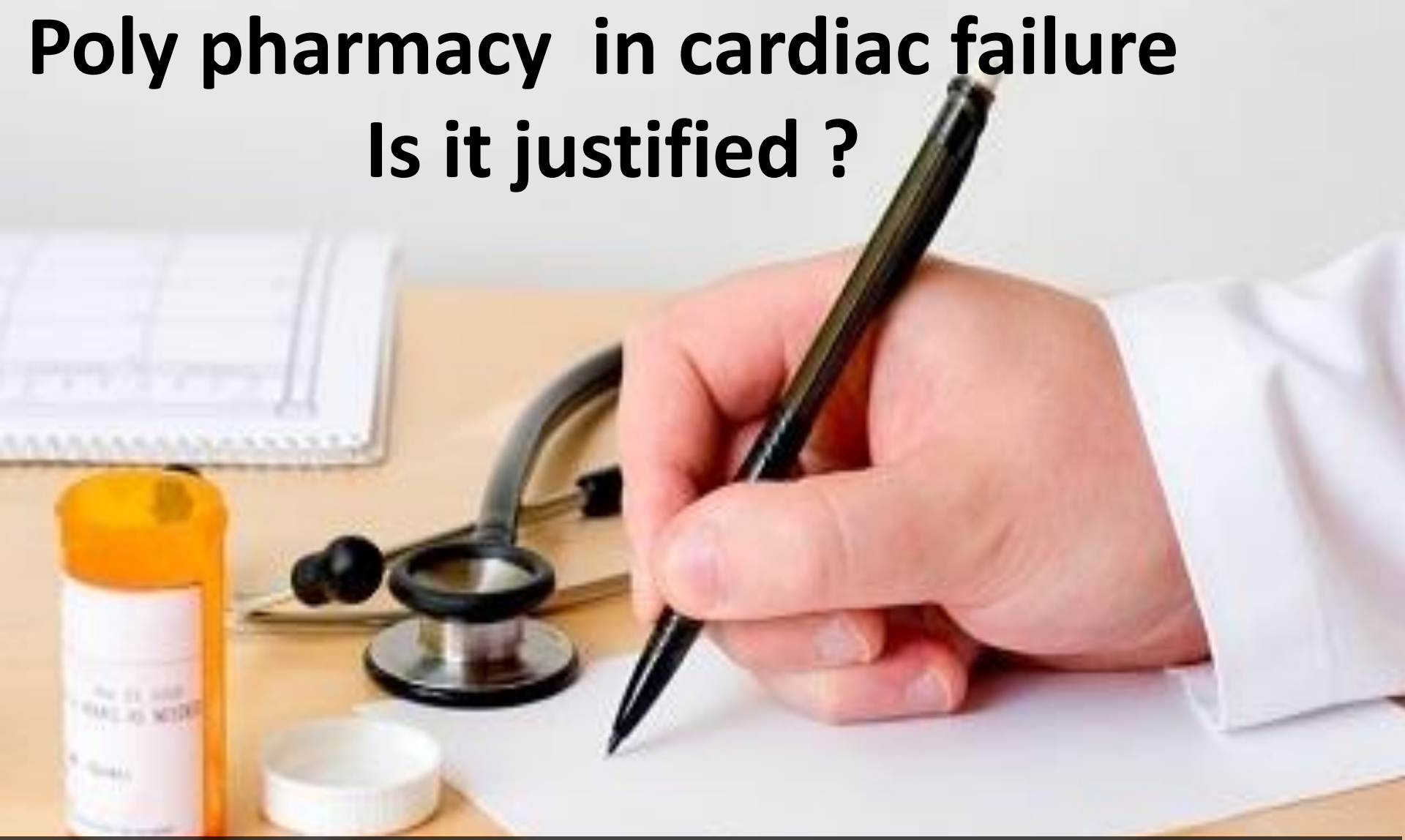
Poly pharmacy in cardiac failure
Is it justified ?



Dr.S.Venkatesan, MD,DM. Cardiologist.

Madras medical college.Chennai.India

Saunders medical dictionary

Administration of ***many drugs together***.
Administration of excessive medication

Dorland‘s

Dispensation of ***unnecessarily numerous*** or complex medicines.

Mosby medical Dictionary,

Use of a number of different drugs, possibly prescribed by ***different doctors*** *and filled in different pharmacies*, by a patient who may have one or several health problems.

Poly-pharmacy is an universal issue

Ethical

Geography

Elderly

(Up to 17 -50 % is admission are due to poly-pharmacy)


Physician
Patient
Hospital
Industry
Administrative
Errors
Polypharmacy

Drug Interactions

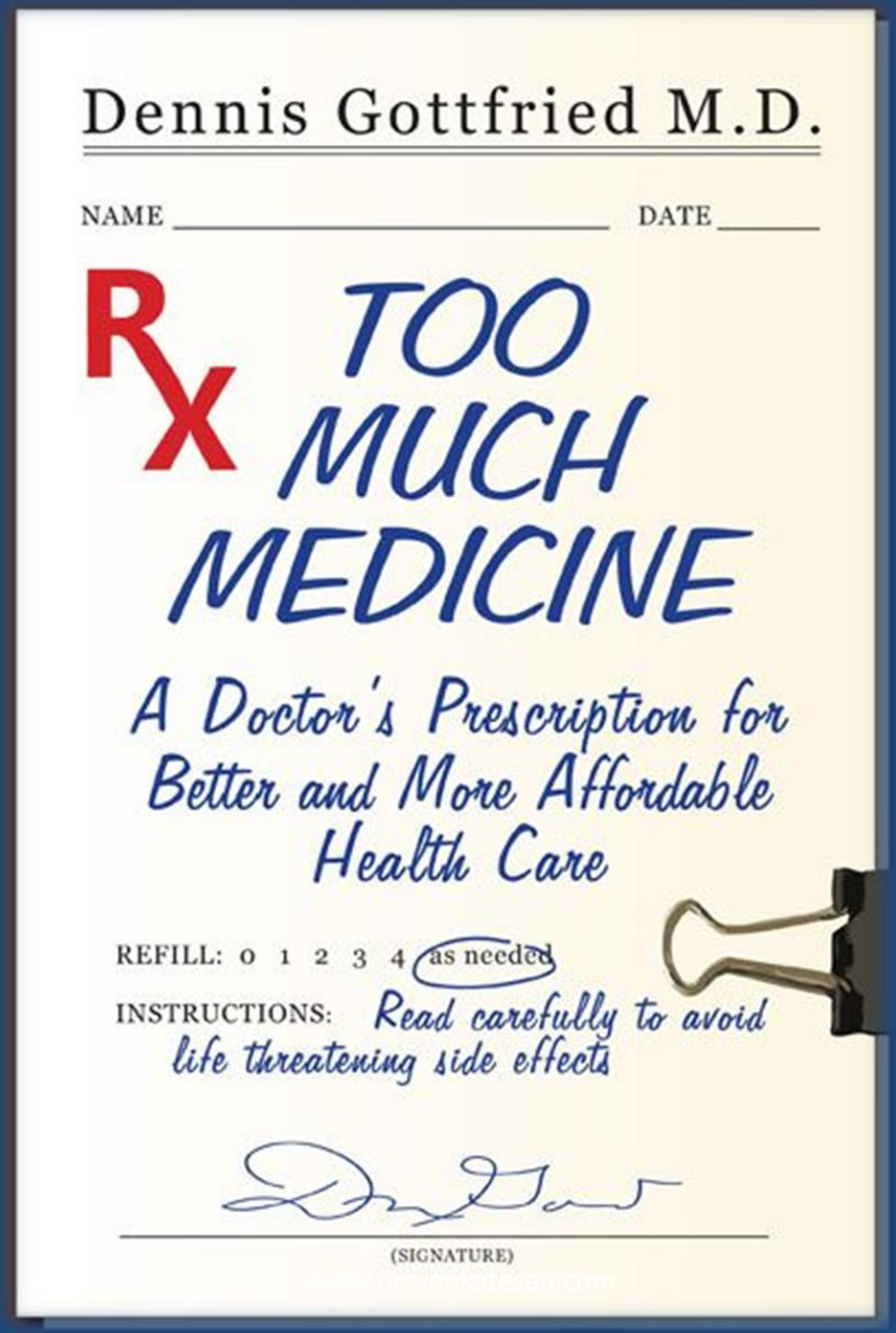
Drug –Drug

Drug –Disease

Drug –Host

“All medicines which are not clinically indicated is referred to poly-pharmacy”

Fulton MM, Allen ER (2005) Polypharmacy in the elderly: a literature review. Journal of the American Academy of Nurse Practitioners, 17, 123–132.



