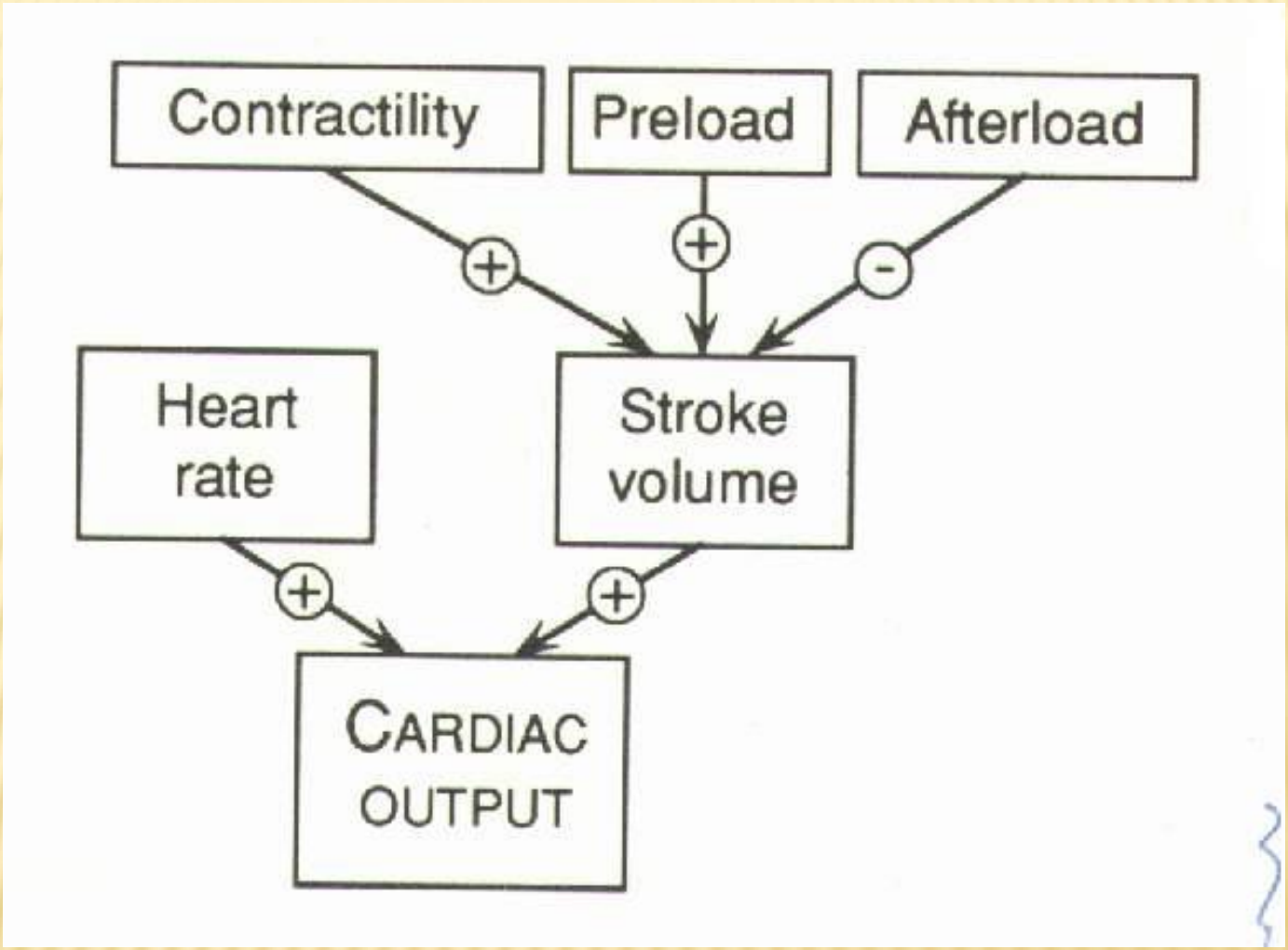
VLA 8. 11. 2016

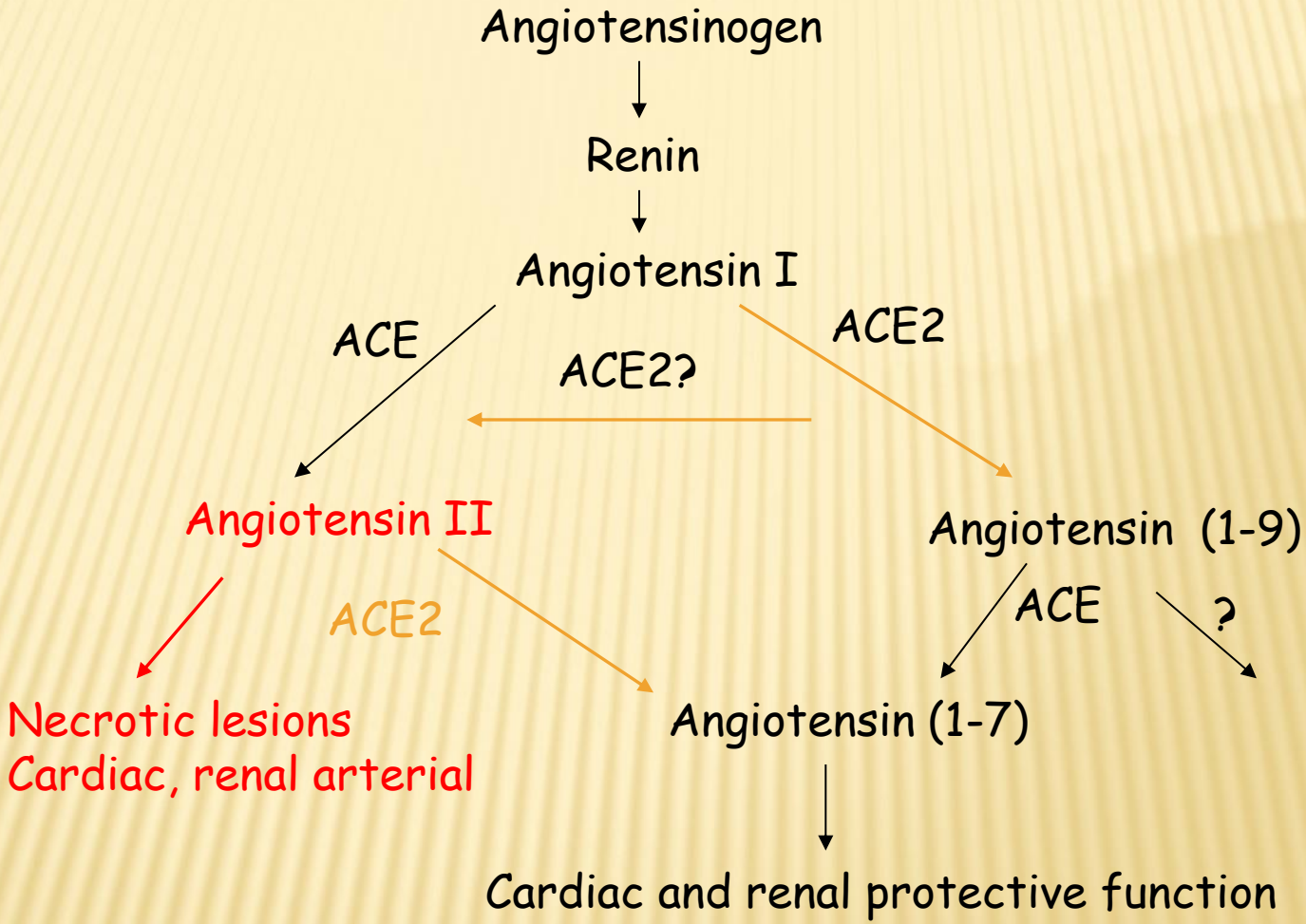
PRESSURE AND VOLUME OVERLOAD. REMODELLING OF THE HEART. CHRONIC HEART FAILURE

NORMAL CARDIAC FUNCTION

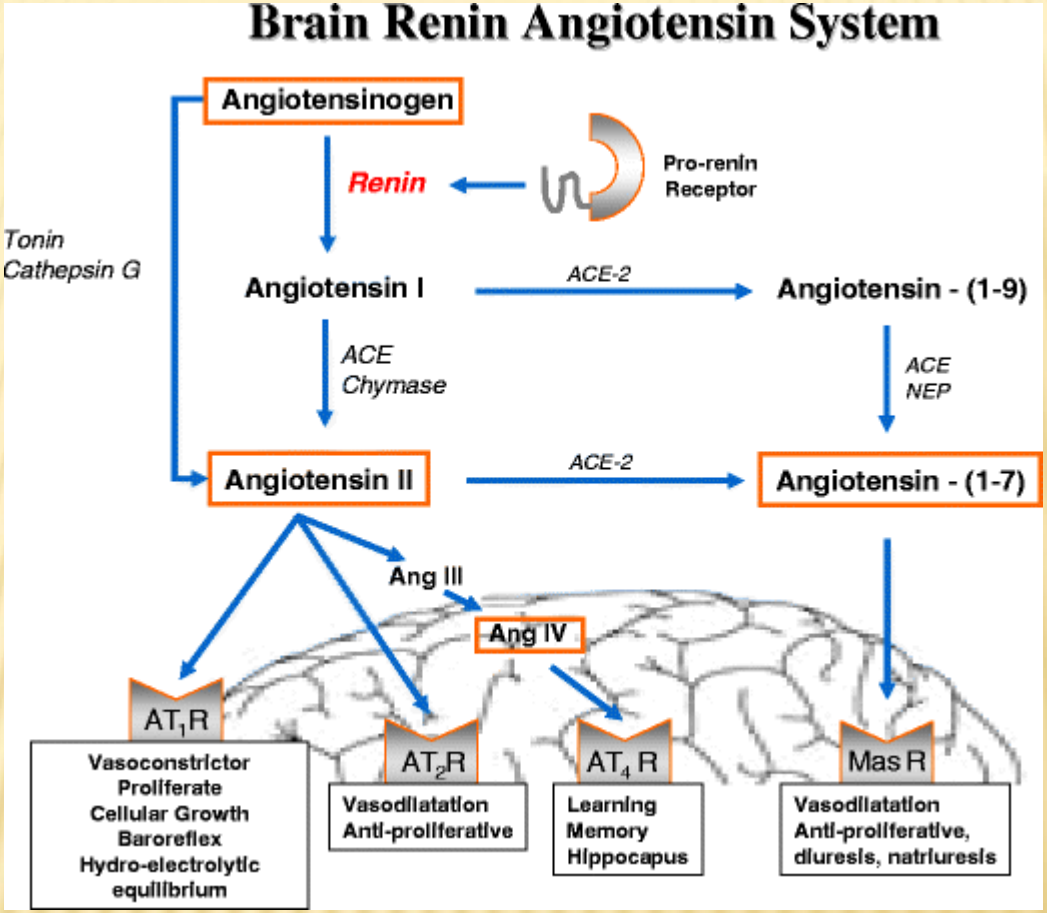
- Cardiac Output = Heart rate x Stroke volume
- Heart rate – controled by SNS and PNS
- Stroke – dependent on preload, afterload and contractility
- Preload = LVEDP and is measured as PCWP (Pulmonary Capillary Wedge Pressure)
- Afterload = SVR
- Contractility: ability of contractile elements to interact and shorten against a load

  (+ inotropy- inotropy)


Contractility
Preload
Afterload
+
+
-
Heart rate
Stroke volume
+
+
CARDIAC OUTPUT

