

Congestive Heart Failure

Quality Assurance Training for Rural Hospitals

Heart Failure Management: New and Emerging Concepts

Kris Vijay, MD
Director, Heart Failure Program
Arizona Heart Institute

When thou examinest the obstruction in his abdomen and thou findest that he is not in a condition to leap the Nile, his stomach is swollen and his chest asthmatic, then say thou to him: "It is Blood that has got itself fixed and does not circulate." Do thou cause and emptying by means of a medicinal remedy. Make him therefore:

Wormwood 1/8	Eldenberries 1/16
Sebesten 1/8	Sasa-chips 1/8

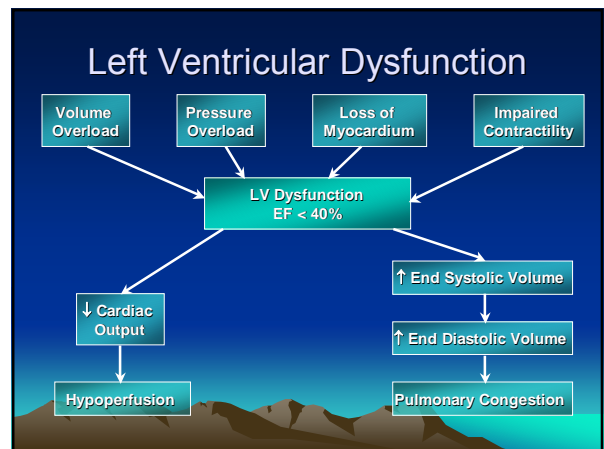
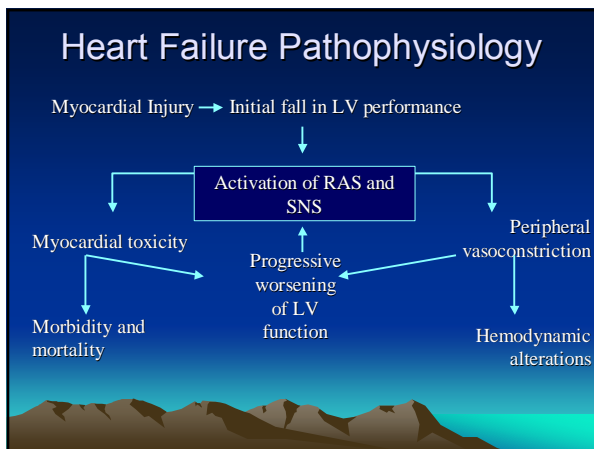
Cook in Beer-that-has-been-brewed-from many-ingredients, strain into one, thoroughly, and let the patient drink.

CHF—Definitions

- **CHF:** A pathophysiologic state in which an abnormality of cardiac function is responsible for failure of the heart to pump blood at a rate commensurate with the requirements of the metabolizing tissues or to do so only when the filling pressure is increased.
- **Diastolic Heart Failure:** A condition in which there is resistance to filling of one or both ventricles leading to increased ventricular filling pressures and congestive symptoms in the presence of normal or near normal systolic function.
- **Asymptomatic LV Dysfunction:** Presence of significant ventricular systolic dysfunction for prolonged periods in the absence of symptoms of, or treatment for, heart failure.

Models of Heart Failure

- Cardiorenal
- Cardiocirculatory
- Neurohormonal
- Independent LV Remodeling



Congestive Heart Failure Quality Assurance Training for Rural Hospitals

Major Risk Factors for CAD

Modifiable risk factors	
Hypertension	Cigarette smoking
Dyslipidemia	Obesity
Diabetes	Physical inactivity
Nonmodifiable risk factors	
Family history	Gender
Age	