Poly-pharmacy in cardiac failure

- Avoidable
- Acceptable (Appropriate)
- Essential

ACC/AHA Guidelines for CHF

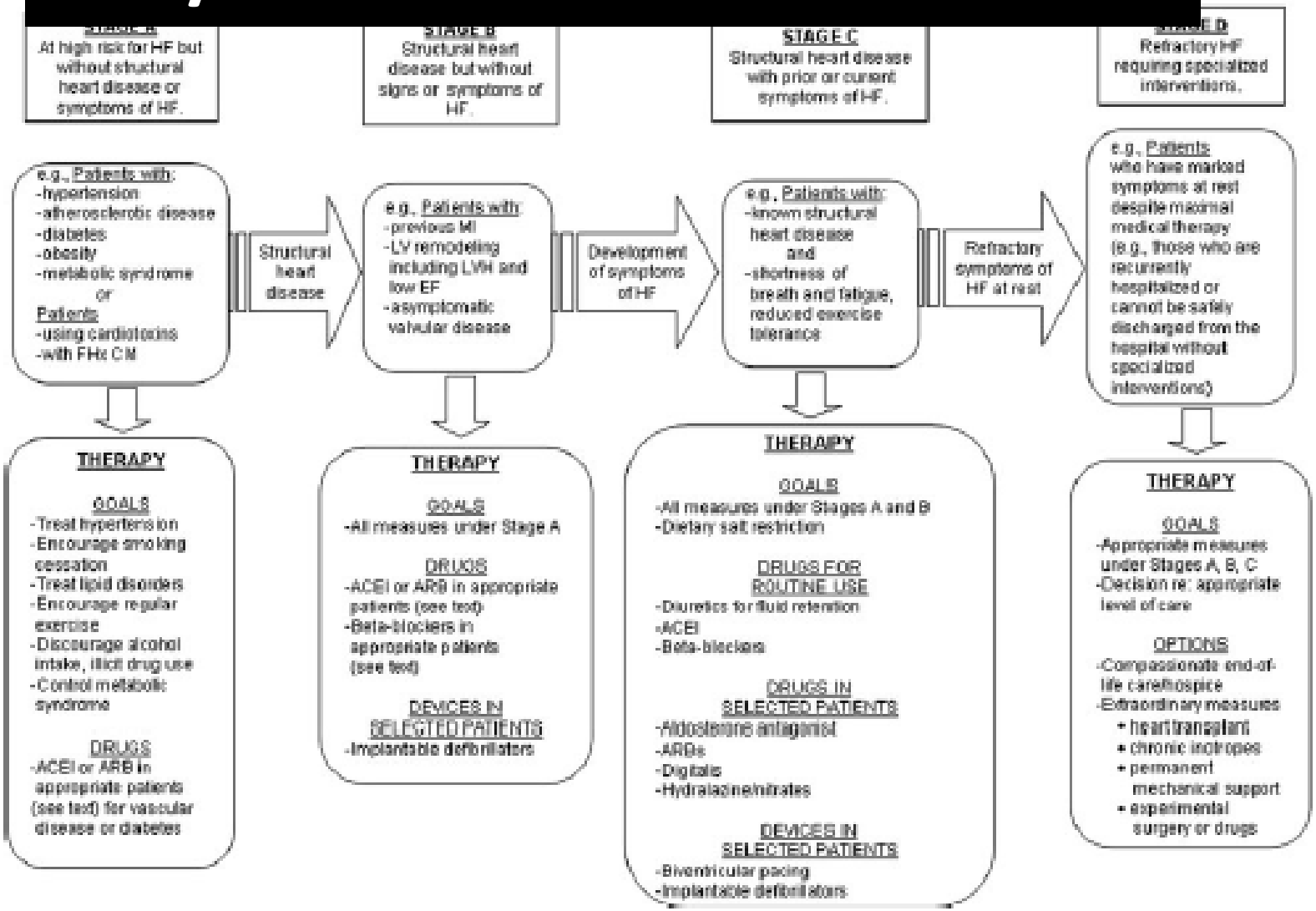


Figure 1. Stages in the Development of Heart Failure/Recommended Therapy by Stage. ACEI indicates angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blocker; EF, ejection fraction; FHx CM, family history of cardiomyopathy; HF, heart failure; LVH, left ventricular hypertrophy; and MI, myocardial infarction.

THERAPY

GOALS
-All measures under Stages A and B
-Dietary salt restriction

DRUGS FOR ROUTINE USE
-Diuretics for fluid retention
-ACEI
-Beta-blockers

DRUGS IN SELECTED PATIENTS
-Aldosterone antagonist
-ARBs
-Digitalis
-Hydralazine/nitrates

DEVICES IN SELECTED PATIENTS
-Biventricular pacing
-Implantable defibrillators

THERAPY

GOALS
-Appropriate measures under Stages A, B, C
-Decision re: appropriate level of care

OPTIONS
-Compassionate end-of-life care/hospice
-Extraordinary measures
- heart transplant
- chronic inotropes
- permanent mechanical support
- experimental surgery or drugs

Non cardiac poly-pharmacy -Appropriate

Diabetes
Arthritis
Depression
Dyspepsia

Inappropriate
(Antacids/Sedatives/Vitamins)

Appropriate

In acute heart failure

Advanced CHF

Atrial fibrillation

Co-existing illness

What is the need for poly-pharmacy in CHF ?

