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CARDIAC MECHANICS

HEART AS A PUMP

CARDIAC CYCLE

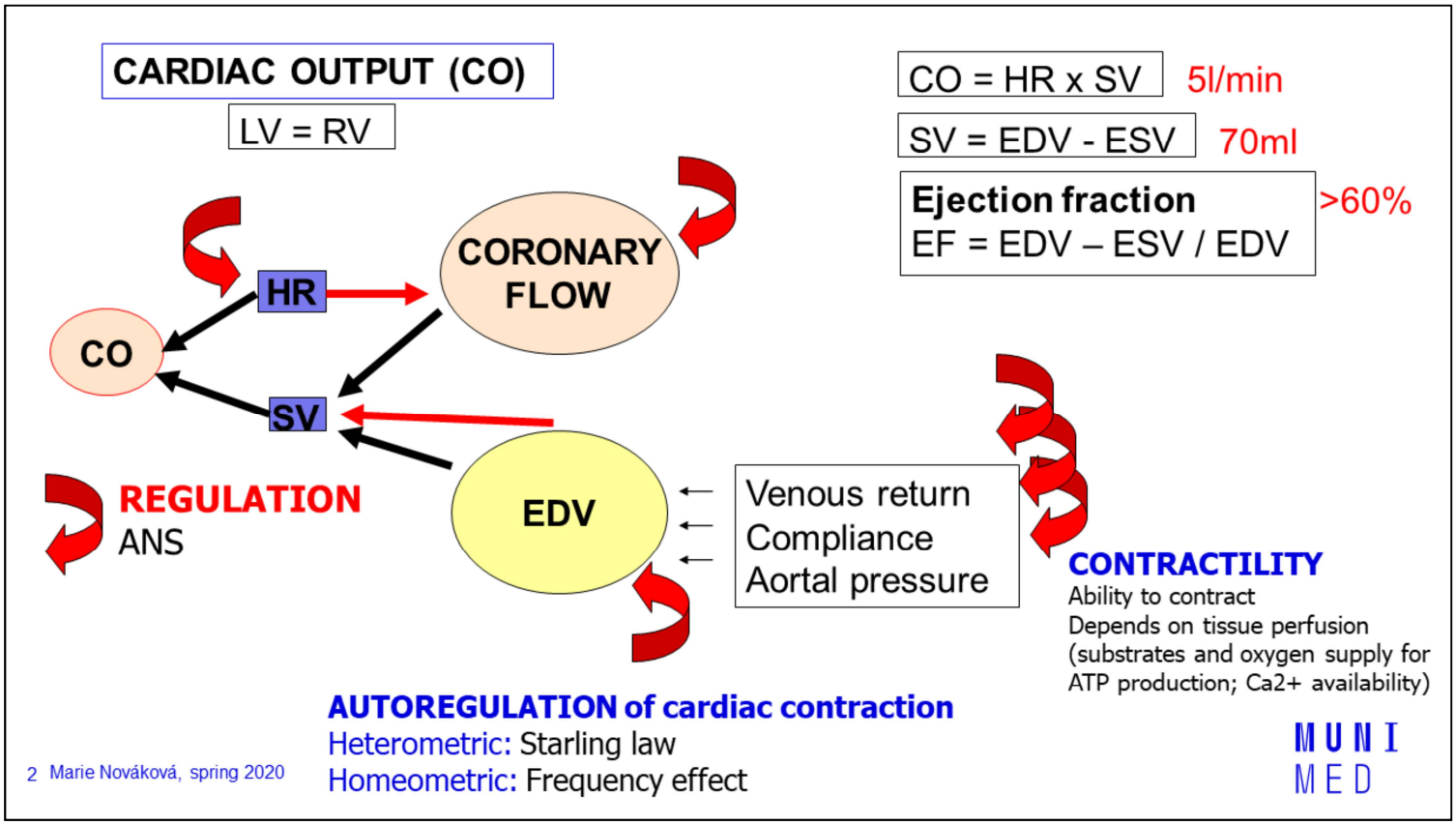
HEART FAILURE

1 Marie Nováková, spring 2020

First, repeat your knowledge about:

- Excitable membranes, ionic channels, ATP-ases
- Regulation of calcium transport mechanisms
- Electrical features of cardiomyocyte
- Conductive system of the heart
- Spread of excitation through myocardium
- Excitation-contraction coupling

- Boron: chapter 22, pp. 507-532



The main role of the heart is pumping of blood into the circulation. Minor functions are endocrine (natriuretic factors) and homeostatic (thermoregulation).

Heart is pressure-volume pump, consisting of two haemodynamically independent units – right and left – connected in series. Each of these units consists of atrium and Coordinated contraction of working myocardial cells ensures pumping of blood from corresponding heart chamber.

Pump can be characterised by its power, e.g. how big volume is pumped during period of time. In case of the heart it is approx. 5 litres of blood per minute. This parameter is called **cardiac output**.

Important terms and relationships – see slide:

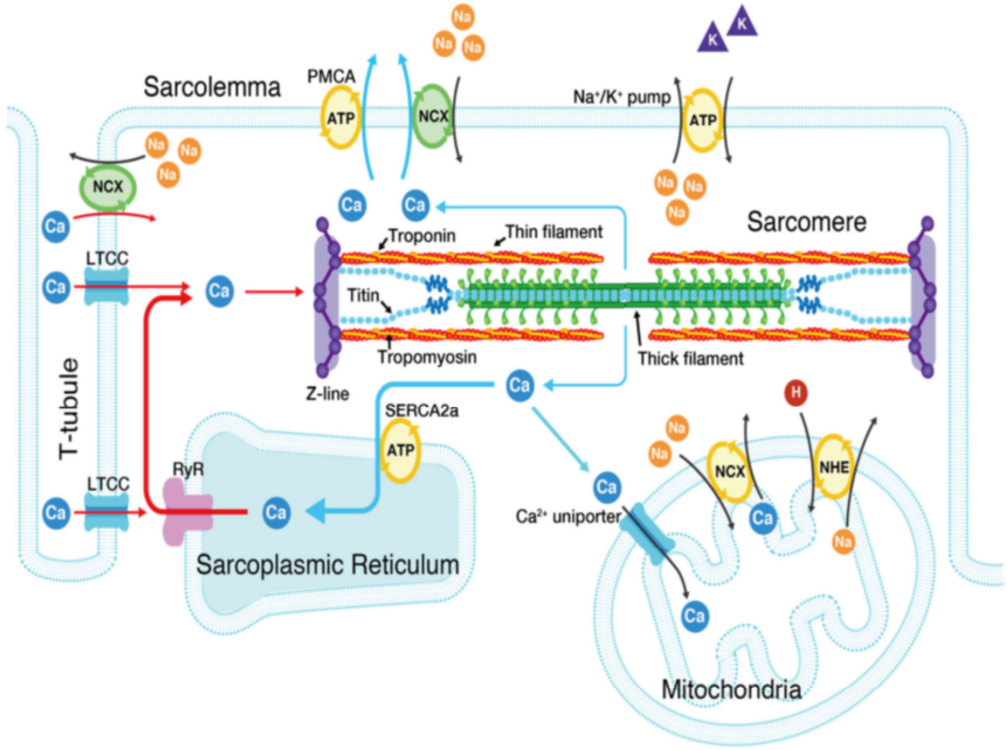
cardiac output = heart rate x systolic volume; it is the same for the right and left ventricle !!!

systolic volume = **enddiastolic volume** – **endsystolic volume** **(residual volume –** ATTENTION residual, not reserve!!!), amount of blood expelled during one systole

ejection fraction (index of contractility, assessed noninvasively, by echocardiography) = how many percent of enddiastolic volume is expelled during ejection phase of systole into the circulation; physiological value is minimally 60%, increases e.g. under sympathetic stimulation, increased temperature, etc., decreases when the **contractility** is decreased (ability of myocardium to contract), e.g. during heart failure

Next to the regulation of contractility by autonomous nervous system, important role is plaied also by autoregulation of the force of contraction (it can be traced down to subcellular level).