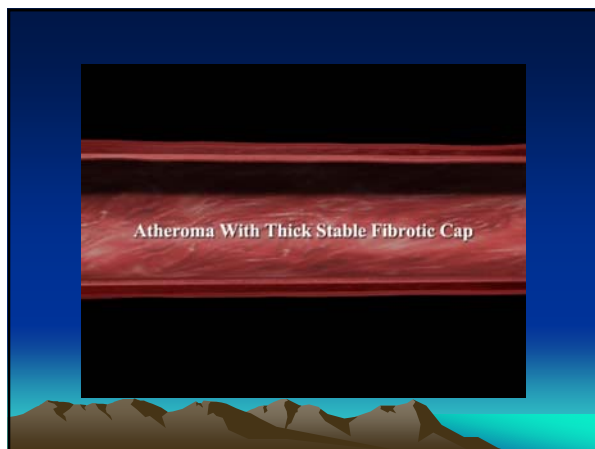
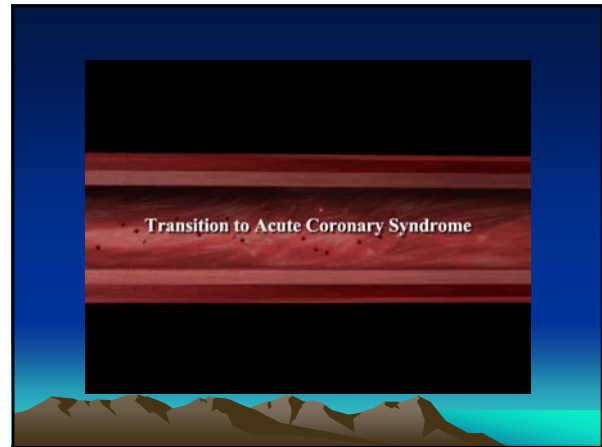
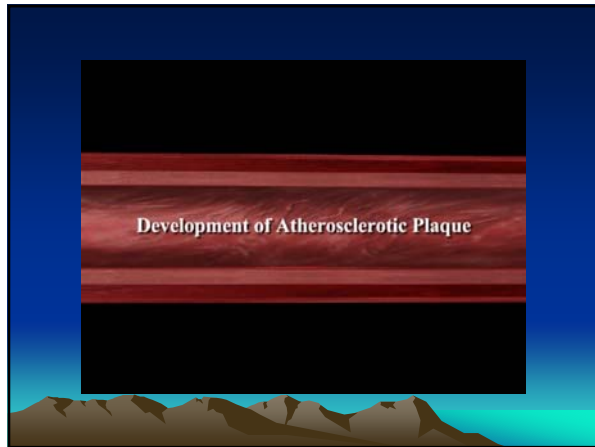
Grundy SM et al., Circulation, 1998; Grundy SM, Circulation, 1999

Most Myocardial Infarctions Are Caused by Low-Grade Stenosis

Coronary stenosis severity prior to MI

Stenosis Severity	Percentage
<50% Stenosis	68%
50%-70% Stenosis	18%
>70% Stenosis	14%

Pooled data from 4 studies: Ambrose et al., 1988; Little et al., 1988; Nobuyoshi et al., 1991; and Giroud et al., 1992. (Adapted from Falk et al.)
Falk E et al., Circulation, 1995

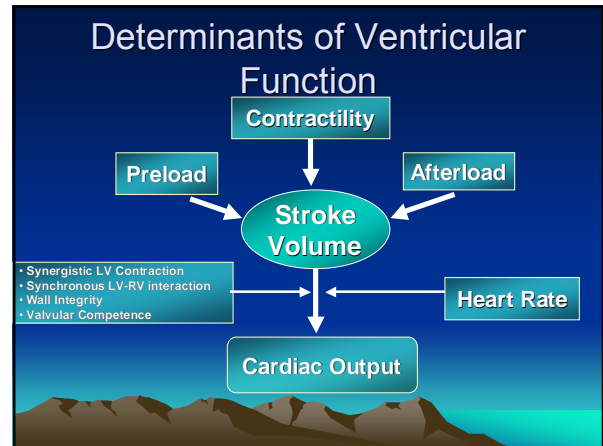
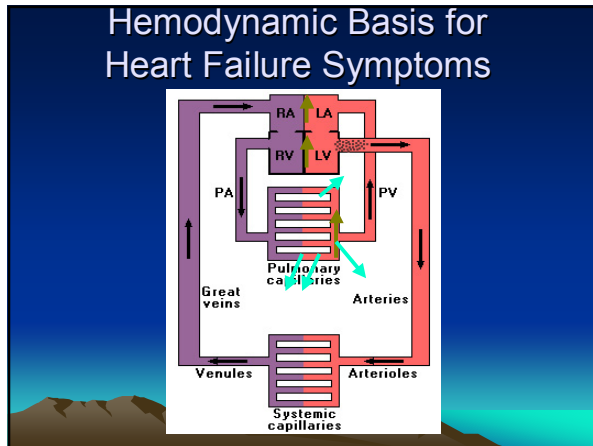


