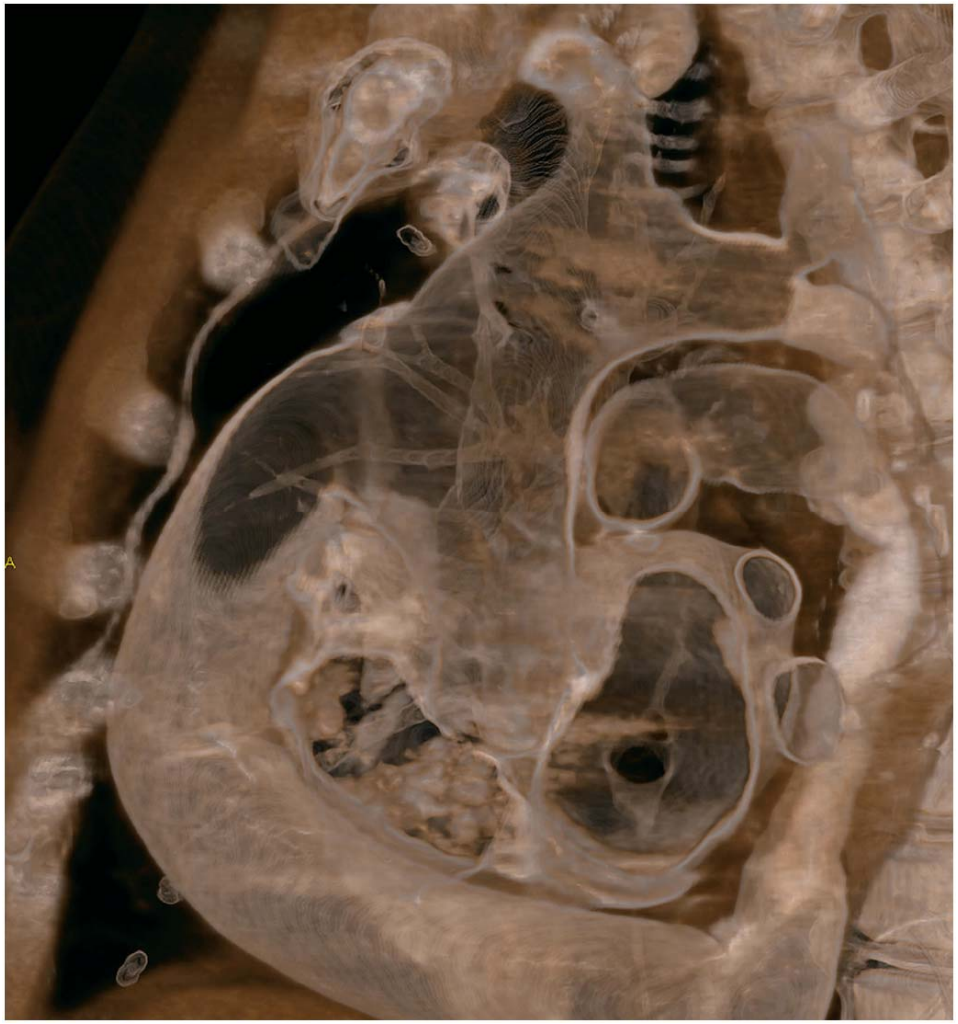
Chapter 19 (3)

# The Cardiac Cycle



# Learning Objectives

- **Describe the Cardiac Cycle**

- **Describe events that occur during the systolic and diastolic phases of the cardiac cycle**

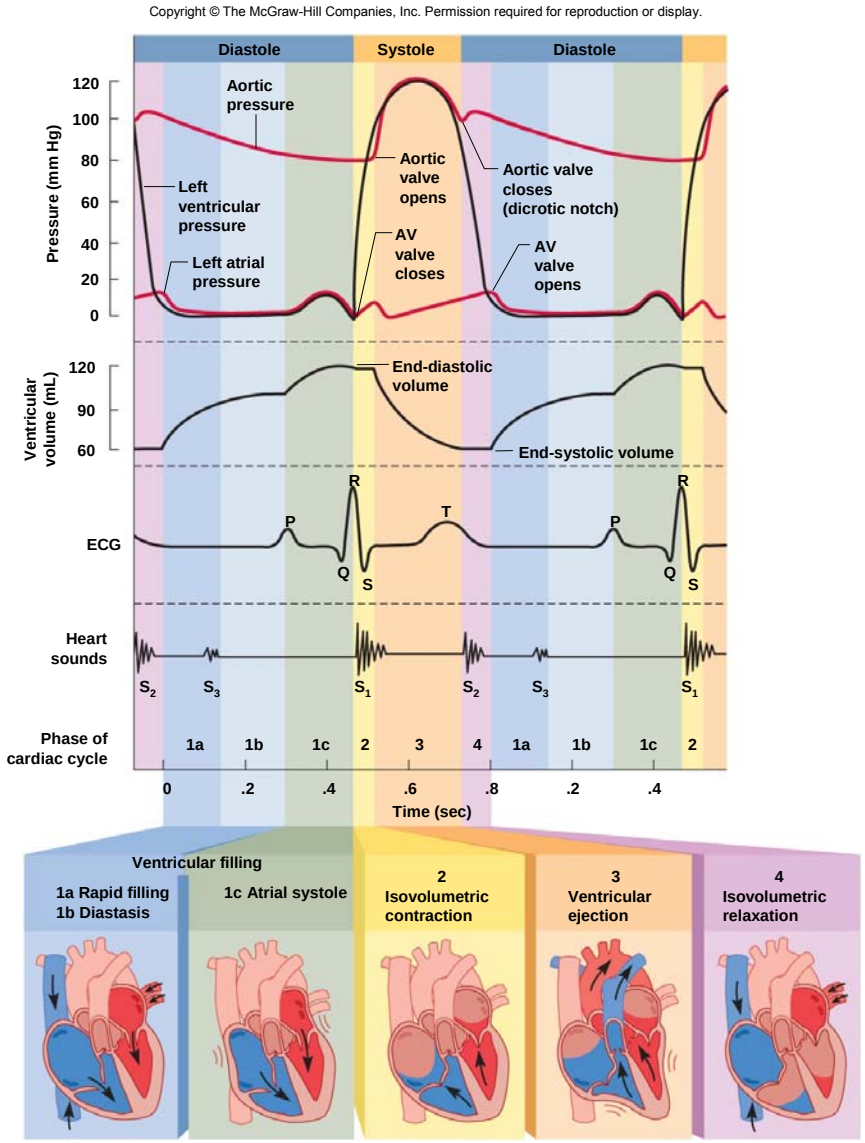
# Cardiac Cycle

- Cardiac cycle - one complete contraction and relaxation of all four chambers of the heart (0.8 sec)
- Atrial systole (atrial contraction) occurs during ventricles diastole (ventricle relaxation)
- Ventricular systole (ventricle contraction) occurs during atrial diastole (atrial relaxation)
- The quiescent period occurs when all four chambers are relaxed (diastolic phase)

# Timing of Cardiac Cycle

- In a resting person
  - atrial systole last about 0.1 sec
  - ventricular systole about 0.3 sec
  - quiescent period, when all four chambers are in diastole, 0.4 sec
- Total duration of the cardiac cycle is therefore 0.8 sec in a heart beating 75 bpm
- To analyze these events which occur in all four chambers, it is best to focus on and follow the events which occur in a single chamber.
- We will focus on events which occur in a ventricle.