STARLING LAW



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Fuyu Kobirumaki-Shimozawa et al., J Physiol Sci (2014) 64:221–232

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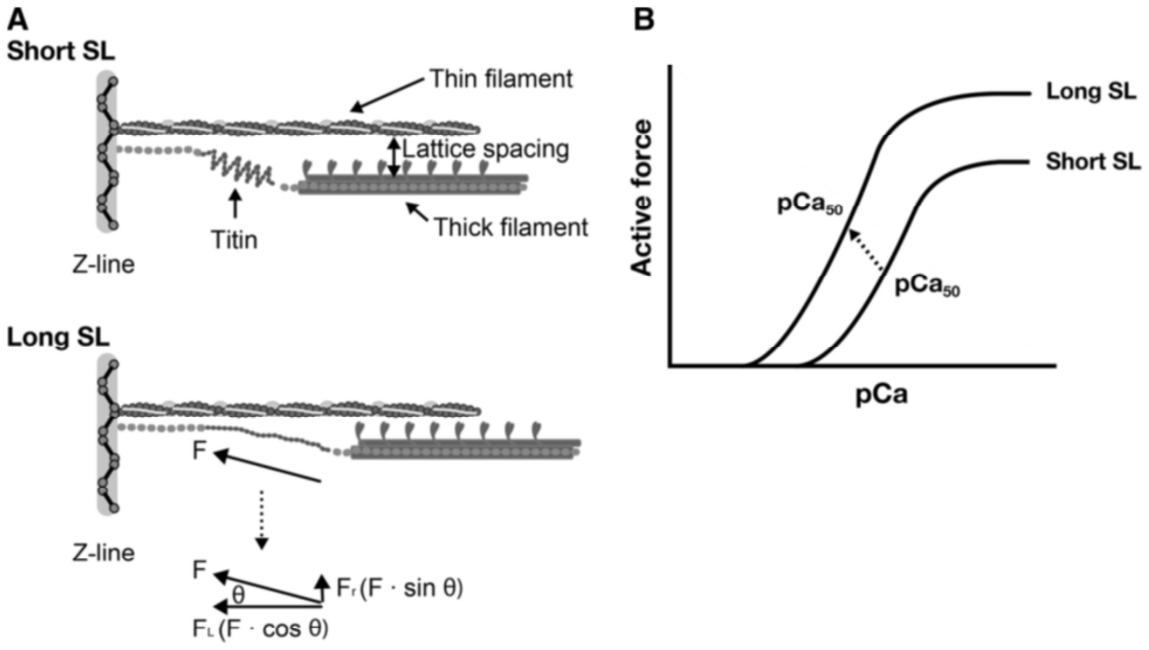
In cardiomyocyte, increased sarcomere length leads to stronger developed force (contraction). This phenomenon is known as heterometeric autoregulation (sarcomere-length dependent). It is autoregulation – it can be observed in single cardiomyocyte (isolated from all regulatory mechanisms, e.g. autonomous nervous system or circulating catecholamines).

This slide summarizes the structures involved in cardiomyocyte contraction and relaxation, ensure movement of calcium between and extra- and intracellular compartment and its intracellular store. These structures also play an important role in excitation-contraction coupling.



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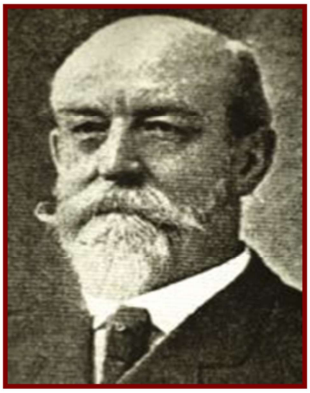
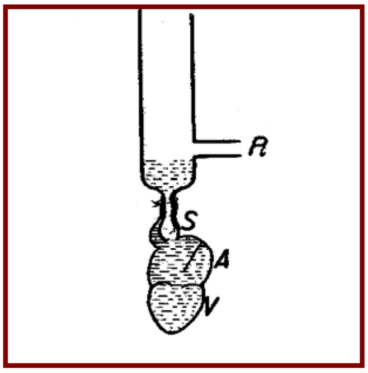
Detailed view of structures which are behind the heterometric autoregulation.

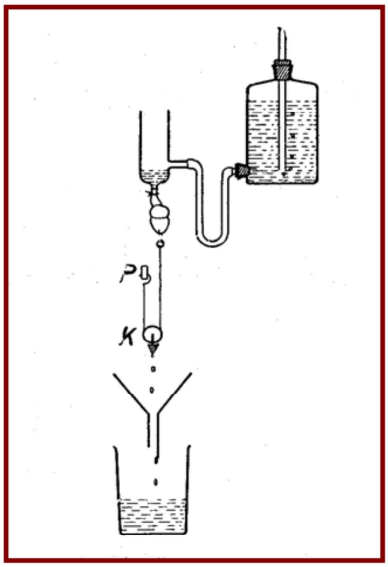
Note especially titin, „giant“ protein ensuring correct mutual position of actin and myosin. Next to increased cross-bridging and increased sensitivity of troponin C to calcium at higher sarcomere length titin is another structure the function of which explains increased developed force.

In the heart *in situ* the analogy of sarcomere lengthening is increased enddiastolic volume in the ventricle (increased filling), e.g. the bigger filling, the stronger contraction (the blood is not accumulated in the heart chamber, any „extra“ load is immediately ejected).



Henry Pickering Bowditch
(1840 – 1911)





HOMEOMETRIC AUTOREGULATION
(FREQUENCY EFFECT)

During increasing HR (stimulation frequency) the force of developed contraction rises
Ratio between intra- and extracellular calcium concentrations increases

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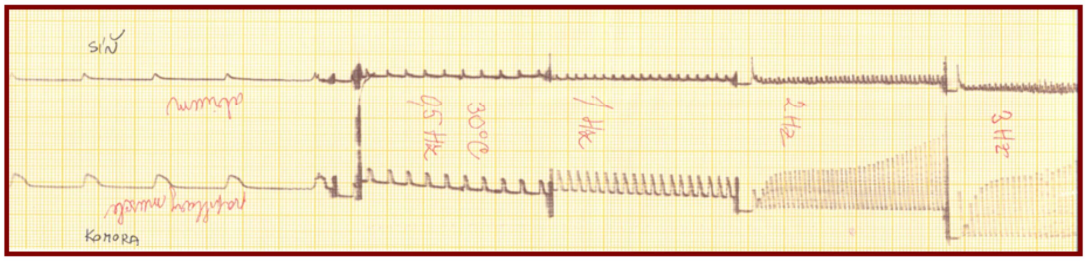
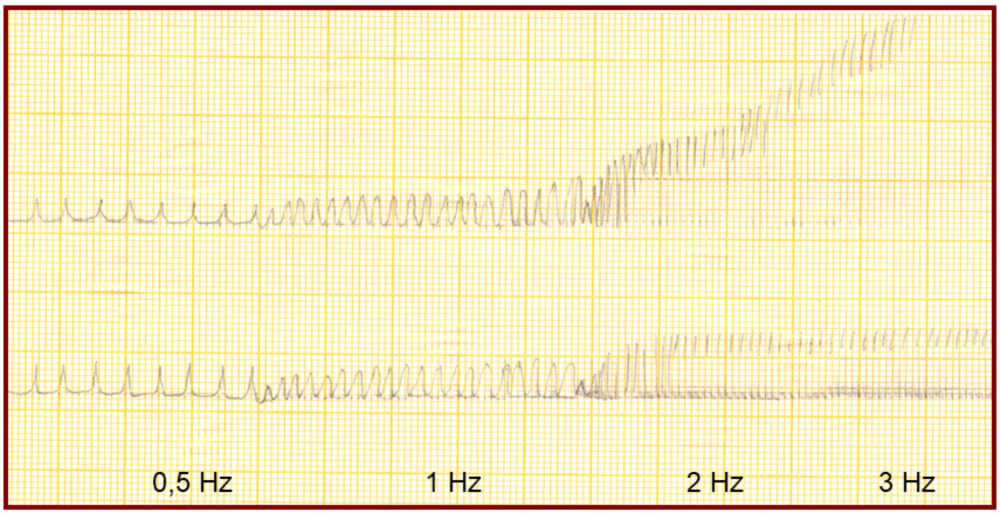
Homeometric autoregulation, also called frequency effect (Bowditch phenomenon, staircase phenomenon) was first described by H. P. Bowditch, based on experiments on the model of isolated frog heart (see picture above). However, this phenomenon is fully applicable in mammalian hearts.

