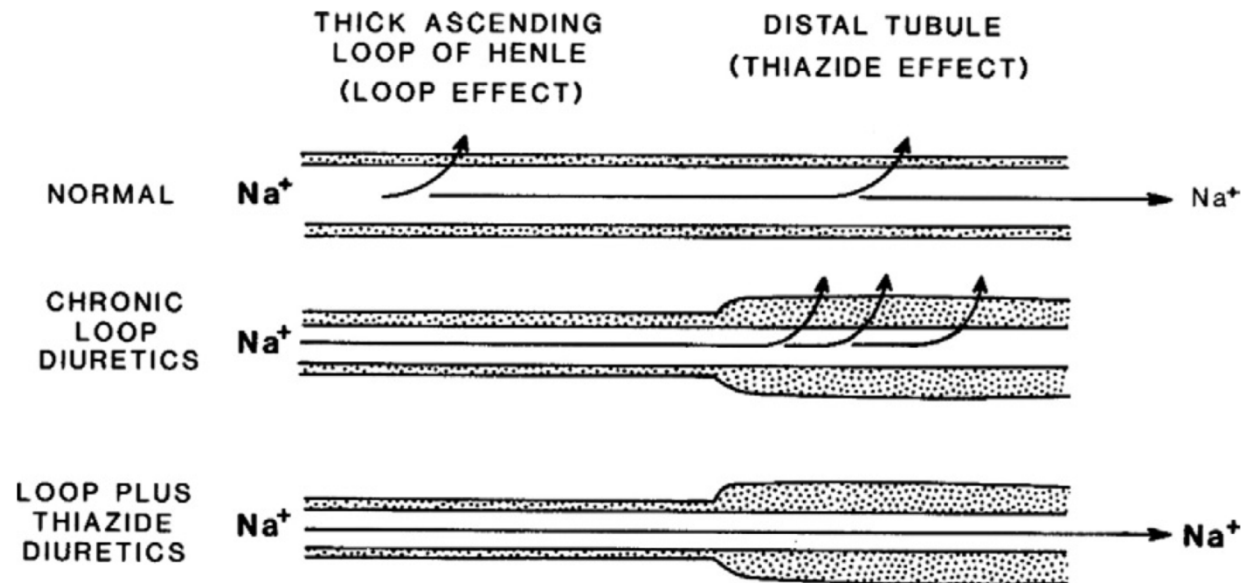
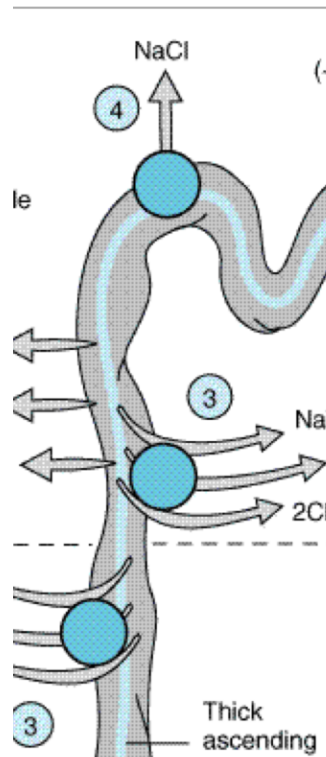
Resting ECG – post cardioversion