LV Remodeling After MI

Acute infarction (hours)
 Infarct expansion (hours to days)
 Global remodeling (days to months)

Congestive Heart Failure

Quality Assurance Training for Rural Hospitals



Cardiac Output

- Cardiac output is the amount of blood that the ventricle ejects per minute.

$$\text{Cardiac Output} = \text{HR} \times \text{SV}$$

Consequences of Decreased Mean Arterial Pressure

$$\downarrow \text{Mean Arterial Pressure (BP)} = \downarrow \text{Cardiac Output} \times \text{Total Peripheral Resistance}$$

Compensatory Mechanisms

- Frank-Starling Mechanism
- Neurohormonal Activation
- Ventricular Remodeling

Compensatory Mechanisms

Frank-Starling Mechanism

- At rest, no HF
- HF due to LV systolic dysfunction
- Advanced HF

The graph shows the relationship between stroke volume per cardiac output (y-axis) and left ventricular end-diastolic pressure (x-axis). Three curves are shown: 'Increased contractility' (top curve), 'Normal' (middle curve), and 'Heart failure' (bottom curve). Point A is on the normal curve, point B is on the heart failure curve at a higher pressure, and point C is on the heart failure curve at a lower pressure. A vertical line labeled 'Primary congestion' is shown at the pressure of point B.

Congestive Heart Failure

Quality Assurance Training for Rural Hospitals

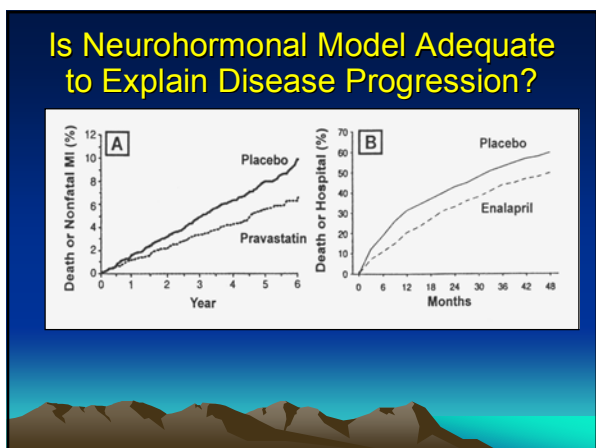
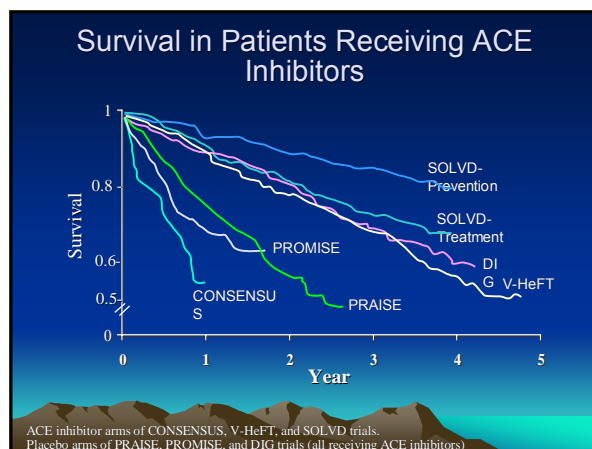
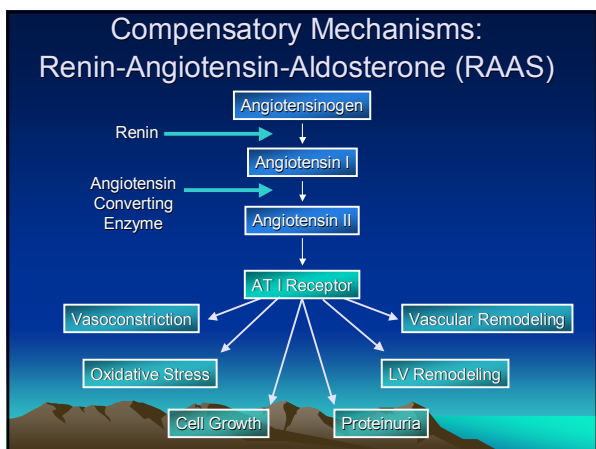
Neurohormonal Activation on Heart Failure

