PHYSIOLOGY

بسم الله الرحمن الرحيم

MID | Lecture 9

Heart as a Pump & Cardiac cycle (Pt.3) & Cardiac output

وَلَقَدْ خَلَقْنَا الْإِنسَانَ وَنَعْلَمُ مَا تُوَسْوِسُ بِهِ نَفْسُهُ ۖ وَنَحْنُ أَقْرَبُ إِلَيْهِ مِنْ حَبْلِ الْوَرِيدِ

اللهم إنّا نعوذ بك من شرور أنفسنا ومن سيئات أعمالنا

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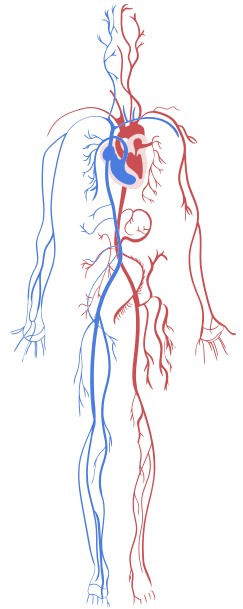
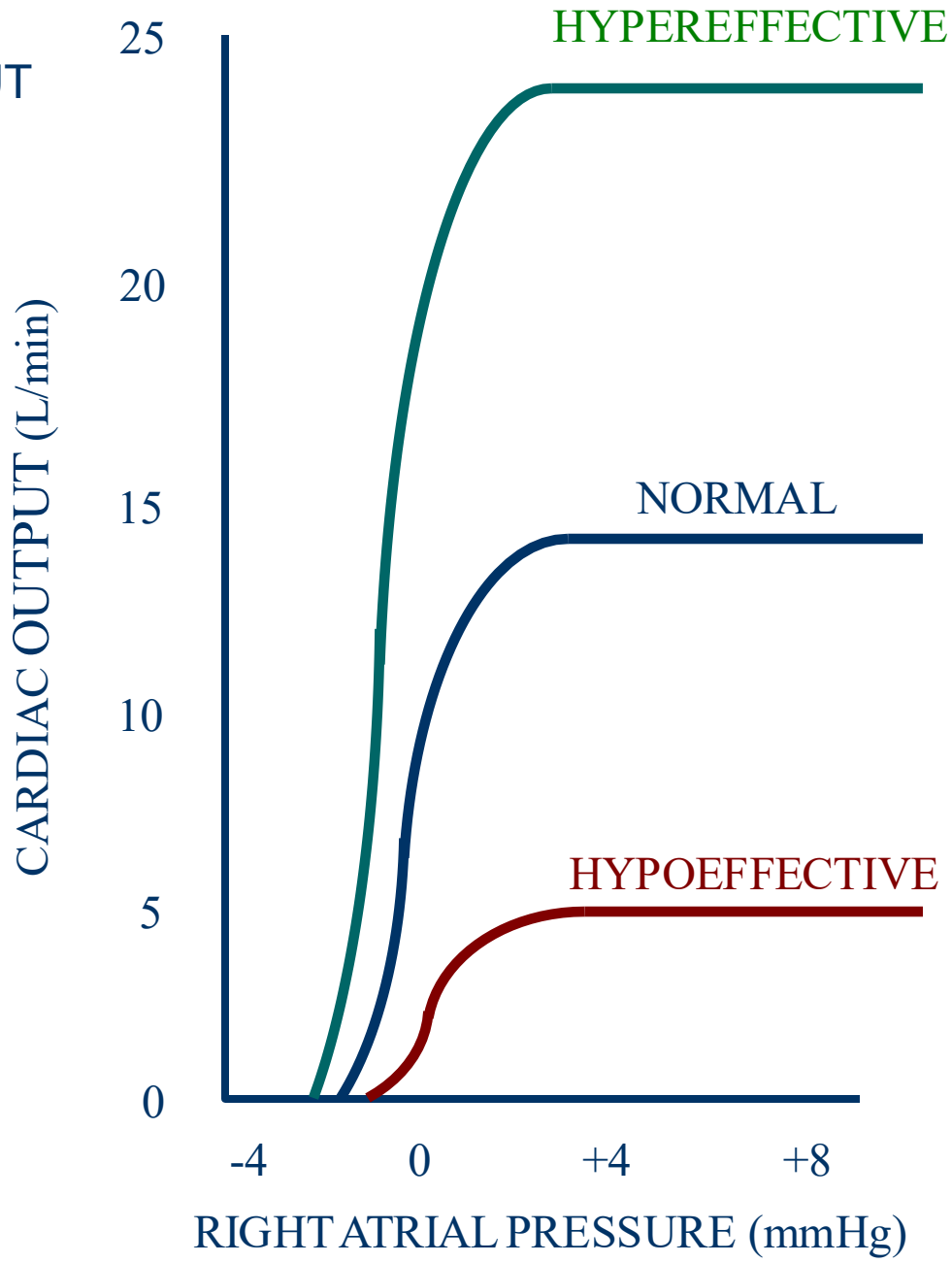


CARDIAC OUTPUT CURVES



Understanding the RAP–Cardiac Output Curve

- The figure plots right atrial pressure (RAP) on the x-axis and cardiac output (CO) on the y-axis.
- RAP is used as an index of venous return because changes in venous return directly influence right atrial pressure: **greater** venous return increases right atrial volume and **therefore raises** RAP.
- Increased venous return increases cardiac output through the Frank–Starling mechanism.
- Thus, RAP indirectly reflects ventricular volume (preload).
- During diastole, atrial pressure must be slightly higher than ventricular pressure to maintain forward blood flow into the ventricle, and **this pressure rises when venous return increases**.

RAP= Right Atrial Pressure

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Cardiac Output in the Normal Heart

- At a right atrial pressure (RAP) of approximately 0 mmHg, the normal cardiac output is about 5 L/min.
- An increase in RAP **indicates** an increase in venous return to the heart.
- According to the Frank–Starling mechanism, greater ventricular filling stretches myocardial fibers, **leading to** a stronger contraction.
- This **increase in contractile force** raises stroke volume, and—assuming heart rate remains constant—cardiac output increases proportionally.
- On the cardiac output curve, increasing RAP progressively elevates cardiac output until the ventricle reaches its maximal capacity to respond to preload **(its maximal end-diastolic volume)**.
- This plateau represents the physiological limit of the Frank–Starling mechanism—approximately 15 L/min—and occurs without any external stimulation, **reflecting an intrinsic cardiac property**.

Length–Tension Relationship in Cardiac Muscle

- In skeletal muscle, contractions typically occur at or near the optimal sarcomere length, where maximal tension can be generated.
- In cardiac muscle, the **resting sarcomere length is shorter than the optimal length**.
- Because of this, increasing ventricular filling **(which increases sarcomere length)** enhances contractile force, allowing greater stroke volume according to the Frank–Starling mechanism.
- This increase in force continues until the sarcomere reaches its **optimal length of about 2.2 µm**, beyond which no further increase in stroke volume occurs.
- At this optimal length, the heart reaches its **intrinsic physiological limit**, corresponding to a cardiac output of approximately **15 L/min** under normal conditions.
- This intrinsic response is **independent of neural regulation**.
- For example, a newly transplanted (denervated) heart still exhibits this Frank–Starling behavior purely due to its **inherent length–tension properties**.
- This description corresponds to the **middle "normal" curve** on the cardiac function graph.

Cardiac Output in the Hypereffective State

- A hypereffective state occurs with **sympathetic stimulation** or with **positive inotropic agents** and can also occur with **athletic cardiovascular adaptation**.
- Positive inotropic effects **increase stroke volume at the same end-diastolic volume (EDV)**. This means the heart contracts more forcefully **without requiring additional preload**.
- This mechanism **differs from the Frank–Starling relationship**:
- **Frank–Starling:** Increasing EDV increases stroke volume, but ejection fraction changes little because **both SV and EDV increase together**.
- **Positive inotropy:** Stroke volume increases **while EDV remains constant**, so **ejection fraction rises**.
- As a result, at any given right atrial pressure (i.e., the same preload), **cardiac output is higher** in a hypereffective state than in the normal state.
- With maximal sympathetic stimulation, **cardiac output can reach about 25 L/min** in healthy individuals, representing the **upper limit** of the hypereffective state.

Athletic Adaptation

- Athletic Adaptation (form of hypereffective heart state):
- Endurance athletes may achieve **cardiac outputs up to 35 L/min during maximal exercise**. This is due to **physiological ventricular hypertrophy**, which increases stroke volume.
- Example comparison:
- **Normal person:** HR ≈ 70 bpm, SV ≈ 70 mL/beat → CO ≈ 5 L/min.
- **Athlete:** SV ≈ 100 mL/beat → to maintain CO ≈ 5 L/min, HR may be **≈ 50 bpm**.
- This lower resting heart rate is **normal in trained athletes** and is **not pathological bradycardia**. Therefore, **clinical interpretation should include assessing physical activity level**, not relying on ECG findings alone.

Cardiac Output in the Hypoeffective State

- **Sympathetic inhibition** or **negative inotropic factors** can produce a hypoeffective heart.
- In this state, **maximal cardiac output decreases**, shifting the cardiac output curve **downward**.

Ventricular Pressure and Volume Curves (cont'd)

- During the latter part of the ejection phase how can blood still leave the ventricle if pressure is higher in the aorta?
- Momentum of blood flow
- Total energy of blood = $P + mV^2/2$ = pressure + kinetic energy
- Under normal conditions, **kinetic energy contributes only about 1%** of the heart's total work, with the majority coming from **pressure (external) work**. However, in **aortic stenosis, kinetic energy can increase to nearly 50%**, making management of aortic stenosis important.
- Aortic valve is narrowed → the blood must pass through a much smaller opening → so it must move faster to maintain flow → higher velocity → higher kinetic energy
- Total energy of blood leaving the ventricle is greater than in the aorta.

Ejection Fraction

- Example of calculation of the ejection fraction:
- **End diastolic volume** = 125 ml
- **End systolic volume** = 55 ml
- **Ejection volume (stroke volume)** = 70 ml
- **Ejection fraction** = 70 ml / 125 ml = **56%** (normally 60%)
- **If heart rate (HR) is 70 beats/minute, what is cardiac output?**
- **Cardiac output** = HR × stroke volume
  = 70/min × 70 ml
  = **4900 ml/min**

Ejection Fraction (cont'd)

- **If:**
  HR = 100
  end diastolic volume = **180 ml**
  end systolic volume = **20 ml**
  what is the cardiac output?
- **C.O. =** 100/min × 160 ml = **16,000 ml/min**
- **Ejection fraction =** 160/180 ≈ **90%**

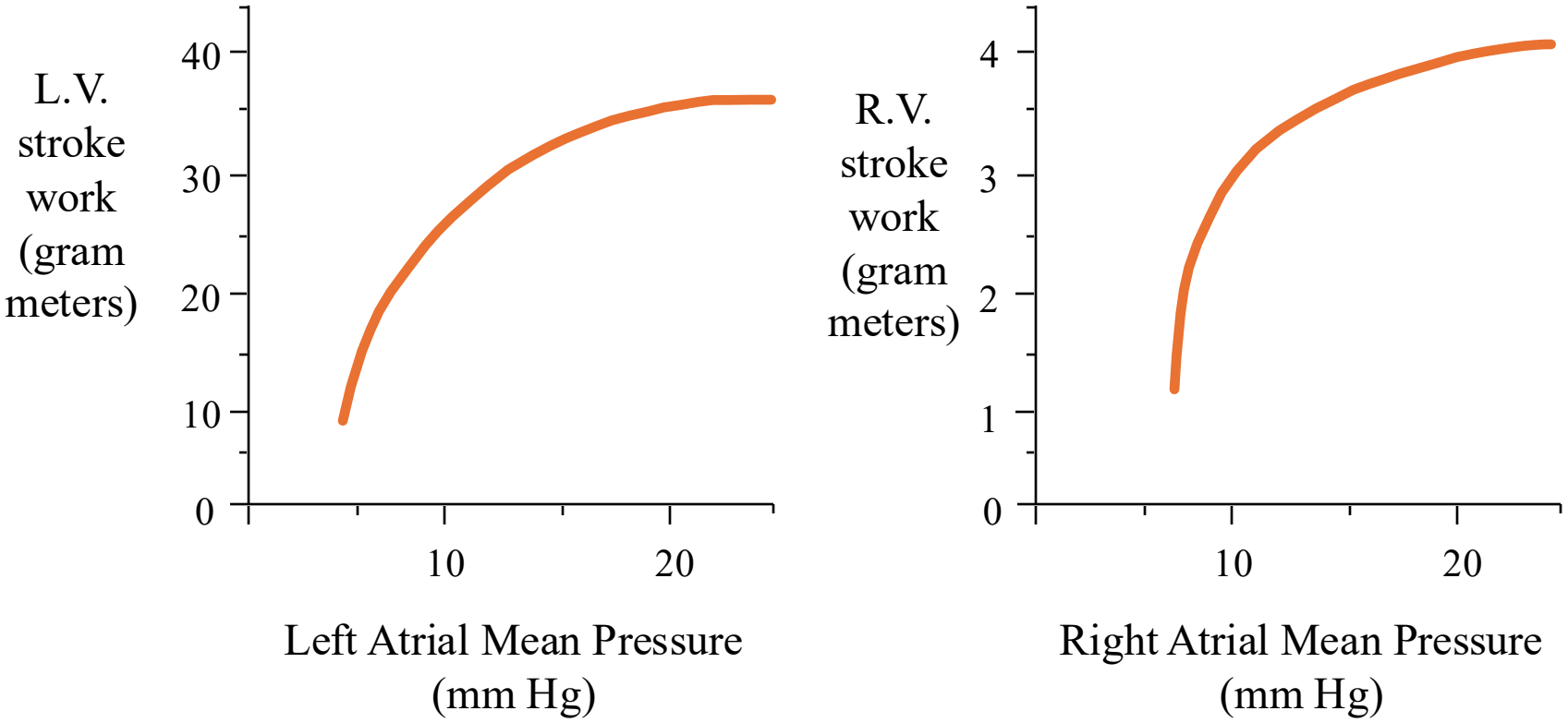
Aortic Pressure Curve

- **Aortic pressure starts increasing during systole** after the **aortic valve opens**.
- **Aortic pressure decreases** toward the end of the ejection phase.
- After the aortic valve closes, an **incisura (dicrotic wave)** occurs because of the sudden cessation of back-flow toward the left ventricle.
- **Aortic pressure decreases slowly during diastole** because of the **elasticity of the aorta**.
- In aortic regurgitation, the aortic valve **fails to close completely**, allowing blood to flow back into the left ventricle during diastole. Because the valve does not form an effective barrier to this **retrograde flow**, the normal dicrotic notch (incisura) on the aortic pressure waveform **may be reduced or absent**.