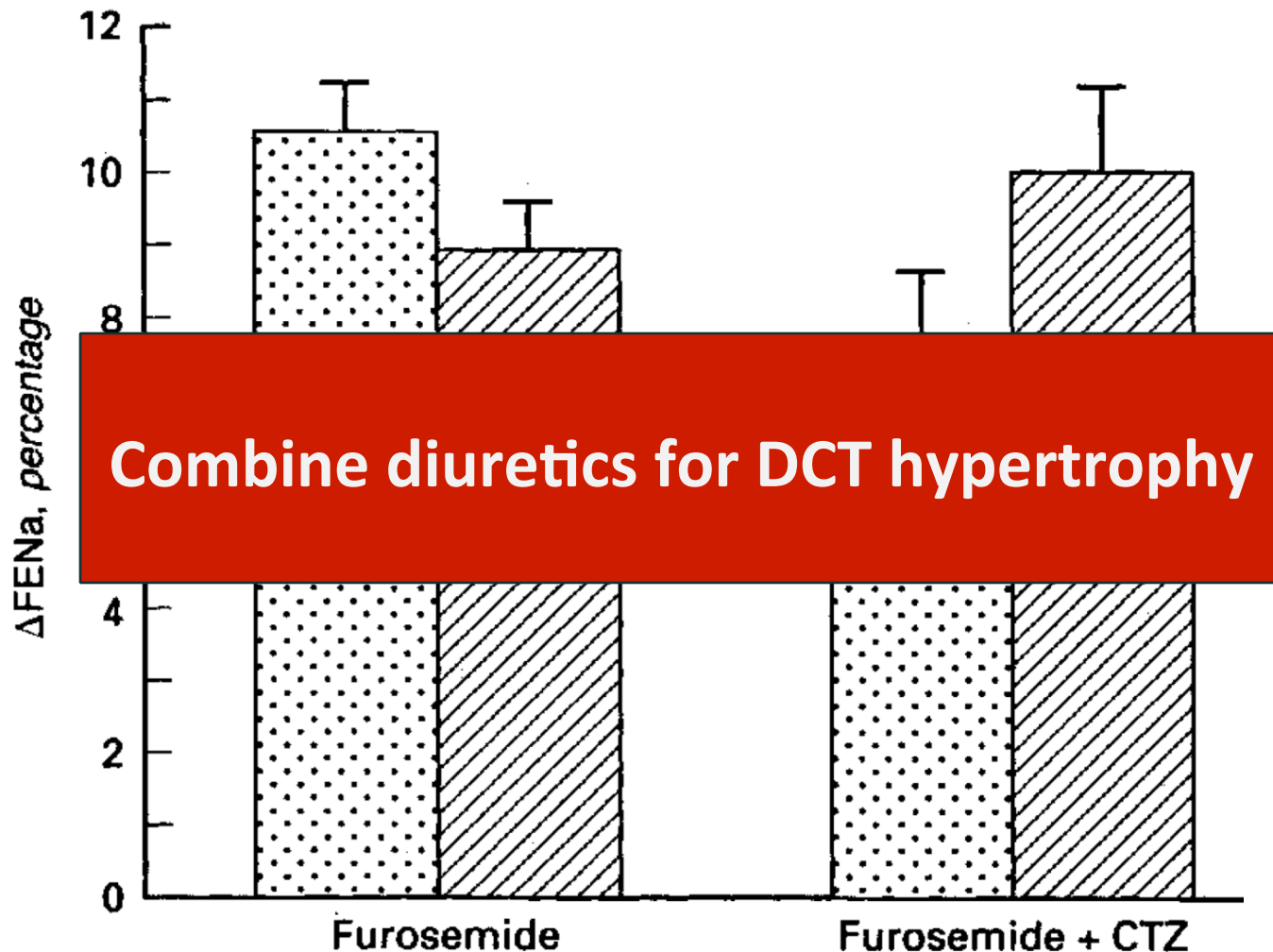
Mechanism of counter- regulation

- Braking
- DCT hypertrophy

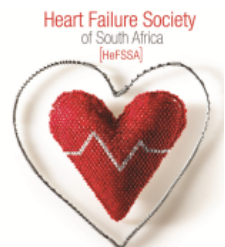
Loop and DCT hypertrophy



Diuretic synergy



Kidney International 1991; 39:336-352



Loop diuretics

DRUG	STRUCTURE	RELATIVE POTENCY
Furosemide		1
Bumetanide		40
Ethacrynic acid		0.7
Torsemide		3

7.5 Diuretics

The effects of diuretics on mortality and morbidity have not been studied in patients with HF, unlike ACE inhibitors, beta-blockers, and MRAs (and other treatments). However, diuretics relieve dyspnoea and oedema and are recommended for this reason in patients with signs and symptoms of congestion, irrespective of EF.