<p>Proliferative, Vasoconstricting, Anti-Natriuretic</p> <ul style="list-style-type: none"> • Adrenergic Nervous System (Norepinephrine) • Renin-Angiotensin System • Non-Osmotic Vasopressin • Endothelin • TNF alpha 	<p>Anti-Proliferative, Vasodilating, Natriuretic</p> <ul style="list-style-type: none"> • Natriuretic Peptides • Nitric Oxide • Kinins • Vasodilating Prostaglandins
--	---

Compensatory Mechanisms

Ventricular Remodeling
Alterations in the heart's size, shape, structure, and function brought about by the chronic hemodynamic stresses experienced by the failing heart.

Curry CW, et al. Mechanical dyssynchrony in dilated cardiomyopathy with intraventricular conduction delay as depicted by 3D tagged magnetic resonance imaging. *Circulation* 2000 Jan 4;101(1):E2.

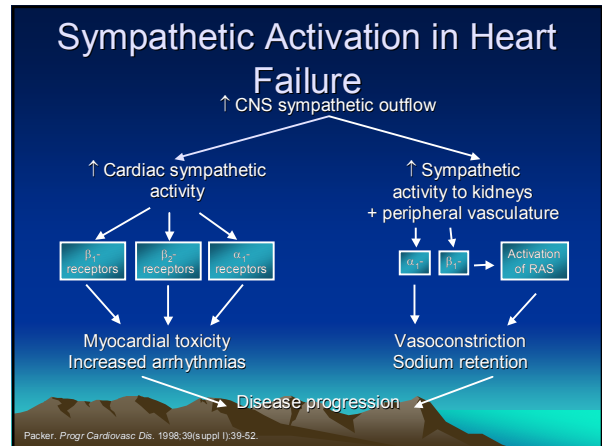
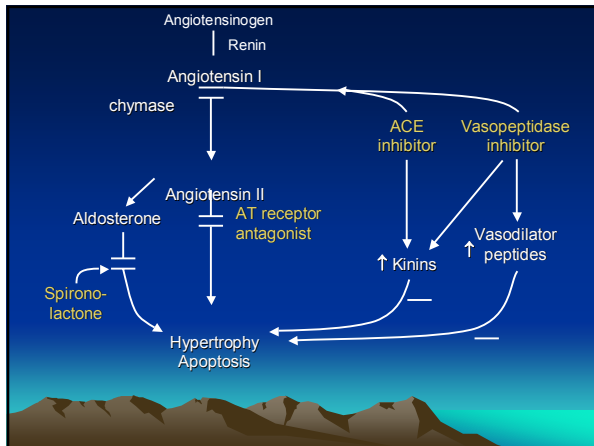


Potential Explanation of Disease Progression

- Incomplete inhibition of RAS due to side effects
- Alternate metabolic pathways in RAS
- Other incipient biologically active systems
 - Speculative: Mechanisms independent of neurohormones.

Congestive Heart Failure

Quality Assurance Training for Rural Hospitals



The Ratio of β_2 - and α_1 -Adrenergic Receptors in the Damaged Heart

In the damaged heart, the ratio of receptors shifts, increasing the relative proportion of β_2 - and α_1 -receptors

	β_1	β_2	α_1
Normal Heart	70	20	10
Damaged Heart	50	25	25

Adapted from Bristow MR. *J Am Coll Cardiol*, 1993;22(4 Suppl A):61A-71A.

- ### Causes of Dilated Cardiomyopathy
- Ischemia
 - Infectious agents: bacterial, viral (including **human immunodeficiency virus**), fungal, **Borrelia burgdorferi (Lyme disease)**
 - Idiopathic
 - Familial
 - Acute rheumatic fever
 - Infiltrative: **amyloid**, hemochromatosis, sarcoid
 - Toxic: heroin, **cocaine**, alcohol, amphetamines, Adriamycin, cyclophosphamide, sulfonamides, lead, arsenic, cobalt, phosphorus, ethylene glycol
 - Nutritional deficiencies: protein, thiamine, selenium

- ### CHF with Normal Systolic Function
- Valve disease
 - Mitral stenosis, tricuspid stenosis
 - Aortic stenosis, pulmonary stenosis
 - Mitral regurgitation, aortic regurgitation
 - Constrictive pericarditis