Frank–Starling Mechanism

- Within physiological limits, the heart pumps all the blood that comes to it **without excessive damming in the veins**.
- Extra stretch on cardiac myocytes makes **actin and myosin filaments interdigitate** to a more optimal degree for **force generation**.

Ventricular Stroke Work Output



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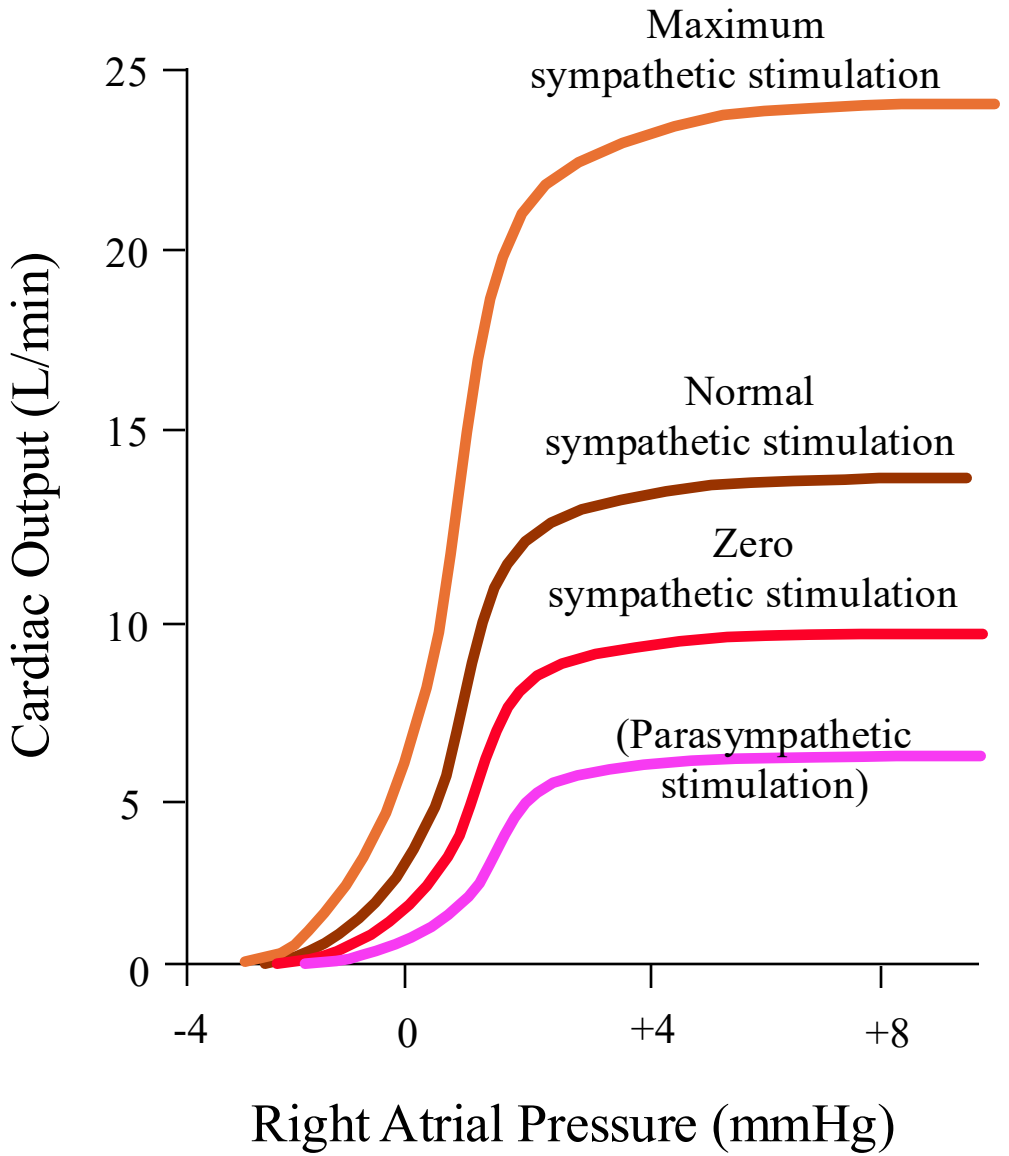
Ventricular Stroke Work Comparison

- This figure illustrates the relationship between **mean right and left atrial pressures** and the stroke work produced by the **right and left ventricles**, respectively.
- Note that although the **x-axis scale is identical** for both graphs, the **y-axis differs by a factor of ten**.
- This indicates that the **left ventricle performs about ten times more stroke work** than the right ventricle.
- The primary reason is that the **left ventricle works against much higher pressures** than the right ventricle, even though both **eject similar volumes of blood**.

Autonomic Effects on Heart

- **Sympathetic stimulation** causes increased HR and increased contractility, with HR = **180–200**, and C.O. = **15–20 L/min**.
- **Parasympathetic stimulation** decreases HR markedly and decreases cardiac contractility slightly.
- Vagal fibers go mainly to the **atria**.
- **Fast heart rate (tachycardia)** can decrease C.O. because there is not enough time for the heart to fill during diastole.

Effect of Sympathetic and Parasympathetic Stimulation on Cardiac Output



Effects of Sympathetic Stimulation on Cardiac Output

1. **Normal sympathetic stimulation**
   - The sympathetic nervous system maintains a **basal firing rate** even without additional stimulation.
   - This basal tone allows both **up-regulation and down-regulation** of cardiac function.
   - Without this baseline activity, **decreasing output would be impossible**, since values cannot fall below zero.
   - In the graph, basal sympathetic stimulation (**brown curve**) produces a cardiac output of **~15 L/min at rest**.
2. **Maximum sympathetic stimulation (positive control)**
   - With increased sympathetic input, cardiac output can rise further, reaching a maximum of **~25 L/min**.

Zero Sympathetic and Parasympathetic Effects on Cardiac Output

3. **Zero sympathetic stimulation (negative control)**
   - With **zero sympathetic input**, cardiac output decreases, with a maximum of about **~10 L/min.**
4. **Parasympathetic stimulation**
   - It decreases cardiac output mainly due to a **marked reduction in heart rate** and a **slight decrease in contractility** (minimal negative inotropic effect).
   - This occurs because parasympathetic fibers (**vagal fibers**) are distributed **mainly to the atria**, not to the ventricles where most of the pumping force is generated.

Cardiac Contractility

- Best is to measure the C.O. curve, but this is nearly impossible in humans.
- Clinically, cardiac contractility is typically assessed using the **ejection fraction**.
- In experimental settings, contractility is quantified by measuring the **slope of ventricular pressure rise during systole (dP/dt)** using specialized equipment.
- **dP/dt is not an accurate measure** because this increases with increasing preload and afterload.
- **(dP/dt) /** $P_{ventricle}$ is better.
  - $P_{Ventricle}$ is instantaneous ventricular pressure.
- Excess **K^+ decreases contractility**.
- Excess **Ca^{2+} causes spastic contraction** (increases contractility), and low Ca^{2+} causes **cardiac dilation**.
- During **isovolumic contraction**, ventricular pressure rises very rapidly. If we calculate the **slope of this rise (dP/dt)**, the slope is **directly proportional to contractility**.

Cardiac output and Venous Return

Faisal I. Mohammed, MD, PhD

Objectives

- Define cardiac output and venous return
- Describe the methods of measurement of CO
- Outline the factors that regulate cardiac output
- Follow up the cardiac output curves at different physiological states
- Define venous return and describe venous return curve
- Outline the factors that regulate venous return curve at different physiological states
- Inter-relate Cardiac output and venous return curves

Important Concepts About Cardiac Output (CO) Control

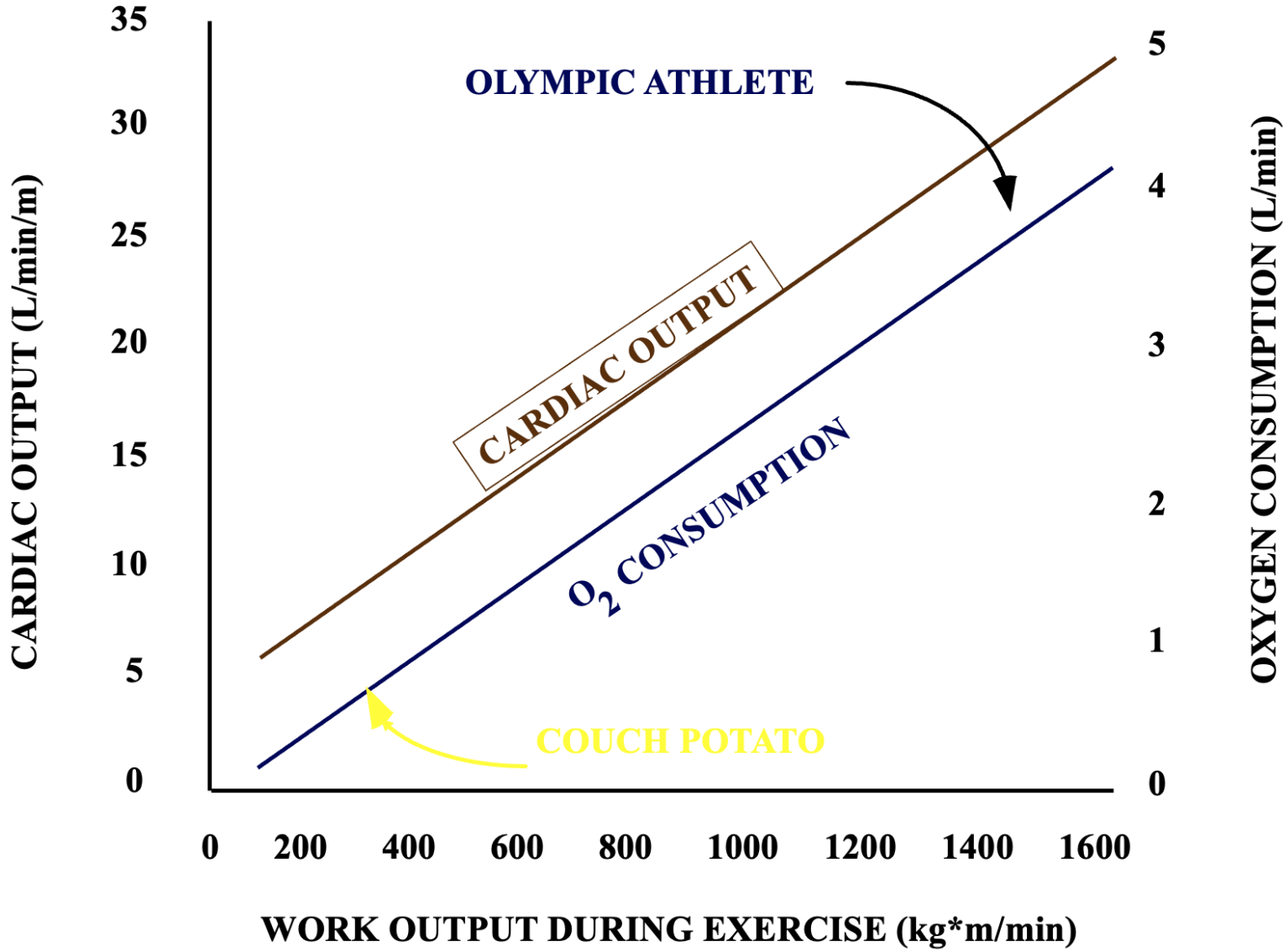
- Cardiac Output is the sum of all tissue flows and is affected by their regulation
  - (CO = **5 L/min**, cardiac index = **3 L/min/m^2**).
- CO is proportional to tissue **O_2 use**.
- CO is proportional to **1/TPR** when AP is constant.
- **F = ΔP / R** (Ohm's law)
- **CO = (MAP – RAP) / TPR**, (RAP = 0) then
- **CO = MAP / TPR ; MAP = CO × TPR**

Legend

- **F = ΔP / R (Ohm's law)**
  - **F** = flow rate
  - **ΔP** = change in pressure (mean arterial pressure – right atrial pressure)
  - **R** = resistance (from the aorta to the right atrium), called **total peripheral resistance** or **total systemic resistance**
- **CO = (MAP – RAP) / TPR**
- If **RAP = 0**, then:
  - **CO = MAP / TPR**
  - **MAP = CO × TPR**
- **Abbreviations:**
  - **CO**: cardiac output
  - **MAP**: mean arterial pressure
  - **RAP**: right atrial pressure
  - **TPR**: total peripheral resistance
- The mean arterial pressure can be changed by modifying **cardiac output** (by altering **stroke volume**, **heart rate**, or both) or by modifying **total peripheral resistance** (through **vasodilation**, which decreases resistance, or **vasoconstriction**, which increases resistance), or by changing **both**.

