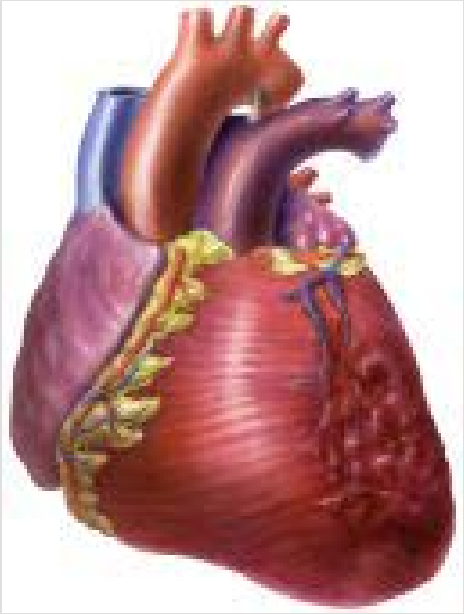
HEART FAILURE



Institute of Pathological Physiology

Martin Vokurka
mvoku@lf1.cuni.cz

WS 2011/12

Case report A

68 year old patient, 10 years of hypertension history, low adherence to the treatment, 5 years ago had acute myocardial infarction

During the last month he complains of growing dyspnea, first exertional but later event at rest and even nocturnal. At acute deterioration he suffered from severe dyspnea, expectoration of watery and foamy fluid.

Case report B

73 year old patient with chronic obstructive pulmonary disease (COPD), heavy smoking from the youth.

In several last weeks he observes intensive lower limb edemas, worsening during the day, improving at night. Mild pain in the right hypochondrium.

Case report A and B

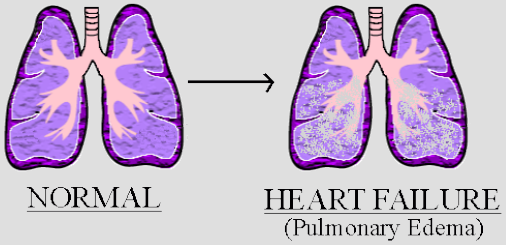
Both patients have edema (fluid and blood congestion).
A – in the lungs
B – at the lower limbs, in the liver…

- **The heart (ventricle) is not capable to pump blood from one circulation to the other – basic hemodynamics**
- **Fluid retention and edemas develop**
- **The organs suffer from inadequate blood supply**
- **Changes of other organs and in the whole organism**

normal situation

heart failure

congestion backward



Case report A and B

The symptoms of BACKWARD failure with the congestion prior to the failing ventricle have been described

A – left ventricle
B – right ventricle

normal situation

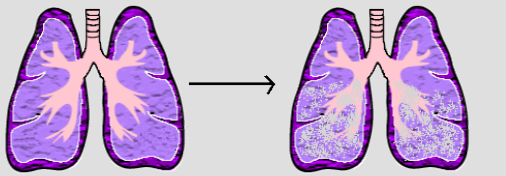
heart failure

congestion
backward

decreased cardiac output

forward

Insufficient organ perfusion
– muscles, kidneys, skin, GIT…



NORMAL

HEART FAILURE
(Pulmonary Edema)

MAIN SYMPTOMES

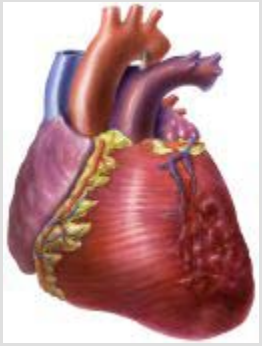
1. *CONGESTION*

- left-sided - DYSPNEA, LUNG EDEMA

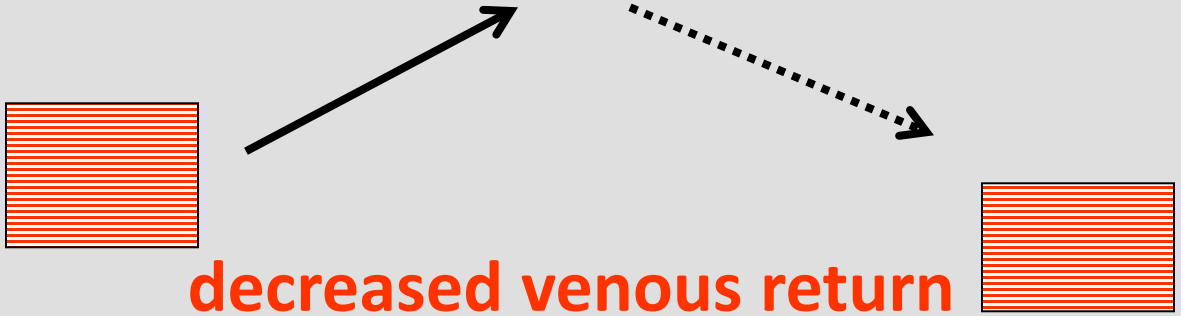
- right-sided - LOWER EXTREMITY EDEMAS, HEPATOMEGALY…

2. *DECREASED CARDIAC OUTPUT*

WEAKNESS, FATIGUE,
DECREASED ORGAN PERFUSION



heart insufficiently filled



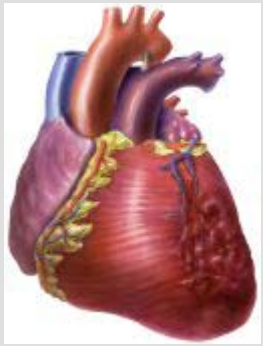
decreased venous return

e.g. shock

decreased cardiac output

bad filling of the ventricles

(e.g. constrictive pericarditis)



heart changes

heart failure

congestion

decreased cardiac output

compensatory events

Frequency of heart failure

In the Czech Rep. the prevalence is about 1-2 %
(i.e. 100 000 of patients)

The number of patients is increasing – among others due to successful treatment of other heart diseases

TYPES OF HEART FAILURE

- LEFT-SIDED

- RIGHT-SIDED

- BOTH-SIDED

according to the failing ventricle

Causes of heart failure

Myocardial failure

- defect in myocardial contraction (ischemia, cardiomyopathy)
- loss of myocardium (myocardial infarction)

Excessive, long-term hemodynamic burden

- increased *pressure* burden (systemic or lung hypertension)
- increased *volume* burden (valvular abnormalities)
- hyperkinetic cirkulation (increased CO)

Most commonly it is the combination of ***CHD and arterial hypertension***

The most frequent causes of LV failure are the combination of

CHD + arterial hypertension

Case report A

68 year old patient, 10 years of hypertension history, low adherence to the treatment, 5 years ago had acute myocardial infarction

During the last month he complains of growing dyspnea, first exertional but later event at rest and even nocturnal. At acute deterioration he suffered from severe dyspnea, expectoration of watery and foamy fluid.

Case report B

73 year old patient with chronic obstructive pulmonary disease (COPD), heavy smoking from the youth.

In several last weeks he observes intensive lower limb edemas, worsening during the day, improving at night. Mild pain in the right hypochondrium.

Case reports A and B

A – left-sided failure: hypertension (pressure damage to LV), myocardial infarction (ischemic damage of the myocardium, loss of the contractility)

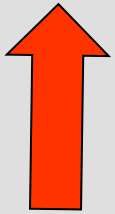
B – right ventricle (pulmonary hypertension due to the lung disease)

Cardiac output

- **volume of the blood pumped by the heart in 1 minute**

In heart failure CO decreases

Activation of compensatory mechanisms trying to increase CO back to normal values



How are the distinct mechanism influencing the CO regulated ?

Cardiac output (CO) =

heart rate (HR) × stroke volume (SV)

70 /min **70 ml**

4 900 ml/min

Heart rate

- vegetative nerves
- (disturbances in) heart rhythm

- has impact of heart cycle duration, mainly shortens diastole – when the heart is filling with blood

Increases CO but high rates decrease the ventricle filling and heart is easier exhausted

Cardiac output (CO) =

heart rate (HR) × stroke volume (SV)

70 /min **70 ml**

4 900 ml/min

Stroke volume

- preload
- contractility
- afterload

* How is the heart filled before the systole
* What is its „force“ of contraction
* What is resistance against the pumping

Preload

is the basic mechanism of the regulation of CO

Preload

filling of the heart at the end of the diastole
enddiastolic volume = EDV
Frank-Starling mechanisms

Volume in the ventricle corresponds to the pressure – ***enddiastolic pressure***, EDP, ***filling pressure***

Factors influencing preload

- ***Venous return***

total blood volume

blood distribution (position of the body, intrathoracic pressure, venous tonus…)

- ***atrial systole***
- ***size of ventricle cavity***
- ***intrapericardial pressure***

Low preload is the cause of the decreased CO in case of syncope and shock

In heart failure the preload is not decreased but it is ***increased*** as one of the the compensatory mechanisms