- ### CHF with Normal Systolic Function
- Restrictive cardiomyopathy
 - Primary
 - Secondary
 - Eosinophilic
 - Infiltrative (amyloidosis)
 - Sarcoidosis
 - Fabry's disease, hemochromatosis
 - Radiation exposure
 - Tumor infiltration

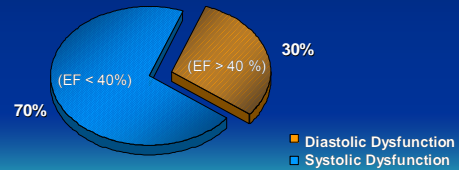
Congestive Heart Failure Quality Assurance Training for Rural Hospitals

CHF with Normal Systolic Function

- Transient ischemia
- Hypertrophic cardiomyopathy
 - Obstructive
 - Nonobstructive
- Hypertensive heart disease
 - Hypertensive hypertrophic cardiomyopathy of the elderly
- Coronary artery disease
- Noncardiac dyspnea

Left Ventricular Dysfunction

- **Systolic:** Impaired contractility/ejection
 - Approximately two-thirds of heart failure patients have systolic dysfunction¹
- **Diastolic:** Impaired filling/relaxation



1 Lilly, L. Pathophysiology of Heart Disease, Second Edition p 200

Precipitating Factors for Acute Decompensation of Chronic Congestive Heart Failure

- | | |
|---|--|
| <ul style="list-style-type: none"> • Noncompliance with diet/therapy • Arrhythmia • Systemic infection • Pulmonary embolism • High-output states—
anemia, pregnancy,
hyperthyroidism • Hypertension | <ul style="list-style-type: none"> • Unrelated illness—renal,
pulmonary, G.I. • Hypothyroidism • Ischemia • Toxins—alcohol, street
drugs • Inappropriate drug
therapy—negative
inotrope, salt-retaining |
|---|--|

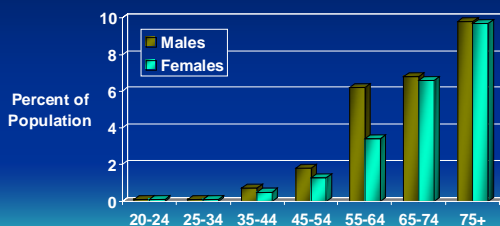
Heart Failure Statistics

- 50% of HF patients have three or more co-morbidities¹
- HF patients take an average of six medications¹
- 78% of HF patients have had at least two hospital admissions per year¹
- Cost of HF in the U.S. is estimated to be between \$10 billion and \$38 billion annually²
- Five-year survival rate for all NYHA classes estimated at 50%³

¹ English M and Mastream M. *Crit Care Nurse* 1996;18:1-6.
² Havranek EP, Abraham WT. *The Healthcare Economics of Heart Failure* 1998; 14:10-18.
³ American Heart Association, 2001 Heart and Stroke Statistical Update.

Prevalence of HF by Age and Gender

United States: 1988–94



Source: NHANES III (1988-94), CDC/NCHS and the American Heart Association

Assessing Heart Failure

- Patient History
- Physical Examination
- Laboratory and Diagnostic Tests

Congestive Heart Failure Quality Assurance Training for Rural Hospitals

Diagnostic Evaluation of New-Onset Heart Failure

- Determine the type of cardiac dysfunction (systolic vs. diastolic)
- Determine etiology
- Define prognosis
- Guide therapy

General Approach to Advanced Heart Failure

- Address clinical profile
- Address reversible components
- Evaluate function and risk
- Tailor standard medical therapy
- Compare to expected outcomes of newer therapies

Left Ventricular Dysfunction Systolic and Diastolic

<ul style="list-style-type: none"> • Symptoms <ul style="list-style-type: none"> – Dyspnea on Exertion – Paroxysmal Nocturnal Dyspnea – Tachycardia – Cough – Hemoptysis 	<ul style="list-style-type: none"> • Physical Signs <ul style="list-style-type: none"> – Basilar Rales – Pulmonary Edema – S3 Gallop – Pleural Effusion – Cheyne-Stokes Respiration
---	--

Right Ventricular Failure Systolic and Diastolic

<ul style="list-style-type: none"> • Symptoms <ul style="list-style-type: none"> – Abdominal Pain – Anorexia – Nausea – Bloating – Swelling 	<ul style="list-style-type: none"> • Physical Signs <ul style="list-style-type: none"> – Peripheral Edema – Jugular Venous Distention – Abdominal-Jugular Reflux – Hepatomegaly
--	---

FACES: A Screening Tool for Heart Failure

- Do you ever feel Fatigue?
- Have you experienced an altered Activity or exercise pattern?
- Do you feel any Congestion in your chest?
- Do you ever get Edema (swelling)?
- Are you ever Short of breath?