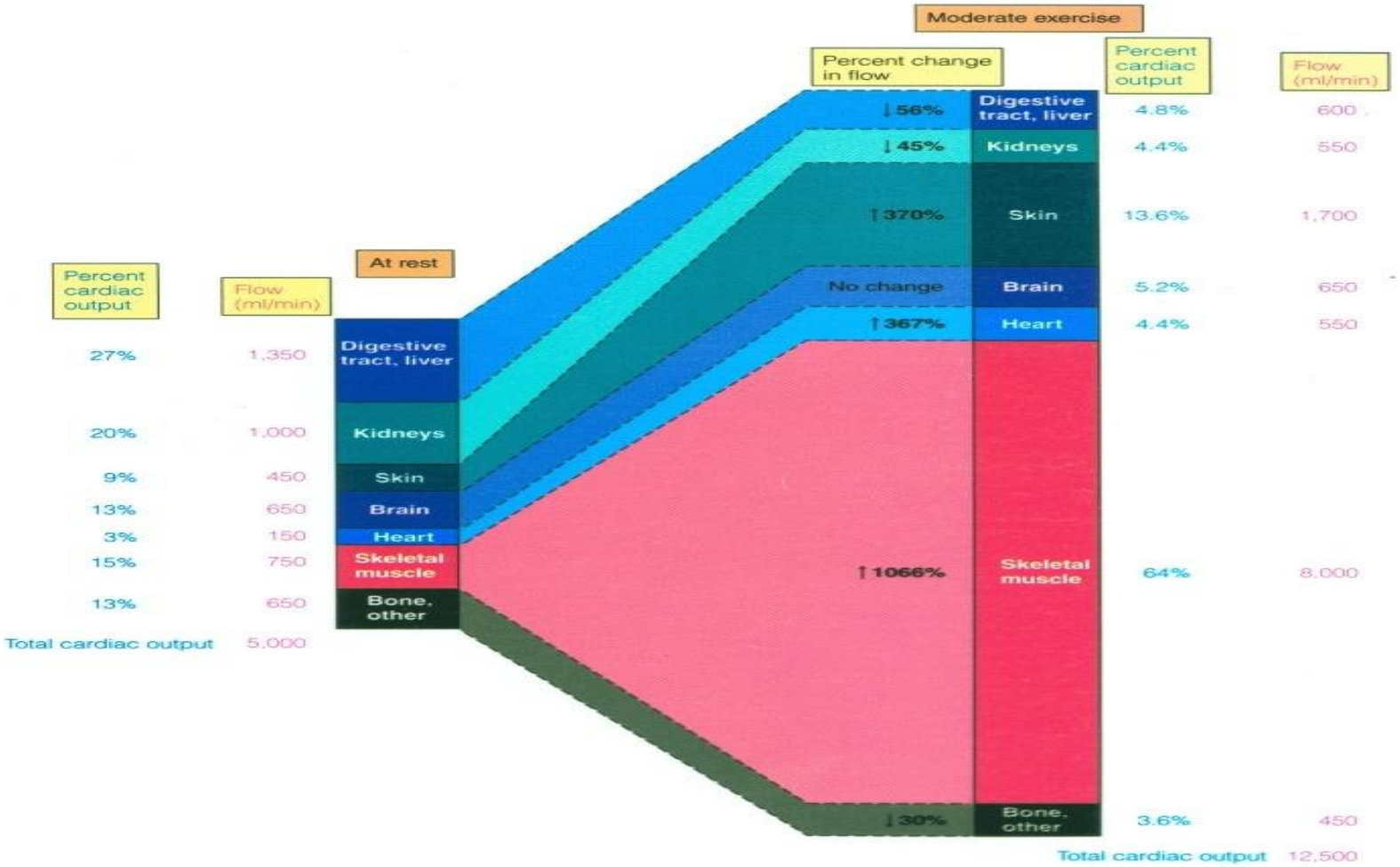
Cardiac Output vs. Cardiac Index

- As mentioned before, cardiac output differs between individuals depending on **their** size and other factors. To compare cardiac function between two different individuals and remove the effect of varying body sizes, we divide the cardiac output (L/min) by the body surface area (m^2) to calculate the **cardiac index (L/min/m^2)**.
- Cardiac output is proportional to **oxygen delivery to the tissues**, because when tissues require more oxygen, **more blood is pumped to them**. As blood flow increases, **cardiac output also increases**, since cardiac output equals the **sum of all blood flow to the tissues**.



This graph shows the relationship between **cardiac output** and **oxygen consumption**. When oxygen consumption increases, **cardiac output also increases**. **Athletes have a higher maximal cardiac output** compared to individuals with no regular physical activity.

Magnitude & Distribution of CO at Rest & During Moderate Exercise



Changes in Tissue Blood Flow with Exercise

- Let's say that cardiac output at rest is **5 L/min**. During exercise, cardiac output increases, but blood flow is **distributed differently** among tissues. Some tissues receive more flow, such as **skeletal muscles** (for example, about **700 mL/min at rest** and up to **8 L/min during exercise**) and the **skin** for temperature regulation (since exercise generates ATP and about **75% of its energy is released as heat**).
- Other tissues, such as the **GI tract**, receive less blood flow, which is why eating before intense exercise may cause **gastrointestinal discomfort**, **reduced digestion**, and, in very severe exercise, may even lead to **GI ischemia**.

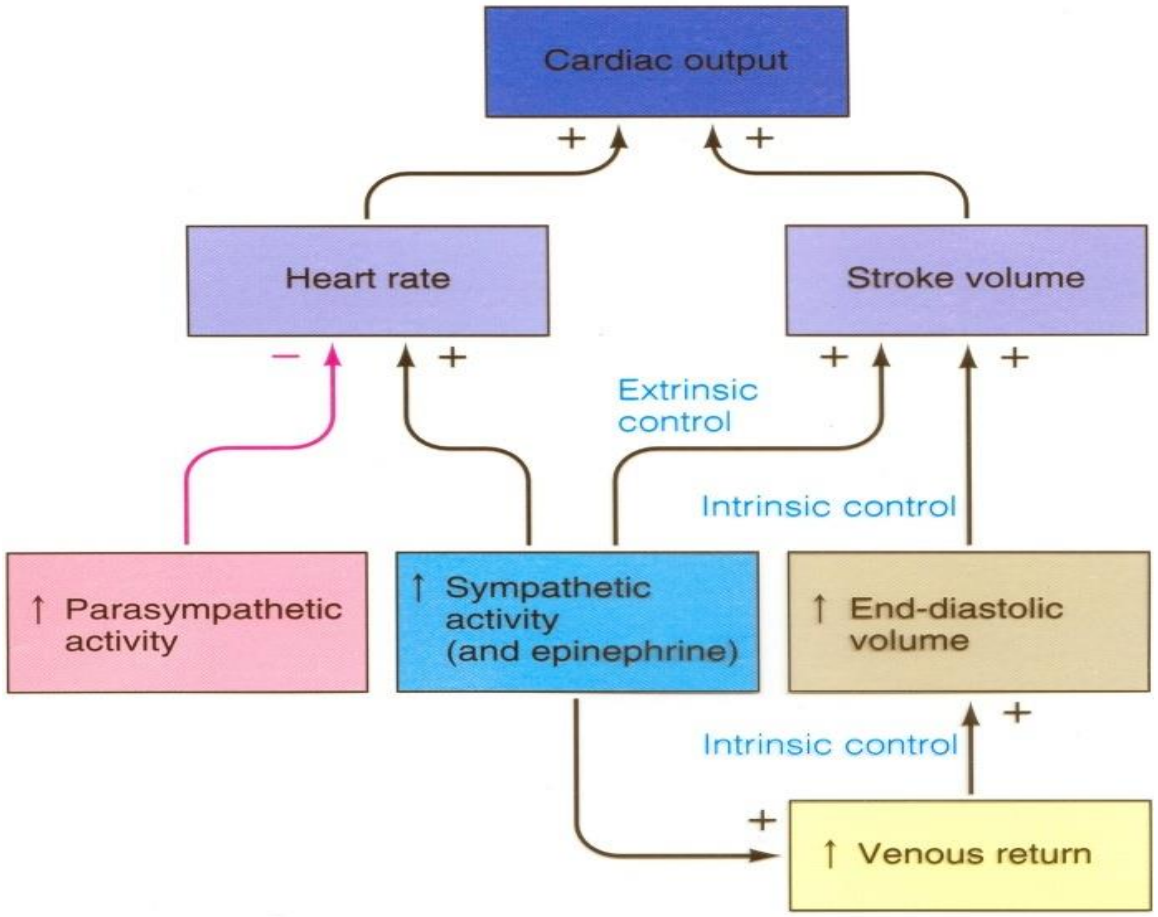
Variations in Tissue Blood Flow

	Per cent	ml/min	ml/min/ 100 gm
Brain	14	700	50
Heart	4	200	70
Bronchi	2	100	25
Kidneys	22	1100	360
Liver	27	1350	95
Portal	(21)	(1050)	
Arterial	(6)	(300)	
Muscle (inactive state)	15	750	4
Bone	5	250	3
Skin (cool weather)	6	300	3
Thyroid gland	1	50	160
Adrenal glands	0.5	25	300
Other tissues	3.5	175	1.3
Total	100.0	5000	---

Understanding Blood Flow per 100 g of Tissue

- The heart has one of the highest **metabolic** blood flows per 100 g of tissue. Someone may ask about organs like the **kidney, thyroid gland,** and **adrenal gland**. The heart receives about **70 mL/100 g/min**, and this flow is mainly for **oxygen supply**. In contrast, the kidney has a very high **normalized** blood flow because a large portion of its circulation is used for **filtration**, not metabolic needs. The thyroid and adrenal glands also show high blood flow per 100 g because they are **endocrine glands** (they release hormones into the bloodstream) and are **very small organs**, so their blood flow per 100 g appears high.
- For clarification:
  - If an organ's total flow is **0.5 mL/min** and its mass is **0.5 g**, its normalized flow is **100 mL/100 g/min**.
  - If an organ's total flow is **500 mL/min** and its mass is **1000 g**, its normalized flow is **50 mL/100 g/min**.