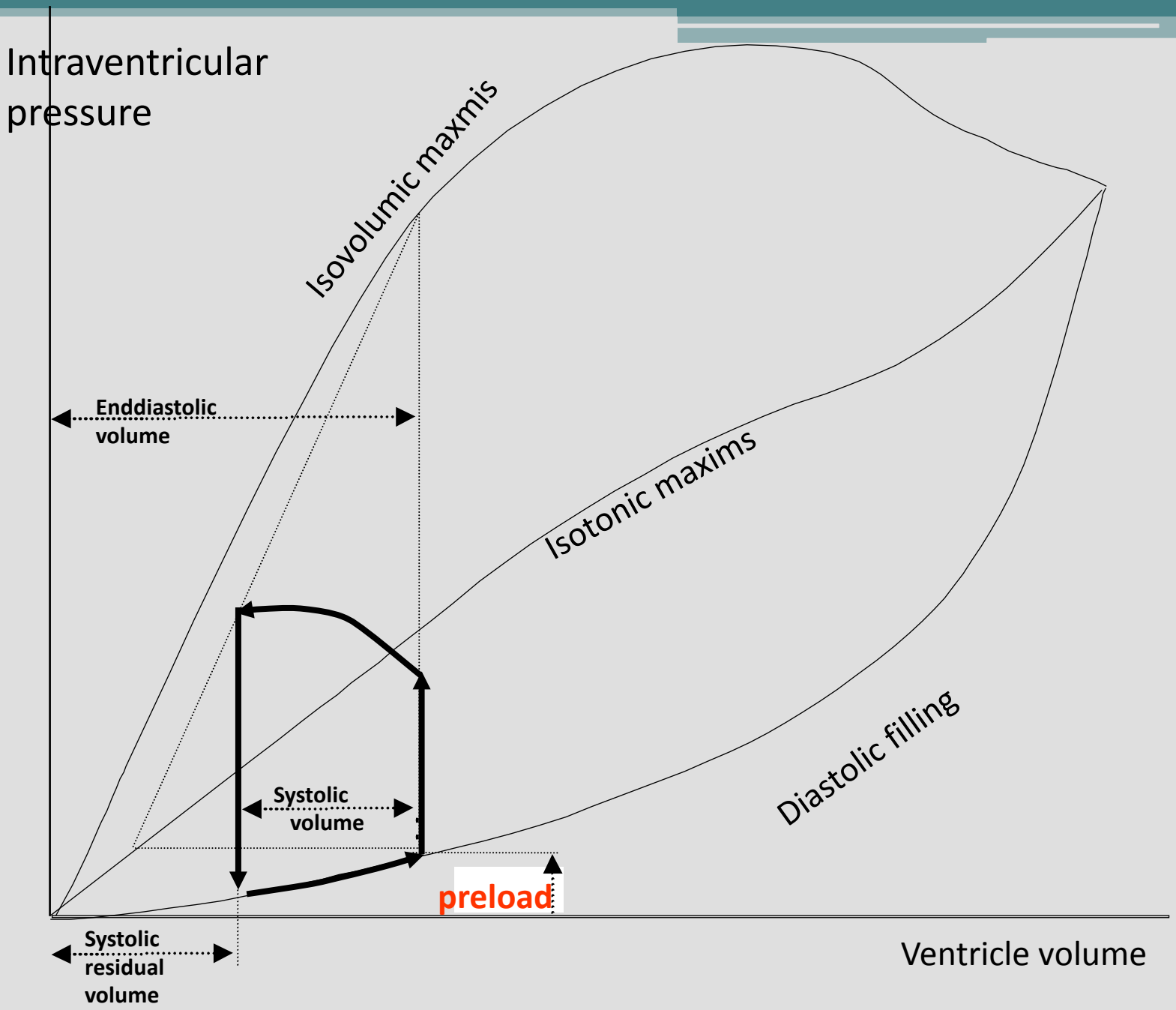
Low preload

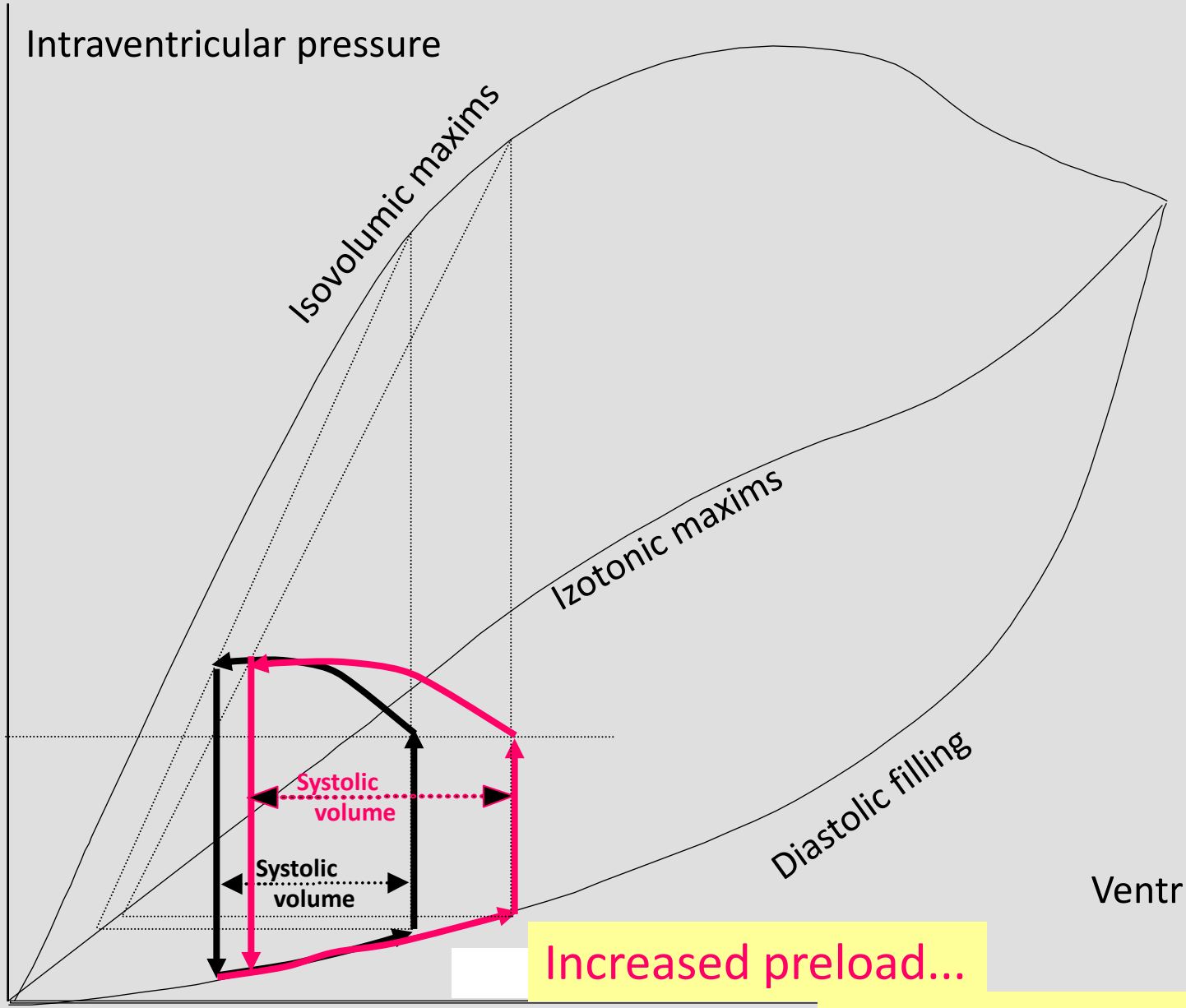
- bleeding, strong vasodilation etc.
- shock, synkope
- THIS IS NOT HEART FAILURE

Failing heart

uses the increase of preload

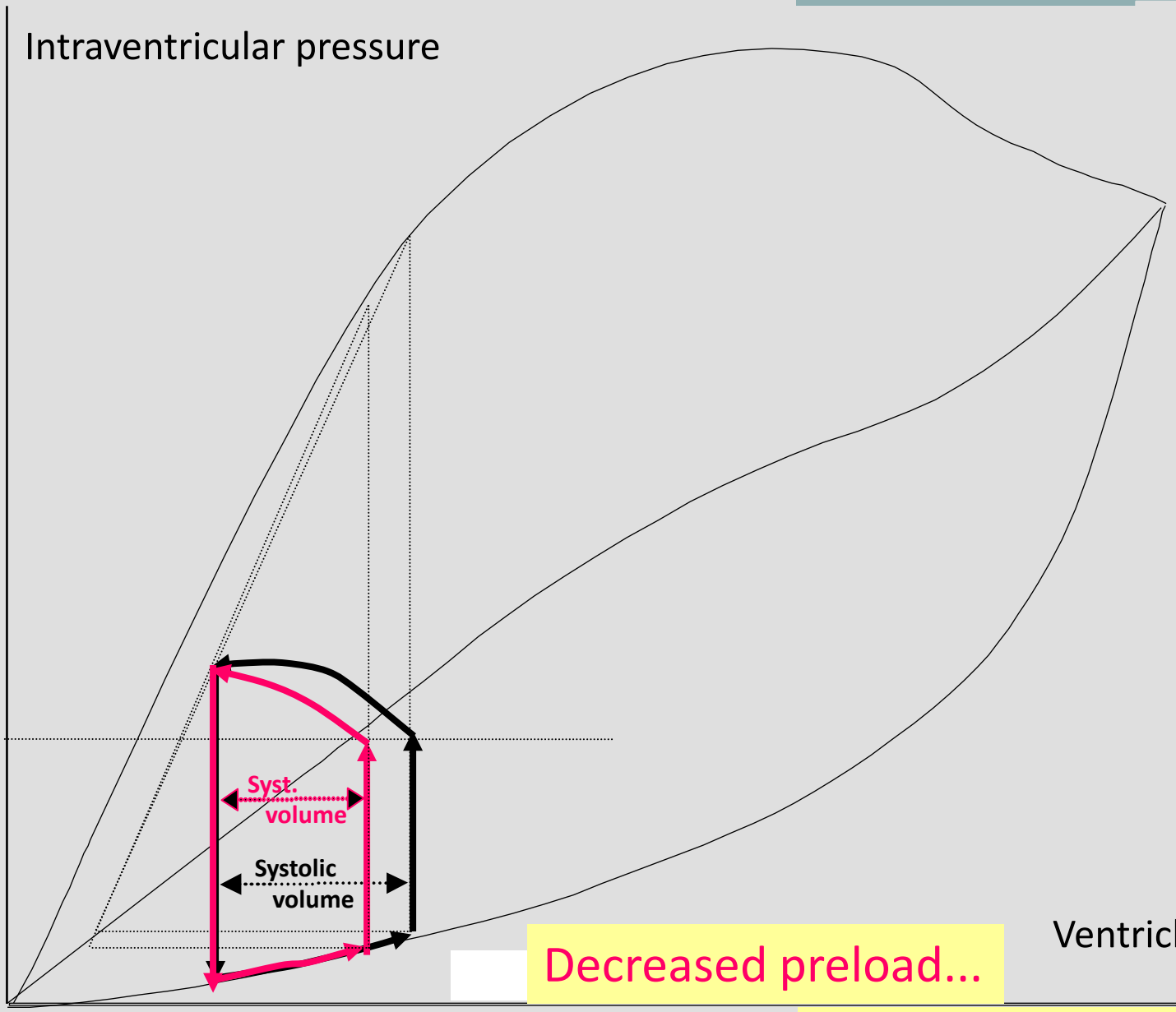
to improve SV and CO


Intraventricular pressure
Isovolumic maxmis
Isotonic maxims
Diastolic filling
Enddiastolic volume
Systolic volume
preload
Systolic residual volume
Ventricle volume



Increased preload...

...increases cardiac output.