Homeometric autoregulation is based on calcium availability for particular contraction (sarcomere length is not changed). The amount of calcium, released from SR terminal is called **recirculation fraction**.

During tachycardia, duration of diastole is shortened (e.g. Shortening of ventricular filling) and therefore enddiastolic volume decreases. Without correction of duration and amplitude of contraction the circulation would stop after a while. (Developed force of contraction will decrease due to heterometric autoregulation!) Thanks to homeometric autoregulation the force of contraction will be preserved even during increasing heart rate.

At higher heart rate, the duration of action potential is shortened, and thus the time during which calcium enters the cardiomyocyte (during plateau phase) decreases. On the other hand, there is higher number of these inward calcium currents per minute and in summary total influx of calcium into the cardiomyocyte at higher heart rate increases.





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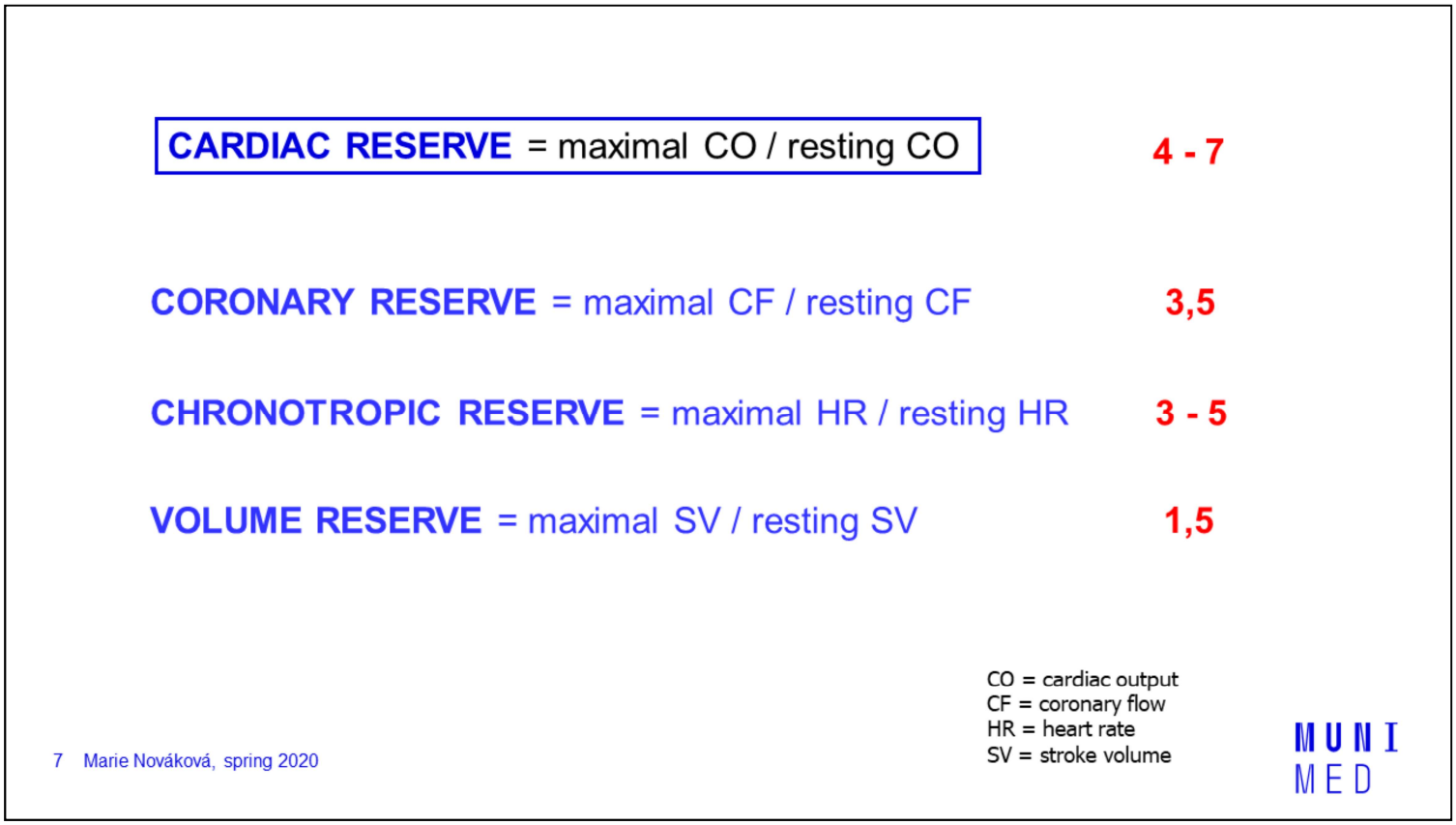
Also, time for extrusion of calcium out of the cardiomyocyte into the extracellular compartment (via Na^+/Ca^{2+}-exchanger and sarcolemmal Ca^{2+}-ATPase) is shorter. As a result, higher intracellular calcium concentration (ATTENTION – intracellular, e.g. total concentration in the cell; of course most of this „extra“ calcium is removed from cytoplasm and stored in the sarcoplasmic reticulum and cytosolic calcium concentration is physiological).

This autoregulation is important for instance during ventricular tachyarrhythmia, when marked shortening of diastole negatively affect cardiac output.

During physical exercise the sympathetic tonus increases, which increases calcium influx into the cardiomyocyte via L-type of Ca^{2+} channels and keeps force of contraction high. Frequency effect plays only modulatory role in such situation.

On original recordings (above) you can see stimulated contractions of isolated papillary muscle from the right ventricle and auricle from the left atrium of guinea pig heart. Note that with increasing stimulation frequency the developed force increases. It is experiment under strictly controlled conditions, without any possible effect of any regulation. This is a proof that we can see autoregulation (these are completely isolated pieces of the heart, without own automaticity).