Adapted from the Heart Failure Society of America.

Two-Minute Assessment of Hemodynamic Profile

Congestion at rest

	NO Warm & Dry	YES Warm & Wet	
<i>Low perfusion at rest</i>	NO A	B	Evidence for Congestion <ul style="list-style-type: none"> • Orthopnea • JVD • Edema • Ascites • Rales (rarely) • Valsalva square wave • Abd-jugular reflux
	YES L	Cold & Wet C	
	Low profile Heart failure "light"	Complex	

Evidence for Low Perfusion

- Narrow pulse pressure
- Cool extremities
- May be sleepy, obtunded
- Suspect from ACEI hypotension and low NA
- One cause or worsening renal fn

Congestive Heart Failure Quality Assurance Training for Rural Hospitals

Diagnostic Evaluation of New-Onset Heart Failure

Initial Work-up:

- ECG
- Chest x-ray
- Blood work including CBC, CMP, H/L profile, U/A and TSH
- Echocardiography

LATER WORK UP THAT MAY BE REQUIRED:

- Stress imaging study
- Radionuclide cine-angiography
- Left heart catheterization

Diagnostic Evaluation of New-Onset Heart Failure

M-Mode Echo 2D Echo

New York Heart Association Functional Classification for CHF

Class I Patients with cardiac disease but without resulting limitations of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.

Class II Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.

New York Heart Association Functional Classification for CHF

Class III Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary physical activity causes fatigue, palpitation, dyspnea, or anginal pain.

Class IV Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of cardiac insufficiency or of anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

Potentially Reversible Components of Heart Failure

- Recent viral illness
- Heavy alcohol consumption
- Drugs that depress contractility or exacerbate fluid retention
- Atrial fibrillation, PAT, slow VT
- Thyroid disease
- Reversible ischemia
- Obesity

Poor Prognostic Factors in Ventricular Dysfunction

- Ischemic cause*
- Advanced age
- Duration of symptoms
- Ejection fraction
 - Left ventricular < 25%
 - Right ventricular < 35%*

*Most useful clinically

Congestive Heart Failure Quality Assurance Training for Rural Hospitals

Poor Prognostic Factors in Ventricular Dysfunction

- Hemodynamics
 - Low cardiac index, stroke work index
 - High pulmonary capillary wedge pressure, pulmonary artery systolic pressure
 - “Restrictive” filling pattern on Doppler
 - Echocardiography

Poor Prognostic Factors in Ventricular Dysfunction

- Functional
 - NYHA functional class III and IV*
 - Decreased exercise duration
 - Peak oxygen consumption < 14 mL/kg per min*
 - Six-minute walking distance < 350 m

**Most useful clinically*

Poor Prognostic Factors in Ventricular Dysfunction

- Neurohumoral factors—increased levels of:
 - Norepinephrine
 - Plasma renin activity
 - Aldosterone
 - Angiotensin II
 - Atrial or brain natriuretic factor
 - Arginine vasopressin
 - Endothelin
 - Tumor necrosis factor

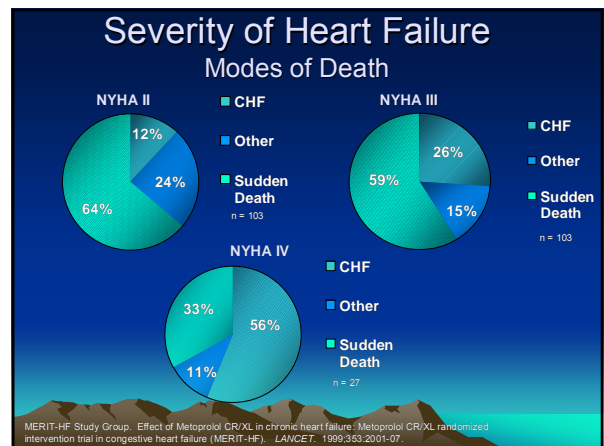
Poor Prognostic Factors in Ventricular Dysfunction