Table 16 Doses of diuretics commonly used to treat heart failure (with and without a preserved ejection fraction, chronic and acute)

Diuretics	Initial dose (mg)	Usual daily dose (mg)		
Loop diuretics ^a				
Furosemide	20–40	40–240		
Bumetanide	0.5–1.0	1–5		
Torsemide	5–10	10–20		
Thiazides ^b				
Bendroflumethiazide	2.5	2.5–10		
Hydrochlorothiazide	25	12.5–100		
Metolazone	2.5	2.5–10		
Indapamide ^c	2.5	2.5–5		
Potassium-sparing diuretics ^d				
	+ACEi/ ARB	–ACEi/ ARB	+ACEi/ ARB	–ACEi/ ARB
Spironolactone/ eplerenone	12.5–25	50	50	100–200
Amiloride	2.5	5	5–10	10–20
Triamterene	25	50	100	200

GUIDELINE

Heart Failure Society of South Africa (HeFSSA) perspective on the European Society of Cardiology (ESC) 2012 chronic heart failure guideline

M T Mpe, MB ChB, FCP, MMed; E Q Klug, MB BCh, FCP, MMed; K S Sliwa, MD, PhD, FESC, FACC; J Hitzeroth, MB BCh, FCP; D A Smith, MB BCh, FCP; on behalf of the Heart Failure Society of South Africa



European Heart Journal (2012) **33**, 1787–1847
doi:10.1093/eurheartj/ehs104



The aim of using diuretics is to achieve and maintain euvolaemia (the patient's 'dry weight') with the lowest achievable dose. This means that the dose must be adjusted, particularly after restoration of dry body weight, to avoid the risk of dehydration leading to hypotension and renal dysfunction. This may reduce cardiac output in patients with HF-PEF and often needlessly prevents the use of (or achievement of the target dose of) other disease-modifying therapies such as ACE inhibitors (or ARBs) and MRAs in patients with HF-REF. Many patients

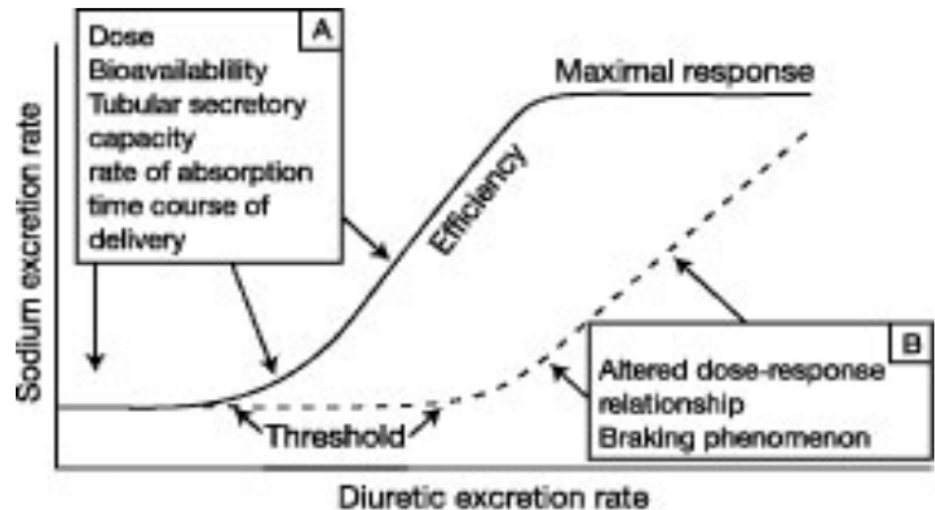
Closing the loop

- Loop diuretics most commonly used drugs in heart failure
- Indicated and highly effective for relief of fluid retention
- No evidence of prognostic benefit, activate the NH system, aggravate renal dysfunction
- Impaired natriuretic and diuretic response in heart failure



Closing the loop

- Pharmacokinetic problems helped by increasing doses to ceiling individual dose
- Pharmacodynamic issues helped by increasing frequency of dose and combining with a thiazide
- Salt restriction in resistant patients
- Beware of OAT system and competing cations/ drugs



The End