Cardiac failure will overtake CAD soon

Shifting concepts , Multiple targets

Still . . . Limited success

Drugs has to catch up with Interventional techniques

More research . . . More drugs

Changing concepts in CHF

Hemodynamic model

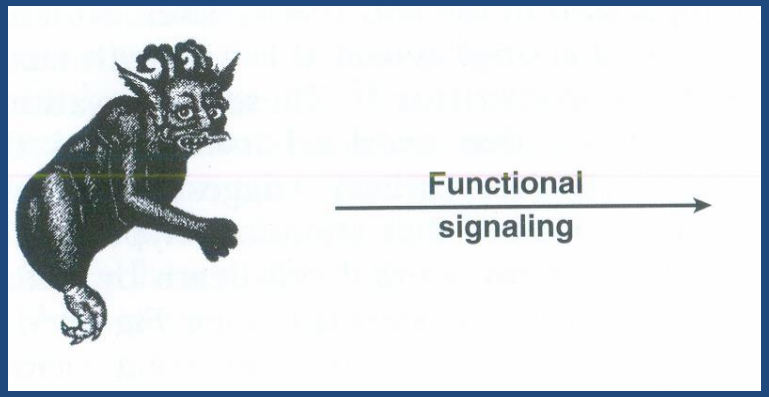
to

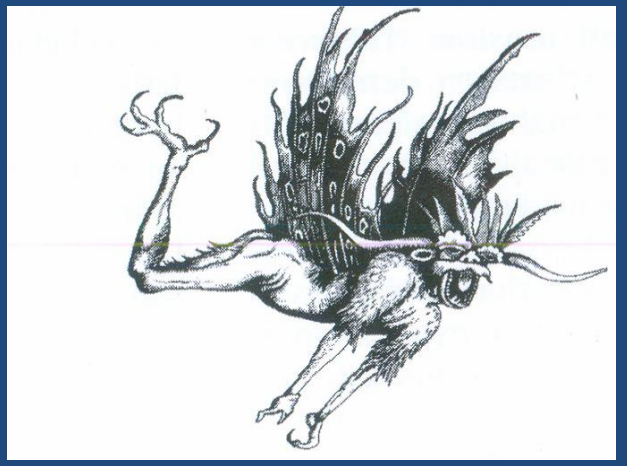
Neuroendocrine model

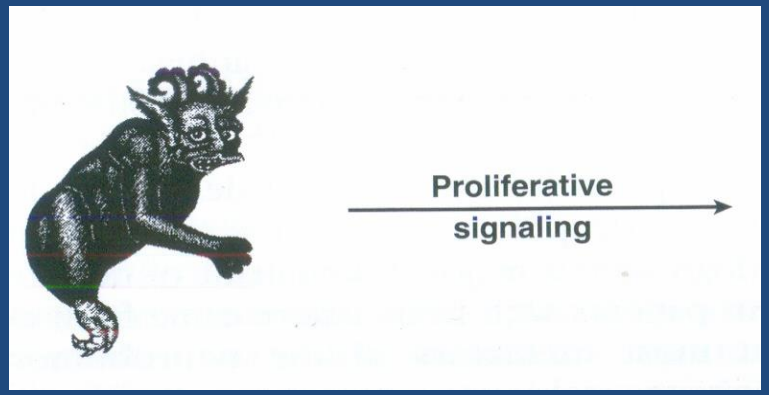
Current definition of cardiac failure

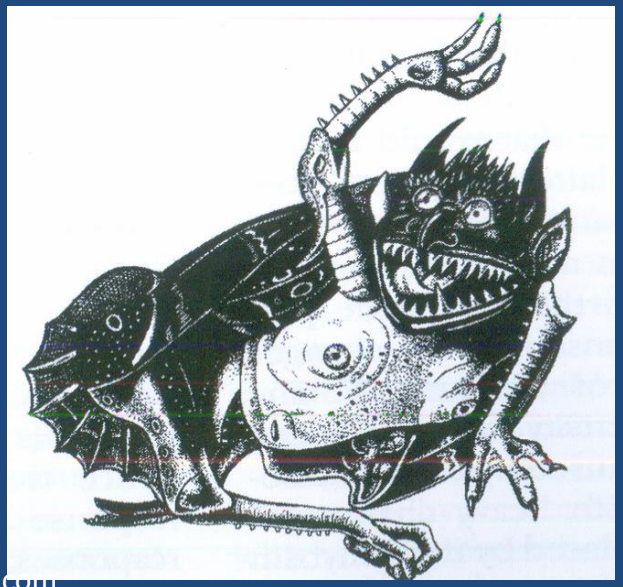
"CHF can be thought of as a state of neurohormonal imbalance, in which the activity of potentially harmful pathways outweighs that of favorable ones"

Going back to the fight/flight model









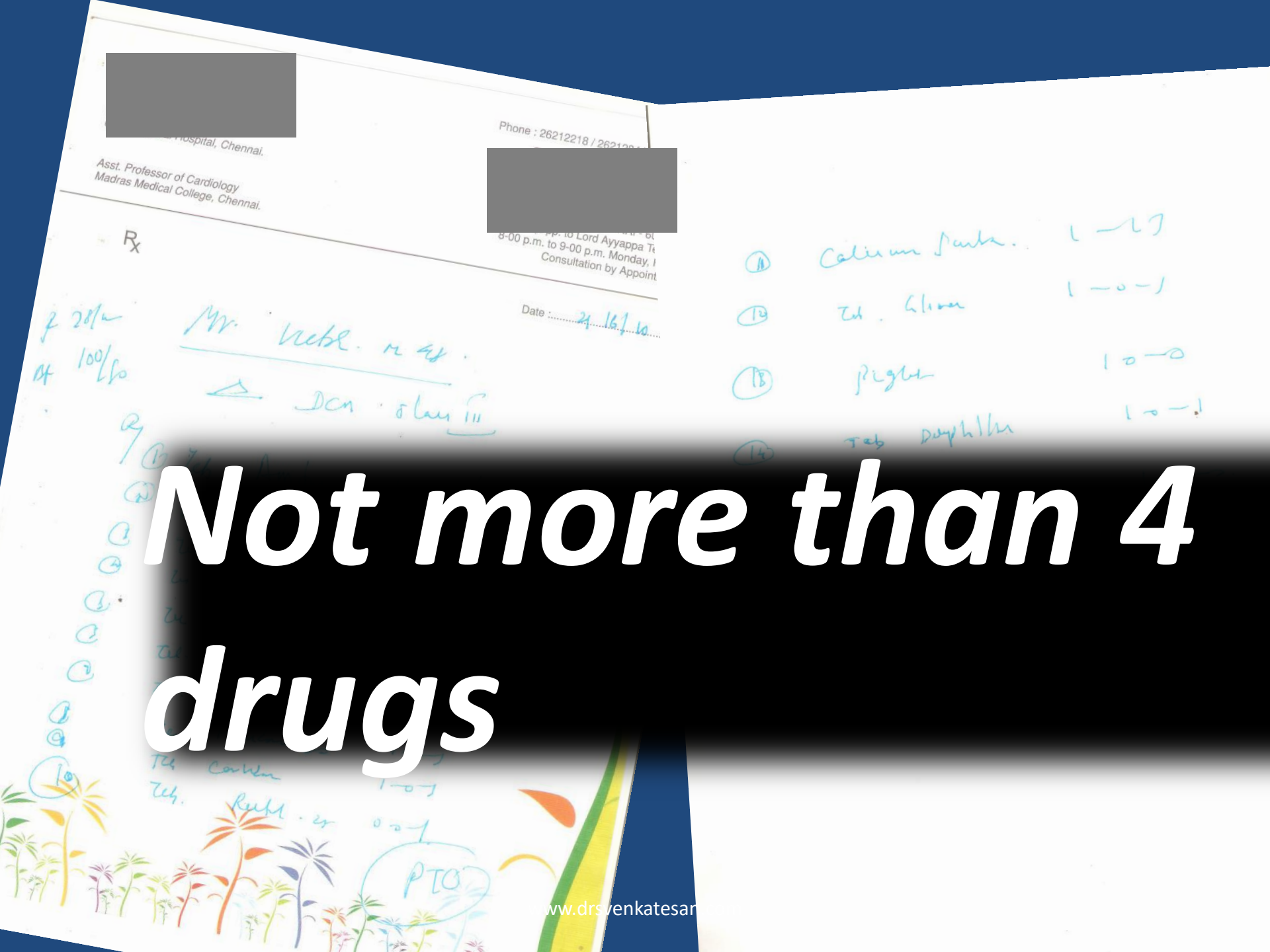
NEUROHORMONE / ENZYME/CYTOKINE	ANTAGONIST	CLINICAL OUTCOME
Norepinephrine	β-Blockers	Reverse remodeling
	Tyrosine hydroxylase inhibitors	?
	Moxonidine	?
Angiotensin II (Ang II)	Angiotensin-converting enzyme inhibitors	↗ bradykinin, ↗ nitric oxide Prevents remodeling Improves survival
	Ang II blockers	?
Tumor necrosis factor–α (TNF-α)	Monoclonal antibodies	?
	Amiodarone	
	Digoxin	?
Endothelin (ET)	Bosentan	Prevents remodeling in animals
	ET_A blockers	
Matrix metalloproteinases (MMPs)	MMP inhibitors	Antislippage?
Atrial natriuretic factor (ANF)	Neutral endopeptidase inhibitors	Natriuresis
Aldosterone	Spironolactone	Improves survival

The Crux of the issue : Balancing the NEM responses

CHF is a condition where both favorable and unfavorable responses occur simultaneously

How to stimulate only the favorable factors and block the unfavorable responses ?

Principles of Prescribing in CHF


Not more than 4 drugs

General principles

Always review the drugs

Listen to the patient

Discourage multiple physician contact

Habitual hospital hoppers ?