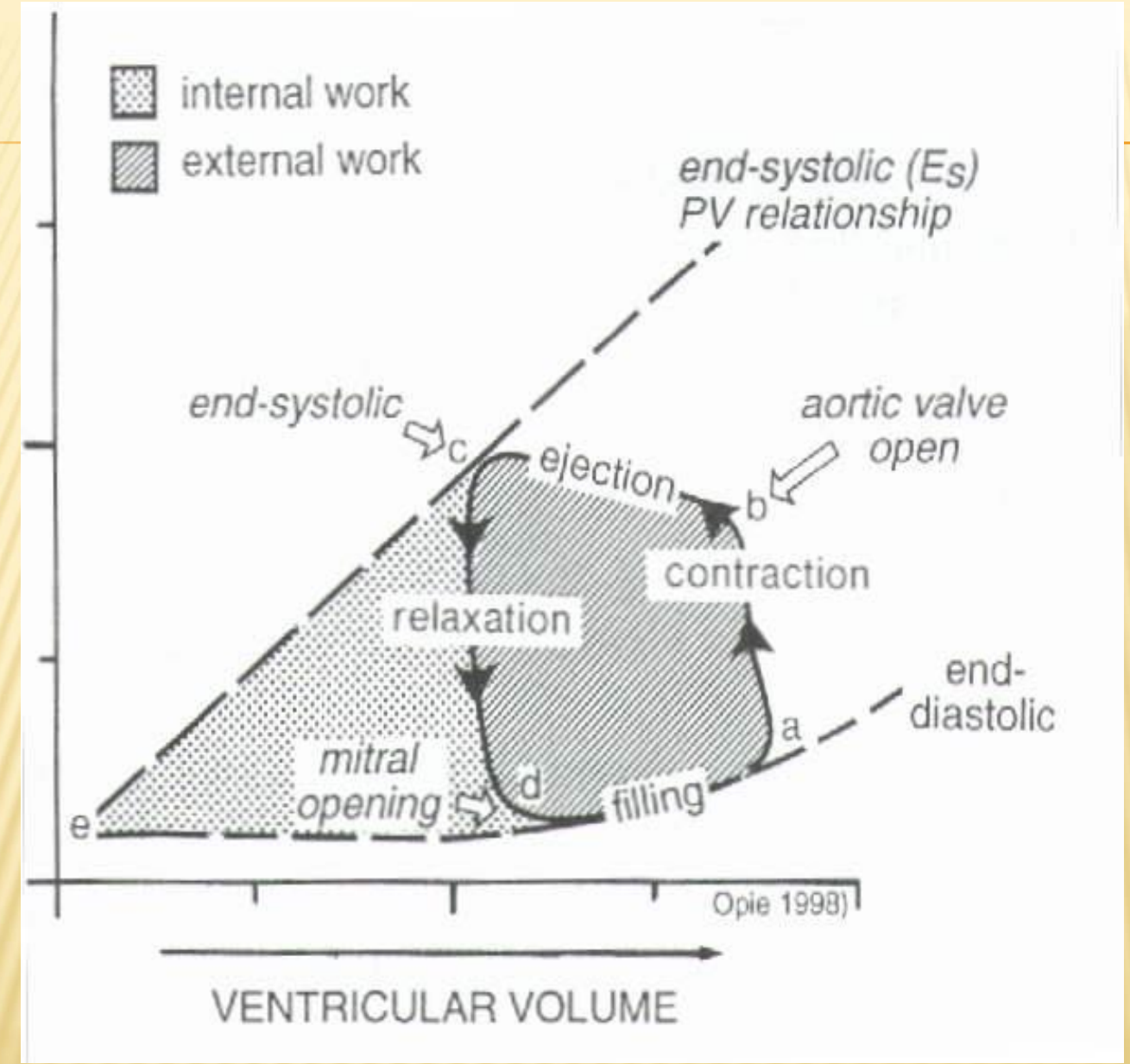


Danilczyk and Penninger, 2006



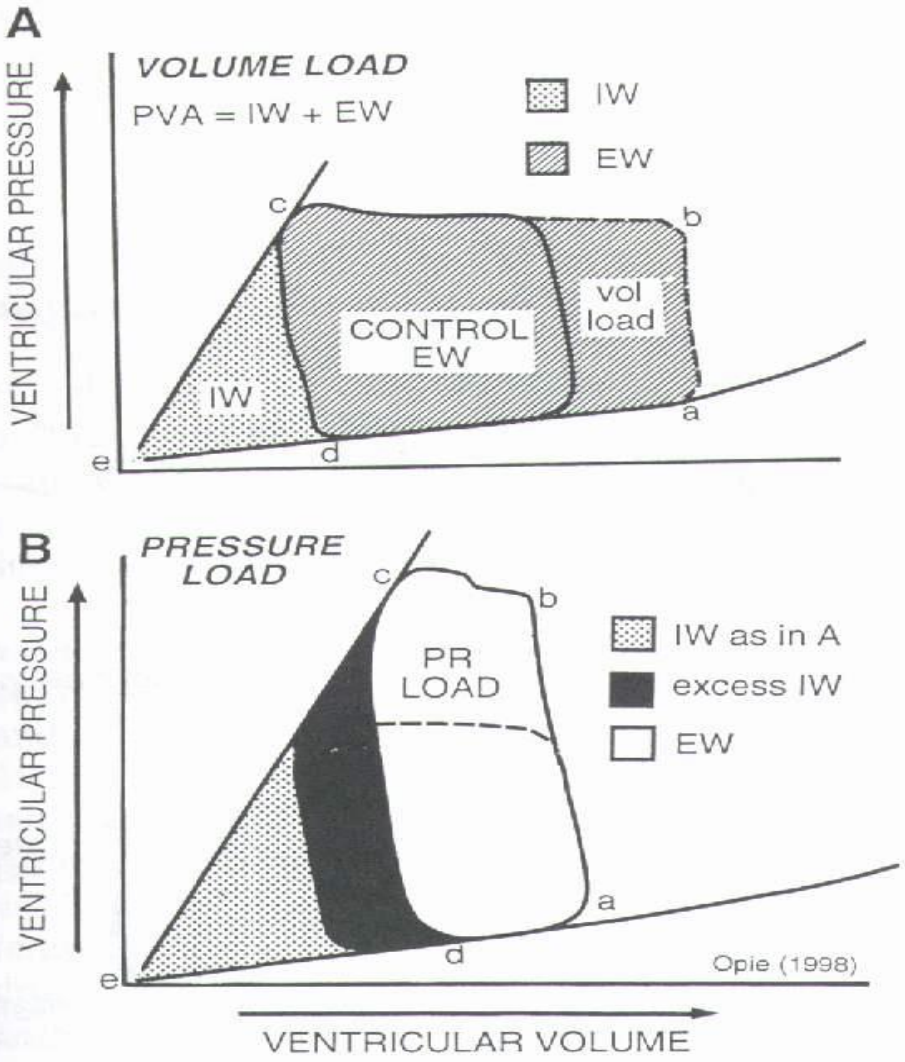
Phillips MI et al., 2008

MASR is highly expressed in myelin-rich tissue, especially in peripheral nerves. Myelin formation marker?



Working diagram

Sum of the external and internal work represents the total mechanical work of contraction and this is directly proportional to oxygen consumption of the myocardium. Pressure work of the heart consumes more oxygen than volume work, so that the effectivity of the former is lower than that of the latter.


A
VOLUME LOAD
PVA = IW + EW
IW
EW
VENTRICULAR PRESSURE
c
b
CONTROL EW
vol load
IW
a
e
d
B
PRESSURE LOAD
c
b
PR LOAD
IW as in A
excess IW
EW
a
d
e
Opie (1998)
VENTRICULAR VOLUME

SYSTOLIC DYSFUNCTION

- Impairment of the contraction of the left ventricle such that stroke volume (SV) is reduced for any given end-diastolic volum (EDV)
- Ejection fraction (EF) is reduced (below 40-45%)
- EF=SV/EDV

SYSTOLIC DYSFUNCTION-ETIOLOGY

- **Dilated Cardiomyopathy**

- Ischemic disease
  - myocardial ischemia
  - myocardial infarction

- Non-ischemic disease
  - Primary myocardium muscle dysfunction
  - Valvular abnormalities
  - Hypertension
  - Alcohol and drug-induced
  - Idiopathic

DIASTOLIC DYSFUNCTION

- Ventricular filling rate and the extent of filling are reduced or a normal extent of filling is associated with an inappropriate rise in ventricular diastolic pressure.

DIASTOLIC DYSFUNCTION-ETIOLOGY

- **Hypertrophic Cardiomyopathy**
- Hypertension
- Myocardial ischemia and infarction

- **Restrictive Cardiomyopathy**
- Amyloidosis
- Sarcoidosis

COMPENSATORY MECHANISMS FOR DECREASED CARDIAC OUTPUT

- Increased SNS activity

  Increase HR and SVR which increases BP
- Frank-Starling mechanism:

  ⇑ LVEDP = ⇑ SV
- Activation of Renin-angiotensinaldosterone
- system (RAAS)
- Myocardial Remodeling