Decreased preload...

...decreases cardiac output.

The relation between the filling of the ventricle and the intraventricular pressure

diastolic filling curve

volume: EDV - enddiastolic volume
pressure: EDP - enddiastolic pressure, filling pressure

- amount of the blood in the ventricle
- properties of the ventricle wall

Stroke volume

- preload
- contractility
- afterload

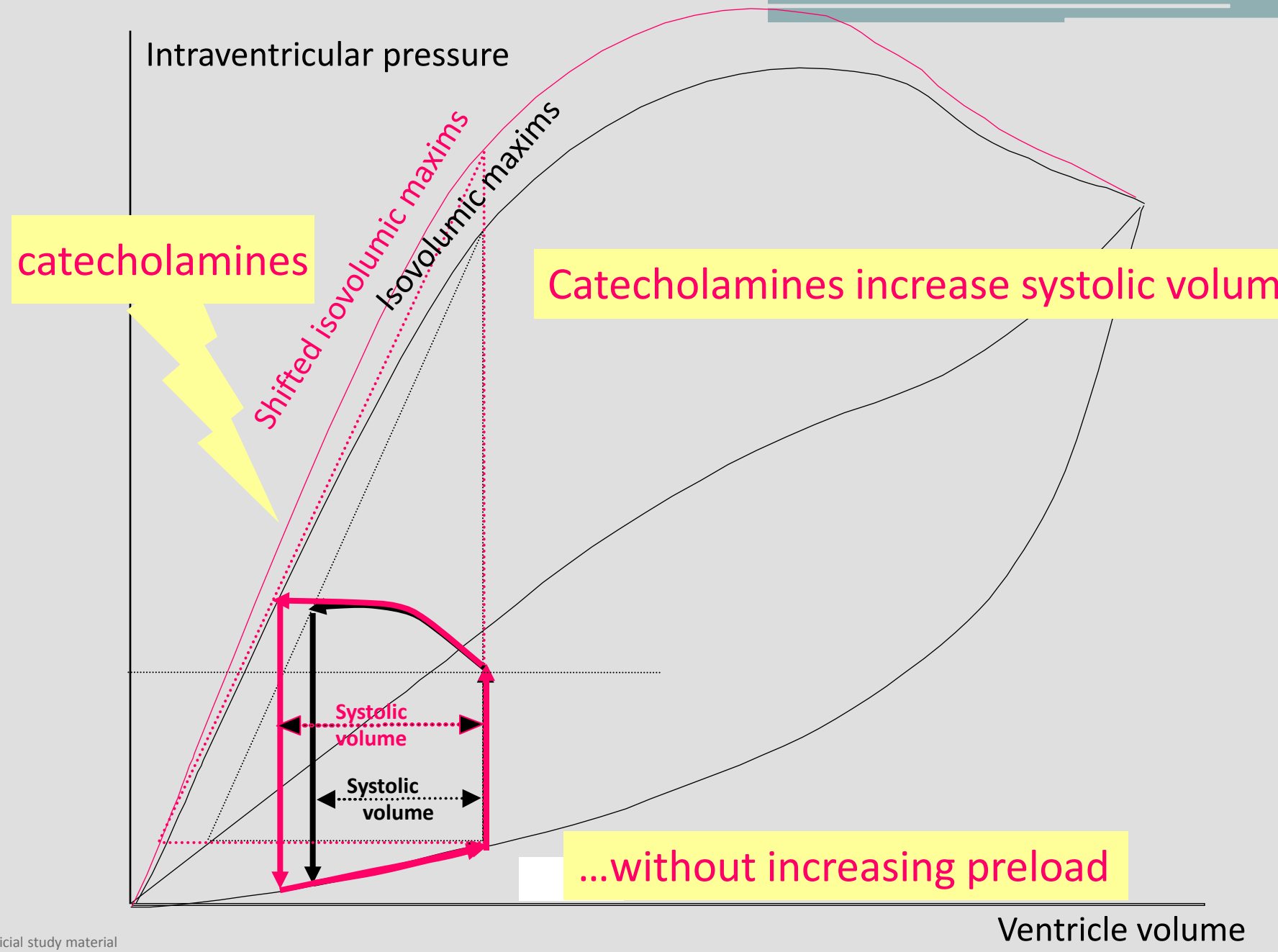
* How is the heart filled before the systole
* What is its „force“ of contraction
* What is resistance against the pumping

Contractility

- **„force“ of the contraction in constant filling (preload, i.e. independent of preload)**

Under physiological conditions the heart

uses the increased contractility to increase SV and CO


Intraventricular pressure
Shifted isovolumic maxims
Isovolumic maxims
catecholamines
Catecholamines increase systolic volume
Systolic volume
Systolic volume
…without increasing preload
Ventricle volume

The decrease of contractility is a frequent cause of heart failure

Contractility

Increase:
sympatic nerves, catecholamines

Decreased
ischemia,
hypoxia,
acidosis,
proinflammatory cytokines,
some drugs etc.

Decreased contractility is often the causative mechanism of heart failure.

Stroke volume

- preload
- contractility
- afterload

* How is the heart filled before the systole
* What is its „force“ of contraction
* What is resistance against the pumping

Afterload

the force against which it contracts, the tension
or stress developed in the ventricular wall during ejection

- arterial pressure
- systemic vascular resistence
- blood viskosity

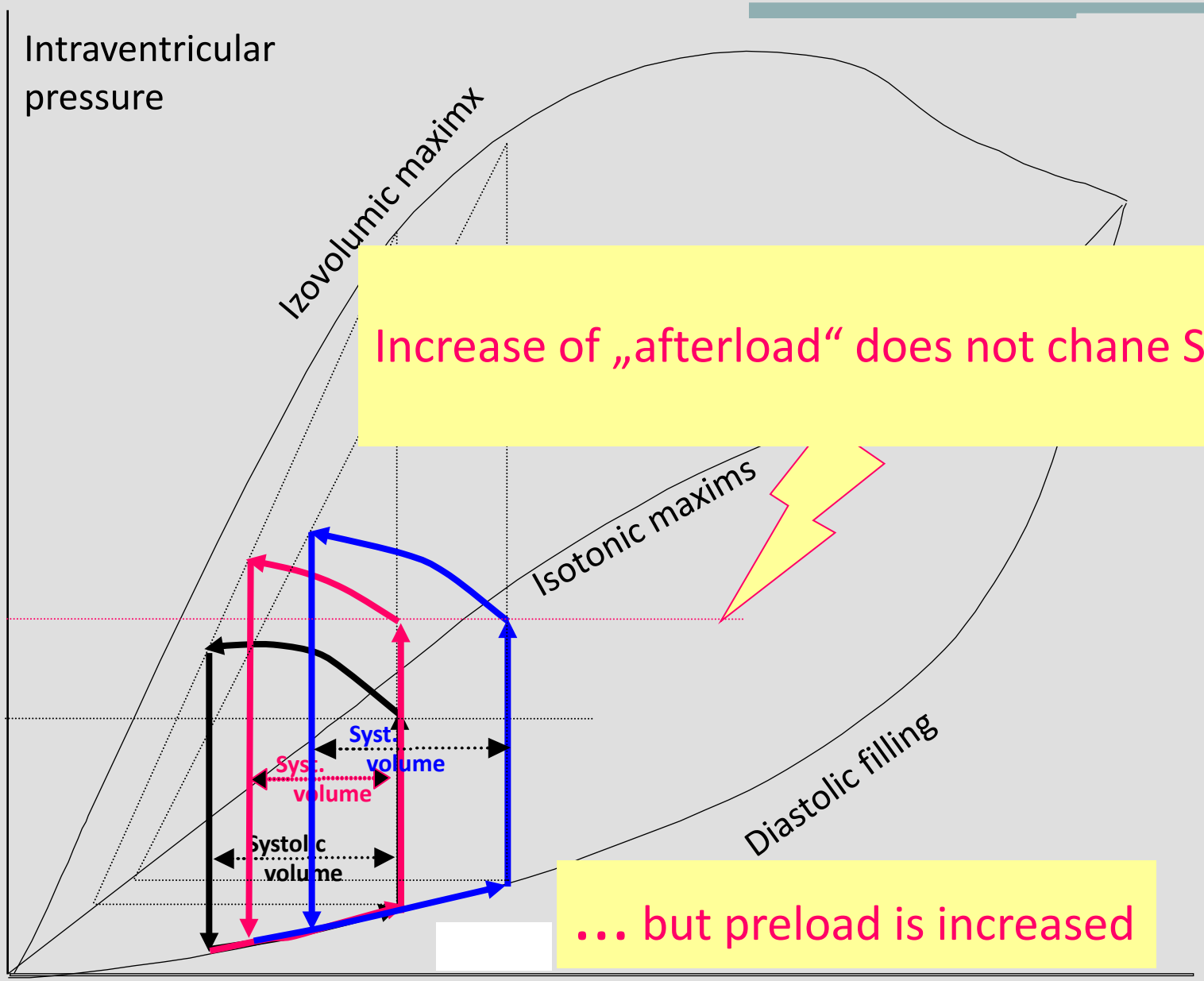
- geometry of the ventricle (***Laplace*** law)

$T = P \times r / d$

Increased volume of the ventricle and thiner wall (i.e. dilatation)
increase afterload
contribute to the decrease of CO
increase requirements for oxygen

Afterload

- arterial pressure
- systemic vascular resistence
- blood viscosity



Increase of „afterload“ does not chane SV

… but preload is increased

Case report A

Why is dyspnea present at night ??

In the supine position the venous return the failing heart increases and thus it accumulates in the lungs.

HEART FAILURE

pathophysiologic state in which an abnormality of *cardiac* function is responsible for the failure of the heart to pump blood at a rate commensurate with the requirements of the metabolizing tissues

decrease of cardiac output

***and/or* can do so only from an abnormally elevated diastolic volume**

increase of the ventricular filling pressure (enddiastolic pressure, EDP)

Types of heart failure

According to the ventricle

- left-sided

- right-sided (cor pulmonale due to lung diseases, lung embolism etc.)