# Major Events of Cardiac Cycle

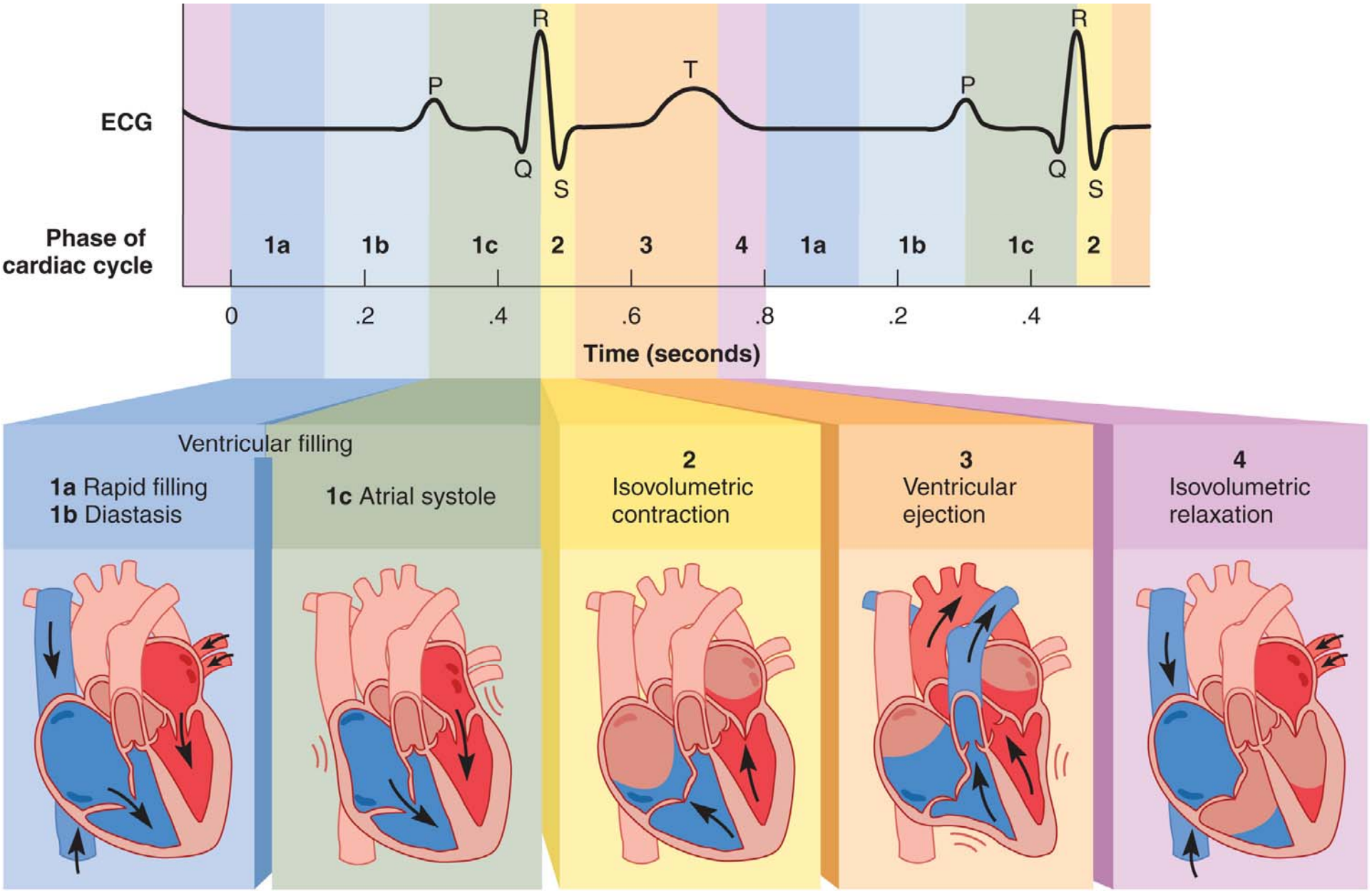



- **ventricular filling**
- **isovolumetric contraction**
- **ventricular ejection**
- **isovolumetric relaxation**

# Phases of Cardiac Cycle

- *ventricular filling / associated in part with atrial systole*
- *isovolumetric contraction of ventricles*
- *ventricular ejection*
- *isovolumetric relaxation*
- *all events in one cardiac cycle are completed in 0.8 second*

# Phases of Cardiac Cycle



# Events of Ventricular Filling (1 of 3)

- Events associated with ventricular diastole = Ventricular Filling
  - Ventricles expand
  - Ventricular pressure drops below pressure in atria
  - AV valves open and blood flows into the ventricles