  - Concentric hypertrophy

  - Eccentric hypertrophy

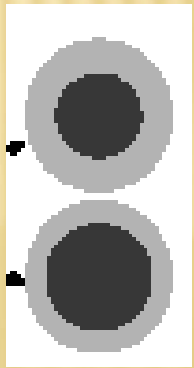
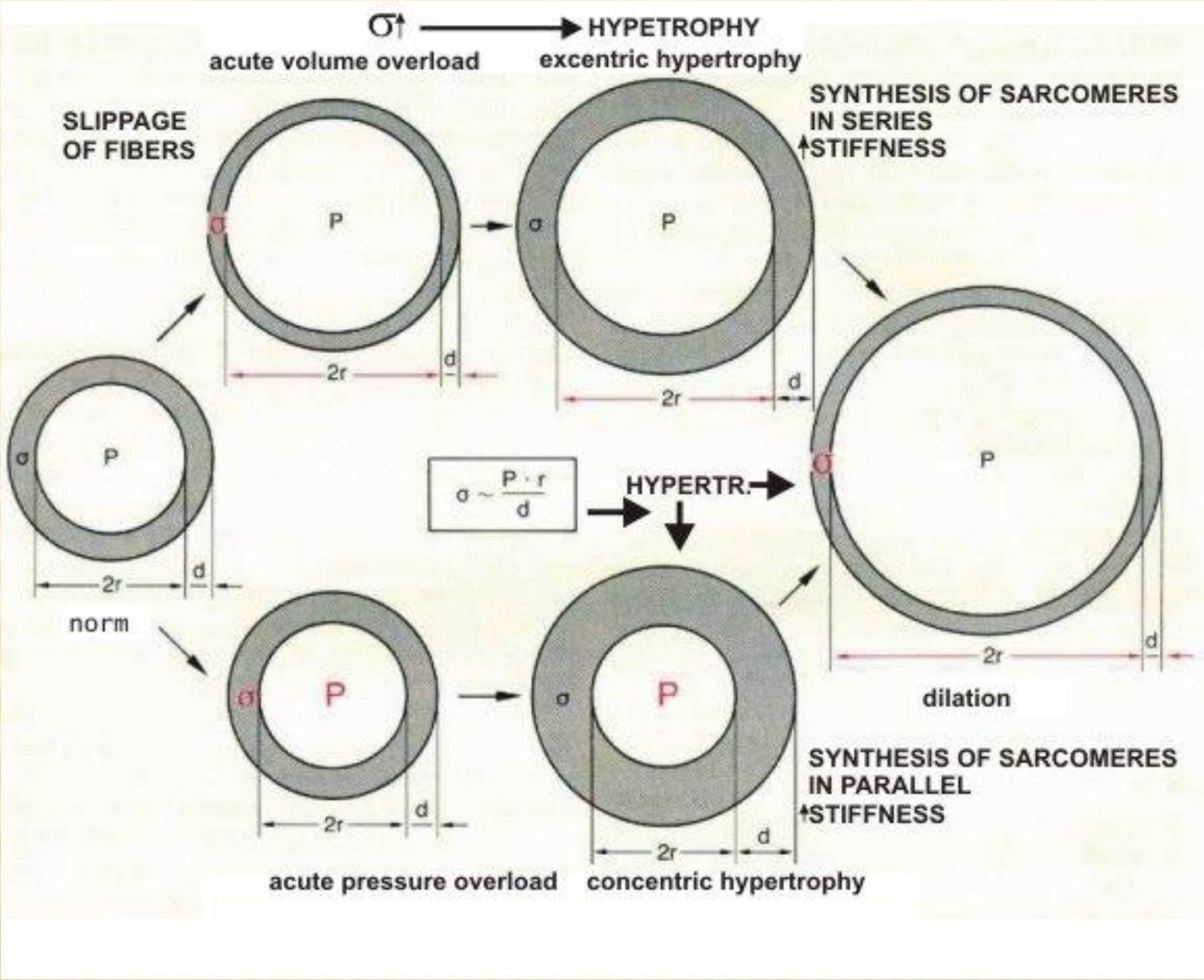


Table 1 Summary of characteristics for the hypertrophy patterns (concentric and eccentric) and haemodynamic mechanisms influencing pathological and physiological left ventricular hypertrophy (LVH)

	Pathological LVH		Physiological LVH	
	Concentric	Eccentric	Concentric	Eccentric
Stimulating haemodynamic mechanism	Increased pressure (afterload)	Increased volume (preload)	Increased pressure (afterload)	Increased volume (preload)
Potential aetiology of stimulus	Hypertension, aortic stenosis	Valvular disease	Strength training	Long-term endurance exercise
Ventricle morphology	Parallel addition of new myofibrils (wall thickening), frequently with myocyte necrosis and increased fibrosis	Series addition of sarcomeres (wall dilation and thinning) frequently with myocyte necrosis	Parallel addition of new myofibrils (wall thickening) with increased capillary density	Series addition of new sarcomeres (chamber volume enlargement)
Ventricular mechanics	Diastolic dysfunction with stiffness and decreased contractility	Decreased contractility often associated with side-to-side slippage of myocytes	Normal or enhanced contractility and myocardial efficiency	Normal or enhanced contractility and myocardial efficiency
Ventricular function	Abnormal	Abnormal	Normal	Normal or supranormal
Potential to regress	No	No	Yes	Yes

Pat


σ↑ → HYPETROPHY
acute volume overload
excentric hypertrophy
SLIPPAGE OF FIBERS
SYNTHESIS OF SARCOMERES IN SERIES
↑STIFFNESS
σ
P
2r
d
$\sigma \sim \frac{P \cdot r}{d}$
HYPERTR.
norm
dilation
SYNTHESIS OF SARCOMERES IN PARALLEL
↑STIFFNESS
acute pressure overload
concentric hypertrophy

HEART FAILURE

- A condition that exist when the heart is unable to pump sufficient blood to meet the metabolic needs of the body.

TYPES OF HEART FAILURE

- **Systolic & Diastolic**
- **High Output Failure**
  - Pregnancy, anemia, thyreotoxicosis
- **Low Output Failure**