- both-sided

Acc. to the intensity

According to the course

- acute

- chronic (development of the compensatory mechanisms):

compensated

decompensated

According to the CO

- low-output (most)

- high-output (hyperkinetic cirkulation)

Pumping disorders of the heart

Systolic failure (dysfunction)

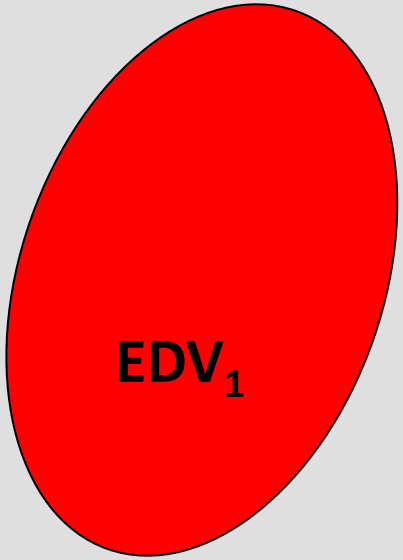
The blood ejection from the ventricle is impaired due to the decrease of the contractility

Ejection fraction

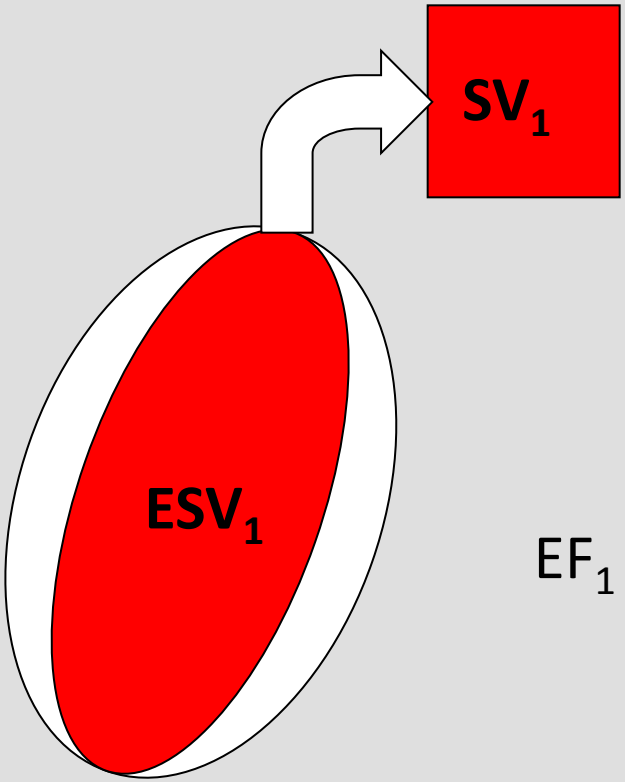
EF = SV / EDV

the ratio of stroke volume to end-diastolic volume
normal value = 67 ± 8 percent

SV = 70 ml, EDV = 120 ml
EF = 70 / 120 = 58 %



End of diastole 1



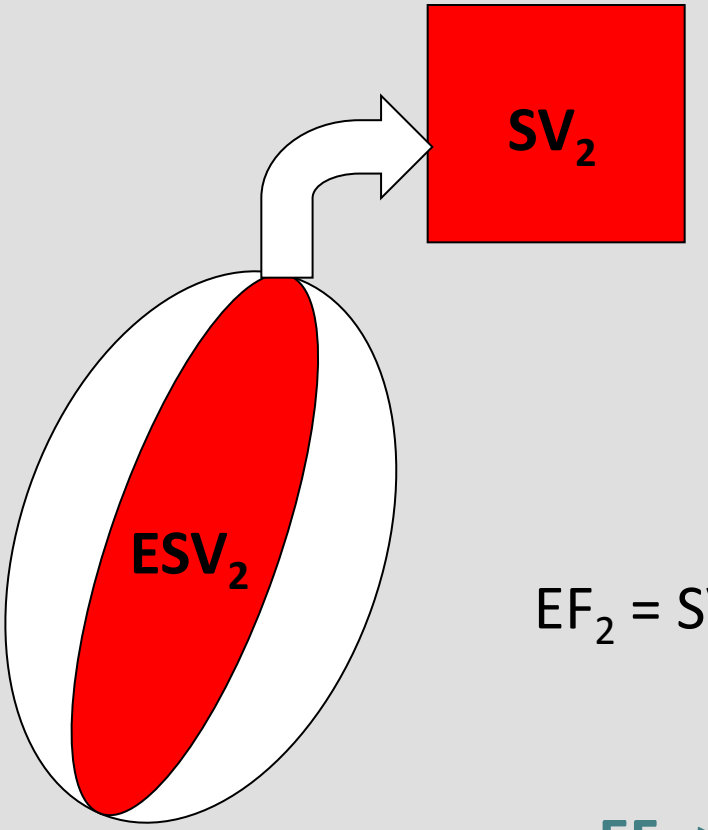
$EF_1 = SV_1/EDV_1$

End of systole 1

Normal heart stimulated by the sympatic nerves
- EF increases, SV increases (contractility increased)

Heart with noncompensated systolic failure
- EF low, SV low

Heart with compensated systolic failure and increased preload
- EF low, SV might be normal (EDV is increased)



$EF_2 = SV_2/EDV_2$

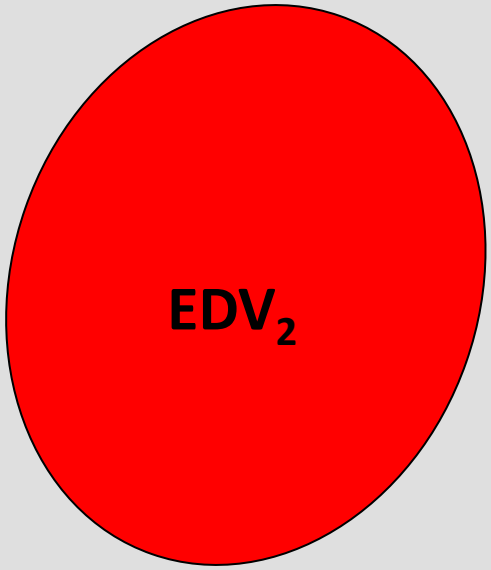
$EF_2 > EF_1$

End of systole 2

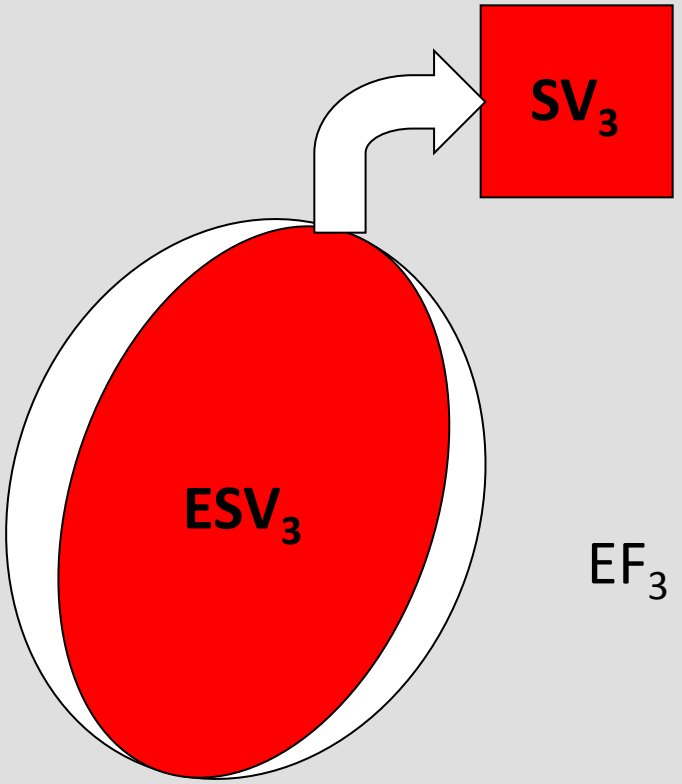
Normal heart stimulated by the sympatic nerves
- EF increases, SV increases (contractility increased)

Heart with noncompensated systolic failure
- EF low, SV low

Heart with compensated systolic failure and increased preload
- EF low, SV might be normal (EDV is increased)

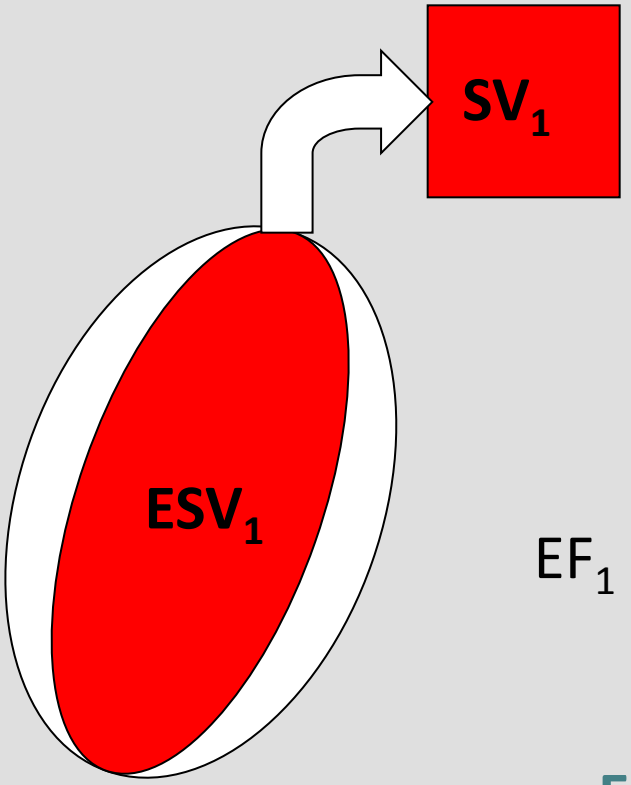


End of diastole 2



$EF_3 = SV_3/EDV_3$

End of systole 3



$EF_1 = SV_1/EDV_1$

$EF_1 > EF_3$

$SV_1 = SV_3$

End of systole 1

Case report A

The patient has decreaed contractility:
ischemia, part of the myocardium was replaced by fibrous tissue (scar) after the myocardial infarction;

Hypertension increases afterload

Case report A

The patient due to the decreased contractility has decreased EF < 35 %

The symptoms of systolic failure

Diastolic failure

The ventricle filling during the diastole is accompanied by increased pressure

usually the decrease in the relaxation and later compliance of heart wall

EDP increases

- CHD
- Hypertension with hypertrophy
- Some cardiomyopathies etc.