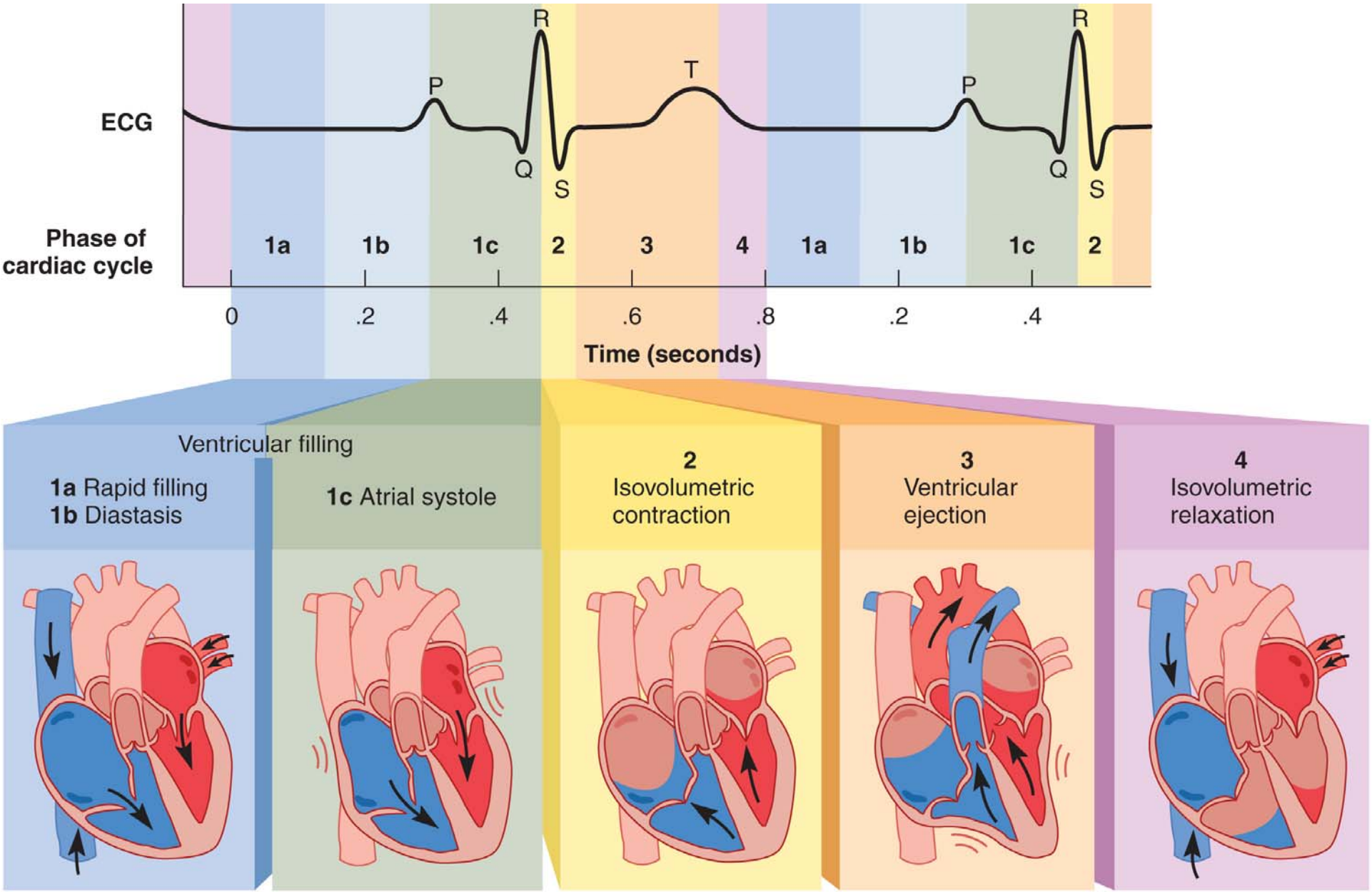
# Events of Ventricular Filling (2 of 3)

- Ventricular filling occurs in three phases:
  - rapid ventricular filling - first one-third
    - blood enters very quickly / before atrial systole begins
  - diastole continues in atria - second one-third
    - marked by slower filling
    - P wave occurs at the end of diastasis
  - atrial systole - final one-third
    - atria contract

## Events of Ventricular Filling (3 of 3)

- Reaching the "end-diastolic volume" of ventricles (EDV)
  - amount of blood contained in ventricles at the end of ventricular filling
  - same volume in right and left ventricle // must never be different
  - 130 mL of blood in each ventricle at end of ventricular diastole

# Events of Ventricular Filling



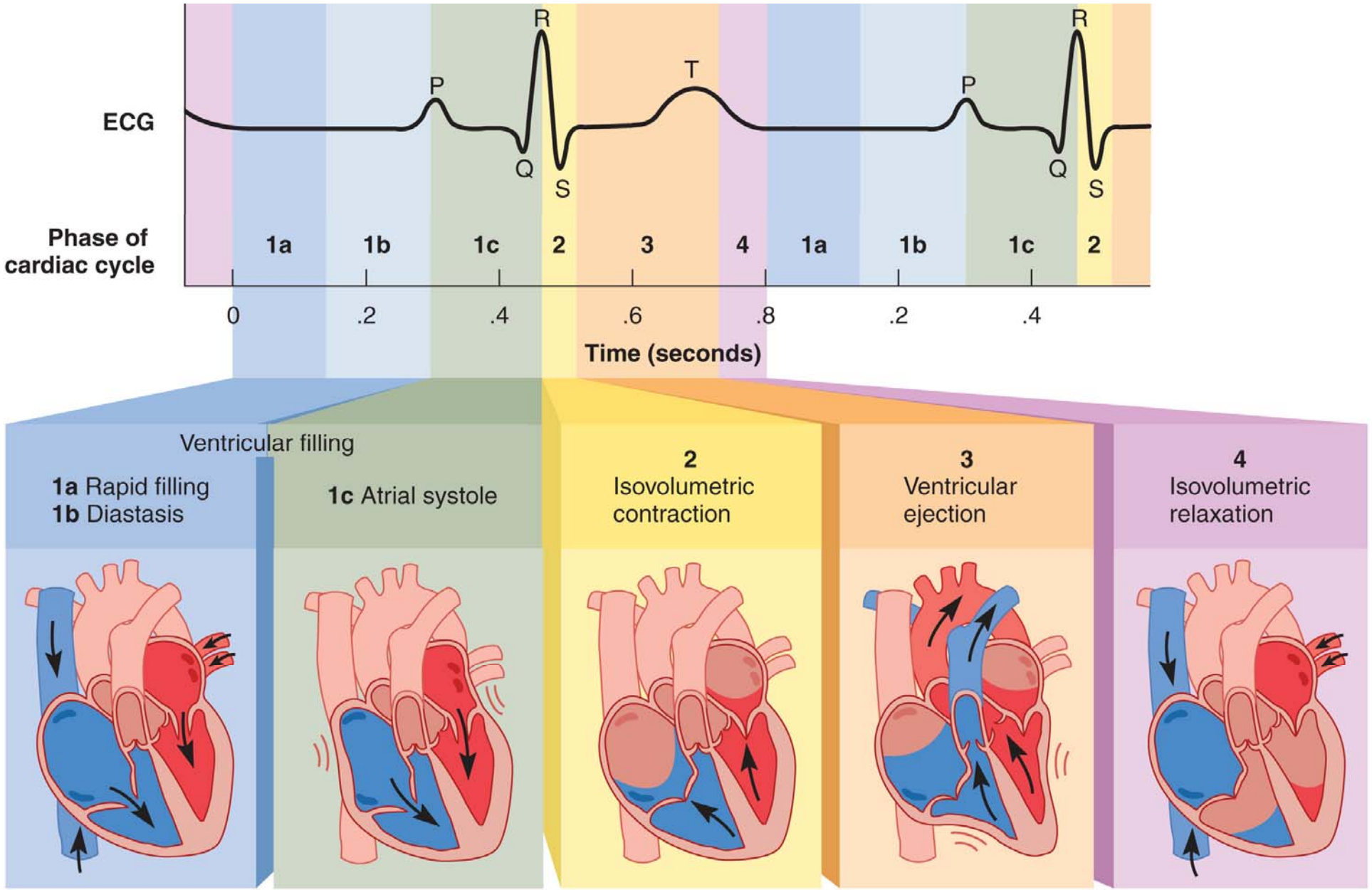
# Events of Iso-volumetric Contraction (1 of 2)