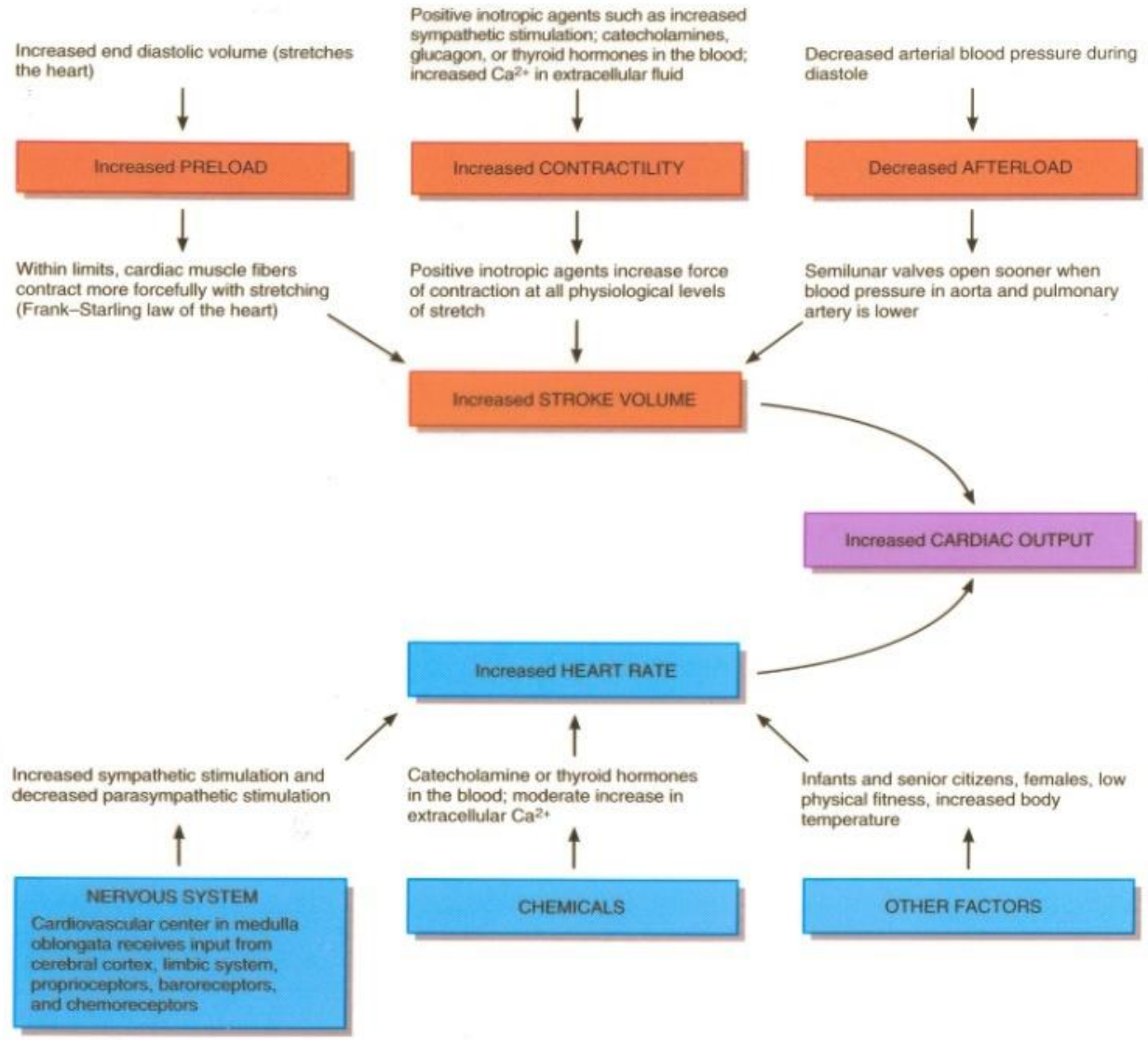
Control of Cardiac Output



Intrinsic and Extrinsic Control of Cardiac Output

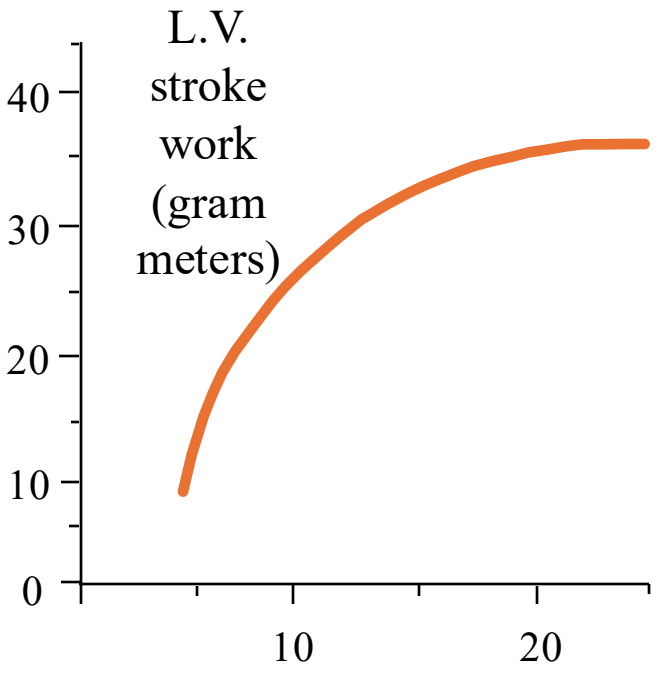
- Cardiac output can be increased by raising either **heart rate** or **stroke volume**. Stroke volume increases when **venous return rises**, leading to a higher **end-diastolic volume**, which represents the intrinsic control of the heart (Frank–Starling law). The extrinsic control occurs through **sympathetic stimulation**, which produces a **positive inotropic effect**. Heart rate is regulated by both the **sympathetic system** (positive chronotropic effect) and the **parasympathetic system** (negative chronotropic effect).

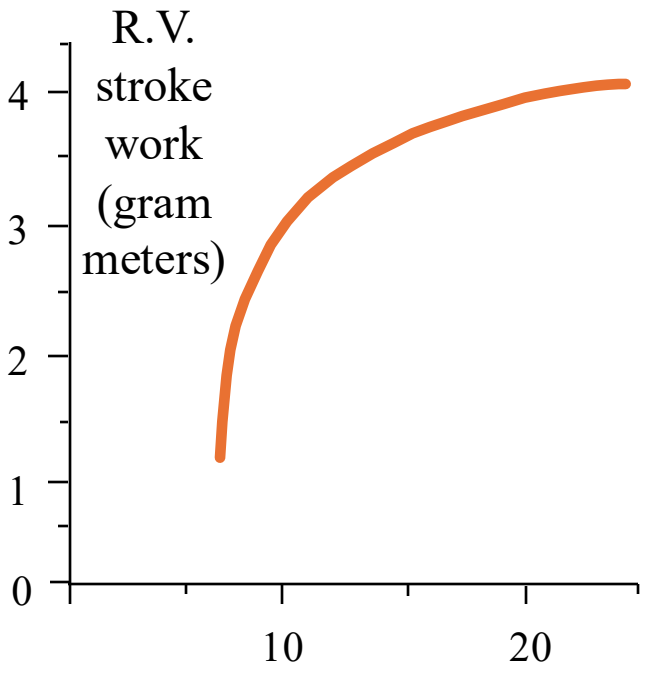
Factors that affect the Cardiac Output



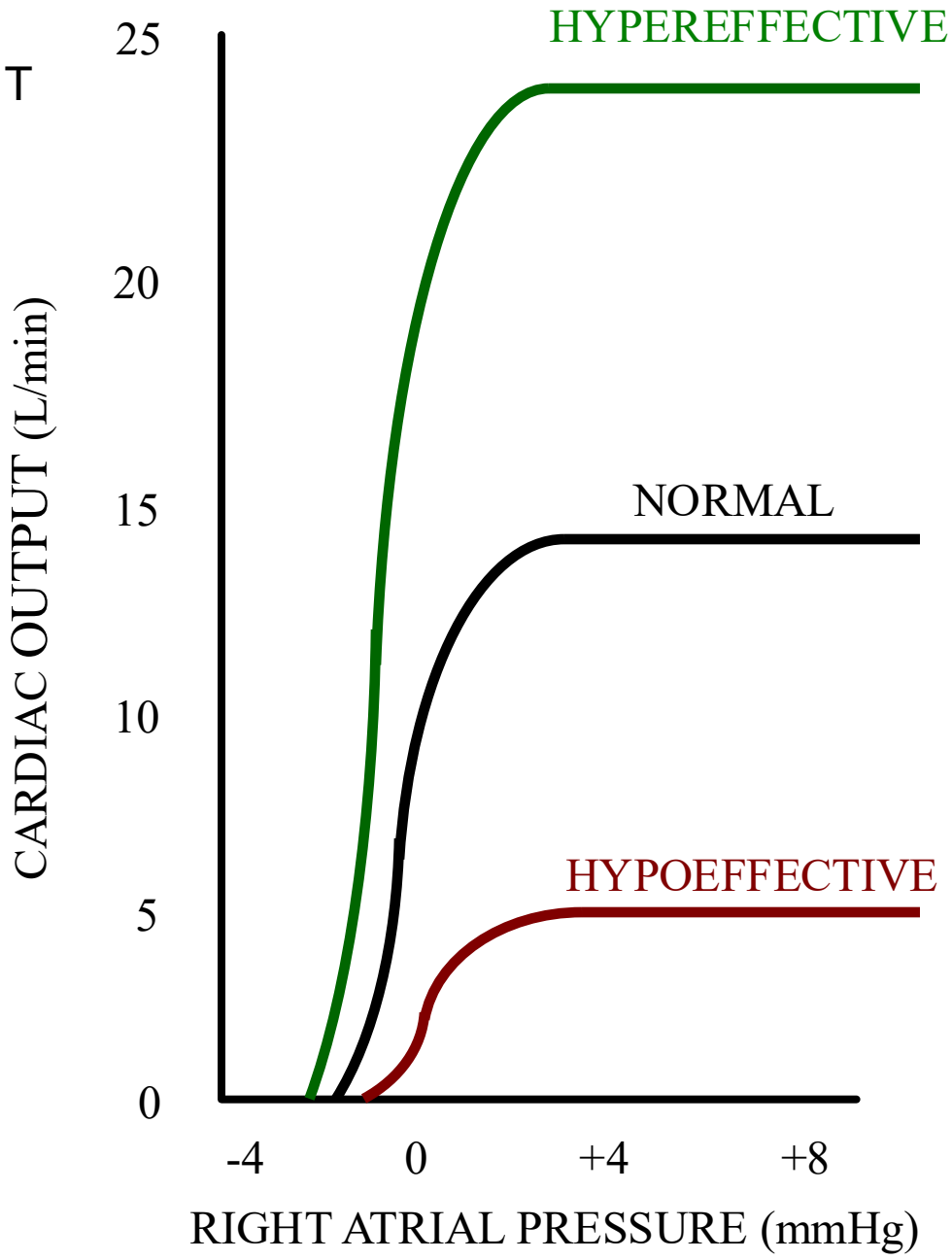
Ventricular Stroke Work Output

The work done by the left ventricle is 10 times the work done by the right.