- Arrhythmias
 - Sudden death and symptomatic ventricular tachycardia*
 - Asymptomatic premature ventricular contraction and non-sustained ventricular tachycardia

**Most useful clinically*

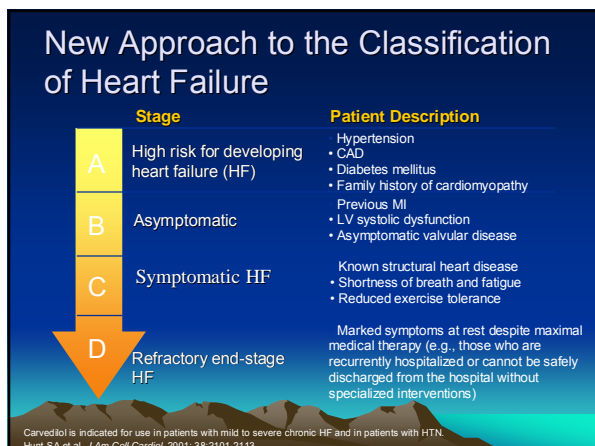
Clinical Class Review The New #1 Predictor of Mortality in CHF

Patient Description	Symptoms	Mortality		
		Hf Death	Unexpected	Disease Progression
I. Asymptomatic			++	++
II. Vigorous activity—limited	(+)	(+)	++	++
III. Routine activity—limited	++	++	+	+
IV. Decompensated—symptoms with rest or minimal activity	+++	+++	+	(+)



Congestive Heart Failure

Quality Assurance Training for Rural Hospitals



- ### Therapies in CHF
- ACE I
 - BB
 - Aldosterone inhibitors
 - Digoxin
 - Diuretics
 - ????

- ### Weight of Evidence: ACE Inhibitors
- Approximately 7,000 patients evaluated in long-term placebo-controlled clinical trials
 - Improvement in cardiac function, symptoms, and clinical status; equivocal effects on exercise tolerance
 - Decrease in all-cause mortality by 20–25 percent ($p < .001$) and decrease in combined risk of death and hospitalization by 30–35 percent ($p < .001$)
 - Effect shown in SOLVD Treatment, CONSENSUS, and V-HeFT II trials.
- Garg and Yusuf, 1995

- ### Weight of Evidence: β -blockade
- Over 10,000 patients have now been evaluated in long-term, placebo-controlled clinical trials
 - Improvement in cardiac function and symptoms; equivocal effects on exercise tolerance
 - Decrease in all-cause mortality by 30–35% ($P < .0001$); effect shown in 4 individual trials
 - Decrease in combined risk of death and hospitalization by 35–40% ($P < .001$); effect shown in 6 individual trials
 - Effect shown in patients *already receiving ACE inhibitors*

- ### ATLAS Trial
- 3,164 patients with Class II-IV heart failure randomized to low-dose (2.5–5.0 mg) or high-dose (32.5–35.0 mg) lisinopril for 3.5–5 years
 - Patients assigned to high doses had an 8% lower risk of death ($P = .128$) and 12% lower risk of death or hospitalization for any reason ($P = .002$) than those assigned to low doses
 - Low and high doses of the ACE inhibitor had similar effects on NYHA class
- Packer et al. Eur Heart J. 1998;19(suppl):142.

Should Physicians Increase the Dose of ACE Inhibitor or Add β -Blockade?

	“Low” dose ACEI → “High” dose ACEI*	“Average” dose ACEI + β -blockade†
Symptoms	Unchanged	Improved
Morbidity/mortality	↓ 12%	↓ 35%–40%
Mortality	↓ 8%	↓ 30%–35%

*Adapted from Packer et al. Eur Heart J. 1998;19(suppl):142.
†Adapted from Lechat et al. Circulation. 1998;98:1184-1191.