- Atria repolarize and relax // remain in diastole for the rest of the cardiac cycle
- Ventricles depolarize
  - this initiates the QRS complex
  - Depolarization followed by the contraction
- AV valves close as ventricular blood pressure increases // forcing blood to surge back against the AV cusps
  - heart sound $S_1$ occurs at the beginning of this phase // closing of AV valves

## Events of Iso-volumetric Contraction (1 of 2)

- Now entering the '**isovolumetric**' contraction phase
  - ventricles contracting but they do not eject blood // why?
  - Note: both AV and semilunar values are STILL CLOSED
  - because pressure in the aorta (80 mm Hg) and in pulmonary trunk (10 mm Hg) is still greater than in the pressure in the two ventricles
- Cardiocytes exert force, but with all four valves closed, the blood cannot go anywhere // rapid increase in pressure

# Events of Iso-volumetric Contraction

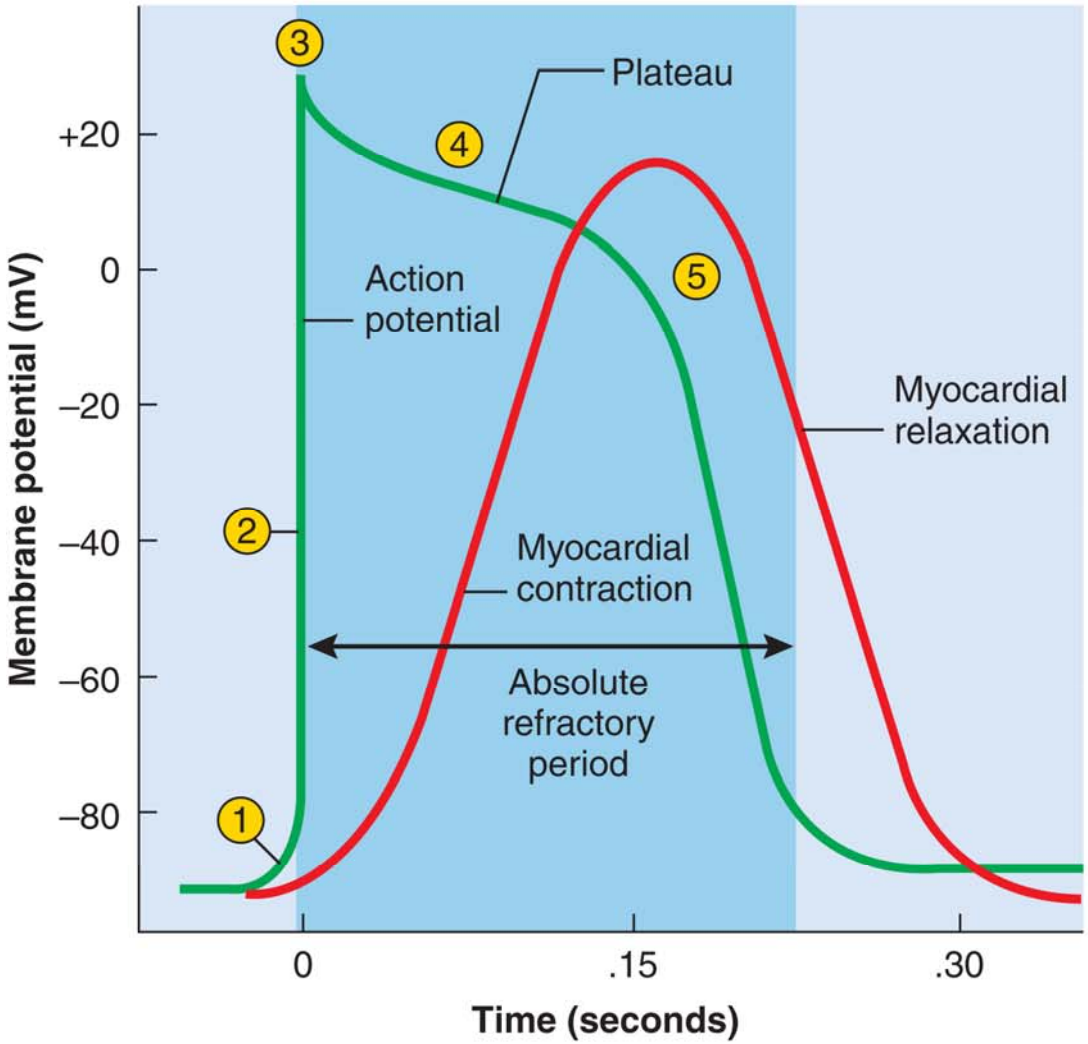


# Events of Ventricular Ejection (1 of 2)

- ejection of blood begins when the ventricular pressure exceeds arterial pressure and forces semilunar valves open
  - pressure peaks in left ventricle at about 120 mm Hg and 25 mm Hg in the right
- blood spurts out of each ventricle rapidly at first – rapid ejection
- then more slowly under reduced pressure – reduced ejection
- ventricular ejections last about 200 – 250 msec
  - corresponds to the plateau phase of the cardiocyte action potential