- **Acute**
  - large MI, aortic valve dysfunction---
- **Chronic**

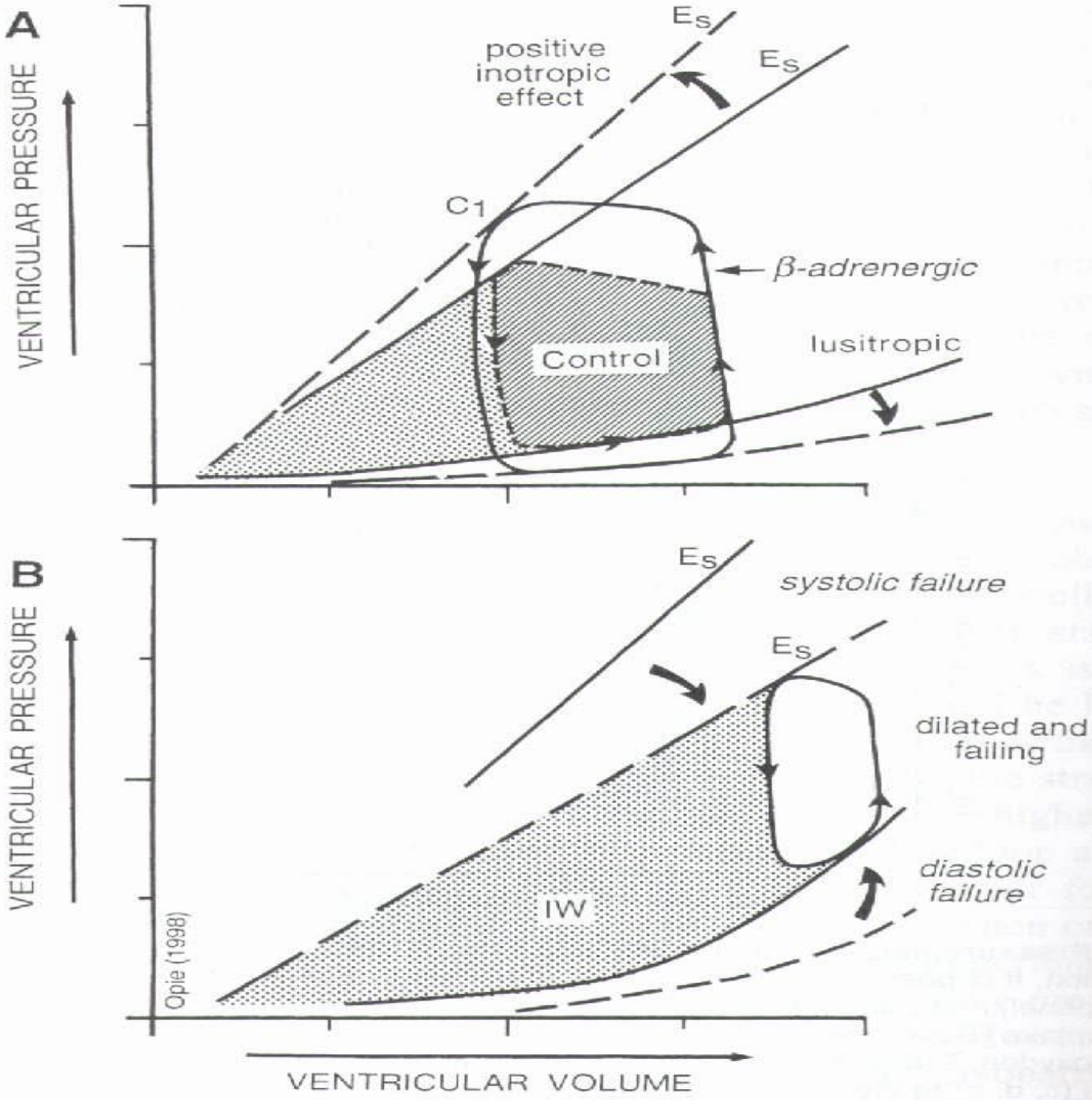
LEFT VS. RIGHT HEART FAILURE

Left Heart Failure

- pulmonary congestion

Right Heart Failure

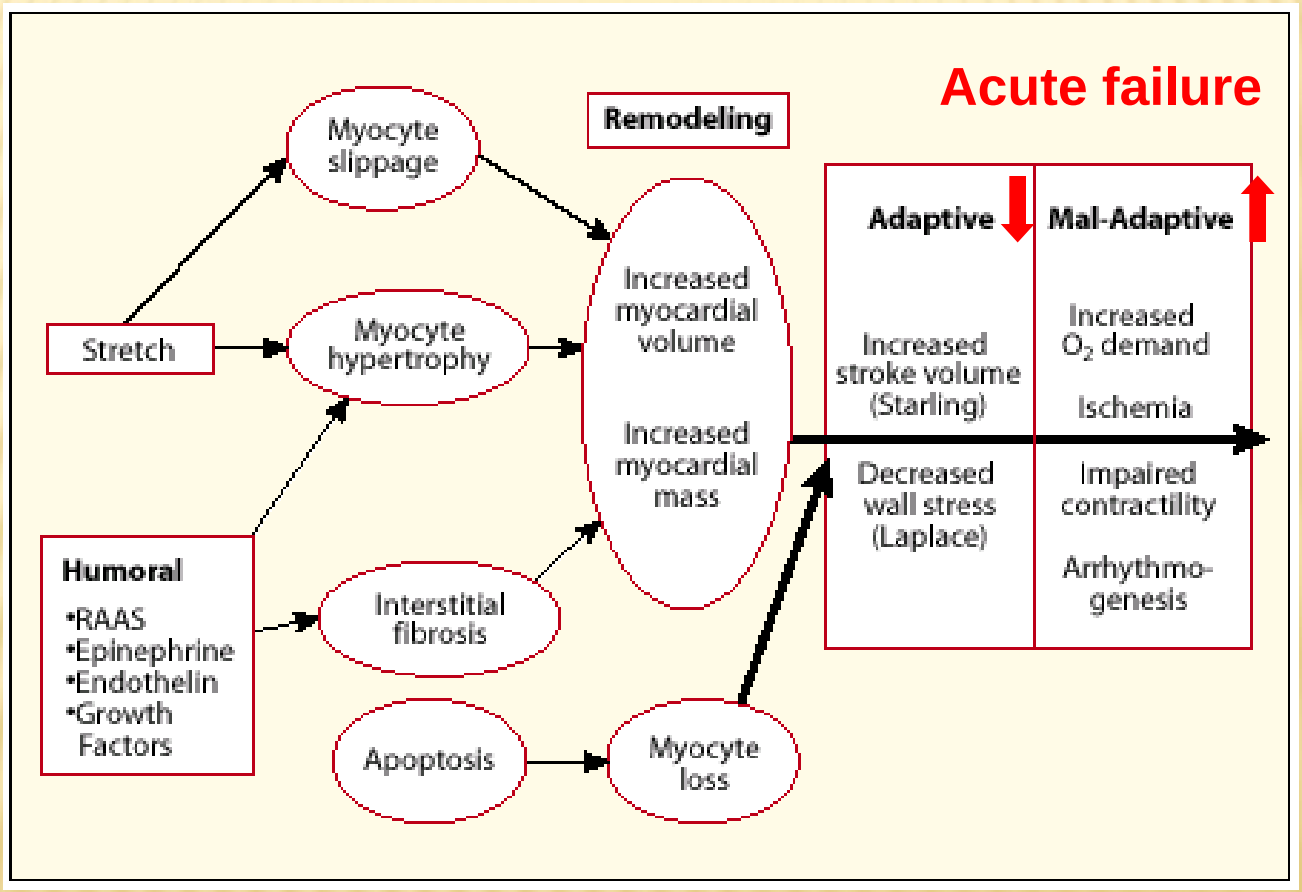
- peripheral edema
- sacral edema
- elevated JVP
- ascites
- hepatomegaly
- splenomegaly
- pleural effusion


A
VENTRICULAR PRESSURE
positive
inotropic
effect
Es
Es
C1
β-adrenergic
Control
lusitropic
B
VENTRICULAR PRESSURE
Es
systolic failure
Es
dilated and
failing
diastolic
failure
IW
Opie (1998)
VENTRICULAR VOLUME