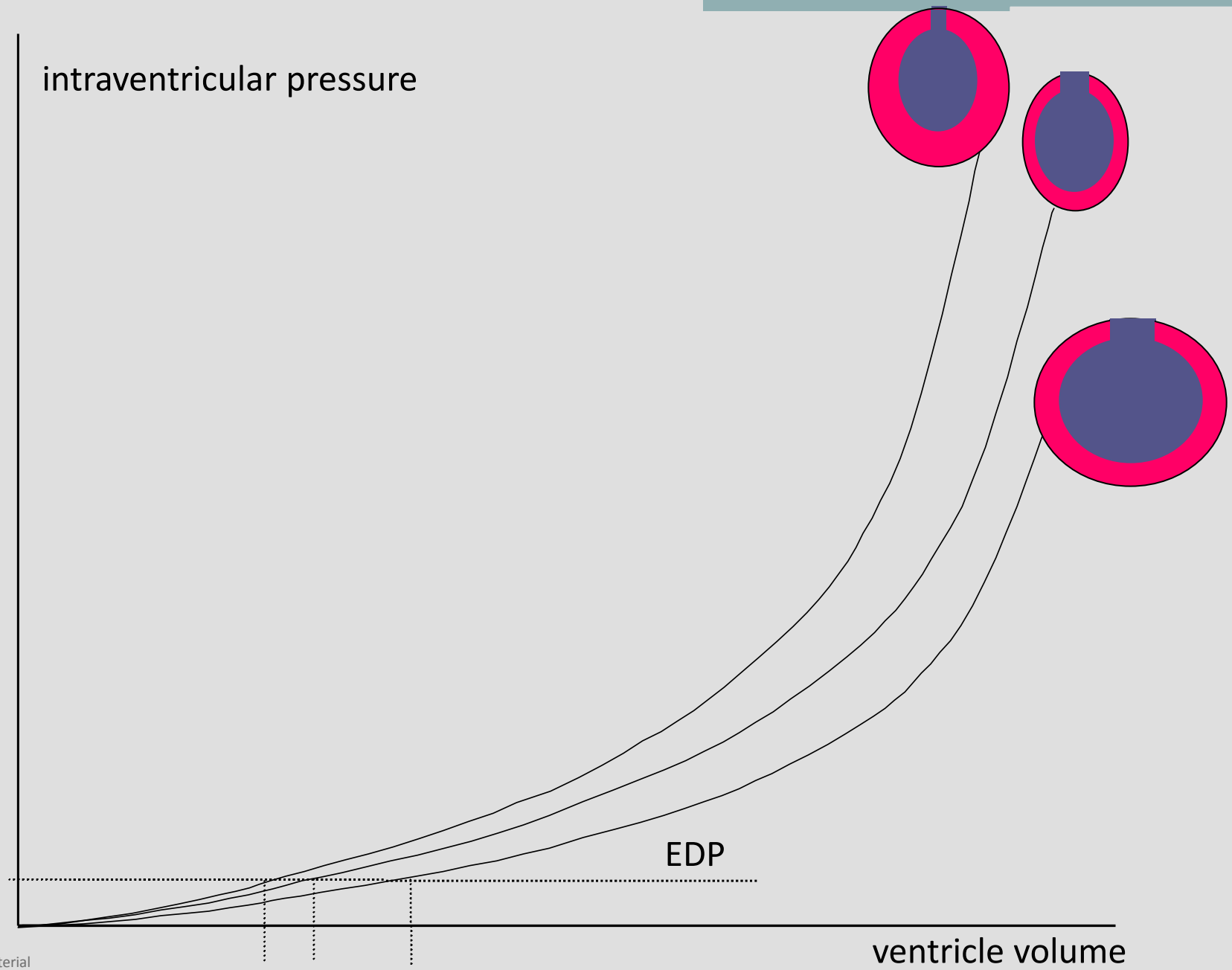
- mainly the congestion symptoms

The relation between the filling of the ventricle and the intraventricular pressure

diastolic filling curve

volume: EDV - enddiastolic volume
pressure: EDP - enddiastolic pressure, filling pressure

- amount of the blood in the ventricle
- properties of the ventricle wall


intraventricular pressure
EDP
ventricle volume

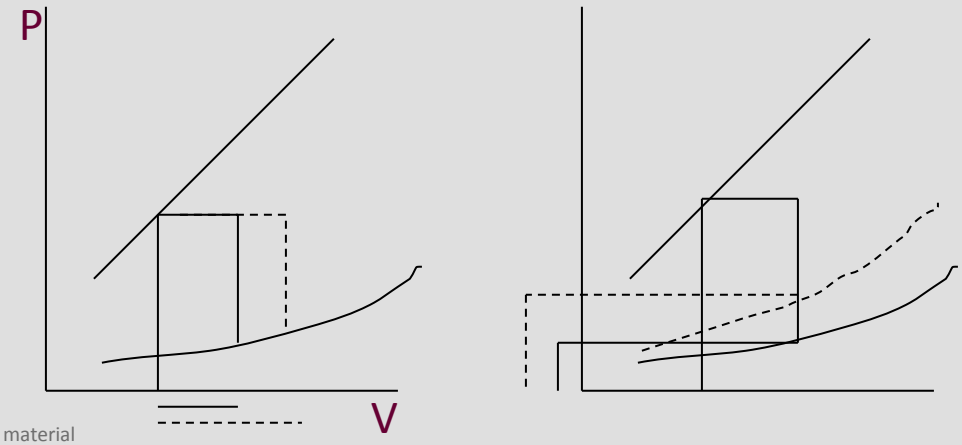
⇧ **preload** → ⇧ enddiastolic volume (EDV) → ⇧ enddiastolic pressure (EDP)

enddiastolic volume (EDV) → changes in the ventricle geometry → dilatation
increased wall tension
increased oxygen consumption
failure of Frank-Starling mech.

enddiastolic pressure (EDP) → pressure "transfer" to the regions „precceding the heart"

ventricle wall properties
(compliance)
ischemia - impaired relaxation
fibrosis
hypertrophy/dilatation

pressure "transfer" to the regions „precceding the heart" → L - lung edema
P - e.g. hepatomegaly



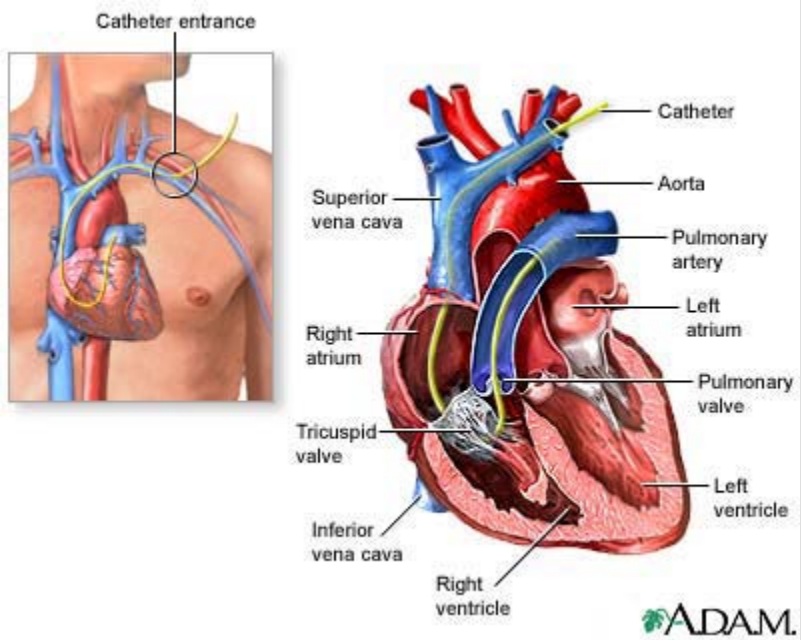
Case report A

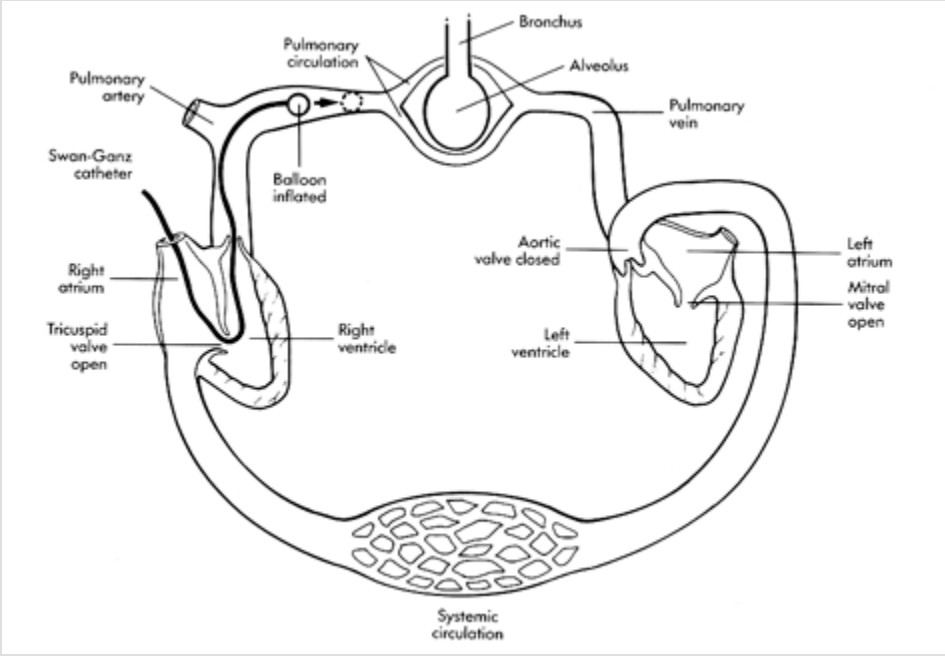
The patient has due to the hypertrophy (caused by systemic hypertension) of the LV decreased compliance, i.e. the increase of EDP is higher for the EDV