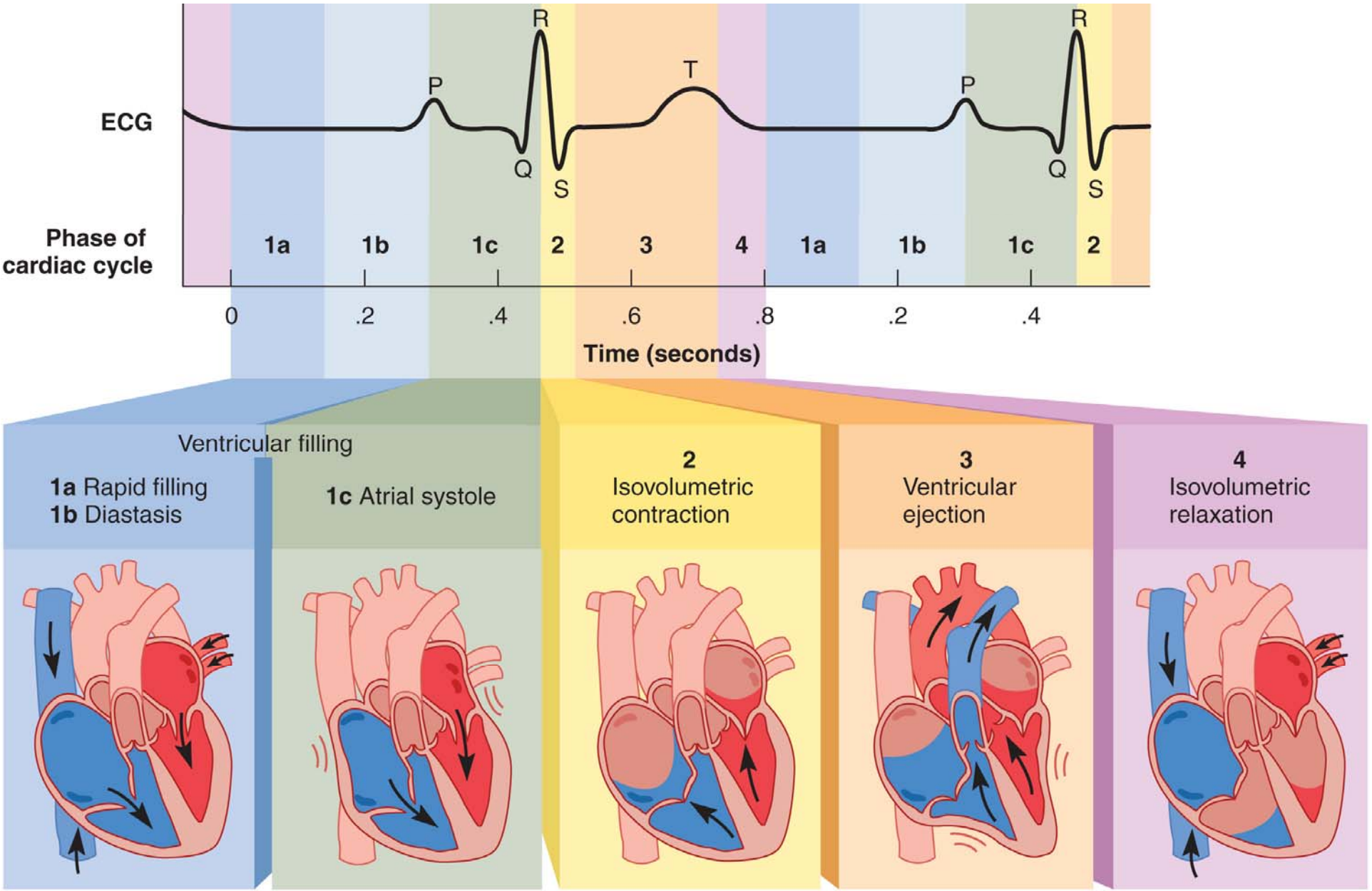
# Events of Ventricular Ejection (2 of 2)

- stroke volume (SV) of about 70 mL of blood is ejected of the 130 mL in each ventricle
  - ejection fraction of about 54%
  - as high as 90% in vigorous exercise
  - long prolonged contraction of ventricles associated with slow calcium channels // the plateau of the myocardiocyte action potential
- end-systolic volume (ESV) // 60 mL of blood left behind
- T wave occurs late in this phase




1. Voltage-gated $Na^+$ channels open.
2. $Na^+$ inflow depolarizes the membrane and triggers the opening of still more $Na^+$ channels, creating a positive feedback cycle and a rapidly rising membrane voltage.
3. $Na^+$ channels close when the cell depolarizes, and the voltage peaks at nearly +30 mV.
4. $Ca^{2+}$ entering through slow $Ca^{2+}$ channels prolongs depolarization of membrane, creating a plateau. Plateau falls slightly because of some $K^+$ leakage, but most $K^+$ channels remain closed until end of plateau.
5. $Ca^{2+}$ channels close and $Ca^{2+}$ is transported out of cell. $K^+$ channels open, and rapid $K^+$ outflow returns membrane to its resting potential.