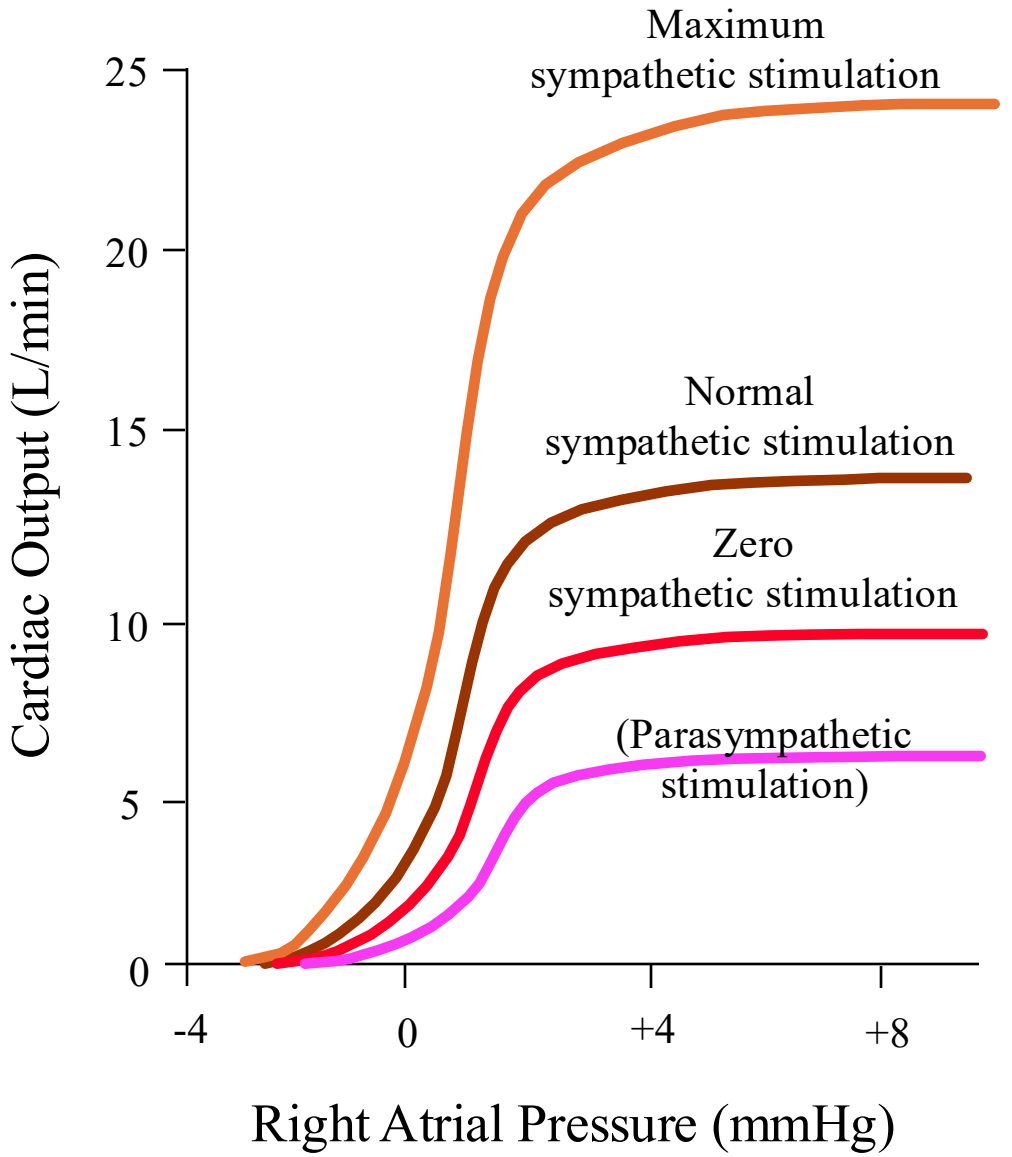




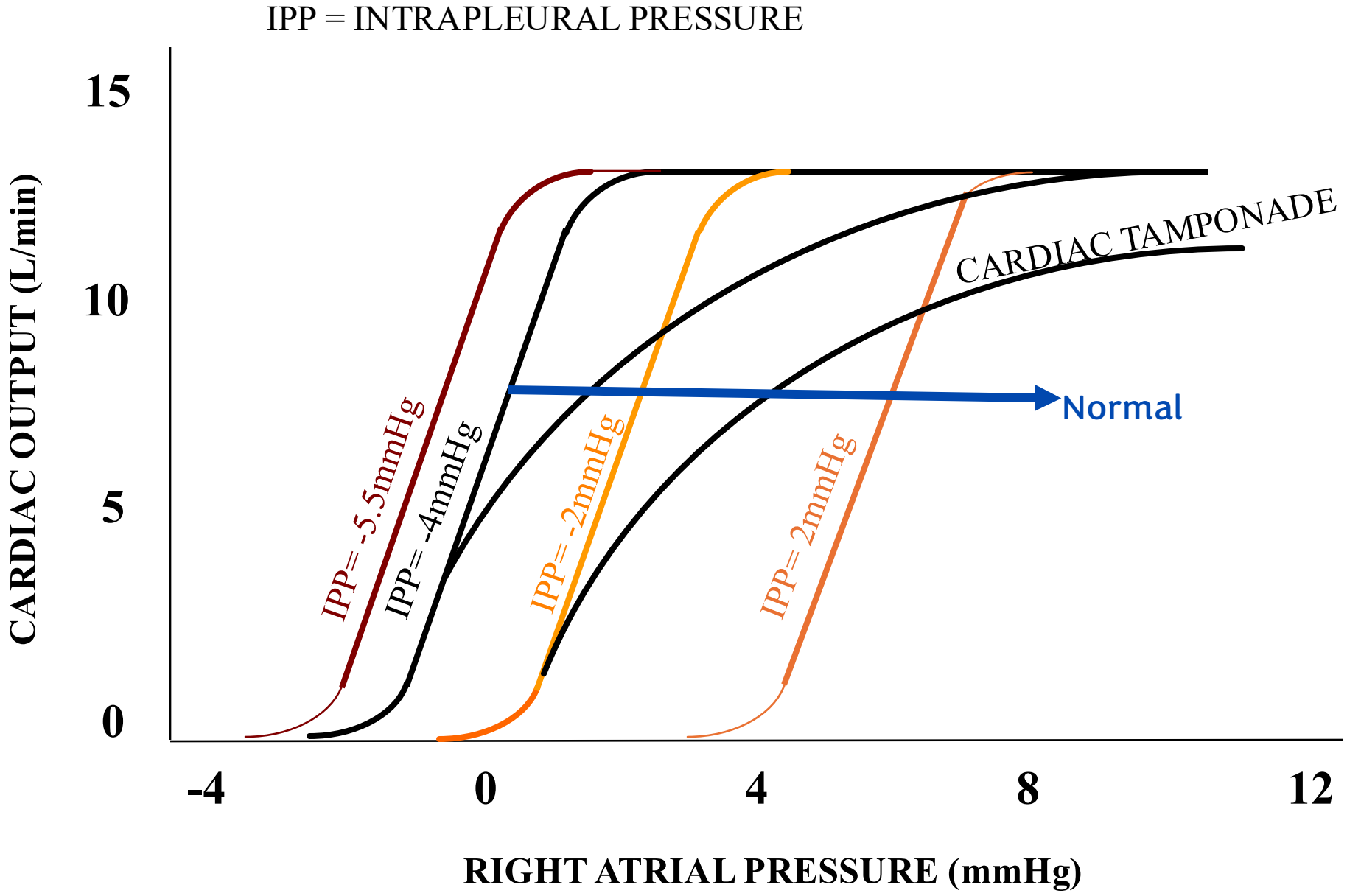
CARDIAC OUTPUT CURVES



Effect of Sympathetic and Parasympathetic Stimulation on Cardiac Output



Theoretically Parasympathetic Stimulation causes hypoeffective heart but in real physiology it does not due to numerous reasons.


IPP = INTRAPLEURAL PRESSURE
15
10
5
0
CARDIAC OUTPUT (L/min)
IPP= -5.5mmHg
IPP= -4mmHg
IPP= -2mmHg
IPP= 2mmHg
CARDIAC TAMPONADE
Normal
-4
0
4
8
12
RIGHT ATRIAL PRESSURE (mmHg)

How Intrapleural Pressure Shifts the Cardiac Function Curve

- The intrapleural pressure is the pressure surrounding the lungs, and it is normally **negative**, about **–4 mmHg (–5cmH2O)**. The intrapleural pressure around the heart is roughly **–5 mmHg**, while the right atrial pressure is close to **0 mmHg**. If intrapleural pressure becomes **less negative** (for example from –5 to –3 mmHg), the external pressure on the heart increases. To fill the right ventricle with the same amount of blood, the **right atrial pressure must rise** (for example from 0 to **+2 mmHg**) to maintain the venous pressure gradient.
- When intrapleural pressure increases, the **cardiac function curve shifts to the right** by the same amount, because the pressure gradient from the systemic veins to the right ventricle decreases, reducing venous return. The increase in right atrial pressure compensates for this reduced gradient. The **maximum cardiac output stays unchanged**, since the Frank–Starling mechanism is unaffected by external pressure.

How Cardiac Tamponade Alters Heart Filling

- Cardiac tamponade is an **increase in intrapericardial pressure**. It is treated by **pericardiocentesis**, which removes the excess pericardial fluid.
- Unlike intrapleural pressure, **intrapericardial pressure acts directly on the heart**, restricting its expansion.
- In cardiac tamponade, the **cardiac function curve does not shift in parallel** because ventricular filling is impaired. It becomes **much harder to reach maximum cardiac output**, since achieving it would require an **abnormally high right atrial pressure**.

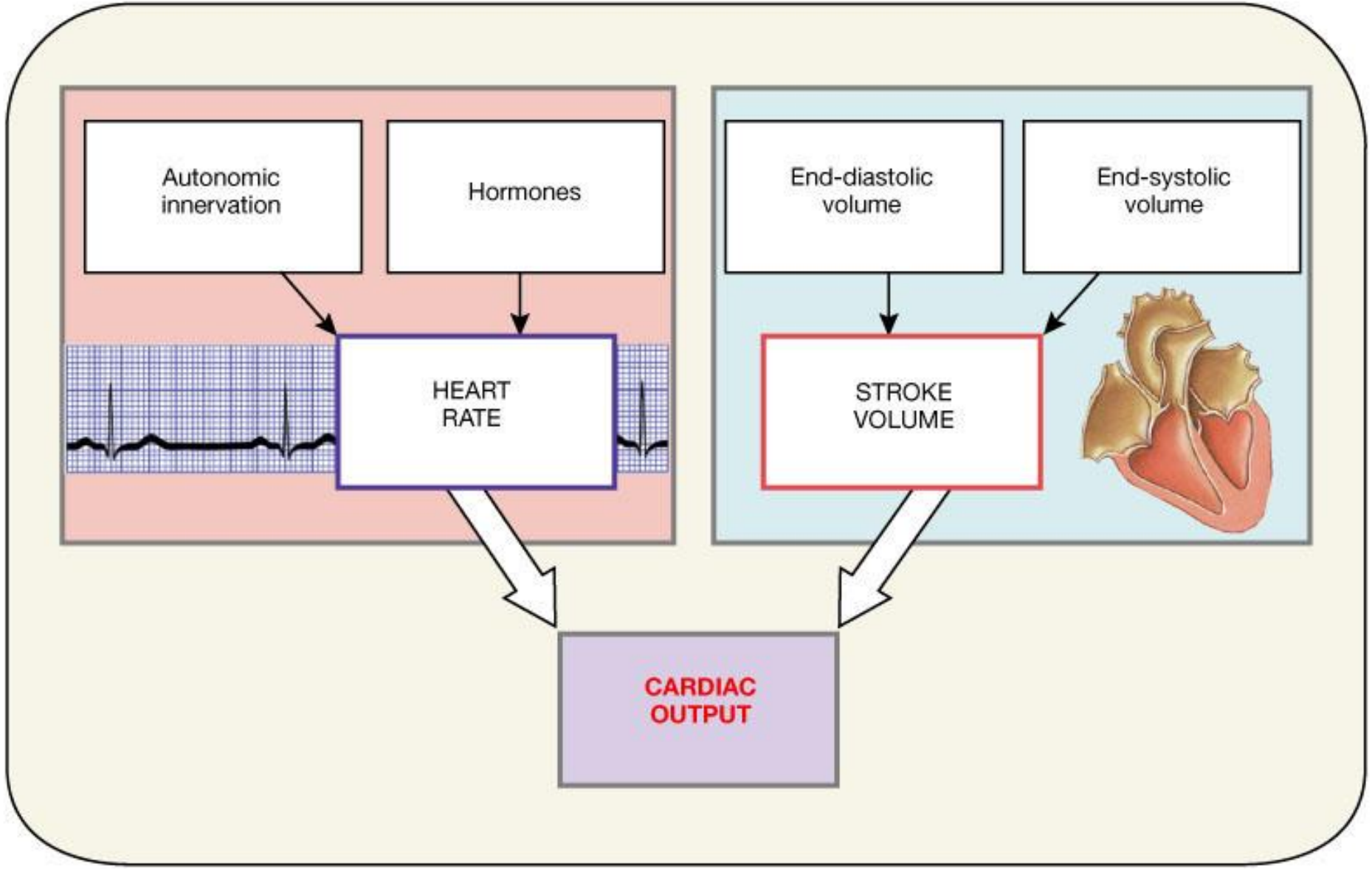
The Cardiac Output Curve

- Plateau of the CO curve is determined by heart strength (contractility + HR).
- ↑ Sympathetics ⇒ ↑ plateau
- ↓ Parasympathetics (HR) ⇒ (? plateau)
- Heart hypertrophy ⇒ ↑ plateau
- Myocardial infarction ⇒ (↓ plateau)
- Sympathetic stimulation and **heart hypertrophy** both **increase the cardiac output plateau.**
- **Myocardial infarction** decreases the plateau because it reduces **functional muscle mass.**

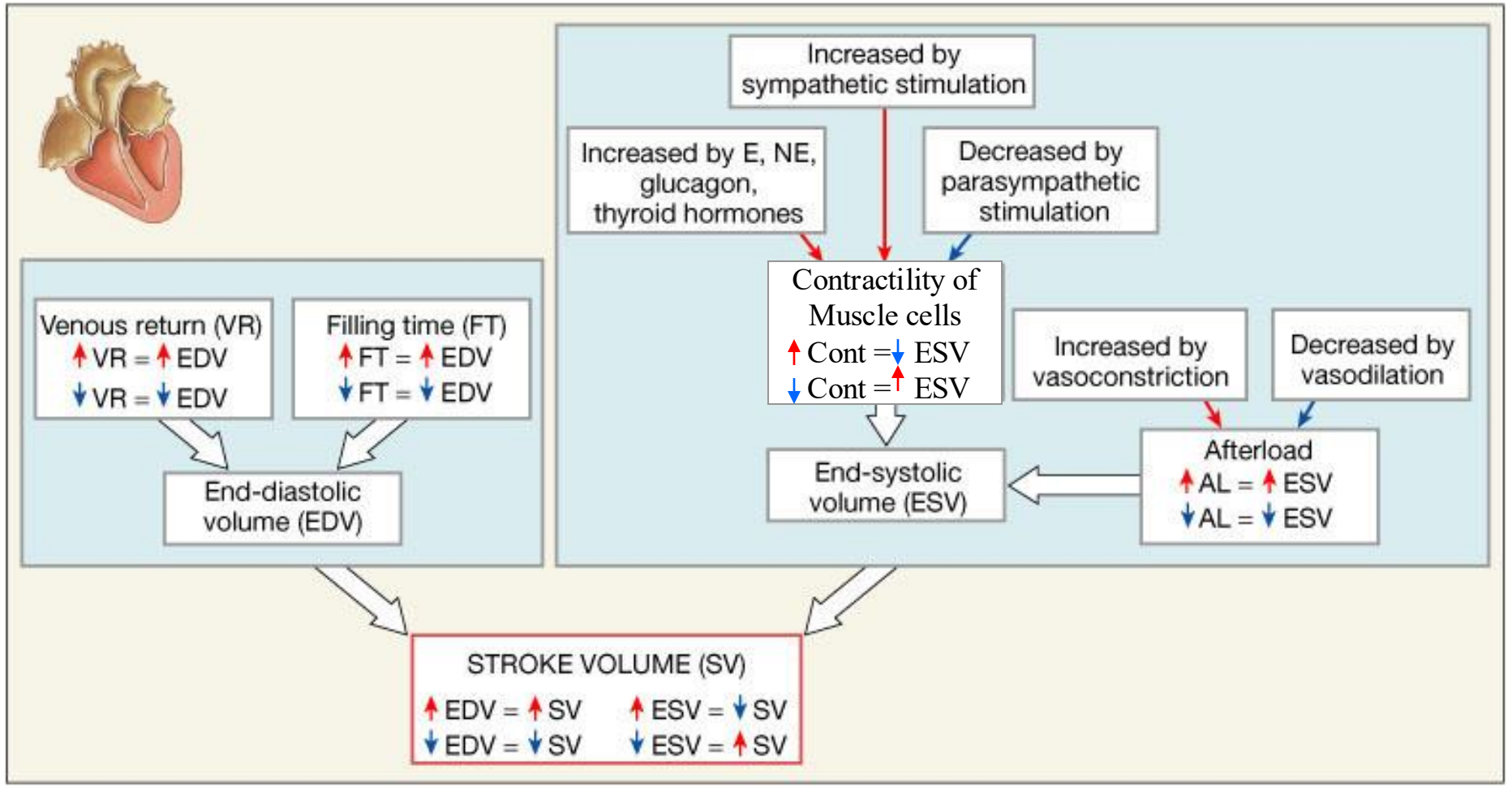
The Cardiac Output Curve (cont'd)

- Valvular disease ⇒ ↓ plateau
  - (stenosis or regurgitation)
- Myocarditis ⇒ ↓ plateau
- Cardiac tamponade ⇒ (↓ plateau)
- Metabolic damage ⇒ ↓ plateau
- **Valvular disease**, such as **aortic regurgitation**, **mitral regurgitation**, or **mitral stenosis**, also decreases the plateau.
- **Myocarditis** reduces the **active contractile mass** of the heart, leading to a lower plateau.
- In **cardiac tamponade**, the heart **never reaches the plateau**.