He has also the symptoms of diastolic failure

EDP measurement

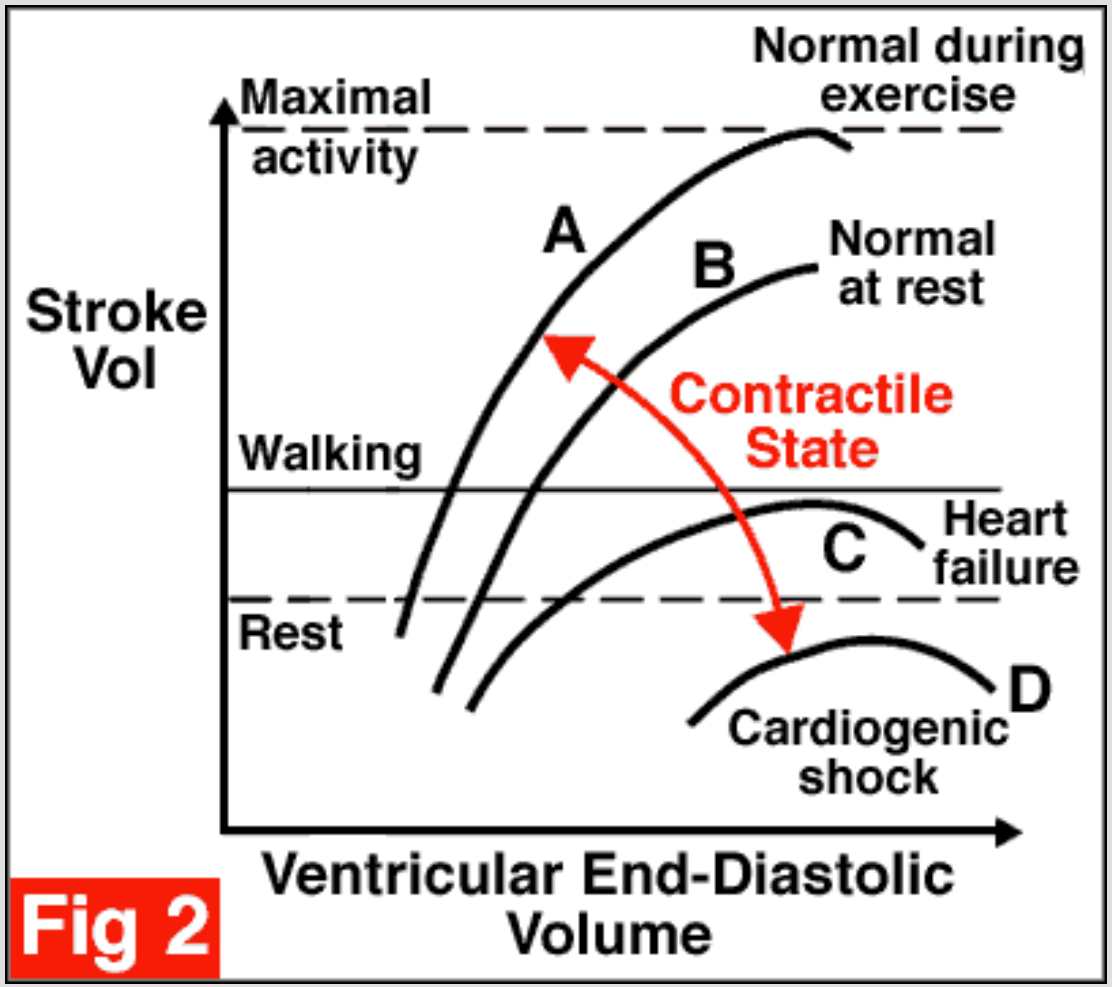
heart catheterization as a pulmonary wedge pressure





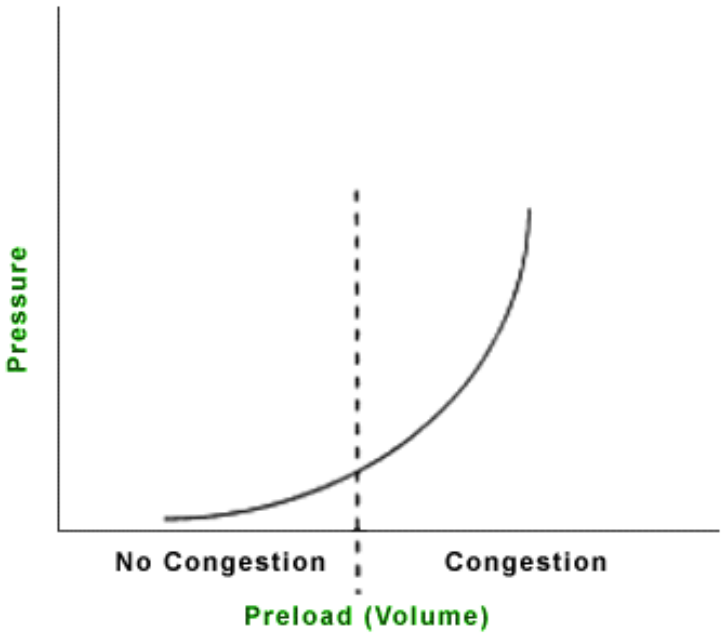
The relation of EDV and stroke volume (Starling curve)

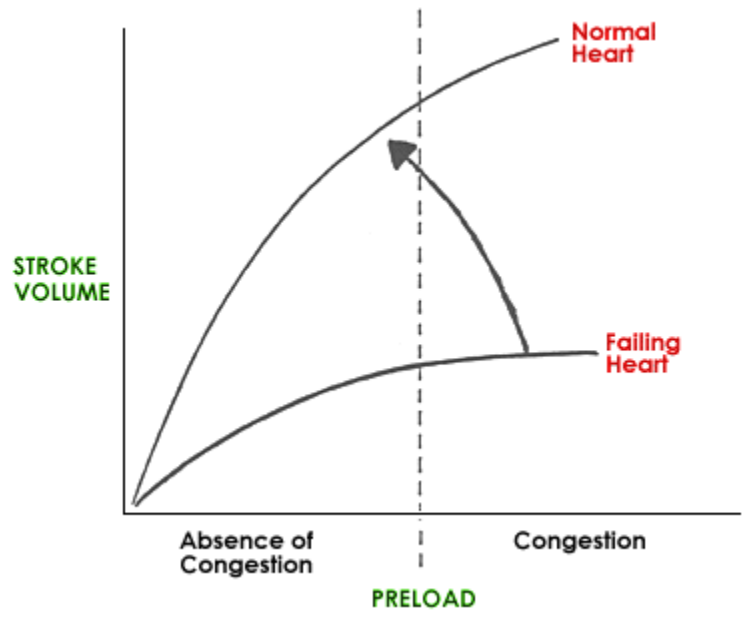
TO (SV)



EDP

The relation of EDP and congestion





Evaluation / monitoring of hemodynamic heart function

- **EF** (ultrasound)

- **cardiac output** (ultrasound or catheterization)

- **EDP** (catheterization)

- **Heart rate (HR)**
- **Blood pressure (BP)**

HEART FAILURE

pathophysiologic state in which an abnormality of *cardiac* function is responsible for the failure of the heart to pump blood at a rate commensurate with the requirements of the metabolizing tissues

and/or can do so only from an abnormally elevated diastolic volume

decrease of cardiac output

increase of the ventricular filling pressure (enddiastolic pressure, EDP)

General symptoms of cardiac failure from the hemodynamic point of view

Low CO

Weakness, fatigue, decreased perfusion of the organs incl. the kidneys, muscles

- ***redistribution of CO***

FORWARD

Accumulation of blood/fluid prior to the failing ventricle

Congestion, edemas

BACKWARD

- The heart (ventricle) is not capable to pump blood from one circulation to the other – basic hemodynamics
- Fluid retention and edemas develop
- The organs suffer from inadequate blood supply
- Changes of other organs and in the whole organism

Systemic changes in heart failure

Heart failure is not only failing of the heart as a pump, but it is ***systemic disorder*** with activation of hormonal processes, with changed metabolism, changed regulation of water-mineral balance, with cytokines involved, heart changes, changes of gene expression etc.

HEMODYNAMIC ASPECTS
NEUROHUMORAL ASPECTS
CELLULAR AND GENE EXPECT

Compensatory mechanisms

short-term action: can be positive (evolutionary are made to be active in acute situation, heart failure is somehow modern disease)

long-term action: have negative effects to further deterioration of heart failure

Prof. MUDr. J. Kvasnička, CSc.
Interní klinika KNP Pardubice, LFUK Hradec Králové

Chronic heart failure. What is it?

- **Heart failure is a pathophysiological error of the organism**:
- To the change of hemodynamic parameters which are under physiological conditions corrected by **short-term** activation of ***sympathetic nerves*** and ***renin-angiotensin-aldosteron*** system [RAAS] the organism reacts by ther **long-term and inadequate** activation**.**

- **Their long-term activation has devastating effects on the organims**.

Katz AM, In discussion, Am J Cardiol 1988;62:82A

konference Důkazy a praxe, 2005

Main compensatory mechanisms in heart failure

They lead to incrase (maintain) CO

1. Sympathetic activity
2. Increase of preload
3. Salt and water retention
4. Myocardium changes

Short-term effective, long-term have deletirious effects themselves and contribute to the symptoms and progression of HF

Vitious circle

Case report

Why these patients have tachycardia?

Sympathetic activity in heart failure

↑ Heart rate
↑ Contractility → ↑ CO
↑ Venous return

Negative consequences

Tachycardia:

Increase in oxygen consumption

shortening of the diastole (impairment of diastolic filling and myocardial blood flow)

Increased risk for arrhytmias

Norepinephrine cardiotoxicity (increase of calcium in myocardium)

Periphery vasoconstriction

increase of afterload

CO/blood flow redistribution

Metabolic action

hyperlipidemia, hyperglycemia

During the heart failure the β receptors in myocardium are down-regulated

Activation of sympathetic nerves improves CO only in short-term but is damaging and exhausting the heart

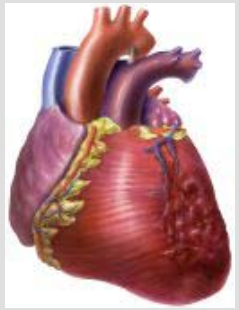
Low doses of betablockers are nowadays used to treat and improve the moderately severe heart failure.

Extremely activated sympatic activity is in SHOCK

Case report

Why do the patients have edemas?

Why patient A urinates often during the night?