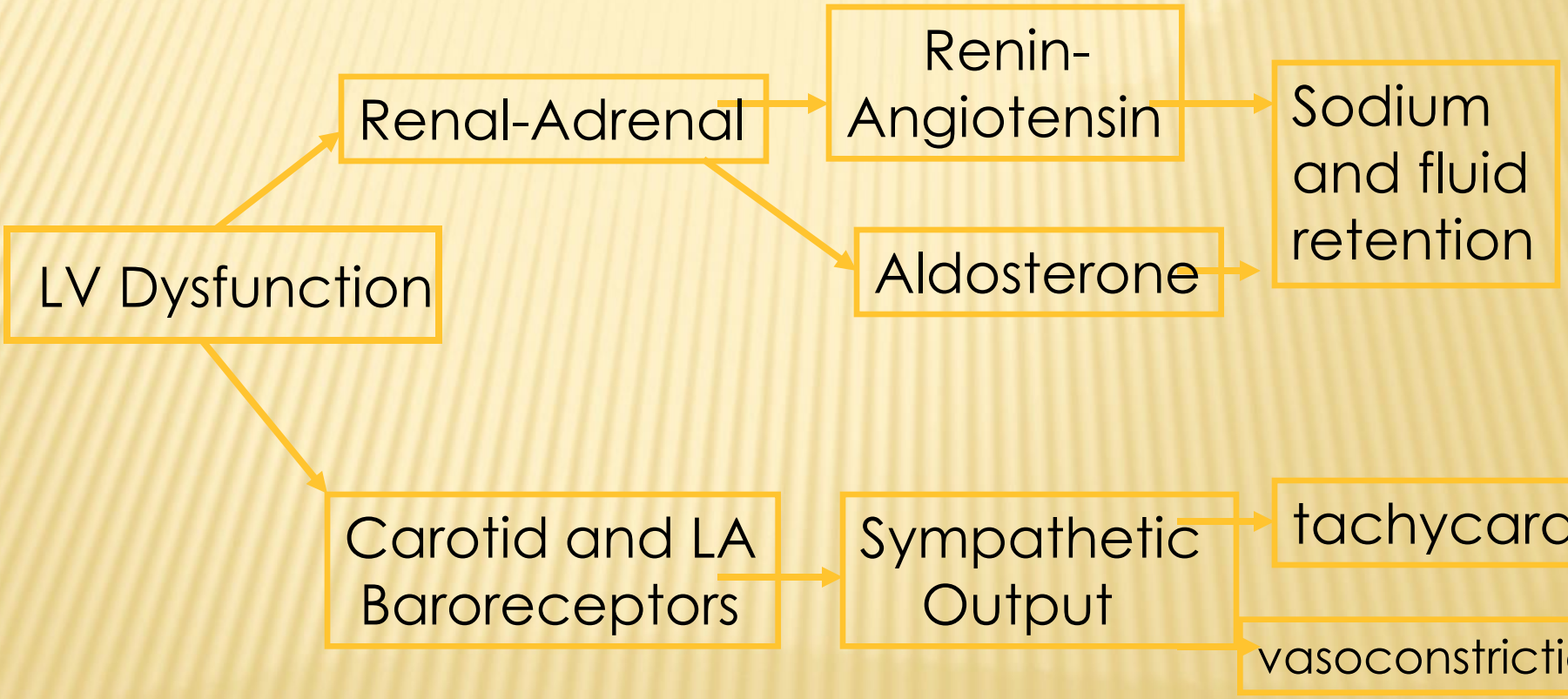
COMPENSATORY MECHANISMS IN HEART FAILURE

- increased preload
- increased sympathetic tone
- increased circulating catecholamines
- increased renin-angiotensin-aldosterone
- increased vasopressin (⇦ CRH)
- increased atrial natriuretic factor

PATHOPHYSIOLOGY OF ACUTE CONGESTIVE HEART FAILURE



PATHOPHYSIOLOGIC RESPONSE TO HEART FAILURE

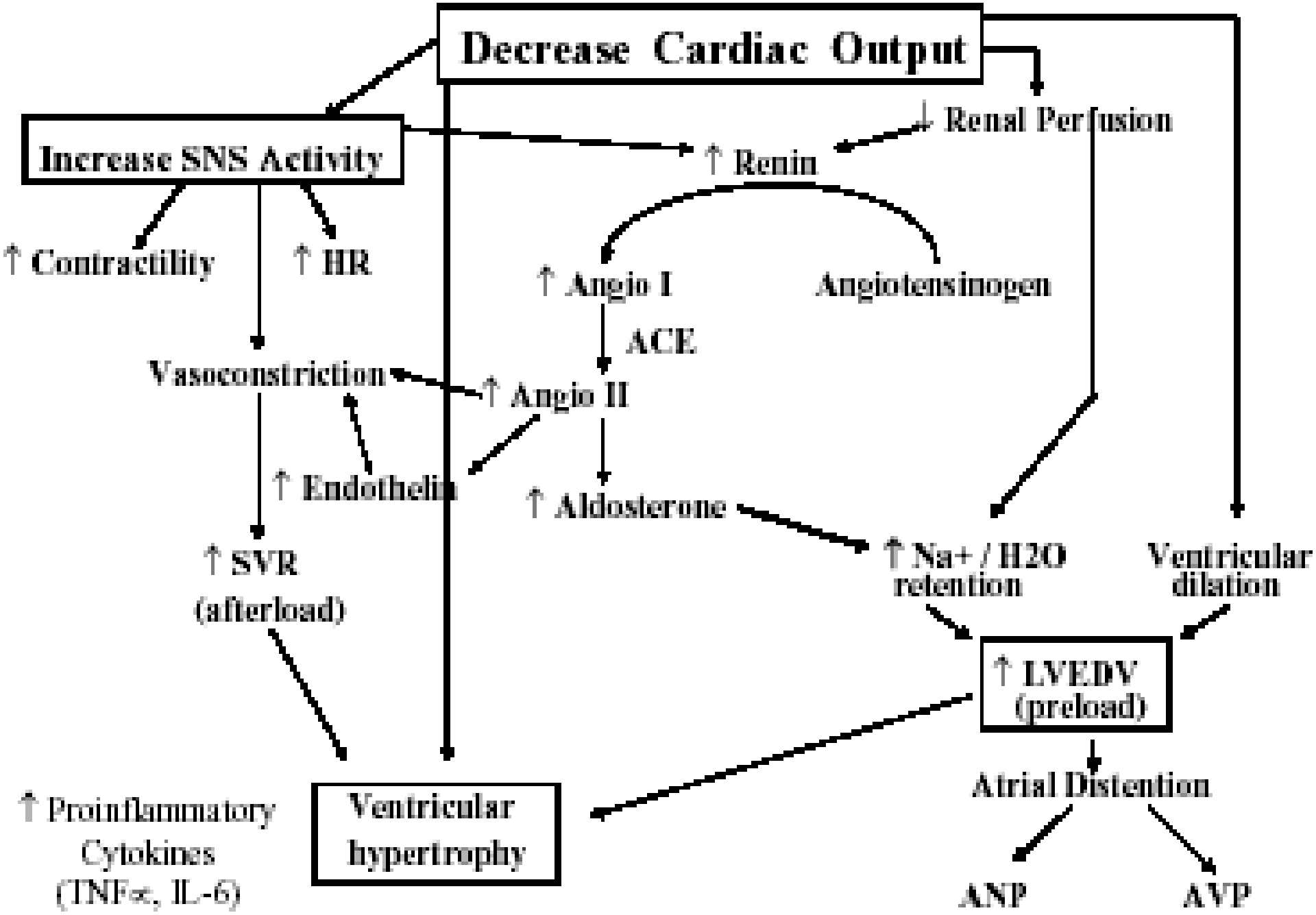


NEUROHUMORAL MECHANISMUS DURING CHF

- Direct toxic effects of Norepinephrine (NE) and AngiotensinII (AII)
  (Arrhythmias, Apoptosis)
- Impaired diastolic filling
- Increased myocardial energy demand
- Increased pre- and after-load
- Platelet aggregation
- Desensitization to catecholamines

NEUROHORMONAL MECHANISM OF CHF

- **Components**
- Endothelin
- Vasopressin (ADH)
- Natriuretic Peptides
- Endothelium-Derived Relaxing Factor
- RAAS
- SNS
- Cytokines


Decrease Cardiac Output
Increase SNS Activity
↓ Renal Perfusion
↑ Renin
↑ Contractility
↑ HR
↑ Angio I
Angiotensinogen
ACE
Vasoconstriction
↑ Angio II
↑ Endothelin
↑ Aldosterone
↑ SVR
(afterload)
↑ Na+ / H2O
retention
Ventricular
dilation
↑ LVEDV
(preload)
↑ Proinflammatory
Cytokines
(TNFα, IL-6)
Ventricular
hypertrophy
Atrial Distention
ANP
AVP

NYHA FUNCTIONAL CLASSIFICATION

- **Class I:** patients with cardiac disease but no limitation of physical activity
- **Class II:** ordinary activity causes fatigue, palpitations, dyspnea or anginal pain
- **Class III:** less than ordinary activity causes fatigue, palpitations, dyspnea or angina
- **Class IV:** symptoms even at rest