Class 1 drugs

Beta blockers

ACEI & ARB

Aldosterone antagonists

Essential

Diuretics and Digoxin

ACEI Inhibitor

ARBs

ELITE 2 / VALIANT

Never both

Beta blockers in CHF

Metoprolol succinate

Carvidilol

Bisoprolol

A word about Aldosterone antoagonist

Aldactone ? Routine

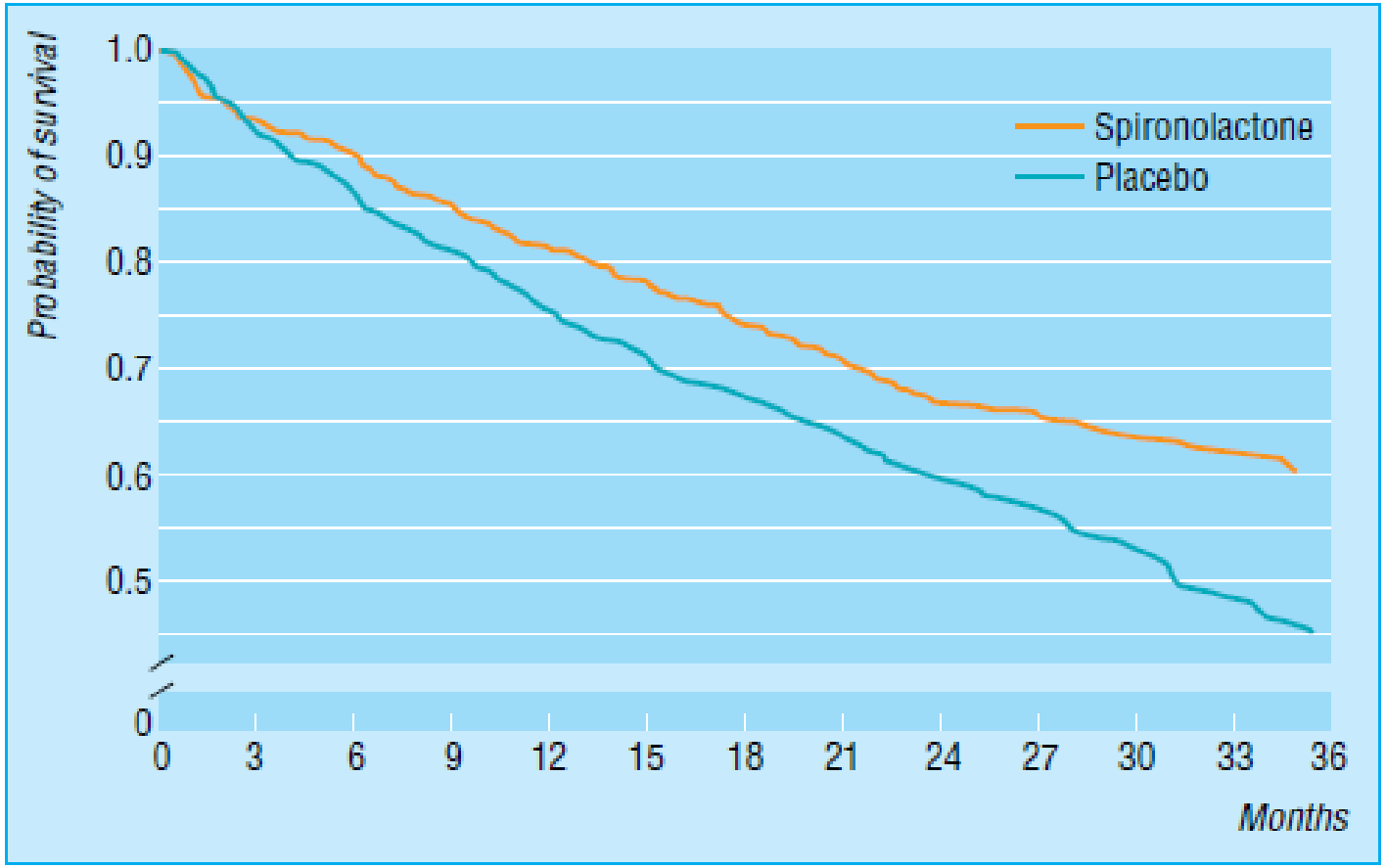
Eplerenone ? (VIP CHFs)

Extreme caution is require d diabetic nephropathy

(ACEI /ARB/ALD) Triple RASS blockade is forbidden

With due respects to RALES /EPHESES

Aldosterone antagonist



Survival curve for randomised aldactone evaluation study (RALES) showing 30% reduction in all cause mortality when spironolactone (up to 25 mg) was added to conventional treatment in patients with severe (New York Heart Association class IV) chronic heart failure

Diuretics

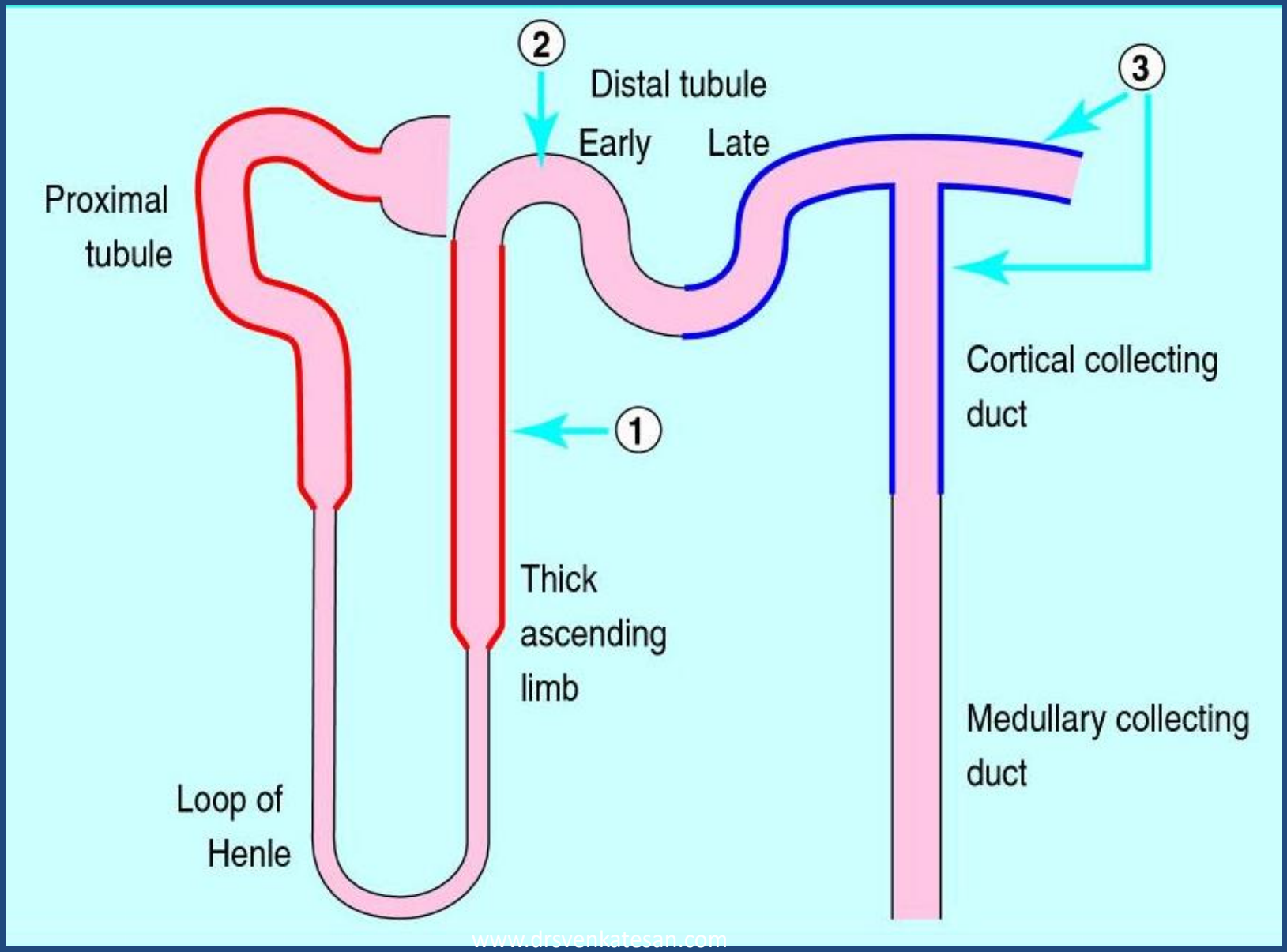


Table 5. Intravenous Diuretic Medications Useful for the Treatment of Severe Heart Failure

Drug	Initial Dose	Maximum Single Dose
Loop Diuretics		
Bumetanide	1.0 mg	4 to 8 mg
Furosemide	40 mg	160 to 200 mg
Torsemide	10 mg	100 to 200 mg
Thiazide Diuretics		
Chlorothiazide	500 mg	1000 mg
Sequential Nephron Blockade		
Chlorothiazide	500 to 1000 mg (IV) once or twice plus loop diuretics once; multiple doses per day	
Metozalone (as Zaroxolyn or Diulo)	2.5 to 5 mg PO once or twice daily with loop diuretic	

Don’t underestimate the value of Digoxin

But , recognise it low safety margin

Point of View

Digoxin

A Neurohormonal Modulator in Heart Failure?

Mihai Gheorghiade, MD, and David Ferguson, MD

It is known that digitalis can exert sympathoinhibitory, sympathoexcitatory, and direct vasoconstricting effects. The relative predominance these differing effects in response to digitalis may depend on the degree of activation of the neuroendocrine

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

M Gheorghiade and D Ferguson
Circulation 1991;84;2181-2186

Diastolic Failure

The NEW ENGLAND JOURNAL of MEDICINE

EDITORIAL

Diastolic Heart Failure — A Common and Lethal Condition by Any Name

Gerard P. Aurigemma, M.D.