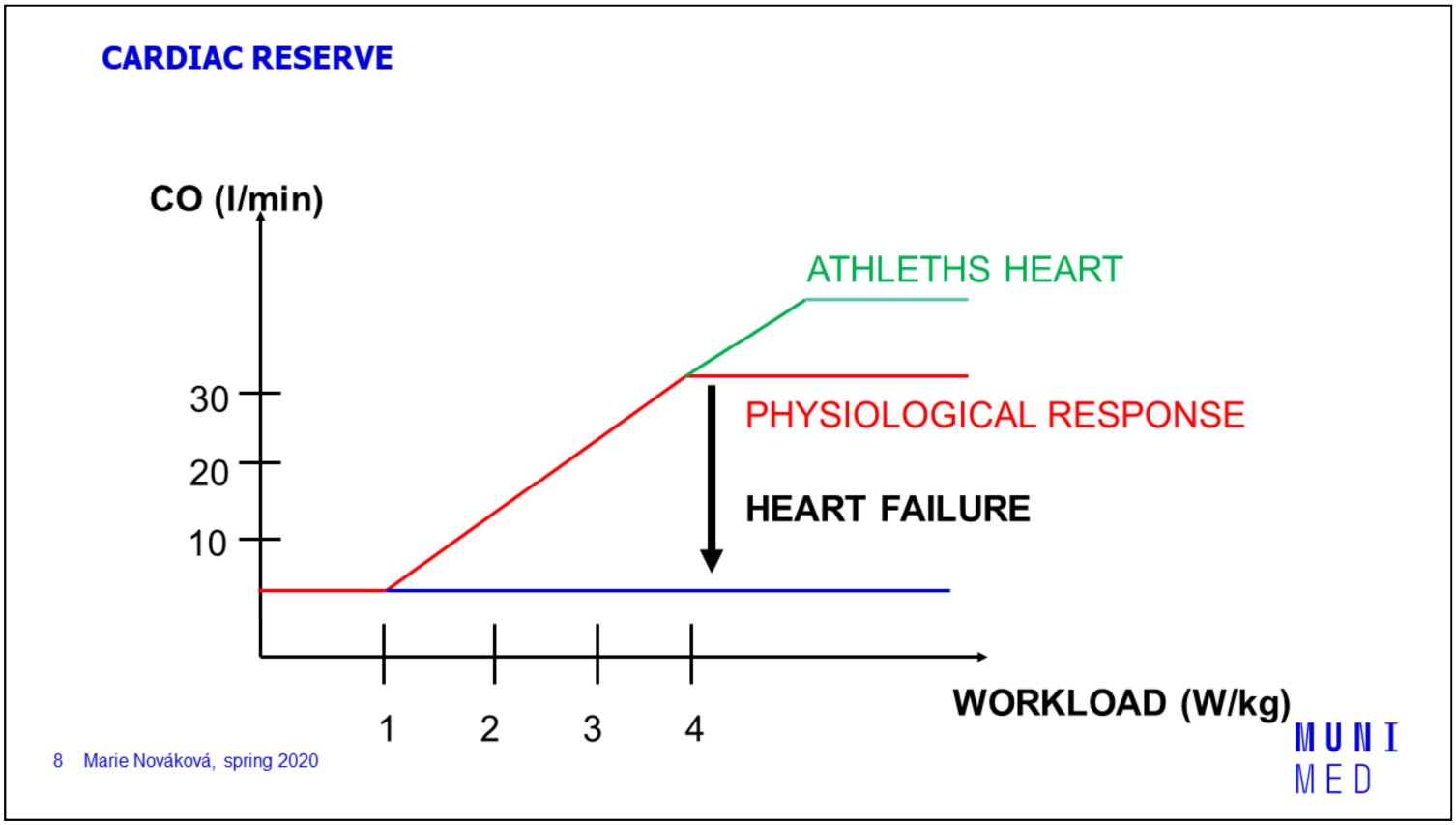


Cardiac reserve is a number (index) which shows how many times the heart can increase its pumping (evaluated by cardiac output) in case of need. Physiological values vary between 4 (healthy non-trained heart) and 7 and more (athletes' heart).

Key parameter for keeping proper heart pumping is sufficient perfusion of working myocardium. No surprise that one of partial heart reserves is coronary reserve (calculation – see slide above). Non-invasively, indirectly, we can get an idea about this reserve e.g. from ergometry (by observation of ECG record, during ischemia – changes of ST segment). It can be assessed invasively, during coronarography, mostly as a part of catheterisation.

Chronotropic reserve (calculation – see slide above) varies from 3 to 5. High value is found in well-trained subjects, with low resting heart rate due to high tonus of parasympathetic system (and due to baroreflex HR decreases too, together with hypertrophy and eventual left ventricle dilation in adapted heart).

Volume reserve (calculation – see slide above) is the smallest partial reserve.



Model example of the heart response to increasing work load (for instance during ergometric examination when the load can be well dosed and measured, according to standard protocols) – evaluated by cardiac output.

Note that physiological cardiac reserve of healthy heart is completely utilized at certain work load and further increasing of work load will not lead to further increase in cardiac output.

Heart adapted to exercise (after sufficiently long time of exercising of sufficient intensity and type, short time or low work load will not lead to adaptation!) has higher cardiac reserve and can therefore work to higher loads and increase its work (as a pump, e.g. cardiac output) more.

Failing heart has very low or no cardiac reserve. During exercise (even of minimal intensity) such heart cannot increase its pumping – such patient cannot perform any significant physical exercise.

IMPORTANT TERMS

Length-tension relationship (curve)

Minimal length l_0

Passive, active, total force

Optimal length

Isometric, **isotonic**, **auxotonic** contraction

Autoregulation of contraction – **heterometric** (Starling)

Preload, **afterload**

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Repeat the terms, which you will need in several questions during final examination.

Key knowledge is that various types of muscles differ in their response to stretching (length- force relationship, see next slide).

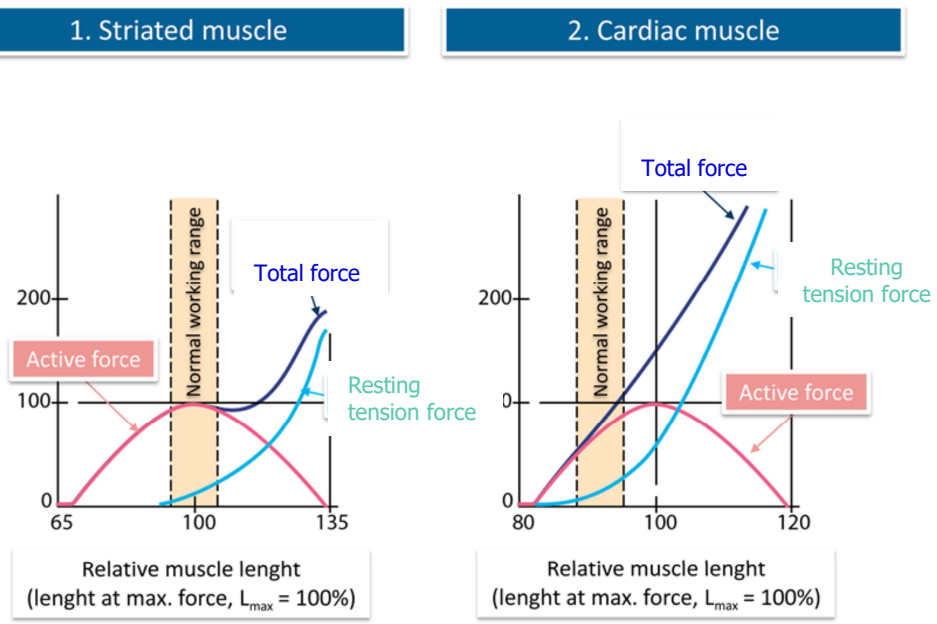
The muscle has to be stretched at least to so-called **minimal length**, otherwise it is not able to contract (not even if stimulated by external stimulus; for instance skeletal muscle which is „torn off“, otherwise under physiological conditions it is kept at minimal length by ligaments inserted to bones).

Optimal length is such length of muscle (resp. sarcomere) at which the muscle develops contraction of maximal amplitude.

There are two important terms for cardiac mechanics:

Preload – you can imagine it either as muscle stretching (in experiment) or filling of cardiac chamber (usually we focus on ventricles, esp. left ventricle).

Afterload – you can imagine it either as a pressure which has to be developed in ventricle (so that valve can open) or resistance against which the ventricle pumps the blood (which has to be overcome).



Passive tension, active tension, isometric contraction, isotonic contraction, auxotonic contraction