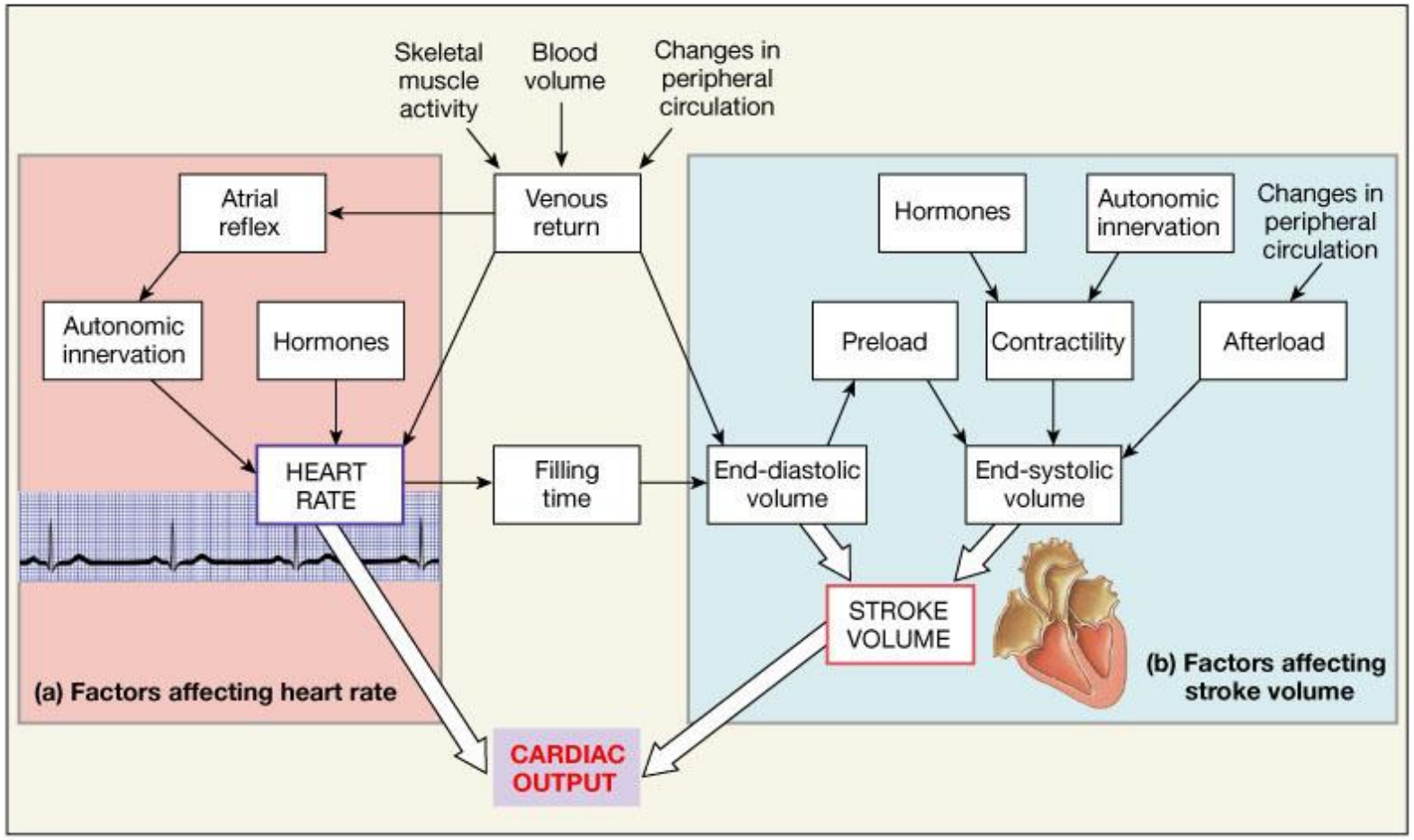
Factors Affecting Cardiac Output



Factors Affecting Stroke Volume

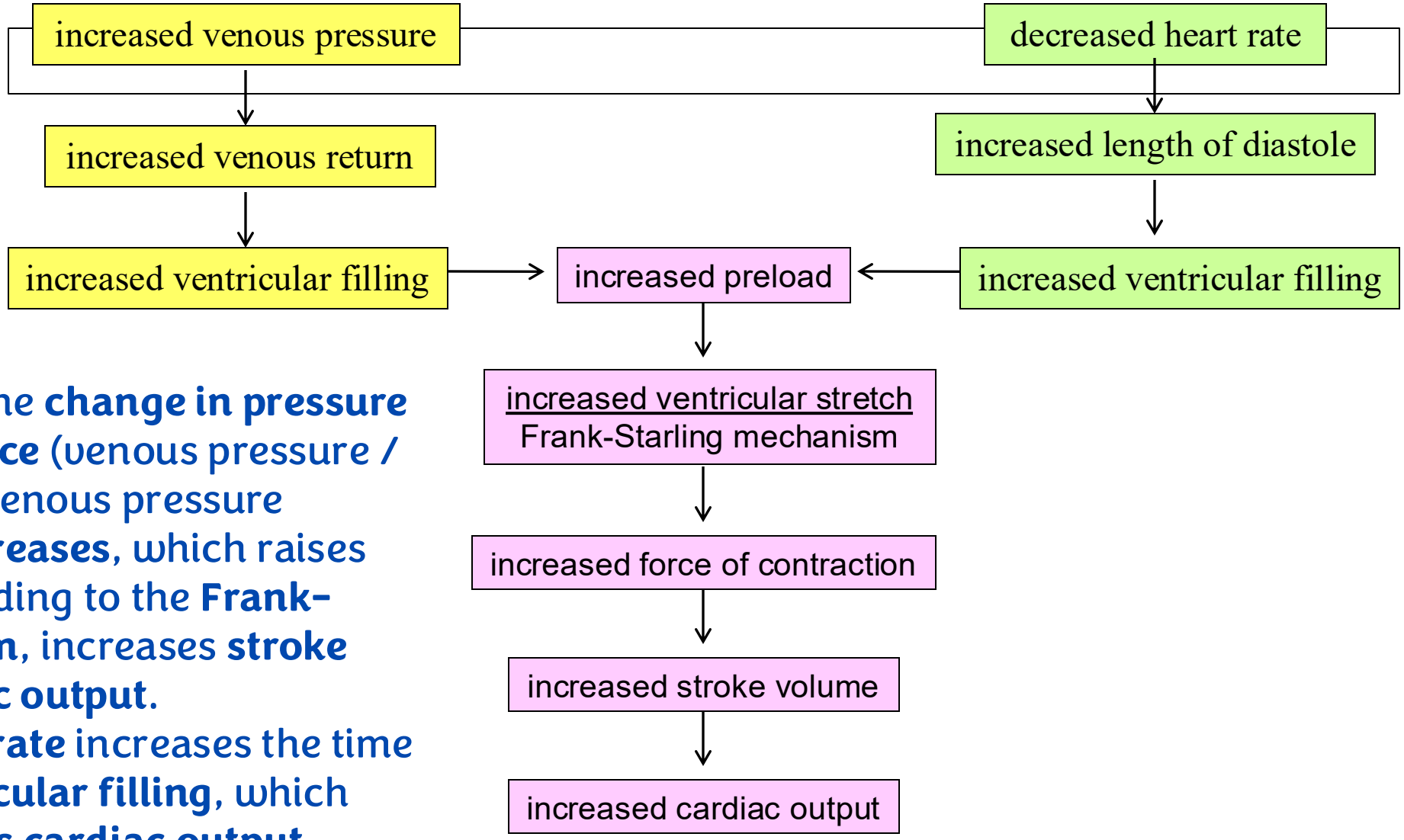


A Summary of the Factors Affecting Cardiac Output



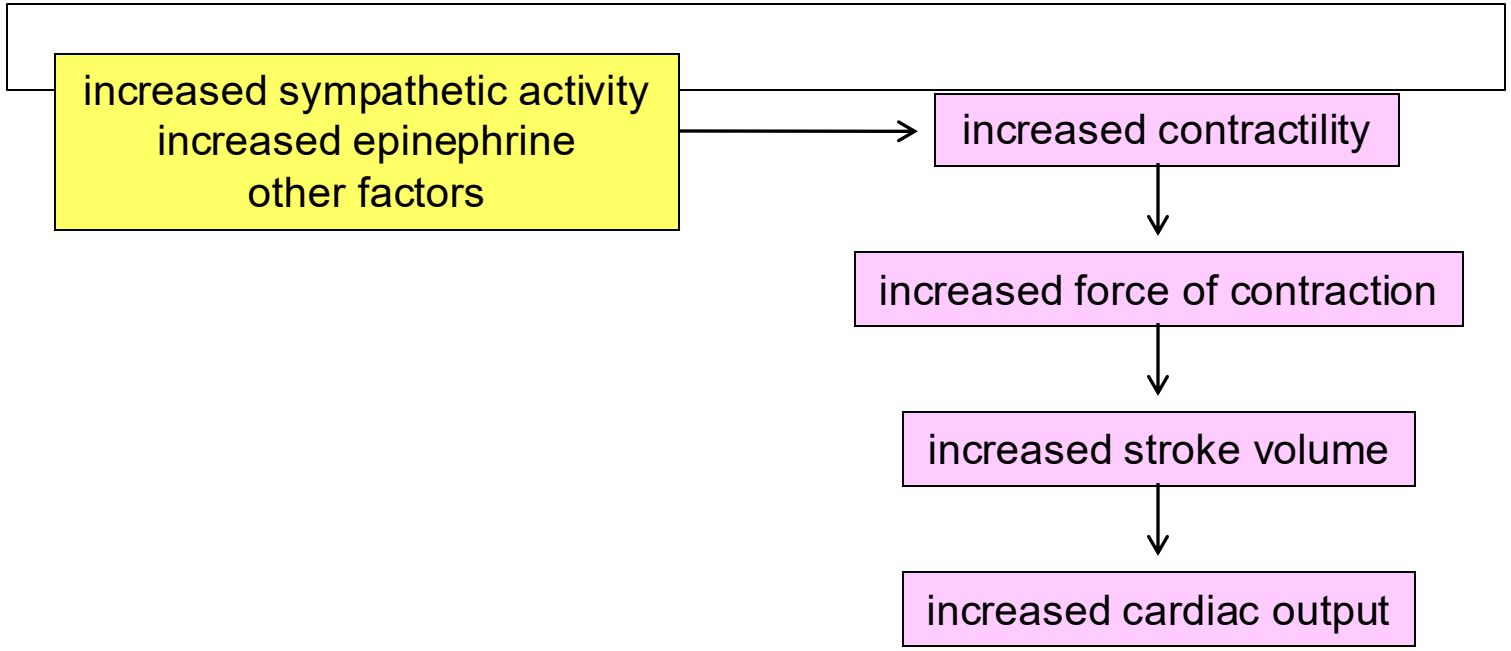
- When heart rate increases, **filling time decreases**, so **end-diastolic volume decreases**.
- When **venous return increases**, **end-diastolic volume increases**.
- When myocardial **contractility increases**—either by sympathetic stimulation or by the secretion of **epinephrine and norepinephrine**—the **end-systolic volume decreases**.
- An increase in **afterload** causes the **end-systolic volume to increase**.
- **Skeletal muscle activity** and **blood volume** both increase **venous return**.