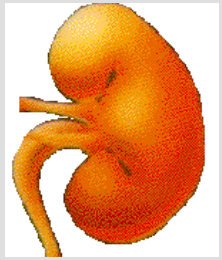
⇩ **cardiac output** - decrease in effective plasmatic volume

⇩ tissue perfusion

⇧ ADH

sympaticus

⇩ glomerular filtration



⇧ renin

⇧ angiotensin II

periphery vasoconstriction

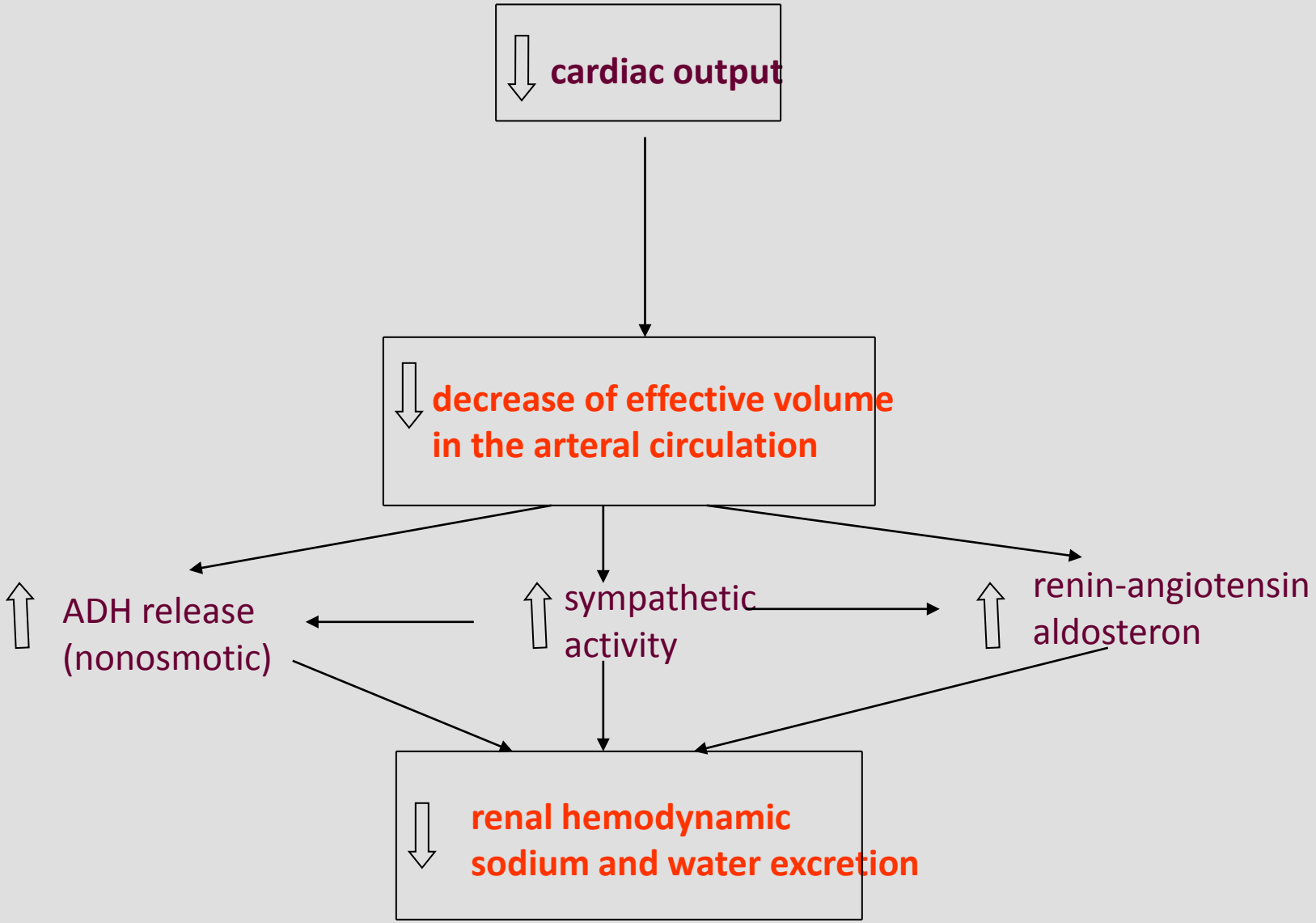
⇧ BP

⇧ afterload

⇧ aldosterone
sec. hyperaldosteronisms

ECT expansion

⇧ preload


cardiac output
decrease of effective volume
in the arteral circulation
ADH release
(nonosmotic)
sympathetic
activity
renin-angiotensin
aldosteron
renal hemodynamic
sodium and water excretion

Water retention and edema in heart failure are cause by the activation of **renin-angiotensin-aldosteron**

Water and salt retention

increase in preload

Negative consequences:

- heart dilatation

- congestion, edemas

- changes in water/mineral equilibrium, sodium retention and potassium depletion – contributes to electrical nestability of the myocardium

Blocking of the RAAS is at present the main treatment of heart failure

-inhibitors of angiotensin converting enzyme (ACE inhibitors)

- angiotensin II receptor antagonists

- aldosterone antagonists

Neurohumoral adjustments

influence vasoconstriction, fluid retention, myocardium
- angiotensin II
- aldosterone
- natriuretic peptids
- norepinephrin
- ADH
- endotelin

- prostaglandins keeping the renal perfusion

Heart changes

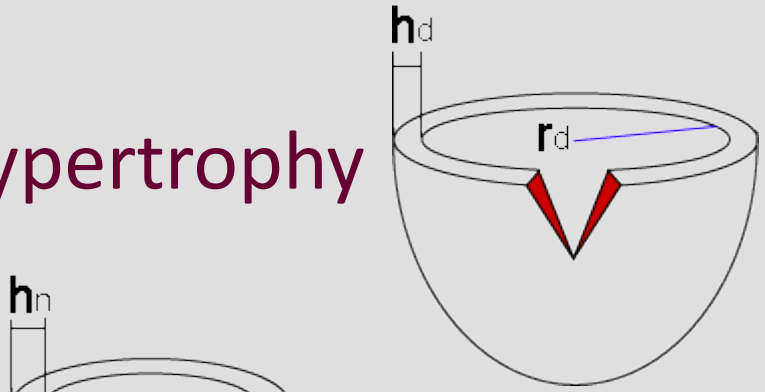
Reaction to ***biomechanical*** stress (tension in the wall)
and to ***neurohumoral*** stimuli

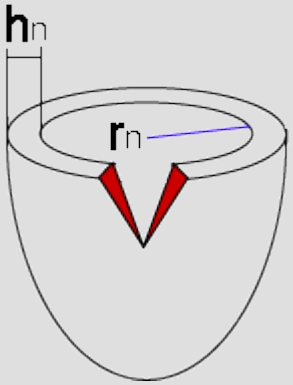
REMODELATION

important for further outcome of heart failure

* Dilatation

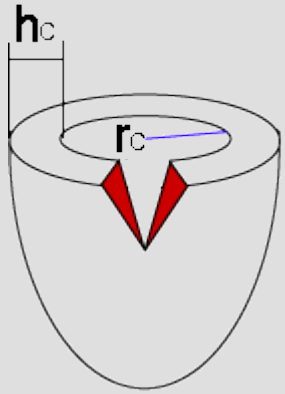
primary du to volume burden
thin wall – increased tension in the wall
(higher *r*, lower *h*)
secondary from previous hypertrophy
(excentric hypertrophy)





* Hypertrophy

concentric in hypertension
excentric secund. in increased volume burden and increased preload



Consequences of heart changes

- increased ***wall tension*** in dilatation - increase in afterload and oxygen consumption

- ***impaired oxygen delivery*** in hypertrophy

- ***decrease of compliance*** - diastolic failure

- ***overstretched dilatation*** impairs contraction and leads to relative valvular insuficiency

- ***arrhytmias***

- ***prognostic*** factor

Heart changes – cellular level

- dysregulated myogenesis (abnormal, „embryonal “ growth)

- apoptosis

Further worsening of heart function

Molecular and cellular changes

Angiotensin II
endotelin
IGF-I
growth factors
cytokins
IL-6
cardiotropin 1 etc.

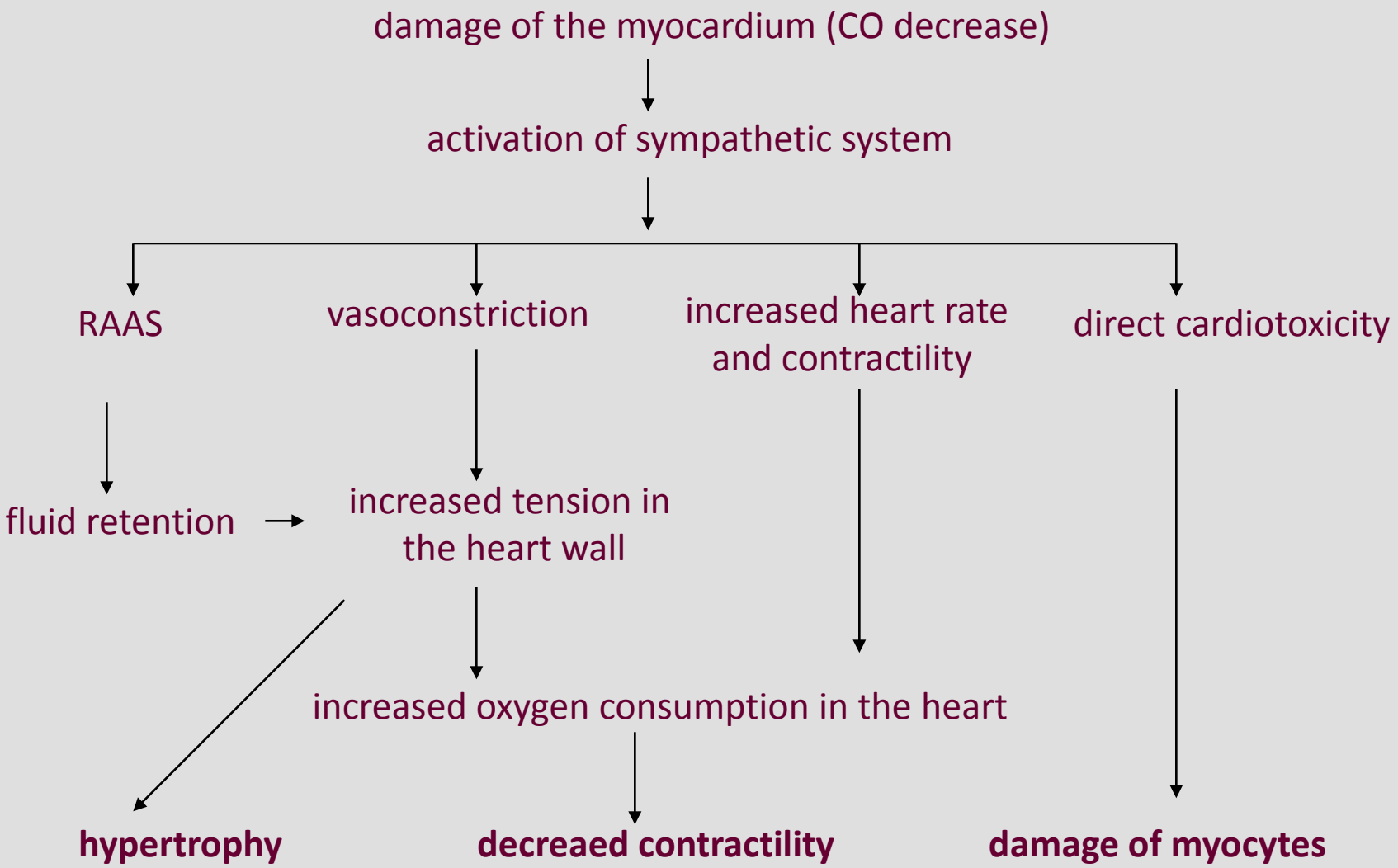
Distension leads to gene expression, e.g. of the genes for natriuretic peptides and fetal genes

Cytokines in heart function / heart failure

Action:
negative inotropic
proapoptotic
fibroplastic
arrhytmogenic etc.