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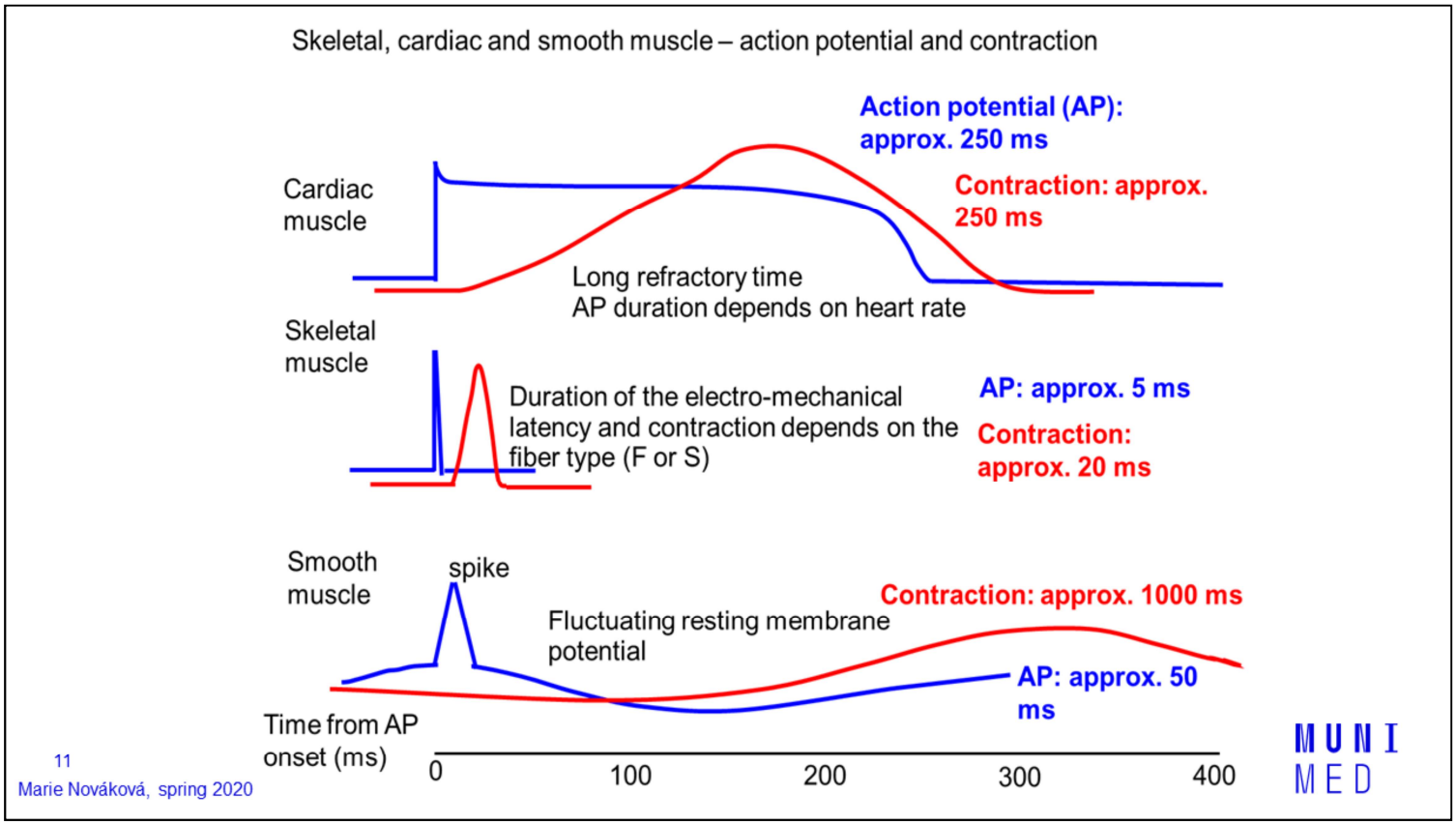
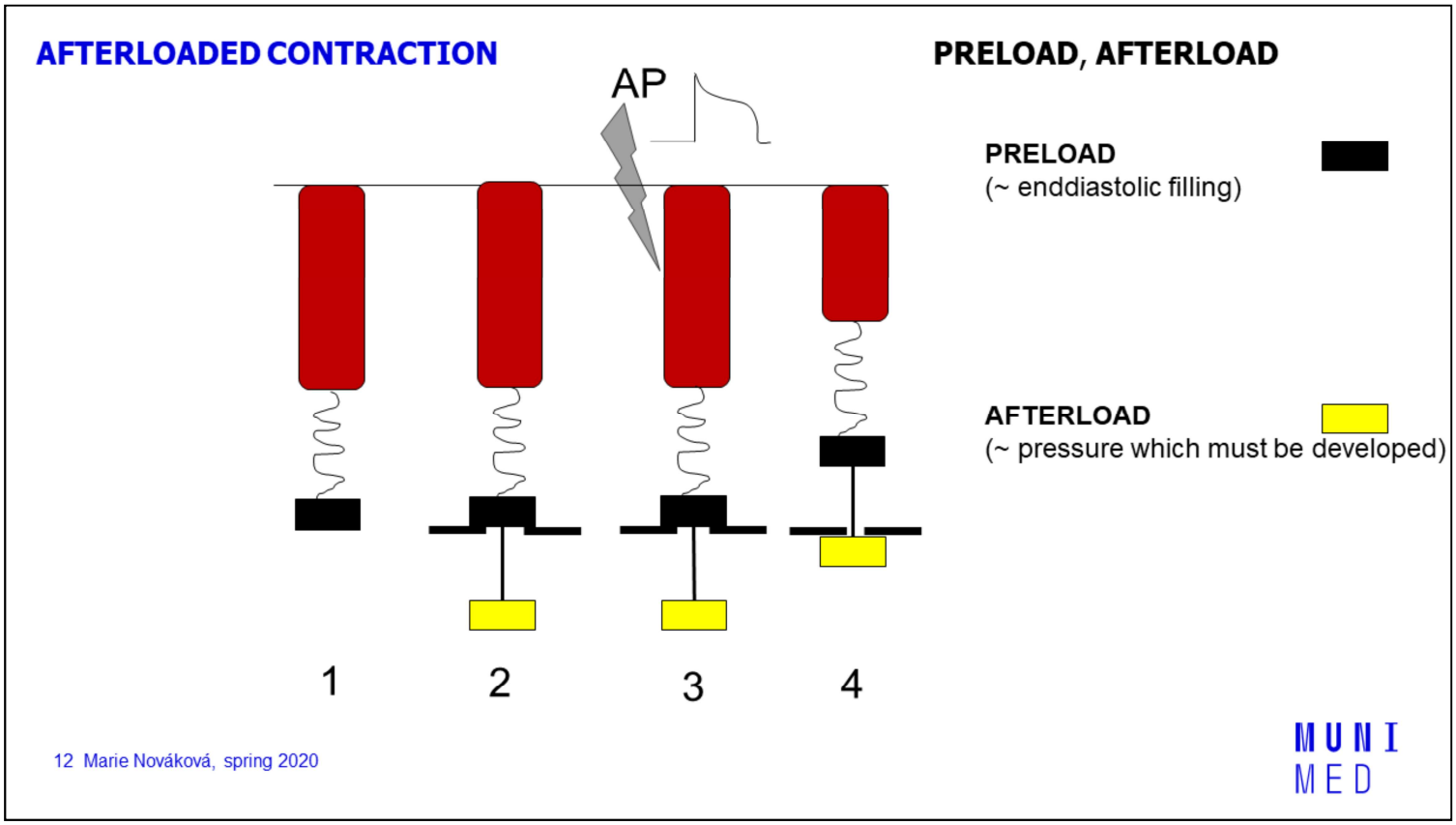
Although working myocardium is a striated muscle, it differs from skeletal muscle by its relationship between length and force. Simply said the main difference is that myocardium works on increasing part of the curve of active tension on contrary to skeletal muscle which develops maximal tension on the top of this curve.



Repeat your knowledge about the relationship between electrical and mechanical events in various types of muscle cells. Focus on the differences between two types of striated muscle.

It is necessary to emphasize that duration of cardiomyocyte action potential is really long (shorter in atrial, longer in ventricular cells) and therefore the refractory period in these cells is very long. This represents very important prevention of time summation of muscle contraction and potential development of tetanic contraction which would compromise pumping of the heart.