N Engl J Med 2006; 355:308-310 | July 20, 2006 | DOI: 10.1056/NEJMe068128

This article has no abstract; the first 100 words appear below.

This issue of the *Journal* contains two provocative contributions to the literature on heart failure. Owan et al.[1] describe the epidemiologic outcomes and survival rates among patients with heart failure who

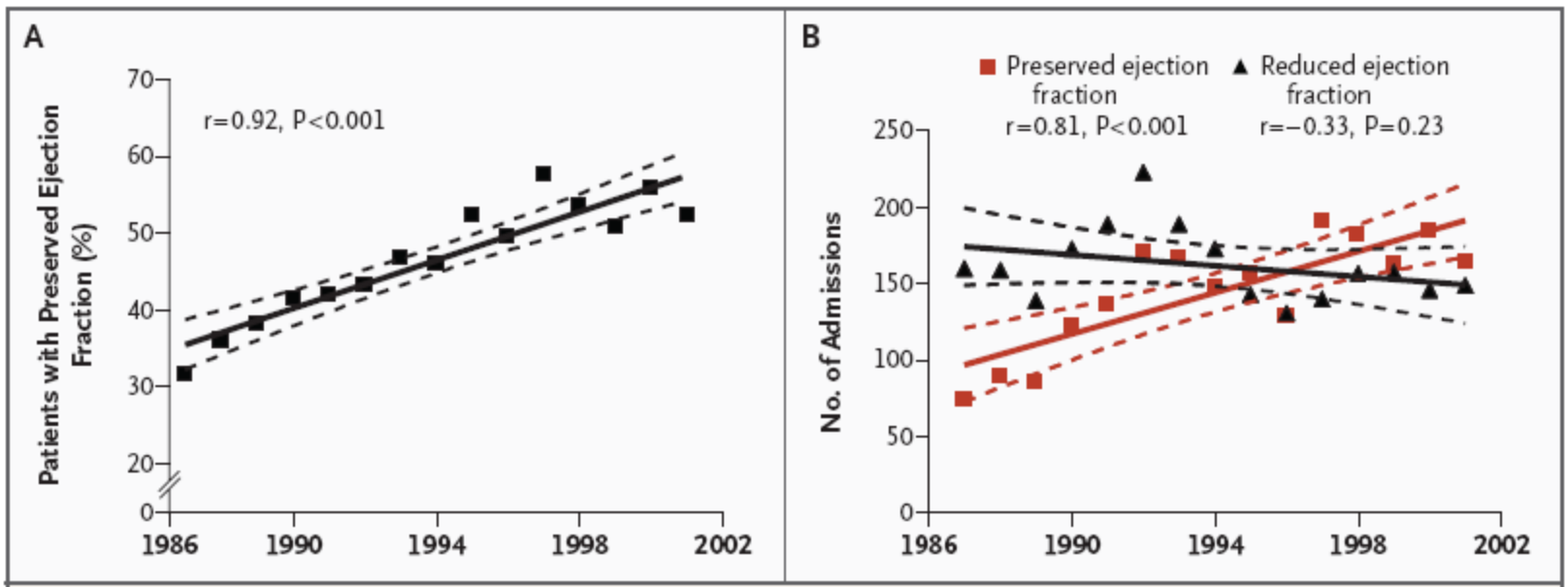


Figure 1. Secular Trends in the Prevalence of Heart Failure with Preserved Ejection Fraction.

Panel A shows the increase during the study in the percentage of patients with heart failure who had preserved ejection fraction. Panel B shows that the number of admissions for heart failure with preserved ejection fraction increased during the study period, whereas the number of admissions for heart failure with reduced ejection fraction did not change. The solid lines represent the regression lines for the relation between the year of admission and the percentage of patients with heart failure who had preserved ejection fraction (Panel A) and the number of admissions for heart failure with preserved or reduced ejection fraction (Panel B). The dashed lines indicate 95 percent confidence intervals.

The enigma of diastolic dysfunction in cardiac failure

- We know the problem is real
- We know it often coexist with systolic dysfunction
- We do not still have specific treatment

Diastolic Failure

No pharmacy ?

Drugs for Diastolic dysfunction

Beta blocker

Primarily HR, BP reduction

(Longitudinal function)

ACEI

CHARM-Preserved -Candesartan

PEP-CHF – Perindopril

Arrhythmia Management in cardiac failure (AF and VPDs)

(Don't panic with few VPDs or transient in CHF as long as LV function is good)

Beta blocker will take care

Don't get tempted by Amiodarone.

Pro-arrhythmic potential can easily exceed benefits

ICD - Always consider (But don't get mad about MADIT)

Handling diabetic heart failure

Very common , Unique situation

Polypharmacy becomes essential

Avoid thioglitazones

Statin ?

Combined cardiac and renal failure ?

Aim should be to reduce the burden

Drug dosage to be reduced

(Except diurteics)

Is polypill an Answer ?

Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association®

The Polypill in the Prevention of Cardiovascular Diseases : Key Concepts, Current Status, Challenges, and Future Directions

Eva Lonn, Jackie Bosch, Koon K. Teo, Prem Pais, Denis Xavier and Salim Yusuf

Circulation. 2010;122:2078-2088

Polypill in cardiac failure

ABCD

ACEI + + **B**etablocker(**C**arvidilol) + **D**iuretic + **D**igoxin

Polypill as a concept CVD prevention . . . not yet for CHF

Yusuf S, Pais P, Afzal The Indian Polycap Study (TIPS). Effects of a polypill (Polycap) on risk factors in middle-aged individuals without cardiovascular disease (TIPS): a phase II, double-blind, randomized trial. *Lancet. 2009;373:1341–1351.*

Drugs with Glamour

L carnitine

Trimetazidine

Ranalozine

Cardio-vitamins

Co-enzyme Q 10

Watch out : Many are waiting on the pipe line

- TNF blocker
- Endothelin antagonist
- NEP antogonist
- Vasopressin antagonist
- Nesiritide


Wisdom
Meta Knowledge
Belief
Knowledge
Information
Data
Noise

Treating chronic heart failure with 4 drugs . Is it possible ?

ACEI

Beta blocker

Diuretic +

Aldosterone anatogonist

Antiplatelet + Anticoagulants

How many class 1 A drugs ?

Do not deny state of the art strategies if eligible and affordable

Revacularisation

Valve surgery

CRT , ICD

Cardiac transplantation

Drug interactions in CHF

1 . Statins

2 . Aspirin

Statin and worsening of CHF

Stain rules the world of coronary syndrome

Dubious role in CHF

Low serum total cholesterol is associated with marked increase in mortality in advanced heart failure. AU Horwich ***Card Fail. 2002;8(4):216.***

Cholesterol levels and in-hospital mortality in patients with acute decompensated heart failure. AU Horwich **TB** **Am Heart J. 2008;156(6):1170.**

CNN Health

Matters of the Heart

Heart failure may worsen with statins, study says

By **Anne Harding,** Health.com
November 5, 2009 -- Updated 2113 GMT (0513 HKT)

Health.com

Some studies have shown that statins can be helpful, while others have found no benefit.

(Health.com) -- It's widely known that cholesterol-lowering statins can benefit patients with heart disease, but a new study suggests they may actually harm some people with heart failure.

Heart disease can occur when arteries become clogged, but in heart failure, the heart gets progressively weaker and larger.