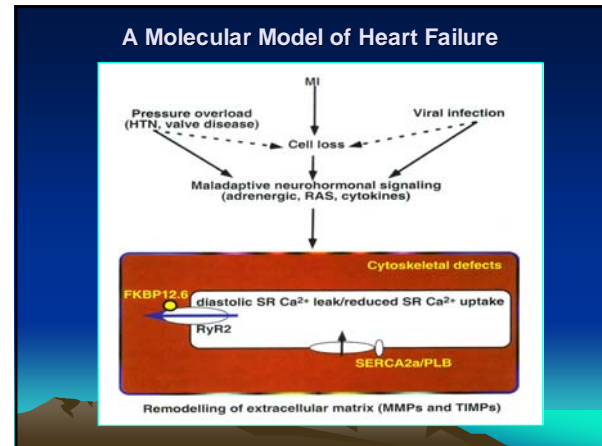
Congestive Heart Failure

Quality Assurance Training for Rural Hospitals

Effect of β -Blockers on Outcomes in Heart Failure

Study	Drug	HF Severity	Target Dosage (mg/day)	Outcome
US Carvedilol ¹	Carvedilol	Mild/moderate	6.25 to 25 ² bid	48% decrease in disease progression* (p=0.001)
CIBIS-II ²	bisoprolol ³	moderate/severe	10 qd	34% mortality (p<0.001)
MERIT-HF ³	Metoprolol succinate	mild/moderate	200 qd	34% mortality (p=0.0062)
COPERNICUS ⁴	carvedilol	severe	25 bid	35% mortality (p=0.0014)

50 mg bid if >85 kg.
¹Disease progression was defined as HF death or hospitalization or the need for sustained increase in medications for HF.
²Colucci WS et al. *Circulation*. 1996;94:2800-2806.
³CIBIS II Investigators and Committees. *Lancet*. 1999;353:9-13.
⁴MERIT-HF Study Group. *Lancet*. 1999;353:2001-2007.
⁵Packer M et al. *N Engl J Med*. 2001;344:1651-1658. *HF NOT AN APPROVED INDICATION



- ### Potential Therapeutic Agents
- Phospholamban inhibitor
 - Ryanodine receptor modulator
 - SOCS
 - BARK inhibitor
 - SERCA 2A gene transfer
 - Myo D gene transfer

- ### Therapeutic Horizons in Heart Failure
- Ca ++ Homeostasis
 - Cardiomyocyte signaling
 - Gene therapies
 - Pharmacological approaches
 - Tap on to currently known genetic defects
 - Cell therapies

- ### Pharmacological Agents
- Antioxidants
 - ARBs
 - Nesiritide
 - Levosimendon
 - Oral PDE inhibitor
 - FFA inhibitor
 - Immune modulator therapy
 - Darbopietin
 - MMP inhibitor
 - Adenosine receptor antagonists
 - Vasopressin inhibitors
 - SNEP inhibitors
 - Dual PPARs
 - Urocortin
 - Anti-inflammatory agents

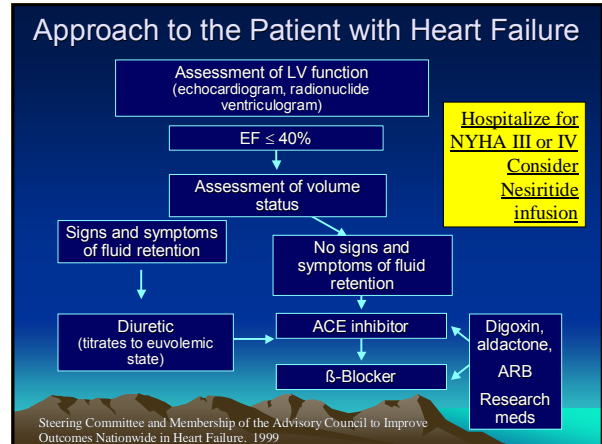
- ### New Options in Research Studies
- Progenitor stem cells
 - Endothelial
 - Bone marrow
 - Mesangioblasts
 - Skeletal muscle cell
 - Gene therapy: Myo D, SERCA, etc.

Congestive Heart Failure

Quality Assurance Training for Rural Hospitals

Summary

- Address clinical profile
- Address reversible components
- Evaluate function and risk
- Tailor standard medical therapy
- Compare to expected outcomes of newer therapies



“You may not be able to change the direction of the wind, but you can adjust the sails to always reach your destination.”

-Jimmy Dean