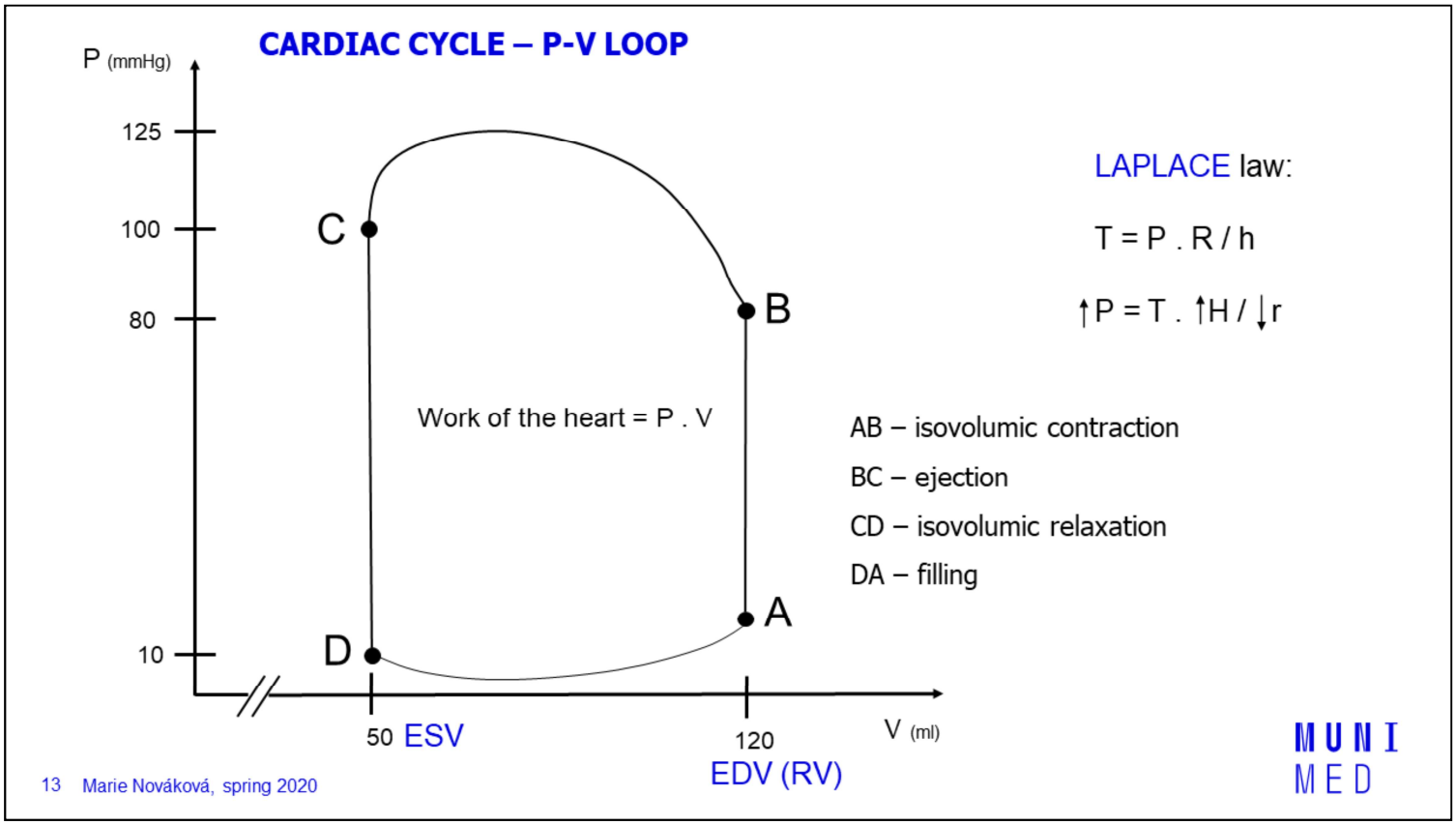


Most muscles contract in an auxotonic way, e.g. isometric contraction (increasing tension, length of sarcomere is constant, muscle doesn't shorten) changes into an isotonic contraction (tension doesn't increase any more, but the muscle shortens, length of sarcomeres is decreasing). Cardiac muscle is not an exception and it is well visible during systole.

On the slide you can see simple experiment on isolated muscle strip. Have a look how cardiac muscle works with preload and afterload (*in situ* with ventricle filling and resistance against which the ventricle pumps).

1. First, the muscle is stretched – black weight (**preload**). (Ventricle contains enddiastolic volume at the end of diastole, sarcomeres are stretched to certain length).
2. Underlay mat is placed under the weight, so the muscle strip will not stretch more (ventricular filling is ended). We add yellow weight (**afterload**). (Ventricle will have to overcome certain resistence in order to expell blood.)
3. Muscle strip is stimulated (AP). It first contracts isometrically (tension increases, isovolumic contraction phase of cardiac cycle).
4. When the afterload is overcome, muscle contracts isotonically (ejection phase of cardiac cycle) and also yellow weight is moved (preload, heart pumps, blood leaves the ventricle).

Imagine how you pull heavy suitcase: first, certain tension has to be developed to overcome its weight and then your muscles shorten and you pull it.



Cardiac cycle can be graphically expressed as pressure-volume diagram (P-V loop).

Systole: A – C

Diastole: C – A

Work of the heart corresponds to area surrounded by the loop. It can be also calculated as product of pumped volume and developed pressure.

Note that in ejection phase the intraventricular pressure increases, although volume of blood in the ventricle decreases. It is helpful to apply Laplace law – see slide above (pressure P increases, tension T is constant – it is isotonic contraction, thickness of the wall H increases and radius of ventricle r decreases).

$P = \underline{T} \cdot 2h \cdot \underline{r^{-1}}$ **Ventricular filling:** r and T rise, P first falls down, then rises up (length/tension relationship)

$\underline{P} = \underline{T} \cdot 2h \cdot r^{-1}$ **Isovolumic contraction**: T rises up, valves closed – increase in P

$\underline{P} = T \cdot 2\underline{h} \cdot r^{-1}$ **Ejection**: r decreases, h rises, thus P increases (even at the same T)

$P = T \cdot 2h \cdot r^{-1}$ **Isovolumic relaxation**: T decreases, valves closed – decrease in P

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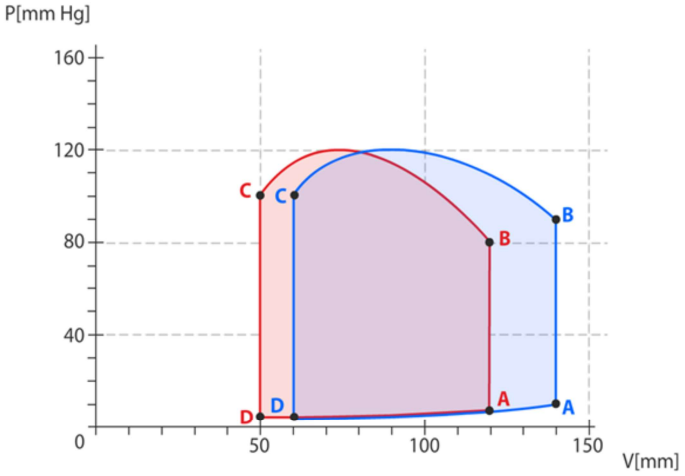
On this slide you can step by step repeat four phases of cardiac cycle. Laplace law will help you to understand relationships among the parameters which are important – pressure, tension, thickness of the wall and diameter of ventricle.

INCREASED PRELOAD

MODEL



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Next three slides describe MODEL SITUATION, when one of parameters affecting cardiac cycle is changed.

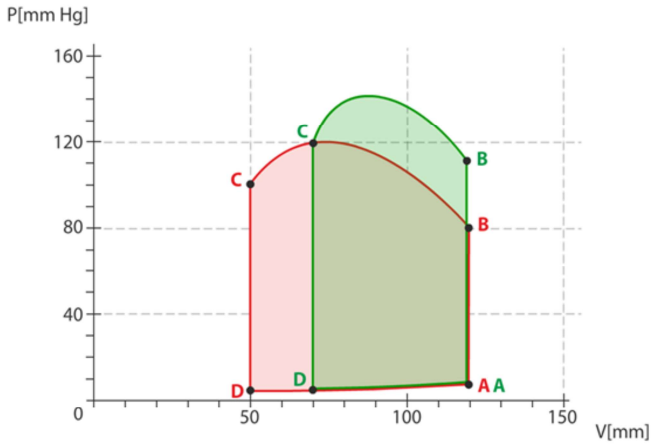
Red loop – resting state. Coloured loop – changed parameter.

The parameter is always changed only for one cardiac cycle.

In case of sudden increase of **preload** (physiological situations – deep breeding, bending forward, clinostatic reaction, etc.), the enddiastolic volume increases, P-V loop shifts to the right, area of P-V diagram increases (the heart performs more). Most of this volume increment is „removed“ immediately in the following cardiac cycle due to heterometric autoregulation. (In case of small change of preload, point B stays at the same value – opening pressure for aortic valve will not change; in case of bigger preload change, it can take several cardiac cycles to „remove“ extra volume in the ventricle, which may lead to slight increase in aortic pressure and shift of point B upwards – however the shift will never be big and permanent, it is case of increased afterload – see next slide).

INCREASED AFTERLOAD

MODEL



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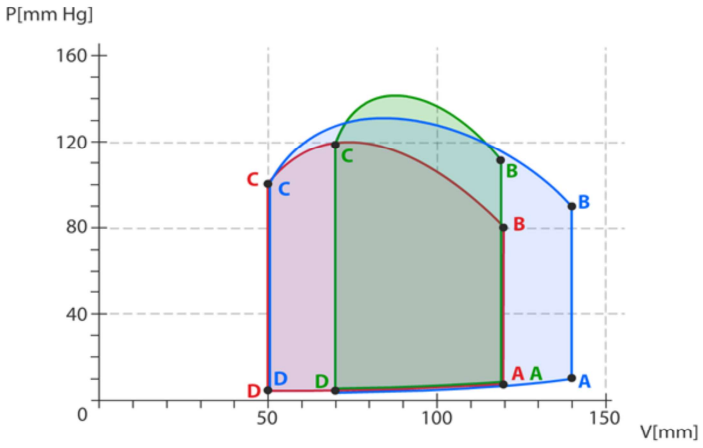
In case of sudden increase of **afterload** (such situation is probably not found under physiological conditions, but in experiment we can for instance mechanically press on the aorta), upwards shift of point B is observed (opening pressure for aortic valve, intraventricular pressure increases, isovolumic contraction phase prolongs, which is energetically very demanding). Again, area inside the P-V loop increases – in another words, heart performs more.