Still, since the study included a small number

The NEW ENGLAND JOURNAL of MEDICINE

November 2007

Rosuvastatin in Older Patients with Systolic Heart Failure

A total of 5011 patients > 60 years

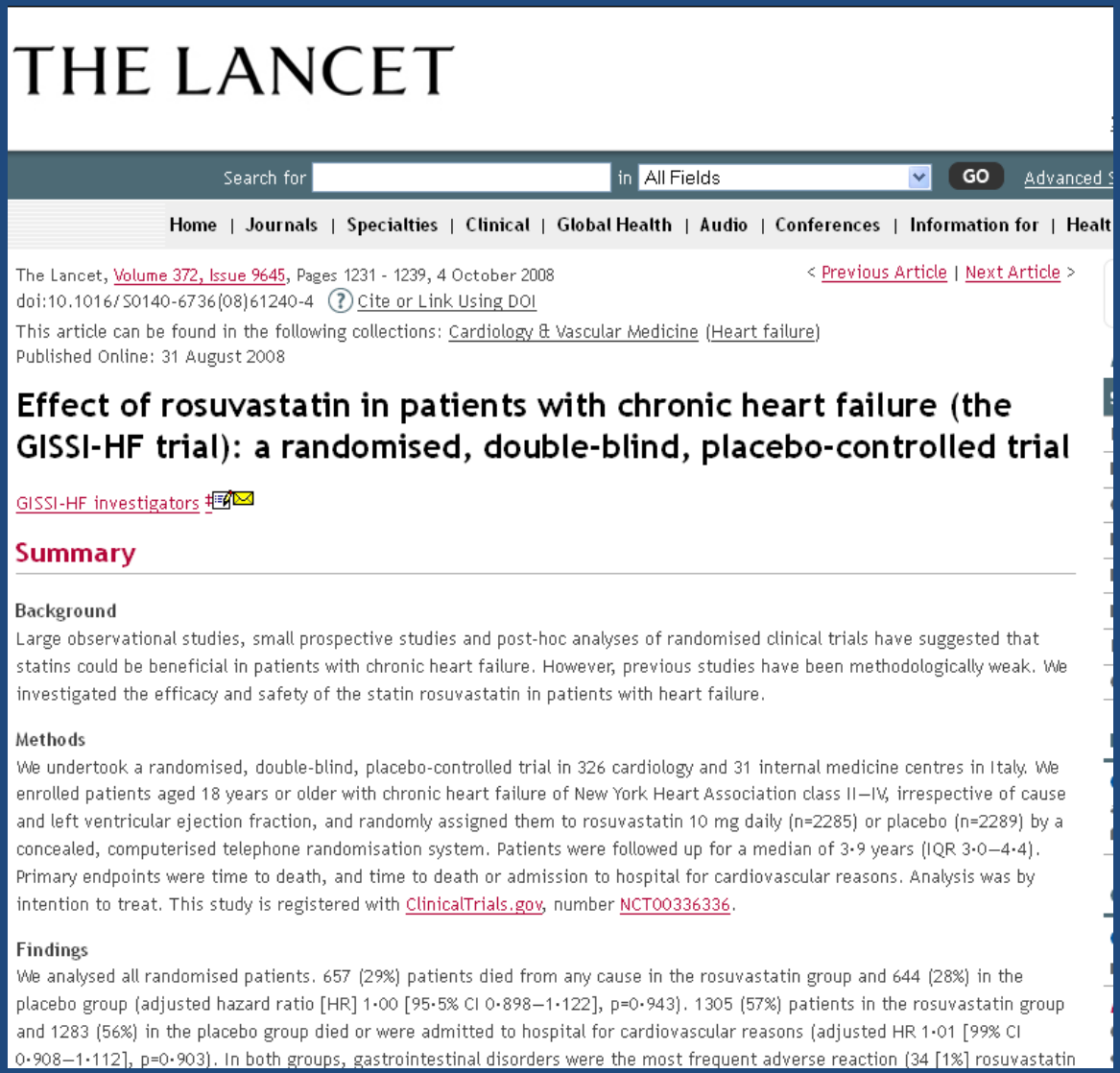
Ischemic cardiac failure

36 month follow up

10 mg of Rosuvastatin

Controlled Rosuvastatin Multinational Trial in Heart Failure (CORONA)

CORONA Group / Norway *



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The Lancet, Volume 372, Issue 9645, Pages 1231 - 1239, 4 October 2008
doi:10.1016/S0140-6736(08)61240-4 Cite or Link Using DOI

< Previous Article | Next Article >

This article can be found in the following collections: Cardiology & Vascular Medicine (Heart failure)
Published Online: 31 August 2008

Effect of rosuvastatin in patients with chronic heart failure (the GISSI-HF trial): a randomised, double-blind, placebo-controlled trial

GISSI-HF investigators

Summary

Background

Large observational studies, small prospective studies and post-hoc analyses of randomised clinical trials have suggested that statins could be beneficial in patients with chronic heart failure. However, previous studies have been methodologically weak. We investigated the efficacy and safety of the statin rosuvastatin in patients with heart failure.

Methods

We undertook a randomised, double-blind, placebo-controlled trial in 326 cardiology and 31 internal medicine centres in Italy. We enrolled patients aged 18 years or older with chronic heart failure of New York Heart Association class II–IV, irrespective of cause and left ventricular ejection fraction, and randomly assigned them to rosuvastatin 10 mg daily (n=2285) or placebo (n=2289) by a concealed, computerised telephone randomisation system. Patients were followed up for a median of 3·9 years (IQR 3·0–4·4). Primary endpoints were time to death, and time to death or admission to hospital for cardiovascular reasons. Analysis was by intention to treat. This study is registered with ClinicalTrials.gov, number NCT00336336.

Findings

We analysed all randomised patients. 657 (29%) patients died from any cause in the rosuvastatin group and 644 (28%) in the placebo group (adjusted hazard ratio [HR] 1·00 [95·5% CI 0·898–1·122], p=0·943). 1305 (57%) patients in the rosuvastatin group and 1283 (56%) in the placebo group died or were admitted to hospital for cardiovascular reasons (adjusted HR 1·01 [99% CI 0·908–1·112], p=0·903). In both groups, gastrointestinal disorders were the most frequent adverse reaction (34 [1%] rosuvastatin

GISSI -HF

Interpretation

Rosuvastatin 10 mg daily did not affect clinical outcomes in patients with chronic heart failure of any cause, in whom the drug was safe

Statin in heart failure –Summary

No benefit

High dose may be detrimental

Need not withhold it ?

Reduce the dose .

Br Heart J 1995;74:215–219

REVIEW

Is aspirin safe for patients with heart failure?

John G F Cleland, Christopher J Bulpitt, Rodney H Falk, Iain N Findlay, Celia M Oakley, Gordon Murray, Philip A Poole-Wilson, Colin R M Prentice, George C Sutton

If NSAIDs are notorious for worsening cardiac failure

Aspirin is the mother of all NSAID

Caution is warranted.

The #1 Hospital
for Heart Care 14 Years in a Row
U.S.News & World Report

The Cleveland Clinic Guide to HEART FAILURE

Everything you need to know about heart failure,
from the #1 heart care experts

Randall C. Starling, MD, MPH
Cardiovascular Medicine

Cleveland Clinic

In spite of all these CHF mortality is prohibitive (5 year 60 %)

Dialogues in Cardiovascular Medicine - Vol 4 · No. 2 · 1999

What has been and can be achieved by pharmacological manipulation of neuroendocrine responses?

Gary S. Francis, MD

Department of Cardiology / F-25 - The Cleveland Clinic Foundation - Cleveland - Ohio - USA

Holistic approach to cardiac failure

Only solution ?