REGULATION OF STROKE VOLUME: PRELOAD

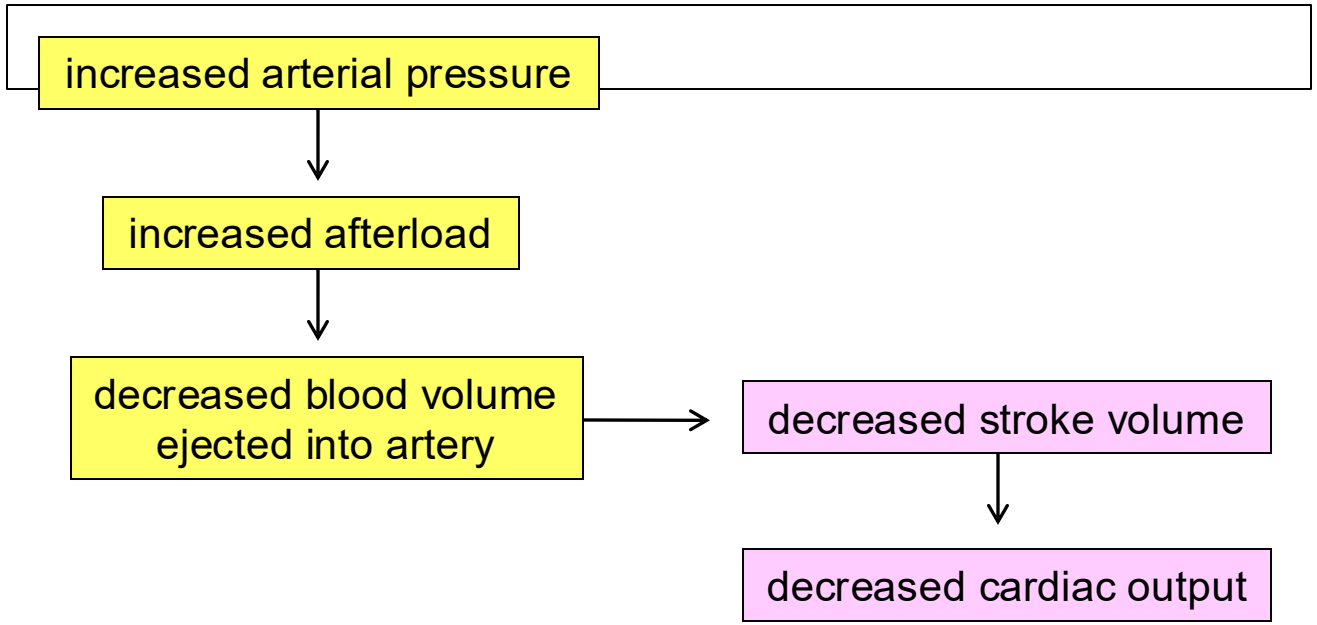


- Blood flow equals the **change in pressure divided by resistance** (venous pressure / resistance). When venous pressure increases, **flow increases**, which raises **preload** and, according to the **Frank–Starling mechanism**, increases **stroke volume** and **cardiac output**.
- A **decreased heart rate** increases the time available for **ventricular filling**, which ultimately **increases cardiac output**.

REGULATION OF STROKE VOLUME: CONTRACTILITY



REGULATION OF STROKE VOLUME: AFTERLOAD

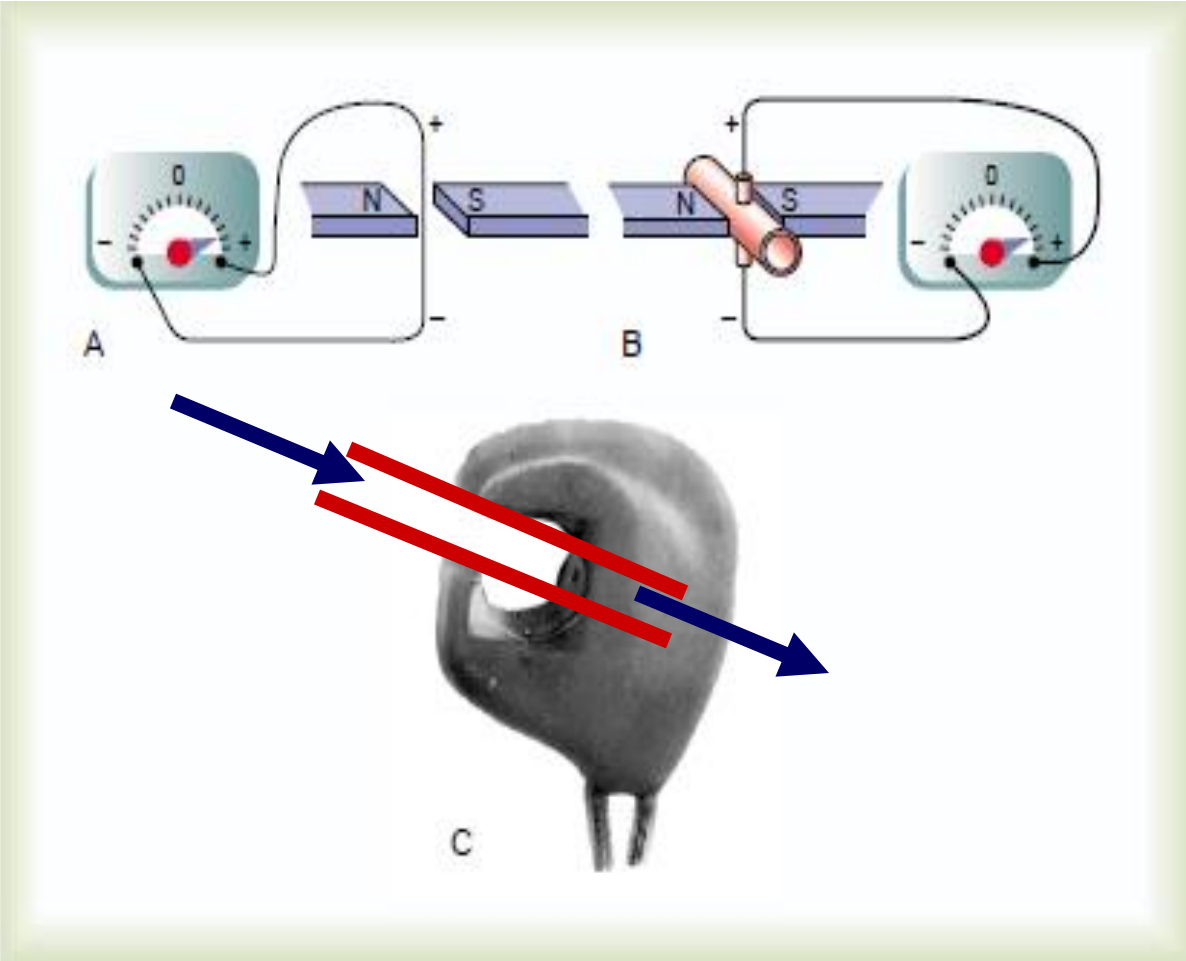


Increased arterial pressure raises **afterload**, which decreases the amount of blood ejected into the artery. This leads to a **reduced stroke volume** and a **decrease in cardiac output**, because the **resistance to blood flow from the ventricle into the aorta becomes higher**.

Measurement of Cardiac Output

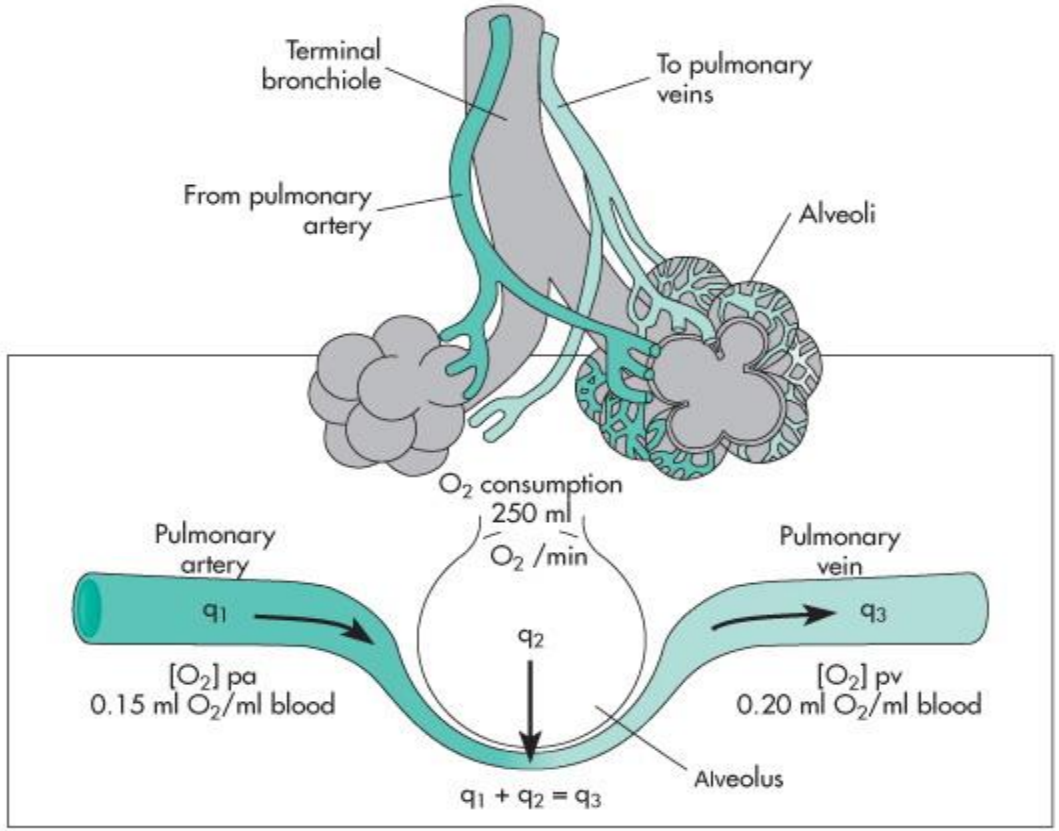
- Electromagnetic flowmeter
- Indicator dilution (dye such as cardiogreen)
- Thermal dilution
- *Oxygen Fick Method*
- **CO = (O_2 consumption) / (A–V O_2 difference)**
- We cannot measure cardiac output directly by cutting the aorta and collecting blood from humans.

Electromagnetic Flowmeter



Measurement of Blood Flow Using an Electromagnetic Flowmeter

- We place the artery between two **magnetic poles** and attach two **electrodes** connected to a galvanometer. Blood flowing through the magnetic field generates an **electromagnetic current** that is directly proportional to the flow. The galvanometer detects the **change in voltage**, which reflects the **speed of blood flow**. The magnitude of the induced voltage is directly proportional to the **velocity of the fluid**, and the device's electronics convert this voltage into a measurable **flow rate**.
- The galv anometer is **calibrated** by running known volumes (for example, 1 liter, then 2 liters) and marking the corresponding changes.
- However, this device is **not practical in humans except during open-chest surgery**.



$q_1 = CO \times C_vO_2$

q_2 = amount of oxygen uptake by the lungs

$q_3 = CO \times C_aO_2$ and equals = $CO \times C_vO_2 + O_2$ uptake

Oxygen uptake = $CO \times (C_aO_2 - C_vO_2)$

CO = Oxygen uptake / $(C_aO_2 - C_vO_2)$

CO = Cardiac Output

C_aO_2 = Arterial oxygen concentration

C_vO_2 = Venous oxygen concentration

q_1 = Amount of O_2 carried to the lungs by the pulmonary artery

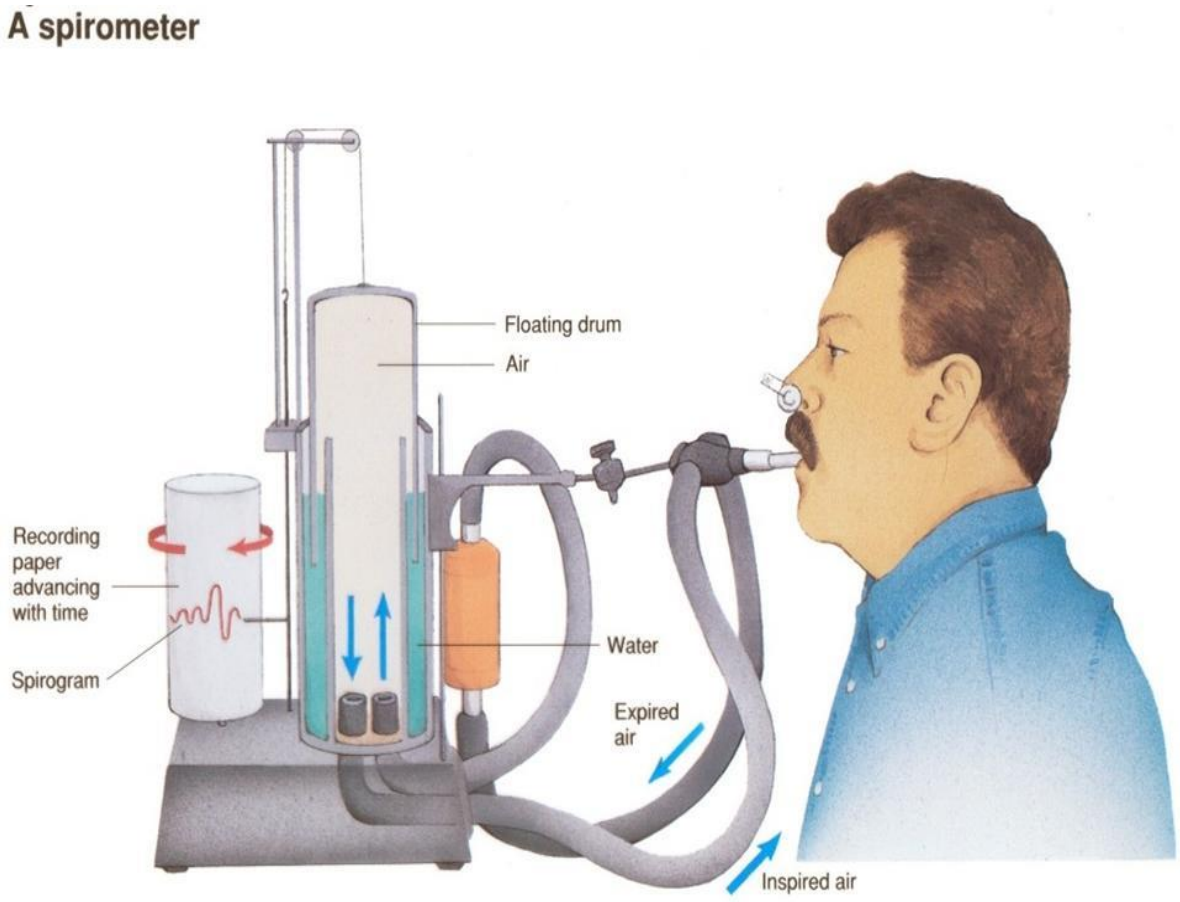
q_2 = Amount of O_2 taken up by the lungs (oxygen uptake)

q_3 = Amount of O_2 carried away from the lungs by arterial blood

Fick principle

- The amount of blood that reaches the lungs through the **pulmonary artery** equals the **cardiac output**. To determine the amount of oxygen carried in that blood, we multiply the **oxygen concentration in the blood** by the **cardiac output**. The **oxygen consumption per minute** is measured using a **spirometer**.
- The amount of oxygen returning from the lungs to the heart through the **pulmonary veins** also equals the **cardiac output times the oxygen concentration** in the pulmonary venous blood.
- q_1 is the **cardiac output** multiplied by the **oxygen concentration in mixed venous blood**.
- Because oxygen concentration varies in different veins, the best place to measure it is the **pulmonary artery**, or, if necessary, the **right ventricle**. Blood taken from these sites is called **mixed venous blood**.
- The **arterial oxygen concentration** is the same throughout the arterial system until the capillaries, since no exchange occurs before them. Arterial samples are usually taken from the **radial artery**.