Duration of systole is quite stable. In case of isovolumic contraction phase prolongation, the ejection phase will shorten. Higher enddiastolic volume is found in the ventricle after such cardiac cycle.

INCREASED PRELOAD AND AFTERLOAD MODEL



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Lets go step by step: if afterload abruptly increases only for one cardiac cycle, volume increment at the end of this cycle will be dispatched in next „normal“ cycle due to heterometric autoregulation (e.g. normal – increased afterload – increased preload – normal.)

HEART SOUNDS

Caused by vibration of various anatomical structures and event. blood:

- **Closure and stretching of valves**
- Isovolumic contraction of heart muscle (papillary muscles, tendons)
- Turbulent blood flow

I. – mitral (+ tricuspidal) valve closure

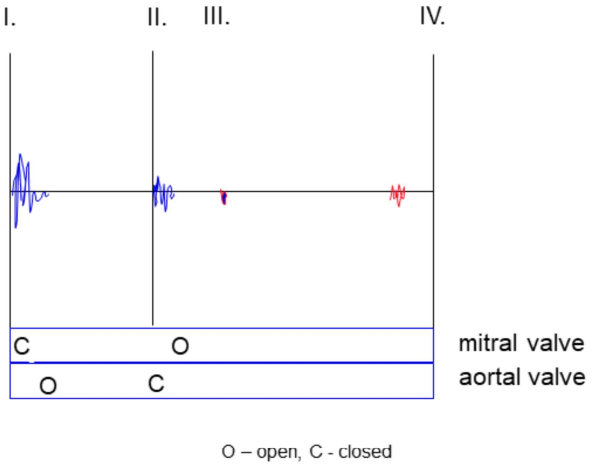
II. - aortal (+ pulmonary) valve closure

III. - fast filling of ventricles - pathological

IV. - contraction of atria – mostly pathological

Vibration of ventricular wall

Splitting of I. or II. sound:
asynchronous closure of M - T valve (I.)
or Ao - P valve (II.)
(inspiration, hypertension….)



O – open, C - closed

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Cardiac cycle can be traced on the body surface by listening to the heart sounds. They can be heard above particular valves, on the spots of „the best audibility“ (see practicals). Main physical event behind this auscultatory phenomenon is VIBRATION of certain structures and blood column (which reflects mechanical events during cardiac cycle).

MURMURS – pathological phenomena based on turbulent blood flow

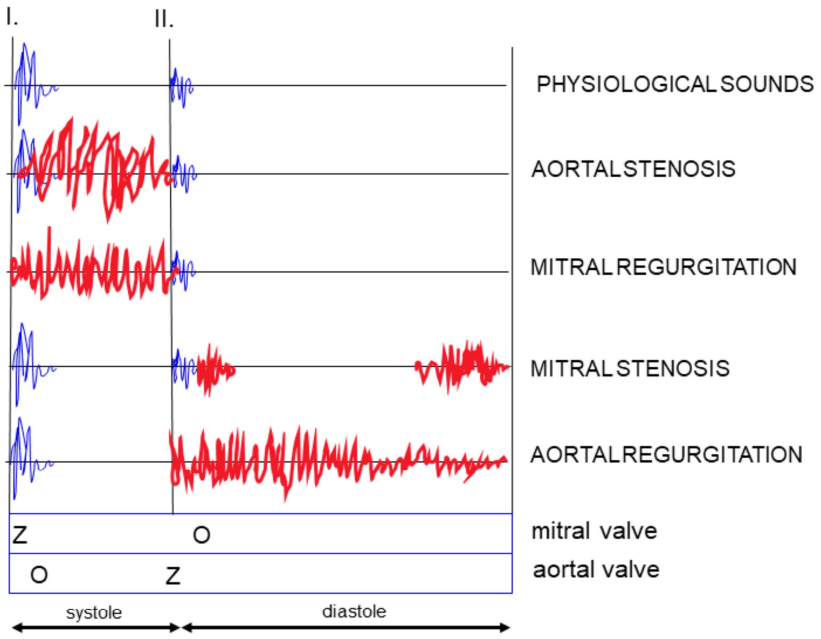
1. **SYSTOLIC**

- Stenosis – aortal, pulmonary **(1)**
- Regurgitation – mitral, tricuspidal **(2)**

2. **DIASTOLIC**

- Stenosis – mitral, tricuspidal **(3)**
- Regurgitation – aortal, pulmonary **(4)**

3. **SUSTAINED**:
- Defects of septum



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O – open, C - closed

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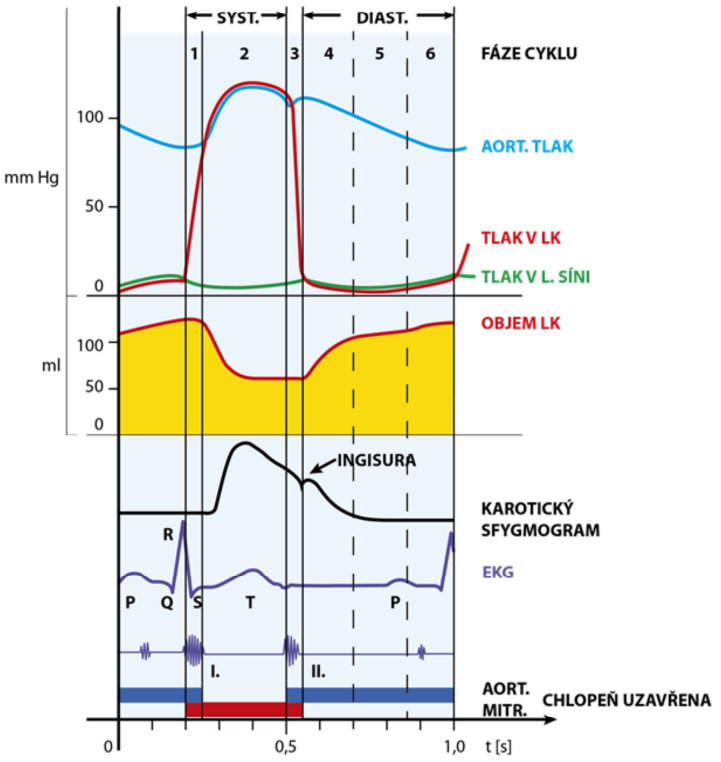
Physiological heart sounds are TWO. They are time limited auscultatory phenomena. In case we hear any other sound between the first and the second heart sound (e.g. during systole), it is **systolic murmur**. In case it is audible between the second heart sound and the first heart sound of the next cardiac cycle, it is **diastolic murmur**.

Murmurs are caused mostly by TURBULENT BLOOD FLOW. There are two situations when laminar blood flow changes into turbulent on valves – either the valve is not open sufficiently – STENOSIS, or the valve is not tightly closed – INSUFICIENCY (blood returns back, regurgitation).

See the slide above and try to figure out how various murmurs originate.

Example: I can hear murmur above aortal valve between the first and the second heart sound, e.g. during the systole, aortal valve should be open widely – however, I can hear the murmur above it, therefore it is systolic murmur due to aortal stenosis.

POLYGRAPHY (polygram)



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Polygram – simultaneous recording of various parameters in time – usually it is registered in order to study mutual relationships of various processes. Polygraphic recording was in past used e.g. for calculation of indexes of contractility – see practicals. Nowadays, echocardiographic examination is used for contractility evaluation (ejection fraction, see slide 2). Polygraphic recording is now used mostly in experiments.

Such picture as on this slide can help you to review your knowledge about mutual time relationships between electrical and mechanical events during cardiac cycle and also relationship to other, peripheral parameters. Try to draw polygram, e.g. according to practicals.