STAGES OF HEART FAILURE

- Stage A
  - High risk for development of heart failure
- Stage B
  - Structural heart disease
  - No symptoms of heart failure
- Stage C
  - Symptomatic heart failure
- Stage D
  - End-stage heart failure

Precipitating causes of heart failure

1. ischemia
2. change in diet, drugs or both
3. increased emotional or physical stress
4. cardiac arrhythmias (eg. atrial fib)
5. infection
6. concurrent illness
7. uncontrolled hypertension
8. new high output state (anemia, thyroid)
9. pulmonary embolism
10. mechanical disruption

HEART FAILURE
CLINICAL MANIFESTATIONS

Symptoms

- dyspnea
- fatigue
- exertional limitation
- weight gain
- poor appetite
- cough

Signs

- tachycardia, tachypnea
- edema
- jugular venous distension
- pulmonary rales
- pleural effusion
- hepato/splenomegaly
- ascites
- cardiomegaly
- S3 gallop

CARDIOMYOPATHIES CLASSIFICATION

- Dilated (congestive)
- Hypertrophic
- Restrictive

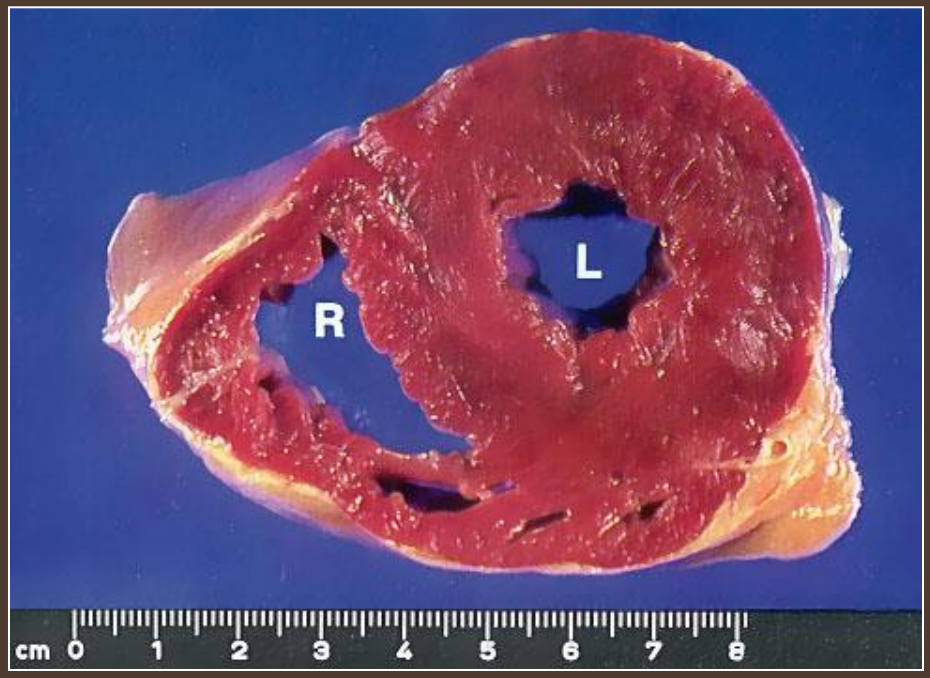
CARDIOMYOPATHIES DILATED (CONGESTIVE)

Ejection fraction-- <40%

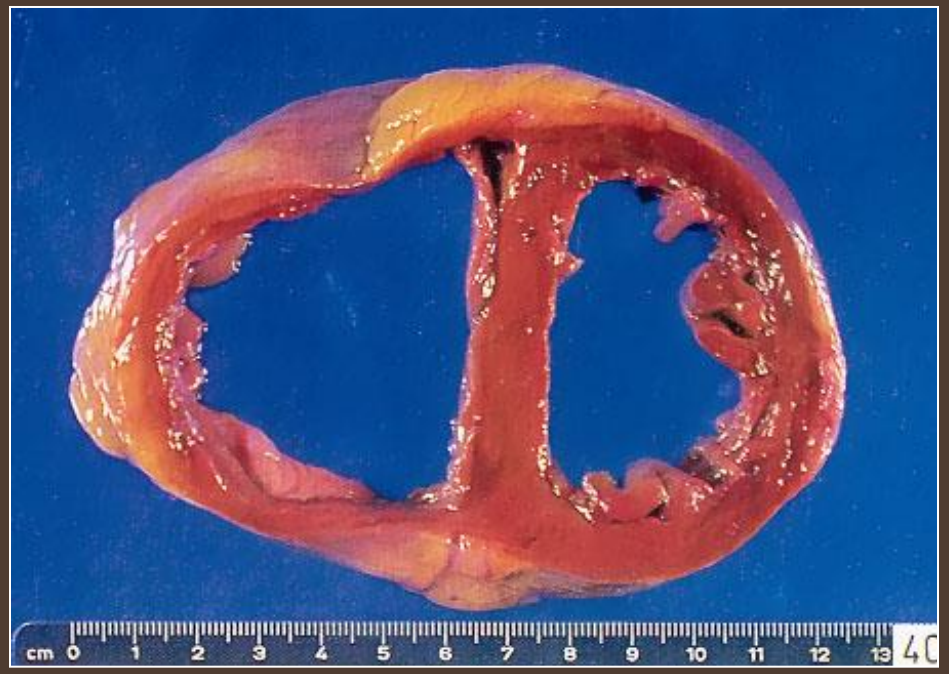
- Mechanism of failure--
  - Impairment of contractility (systolic dysfunction)
- Causes--
  - Idiopathic, alcohol, peripartum, genetic, myocarditis, hemochromatosis, chronic anemia, doxorubicin, sarcoidosis
- Indirect causes (not considered cardiomyopathies)--
  - Ischemic heart disease, valvular disease, congenital heart disease

Cross section of a normal heart, with right and left ventricles (R &L) having normal myocardial thickness and chamber size.

normal thickness LV 1.3-1.5 cm; RV 0.3-0.5 cm



Dilated cardiomyopathy (cross section), with both right and left ventricular chambers showing dilatation. The myocardium appears to be normal or slightly thin in this case.



CARDIOMYOPATHIES HYPERTROPHIC

- Ejection fraction-- 50-80%
- Mechanism of failure-- impairment of compliance (diastolic dysfunction)
- Causes-- Idiopathic, genetic, Friedreich ataxia, storage diseases, DM mother
- Indirect causes– hypertesion heart, aortic stenosis