Spirometer



Oxygen is supplied to the device, and the tester is asked to breathe through it for a set period of time. We then measure the **oxygen uptake per minute**.

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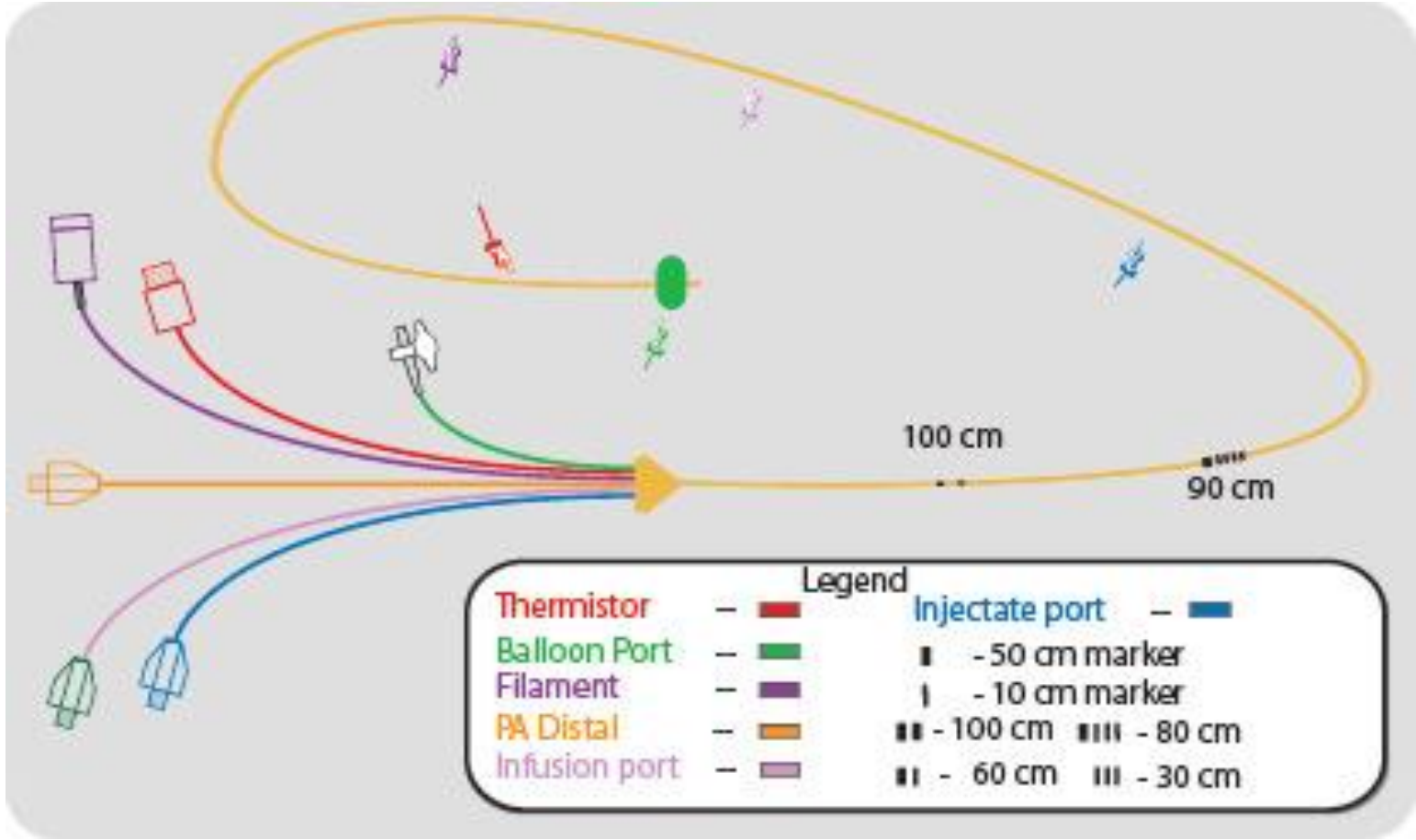
Swan-Ganz Catheter

The Swan-Ganz catheter is inserted through a central vein and advanced through the right atrium and right ventricle until it reaches the pulmonary artery. The catheter has several ports, such as one for temperature measurement, one for injections or blood sampling, and a balloon port at the tip. It is used mainly in anesthesia and critical care for hemodynamic monitoring.



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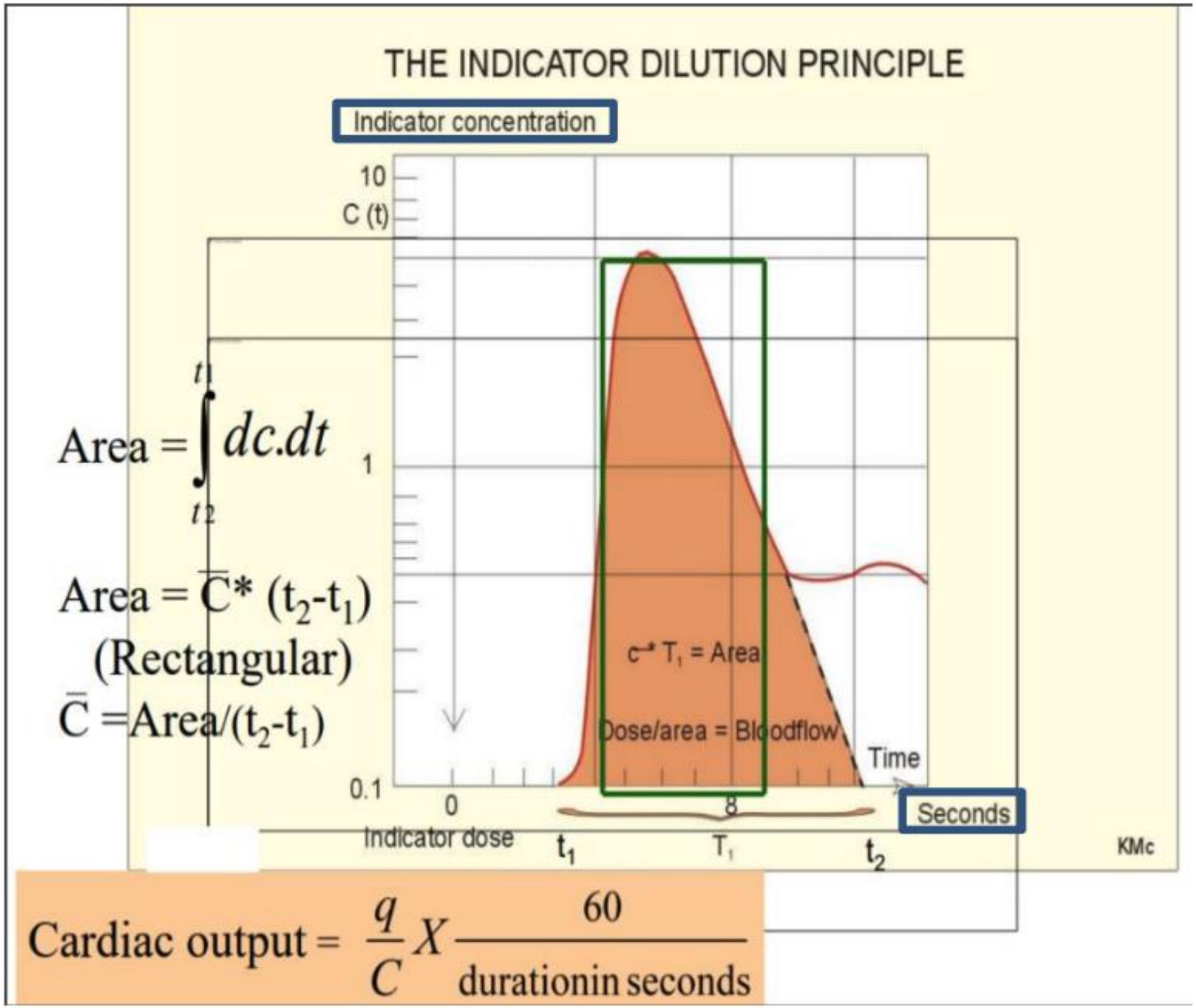
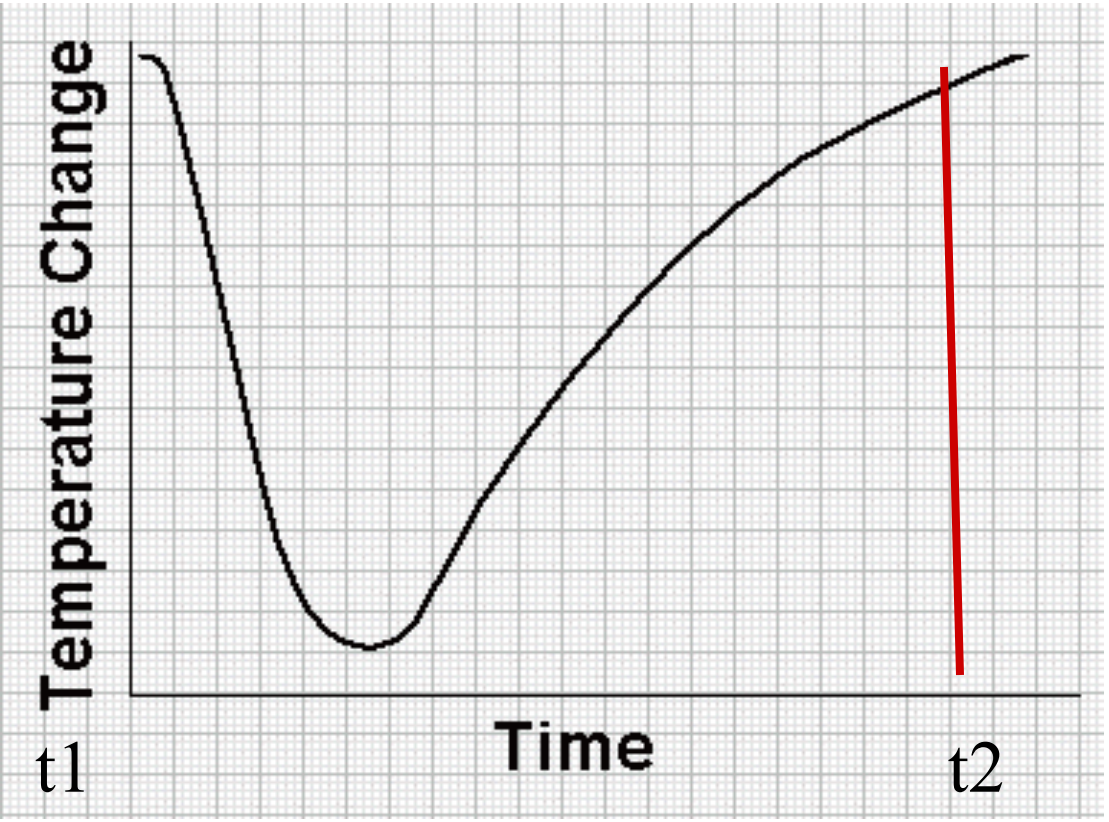
O_2 Fick Problem

- If pulmonary vein O_2 content = **200 ml O_2/L blood**
- Pulmonary artery O_2 content = **160 ml O_2/L blood**
- Lungs add **400 ml O_2/min**
- What is cardiac output?
- **Answer:** 400 / (200 – 160) = **10 L/min**
- The cardiac output equals the oxygen uptake over the difference between the arterial and venous blood.

An indicator is given and it's concentration is measured over time



Thermodilution Method Curve



$$\text{AREA} = \int_{t1}^{t2} dT.dt$$

Cold saline is injected into the blood through the **Swan-Ganz catheter**, and the resulting **change in temperature** is recorded. This produces a curve, and the **area under the curve** is used to calculate cardiac output.

PHYSIOLOGY QUIZ

LECTURE 9

رسالة من الفريق العلمي

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Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1	Slide #58	Wrong quiz link	Working quiz link
V1 → V2	Slide #18, 4th point of the 1st point	Red curve	Brown curve