Clinical review

ABC of heart failure

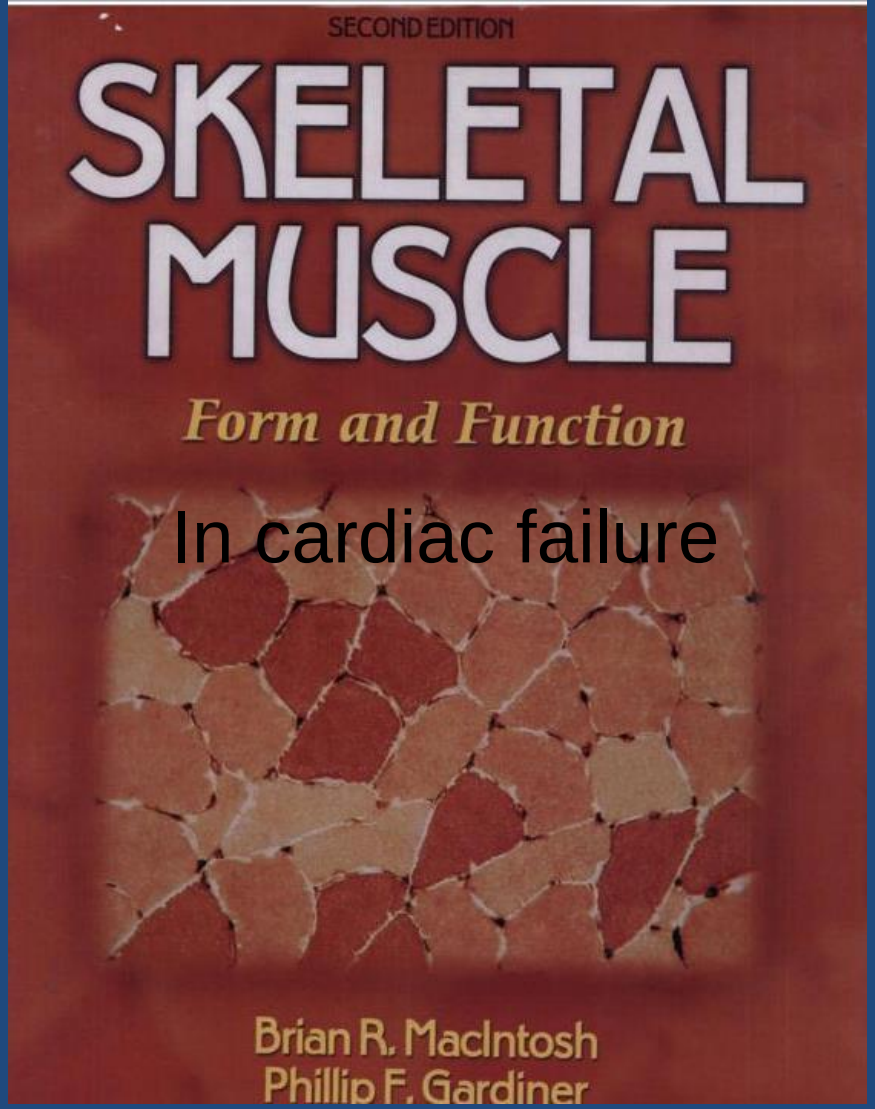
Non-drug management

C R Gibbs, G Jackson, G Y H Lip

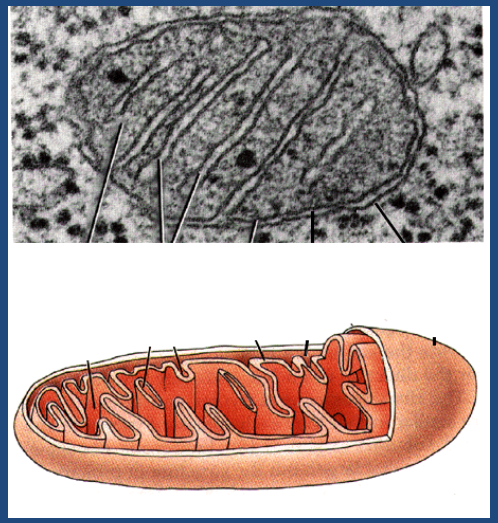
Approa
non-ph
compl
non-pharmacological management.

Comes free

Drug less pharmacotherapy



Skeletal muscle mitochondrial Dysfunction due to sustained Muscle sympathetic activity



Functional capacity directly related to skeletal muscle function

skeletal muscle dysfunction in cardiac failure

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... heart **failure**: role of **cardiac** pump **dysfunction** as ... - Wilson - Cited by 140
Exertional fatigue due to **skeletal muscle dysfunction** in ... - Wilson - Cited by 200
Skeletal muscle dysfunction in chronic obstructive ... - Gosker - Cited by 235

Skeletal muscle dysfunction in chronic obstructive pulmonary ...
www.ncbi.nlm.nih.gov/pubmed/10799364
by HR Gosker - 2000 - Cited by 235 - Related articles
Skeletal muscle dysfunction in chronic obstructive pulmonary disease and chronic **heart failure**: underlying mechanisms and therapy perspectives. Gosker HR ...

Skeletal muscle dysfunction and exercise intolerance in **heart failure**
www.uptodate.com/.../**skeletal-muscle-dysfunction**-and-exercise-intol...
27 Jan 2012 – The hallmark of **heart failure** (HF) is exercise intolerance due to dyspnea and fatigue. These symptoms were, in the past, thought to result ...

Exertional fatigue due to **skeletal muscle dysfunction** in patients with ...
circ.ahajournals.org/content/87/2/470.abstract
by JR Wilson - 1993 - Cited by 198 - Related articles
The present study was undertaken to determine if a subpopulation of patients with **heart failure** develops exertional fatigue due to **skeletal muscle dysfunction** ...

Skeletal Muscle Function and Its Relation to Exercise Tolerance in ...
content.onlinejacc.org/article.aspx?articleid=1124297
by D Harrington - 1997 - Cited by 204 - Related articles

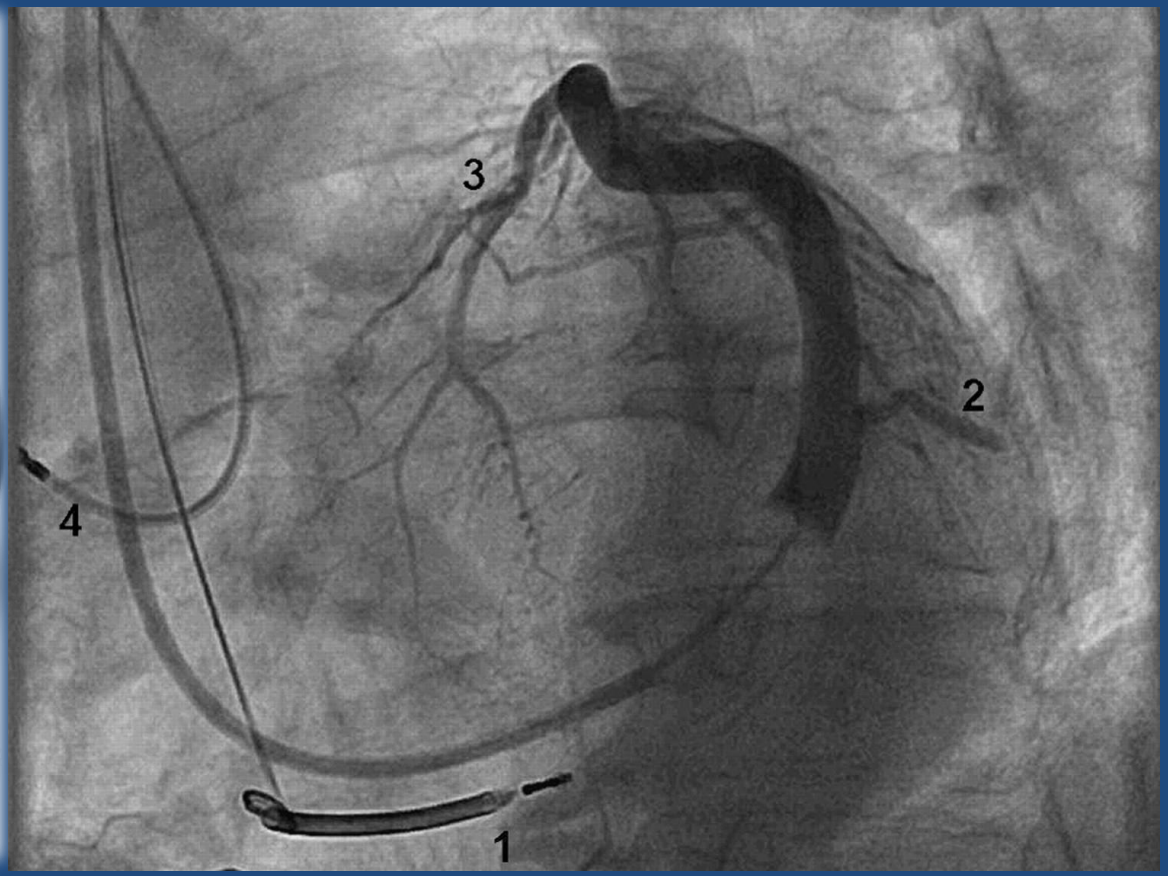
Is exercise training increase stress to heart ?

- Isometric exercise > 3 minutes was shown to increase after load and transient reduction in EF %

- Leg press exercise at 70 % of max capacity

  Increases muscle power without VO2 increase


MyoStim


3
2
4
1

CRT vs Skeletal muscle training

Simple exercise can achieve the same result

(Miracle 28 meter extra in 6 minute walk)

Combining Heart failure and Diabetes clinics

Jennifer Gow – HF Specialist Nurse
Jackie Price – Diabetes Specialist Nurse

Date										
Pulse										
BP (lying)										
BP (standing)										
Drug 2										
Drug 3										
Drug 4										
Drug 5										
Serum potassium										
Other investigations										
Next visit										
Doctor's signature										

Self empowered patients !