Mainly proinflammatory cytokines: TNFα, IL-1, IL-6

Originate in systemic inflammatory reaction (inflammation, tumor)
locally in heart failure as a response to hemodynamic changes


damage of the myocardium (CO decrease)
activation of sympathetic system
RAAS
vasoconstriction
increased heart rate and contractility
direct cardiotoxicity
fluid retention
increased tension in the heart wall
increased oxygen consumption in the heart
hypertrophy
decreaed contractility
damage of myocytes

Overview of clinical symptoms

Symptoms of heart failure from the hemodynamic point of view

Low CO

Weakness, fatigue, decreased organ perfusion
incl. kidneys, muscles - ***redistribution of CO***
FORWARD

Blood congestion in organs from which blood is collected to the failing ventricle

Edemas etc.
BACKWARD

Right-sided failure

BACKWARD

decreased ejection from RV

⇑ EDV, EDP in RV

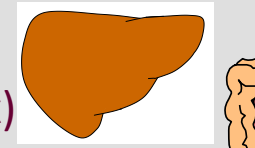
⇑ pressure in R atrium

⇑ volume and pressure in large veins

⇑ capillary pressure

edemas, transsudation (ascites, hydrothorax)

⇑ volume in distensible organs (hepatosplenomegaly)



FORWARD

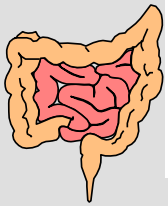
decreased flow from RV to the lungs

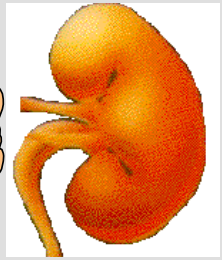
decreased flow to the left atrium

⇓ cardiac output

fluid retention

symptomes of decreased CO





Left-sided failure

BACKWARD

decreased ejection from LV

⇑ EDV, EDP in LV

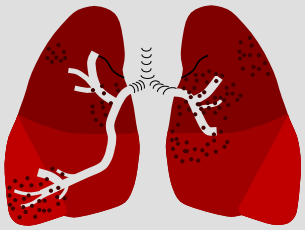
⇑ pressure in L atrium

⇑ volume and pressure in pulmonary veins

⇑ capillary pressure

⇑ fluid volume in the lung
fluid transsudation to the alveoli

pulmonary edema, dyspnea



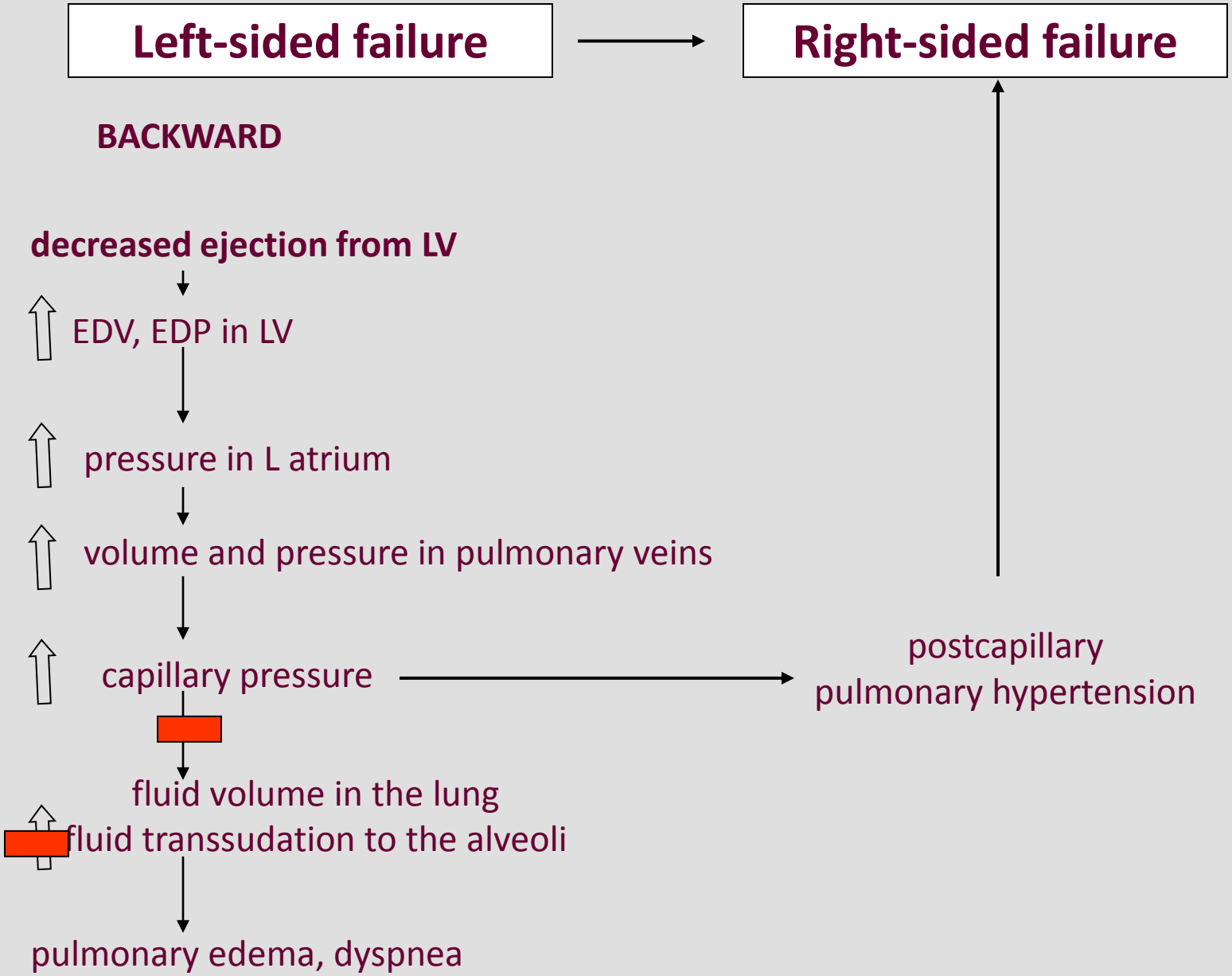
FORWARD

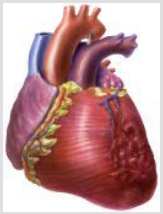
decreased ejection from LV → ⇓ cardiac output

⇓ kidney perfusion → fluid retention

⇓ tissue perfusion → symptomes of decreased CO

fatigue, weakness
pale skin
impairment of organ functions


Left-sided failure
Right-sided failure
BACKWARD
decreased ejection from LV
EDV, EDP in LV
pressure in L atrium
volume and pressure in pulmonary veins
capillary pressure
postcapillary
pulmonary hypertension
fluid volume in the lung
fluid transsudation to the alveoli
pulmonary edema, dyspnea



left-sided failure

increase of filling pressure + fluid retention

pulmonary edema

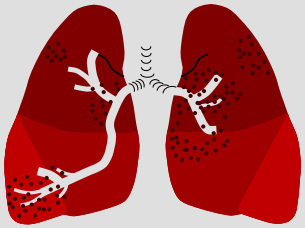
hypoxemia

dyspnea

myocardial hypoxia

increase burden for respiratory muscles

impairment of myocardial contractility



Heart failure classification

NYHA -New York Heart Association: according to the dyspnea

- Class I: patients with no limitation of activities; they suffer no symptoms from ordinary activities.
- Class II: patients with slight, mild limitation of activity; they are comfortable with rest or with mild exertion.
- Class III: patients with marked limitation of activity; they are comfortable only at rest.
- Class IV: patients who should be at complete rest, confined to bed or chair; any physical activity brings on discomfort and symptoms occur at rest.

Principles of the treatment

- action against the negative effects of compensatory mechanism
  betablockers
  inhibitors of RAAS
- increase of the contractility – digitalis (only in some cases)
- reduction of cardiac work load
- control of excessive fluid retention - diuretics
- vasodilator therapy - improves (decreases) afterload
- perspective: natriuretic peptids, anticytokine treatment, antiendothelins…
- mechanical support
- transplantation

Conclusions I

- Hemodynamics: decrease of CO and congestion
- CO decrease: weakness, fatigue, cold skin, even deterioration of consciousness in worst cases. Decrease of kidney perfusion!
- Preload increase: high enddiastolic pressure and congestion –
  in the lungs or in the systemic circulation

Conclusions II

- Failing heart works with low contractility, high enddiastolic pressure
- Systolic failure means low contractility, low ejection fraction
- Diastolic failure means low compliance komory, increase of enddiastolic

Conclusions III

- HF is a systemic disease with changes in the heart but also other organs with strong neuroendocrine response and activation
- Compensatory mechanisms have short-term effect, later they contribute to the deterioration of the disease
- Important is mainly activation of sympathetic systém and RAAS. The modern treatment acts against them.

The End