# Events of Ventricular Ejection



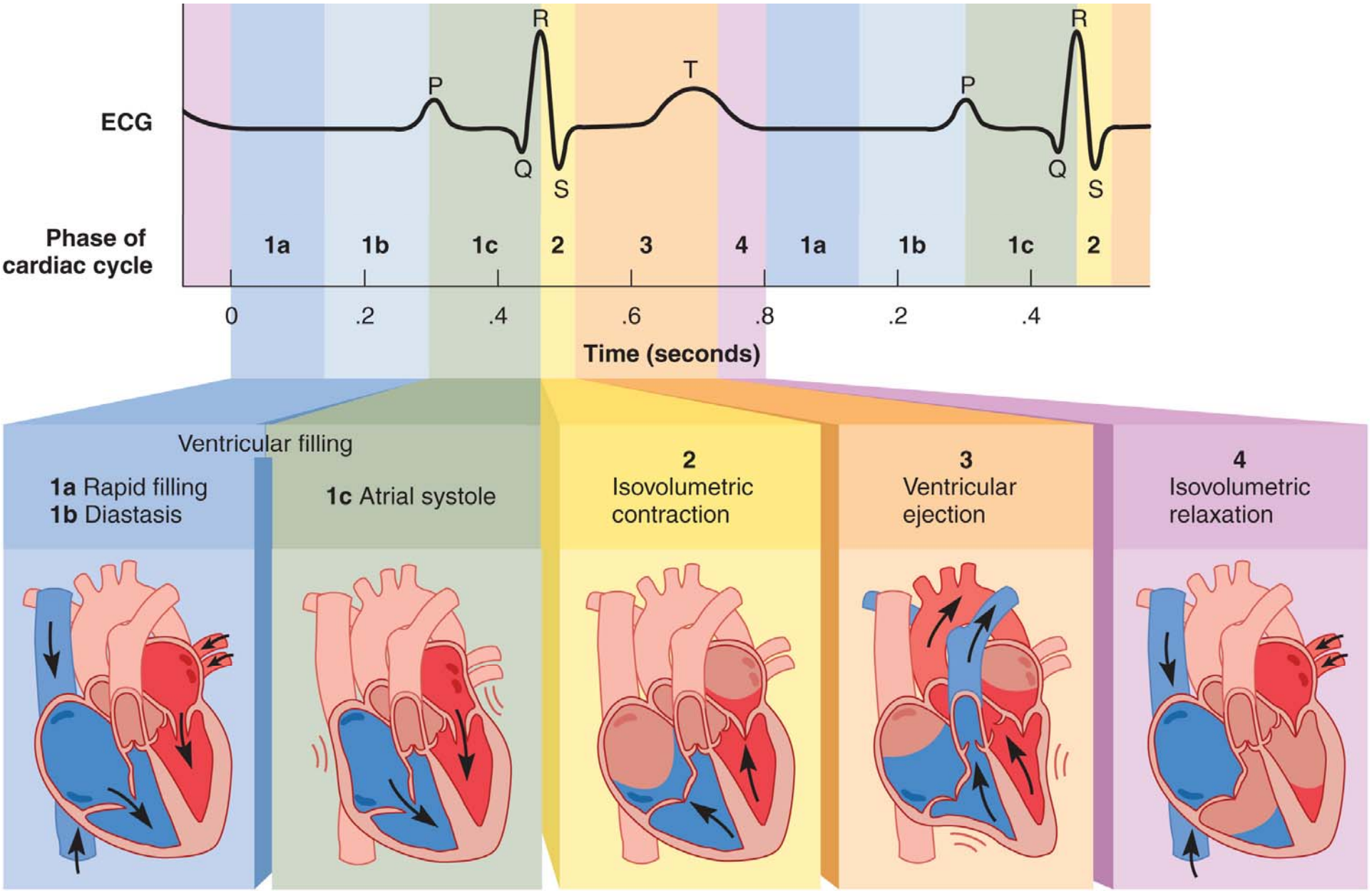
# Isovolumetric Relaxation

- Early **ventricular diastole *///*** when **T wave ends** and **the ventricles begin to expand**
- Elastic recoil and expansion would cause pressure to drop rapidly and suck blood into the ventricles
  - blood from the aorta and pulmonary briefly **flows backwards**
  - **filling the semilunar valves** and **closing the cusps**
  - creates a **slight pressure rebound** that appears as the **dicrotic notch** of the aortic pressure curve

# Isovolumetric Relaxation

- heart sound $S_2$ occurs as blood rebounds from the closed semilunar valves and the ventricle expands
- 'isovolumetric' because semilunar valves are closed and AV valves have not yet opened // ventricles are therefore taking in no blood
- when AV valves open, ventricular filling begins again

# Isovolumetric Relaxation

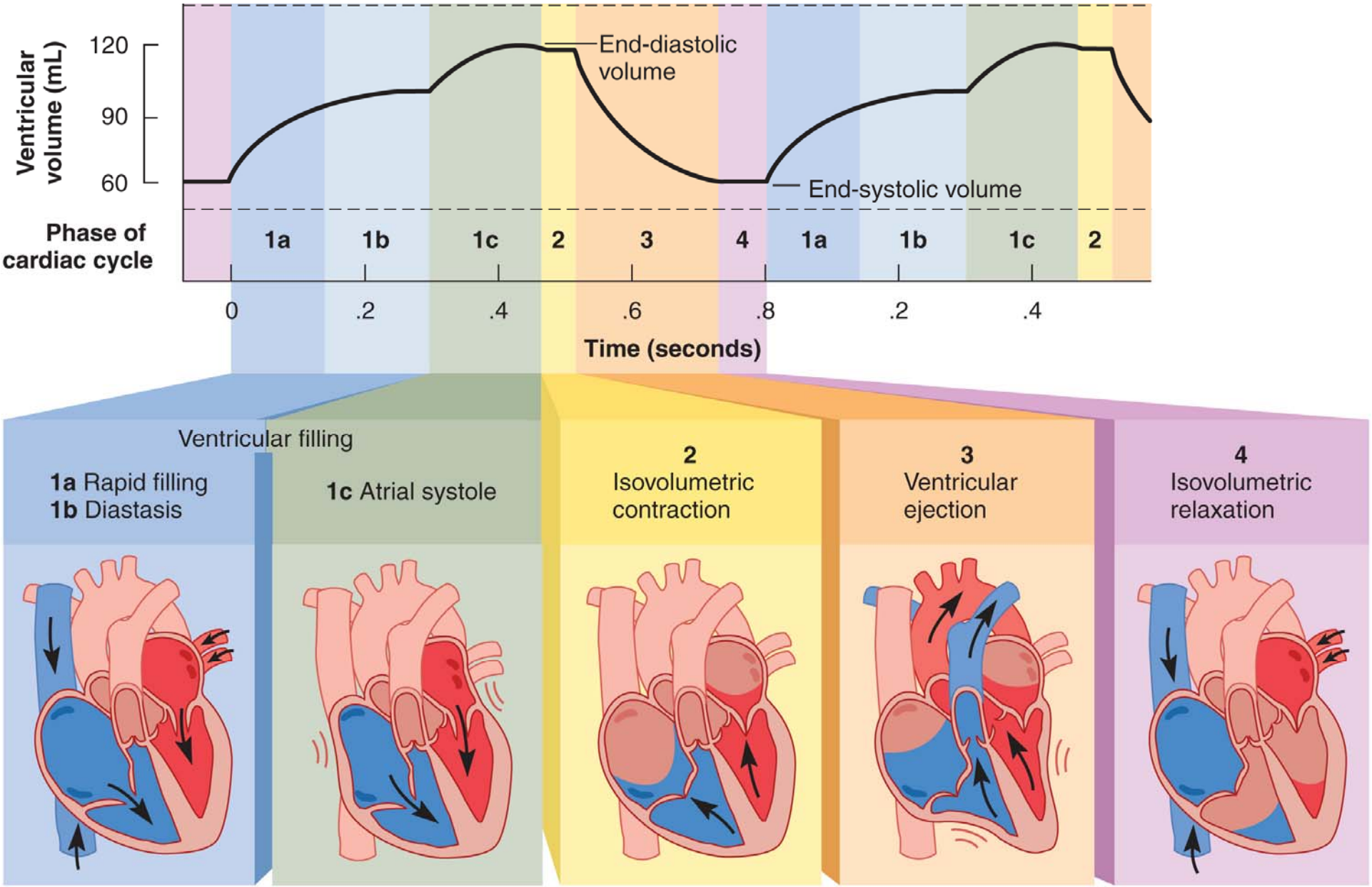


# Overview of Volume Changes

| | |
|---|---|
| end-systolic volume (ESV) | 60 ml |
| - passively added to ESV during atrial diastole | 30 ml |
| - added to ESV by atrial systole | 40 ml |
| Total end-diastolic volume (EDV) | 130 ml |
| stroke volume (SV) / blood ejected ejected by ventricular systole | -70 ml |
| end-systolic volume (ESV) | 60 ml |