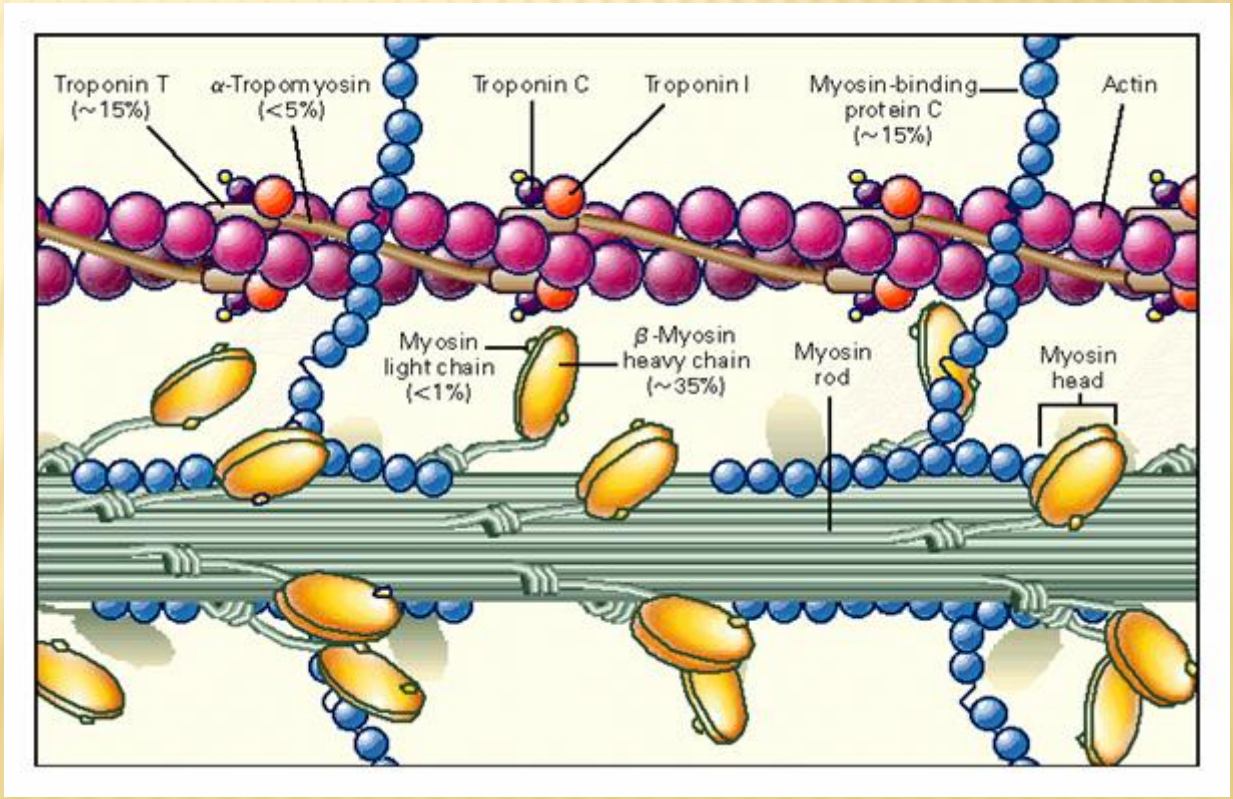
ETIOLOGY

Familial in ~ 55% of cases with autosomal dominant transmission

Mutations in one of 4 genes encoding proteins of cardiac sarcomere account for majority of familial cases

Remainder cases are spontaneous mutations

β-MHC
cardiac troponin T
myosin binding protein C
α-tropomyosin



CARDIOMYOPATHIES RESTRICTIVE

- Ejection fraction-- 45-90%
- Mechanisms of failure-- Impairment of compliance (diastolic dysfuntion)
- Causes-- Idiopathic, amyloidosis, radiation-induced fibrosis
- Indirect causes-- pericardial constriction

RESTRICTIVE (INFILTRATIVE) CARDIOMYOPATHY-ETIOLOGY

- Infiltration of the myocardium with something other than muscle
- Stiff heart that cannot fill or pump well
  (Filling appears to be the main problem)

ETIOLOGIES

TABLE 4. CAUSES OF RESTRICTIVE CARDIOMYOPATHY.

Myocardial

Noninfiltrative disorders
- Idiopathic disease
- Familial disease
- Hypertrophy
- Scleroderma
- Diabetes mellitus
- Pseudoxanthoma elasticum

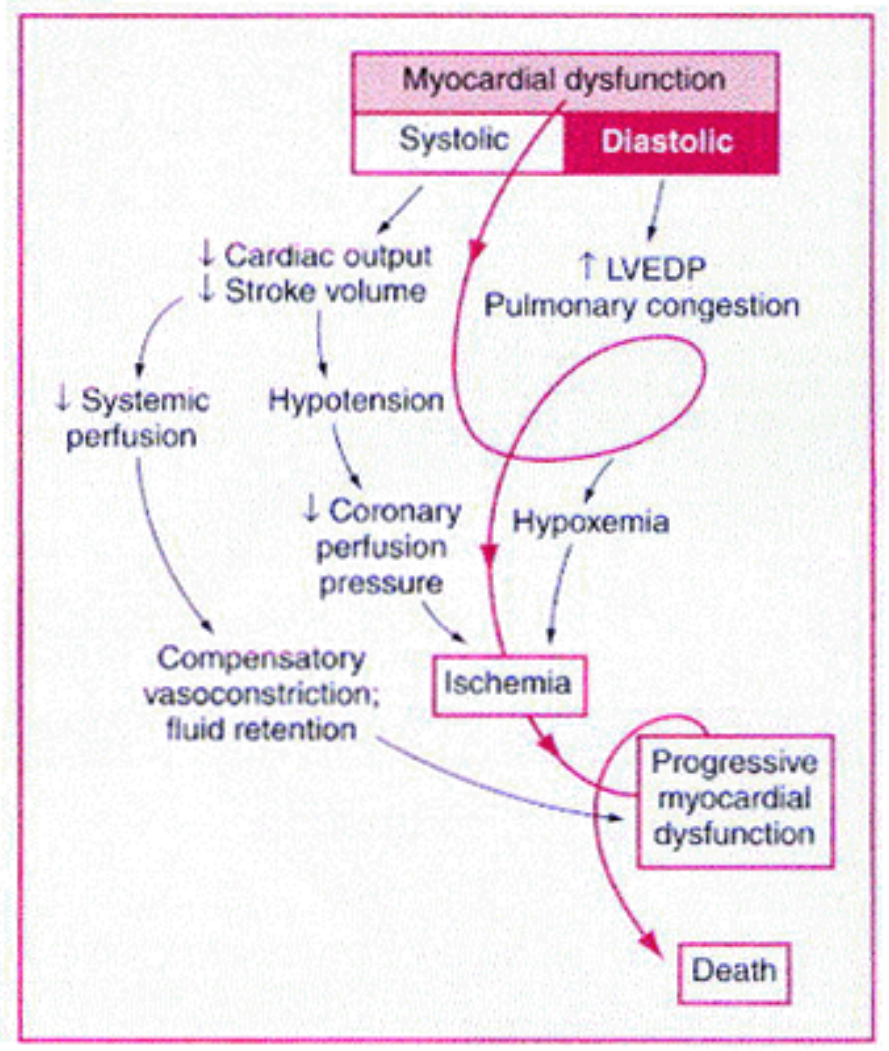
Infiltrative disorders
- Amyloidosis
- Sarcoidosis
- Gaucher's disease
- Hurler's syndrome
- Fatty infiltration

Storage disorders
- Hemochromatosis
- Fabry's disease
- Glycogen storage disease

Endomyocardial

Endomyocardial fibrosis
Hypereosinophilic (Löffler's) syndrome
Carcinoid syndrome
Metastatic cancer
Exposure to radiation
Toxins
Anthracycline (doxorubicin or daunorubicin)
Serotonin
Methysergide
Ergotamine
Mercurial agents
Busulfan

THE VICIOUS CIRCLE IN CARDIOGENIC SHOCK



Ann Intern Med 131:47–59, 1999

DĚKUJI ZA POZORNOST!