HEART FAILURE = loss of cardiac reserve

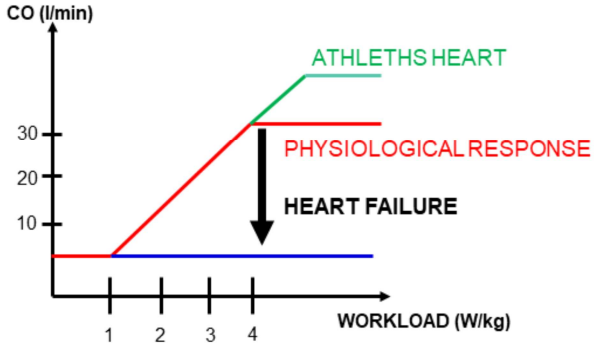
The heart is not able pump sufficient amount of blood into periphery at normal venous return.

SYMPTOMS
fatigue, oedemas, venostasis, dyspnoea, cyanosis

ACUTE x CHRONIC.

COMPENSATED x DECOMPENSATED.

MOST FREQUENT CAUSES:
- Severe arrhythmias
- Overload – *volume* (aortal insufficiency, a-v shunts) or *pressure* (hypertension and aortal stenosis – left overload, pulmonary hypertension and stenosis of pulmonary valve – right overload)
- Cardiomyopathy



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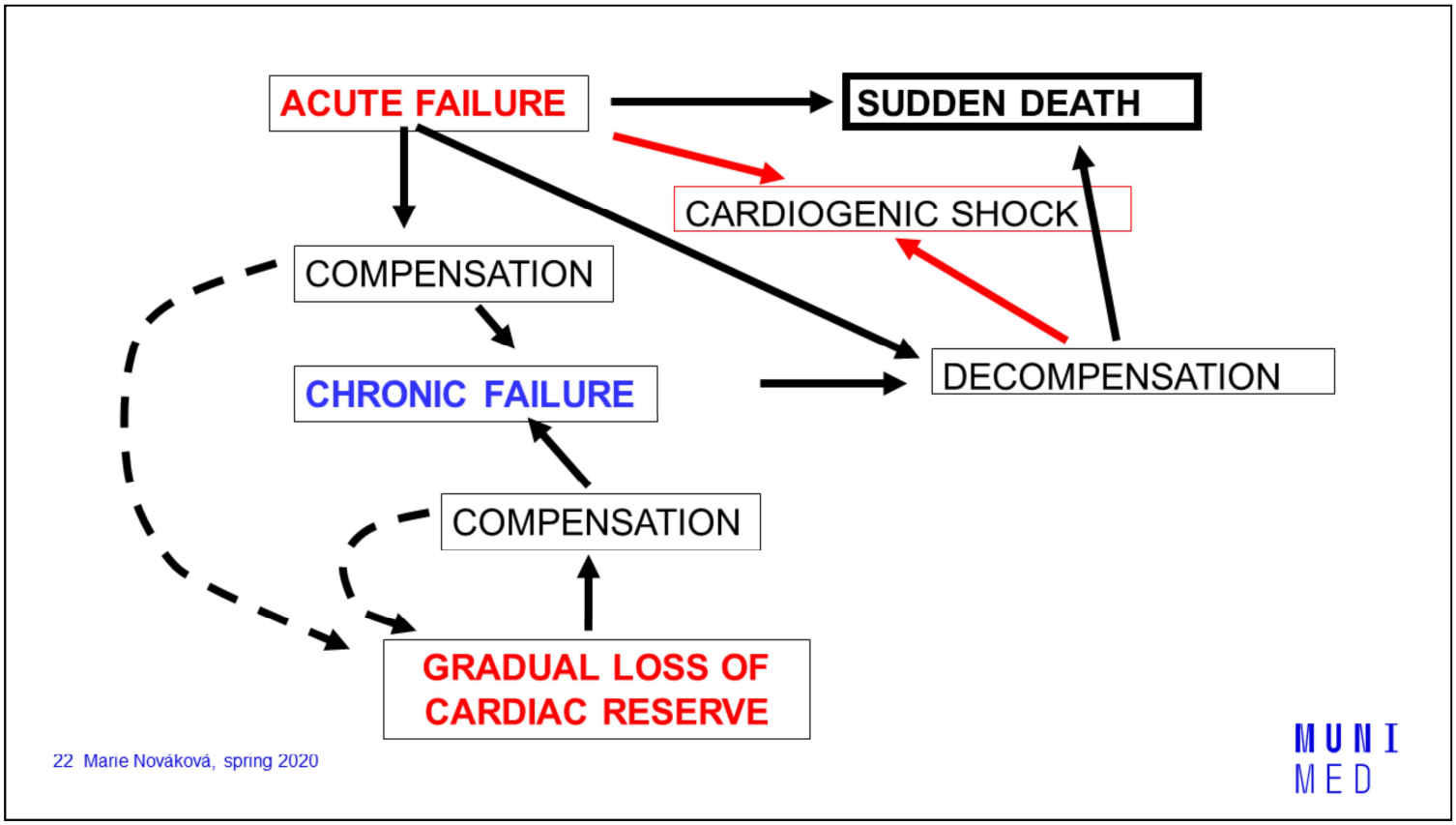
Repeat your knowledge about cardiac reserve (see above).

Loss of cardiac reserve – e.g. inability to increase the heart performance (its pumping) – is characteristic for heart failure. It is very serious health condition, frequently observed as end-stage of various chronic cardiovascular disorders (hypertension, CAD, etc.). However, it can be an acute situation as well.



This slide is voluntary – you can think about the possibilities how the heart failure can originate (ACUTE – for instance post-infection complication of influenza, myocarditis, CHRONIC – gradual loss of cardiac reserve, see commentary to previous slide) and what are possible next steps in its progression (sudden death, compensation, decompensation).

HEART FAILURE - COMPENSATION

BAROREFLEX

Physiological role: compensation of decrease in minimal volume of circulating fluids
Signal: BP decrease (orthostase, work vasodilatation)
Sensor: baroreceptors
Response: activation of SAS (increased HR, inotropy, BP)
Pathological signal: long-lasting decrease of BP due to heart insufficiency
Results: increased energy outcome – **vicious circle**

Ca^{2+} - antagonists

β – sympatolytics

ACTIVATION OF RAAS

Physiological role: compensation of loss of circulating fluids (bleeding)
Signal: decrease in renal perfusion
Sensor: juxtaglomerular system of kidney
Response: BP increase (angiotenzin II.), water retention (aldosteron)
Pathological signal: decrease in renal perfusion due to heart insufficiency
Results: increased preload and afterload, increased energy outcome – **vicious circle**

angiotenzin-converting enzyme inhibitors (AT II. receptors)

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This and following slide summarize some PHYSIOLOGICAL mechanisms involved in correction of certain symptoms of heart failure.

Particular mechanisms, their physiological role, physiological triggers and detection of parameter (sensors) and signals which trigger these mechanisms in heart failure are listed. Triggering these mechanisms in organism with failing heart leads to negative impacts and to so-called vicious circle. The overall situation of such heart worsens unless this vicious circle is cut (for instance by pharmacotherapy).

You don't need to study pharmacotherapy ☺

DILATATION (STARLING PRINCIPLE)

Physiological role: compensation of momentary right-left differences

Signal: orthostase, deep breathing, beginning of exercise

Pathological signal: continual blood stasis in the heart

Results: increased energy outcome – **vicious circle**

HYPERTROPHY

Physiological role: preservation of energetically demanding tension of ventricular wall

Signal: P = s . 2 h / r, intermittent BP increase (athletes heart)

Response: concentric remodelling

Pathological signal: continual increase of preload or afterload

Results: worsening of oxygenation, fibrotisation – **vicious circle**

diuretics

cardiac glycosides (digitalis)

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See the comment to the previous slide.

Ad HYPERTROPHY:

Heart pumping against high afterload (e.g. in arterial hypertension) must develop higher tension in the isovolumic contraction phase of cardiac cycle. It is energetically demanding. Higher tension leads to increased oxygen consumption in the myocardium (in the wall of the ventricle). It may lead to myocardium remodelling – from pathological reasons, on contrary to „physiological“ remodelling in athletes heart. This remodelling is macroscopically observable as thickening of the ventricular wall (h).