*Note: both ventricles must eject same amount of blood*

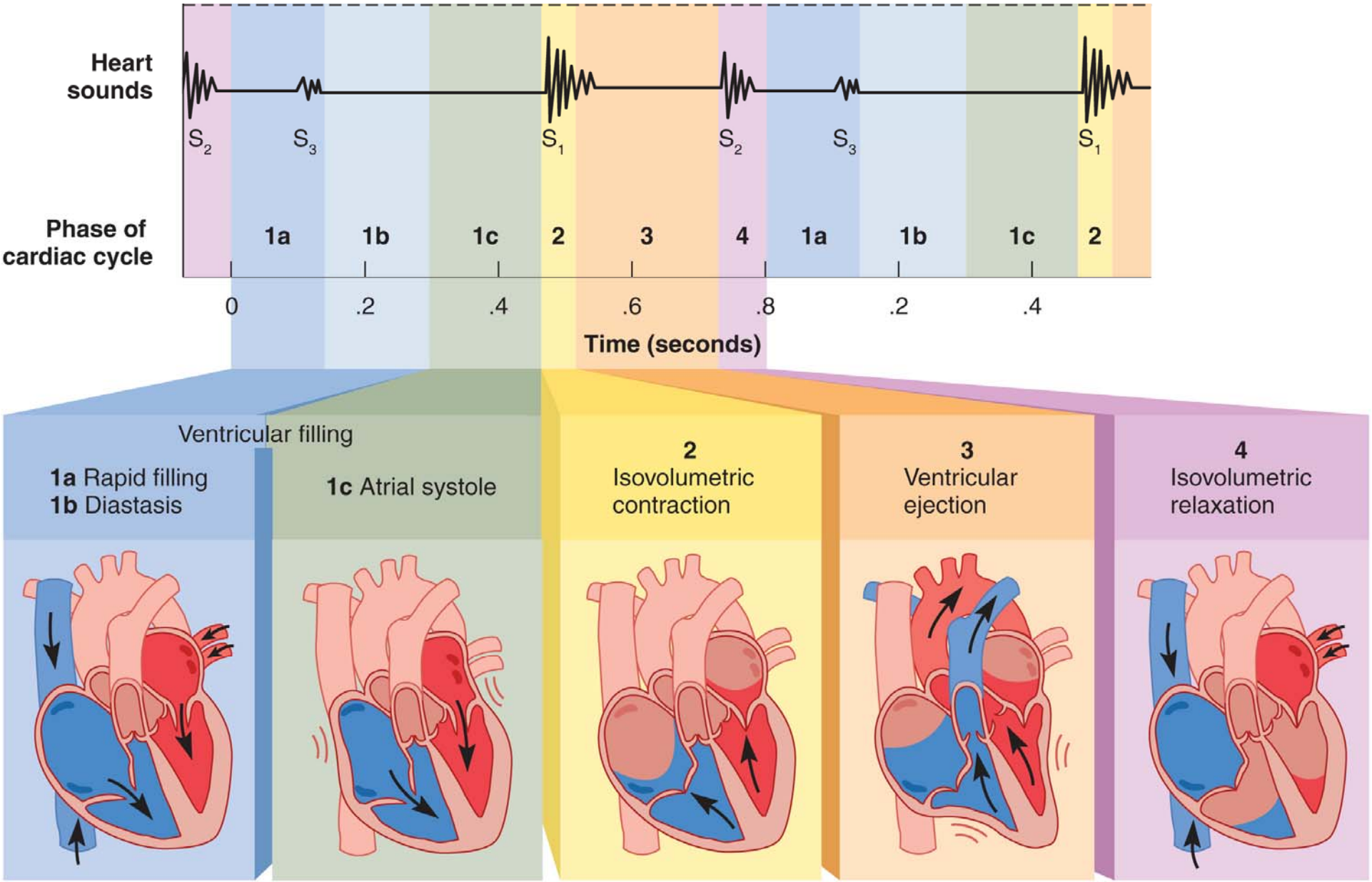
# Overview of Volume Changes



# Heart Sounds

- auscultation - listening to sounds made by body
- first heart sound ($S_1$), louder and longer “lubb”, occurs with closure of AV valves, turbulence in the bloodstream, and movements of the heart wall
- second heart sound ($S_2$), softer and sharper “dupp” occurs with closure of semilunar valves, turbulence in the bloodstream, and movements of the heart wall
- $S_3$ - rarely heard in people over 30

# Heart Sounds



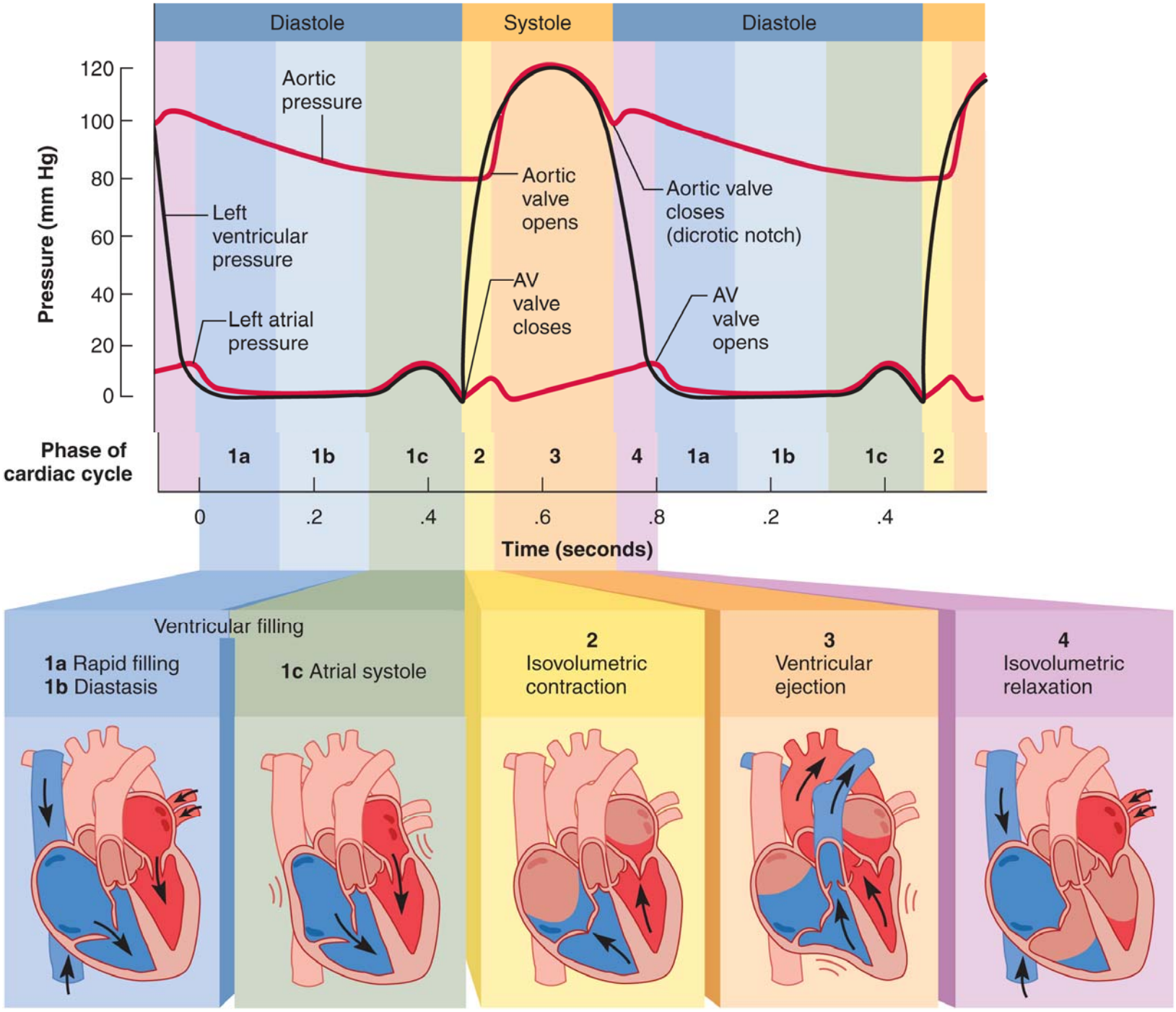
## Pressure Gradients / Blood Flow / Valve Function