Patient guided dose adjustments

Heart failure cooperation card: patients and doctors are able to monitor changes in clinical signs (including weight), drug treatment, and baseline investigations. Patients should be encouraged to monitor their weight between clinic visits

Role of Family , Spouse , community

Table 2 Core concepts and Sub-concepts

Central Concepts	No of papers (n = 30)	Sub-concepts
1. Impact of CHF on everyday life		
Social isolation	20	Feeling abandoned; Physical restrictions; Food and diet; Medication; Fatigue; Relationships with family and friends
Living in fear	16	Uncertainty; Frustrated; Sleep; Work restrictions; Being limited; Behaviour change
Losing a sense of control	15	Symptoms; Being limited; Helplessness; Unpredictable
2. Common patterns of coping strategies		
Sharing experiences	13	Practical support; Psychological support; Emotional support; Knowledge; Assistance; Friends/family; Comfort
Being flexible to changing circumstances	14	Coping; Adjustment; Awareness; Acceptance; Making changes
3. Factors influencing self care and/or the provision of good care		
Knowledge	17	Knowledge; lack of knowledge; Acquiring information; Self-management; Self care; Emotional benefit; Navigating health services; Access to services
Health Services – availability and access	3	Time constraints; Communication; Negative experience; Patient satisfaction
Health Services – continuity and quality of care	15	Advice; Self care; Time constraints; Self care; Trust; Multiple care providers; Conflicting advice; Confusion; Education
Co-morbidity	11	Depression; Diabetes; Arthritis; Dietary restriction; Exercise; Sexual life
Personal Relationships	26	Family; Friends; Sexual life; Peers with CHF; Changing roles; Social isolation

CHF : A behavioral disorder

Emotional support and Ejection fraction !

Social isolation

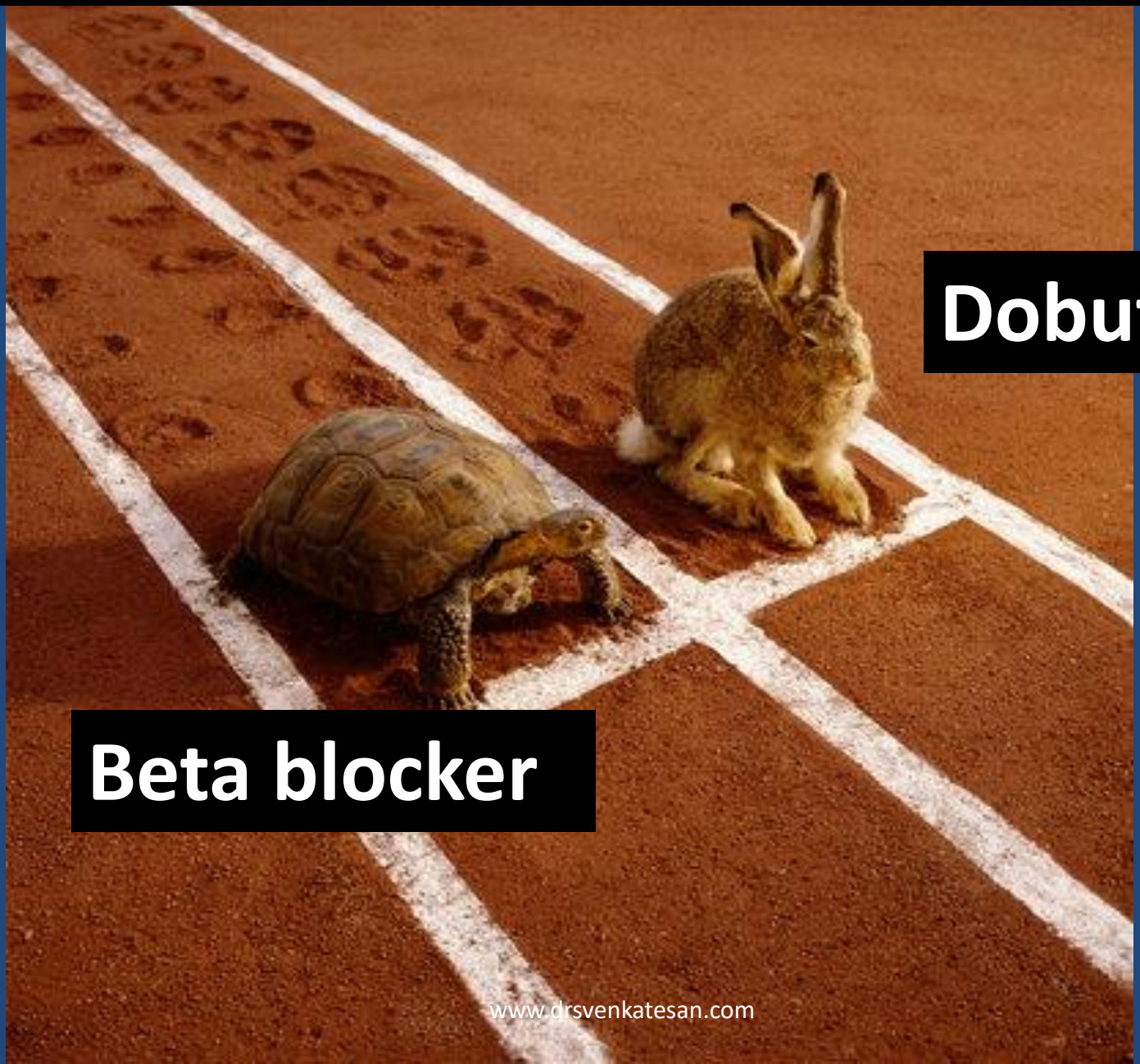
Living in fear (visiting death's door)

Losing a sense of control

Knowledge anxiety

(Addressing these issues can drastically reduce drug burden)

Make the life simple slow .



Summary

Cardiac failure is like management of cancer

Optimal drugs ,constant vigil ,Resist temptation

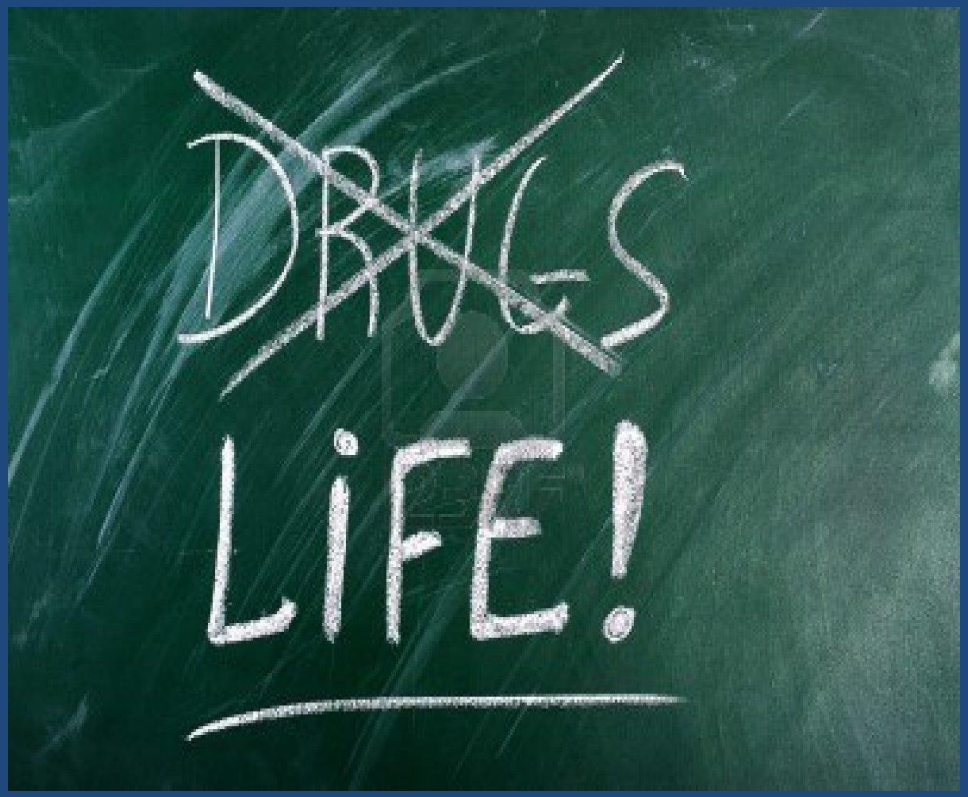
***Do not banish polypharmacy . Use it judiciously*.**

Use non pharmacological methods liberally

Consider ICD/CRT/Surgical option whenever possible

Aim for peace in patient mind

Future looks bright A drug less world ?



Thank you