- fluid flows only if it is subject to a pressure gradient /// fluid flows down a pressure gradient from high pressure to low pressure

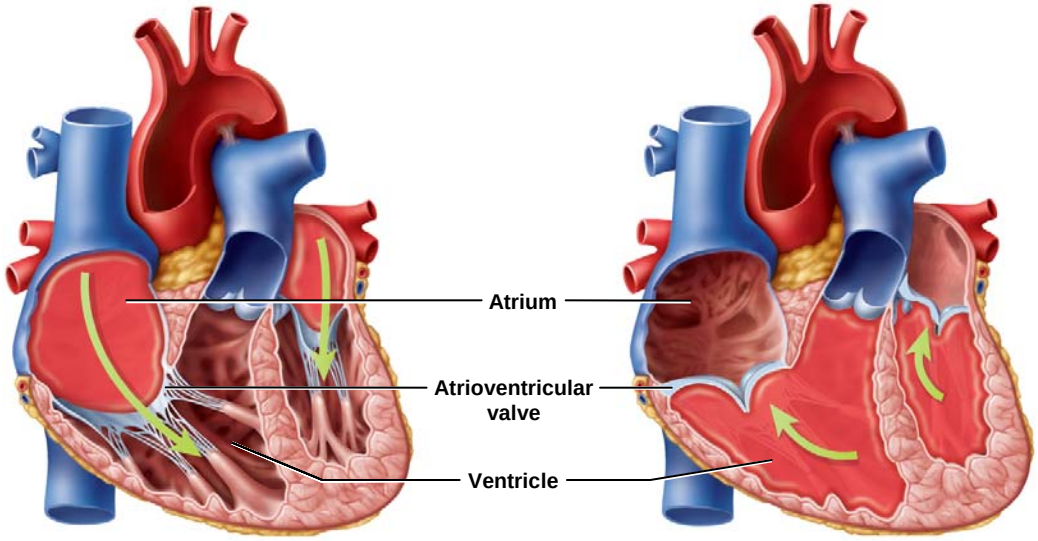
- Follow events that occur on left side of heart (note: similar events occur on the right side of the heart but with lower blood pressure / left and right heart functions must occur simultaneously)
  - when ventricle relaxes and expands (this is the **pre-load** in ventricle) // its internal pressure falls
  - if bicuspid valve is open, blood flows into left ventricle
  - when ventricle contracts, blood flow towards atria / internal pressure rises
  - AV valves close, pressure in ventricle continues rise // the aortic valve is pushed open (overcoming **after-load**) and blood flows into aorta from left ventricle

## Pressure Gradients / Blood Flow / Valve Function

- Opening and closing of valves are governed by these pressure changes
  - AV valves limp when ventricles relaxed
  - semilunar valves under pressure from blood in pulmonary truck and aorta at time when ventricles relaxed (the afterload)



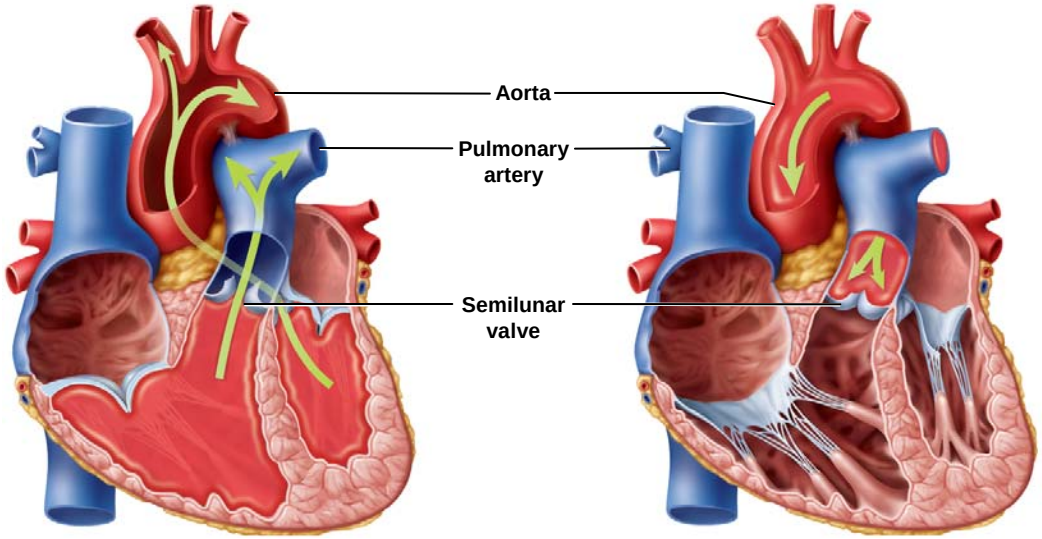
# Operation of Heart Valves




Atrioventricular valves open

Atrioventricular valves closed

(a)



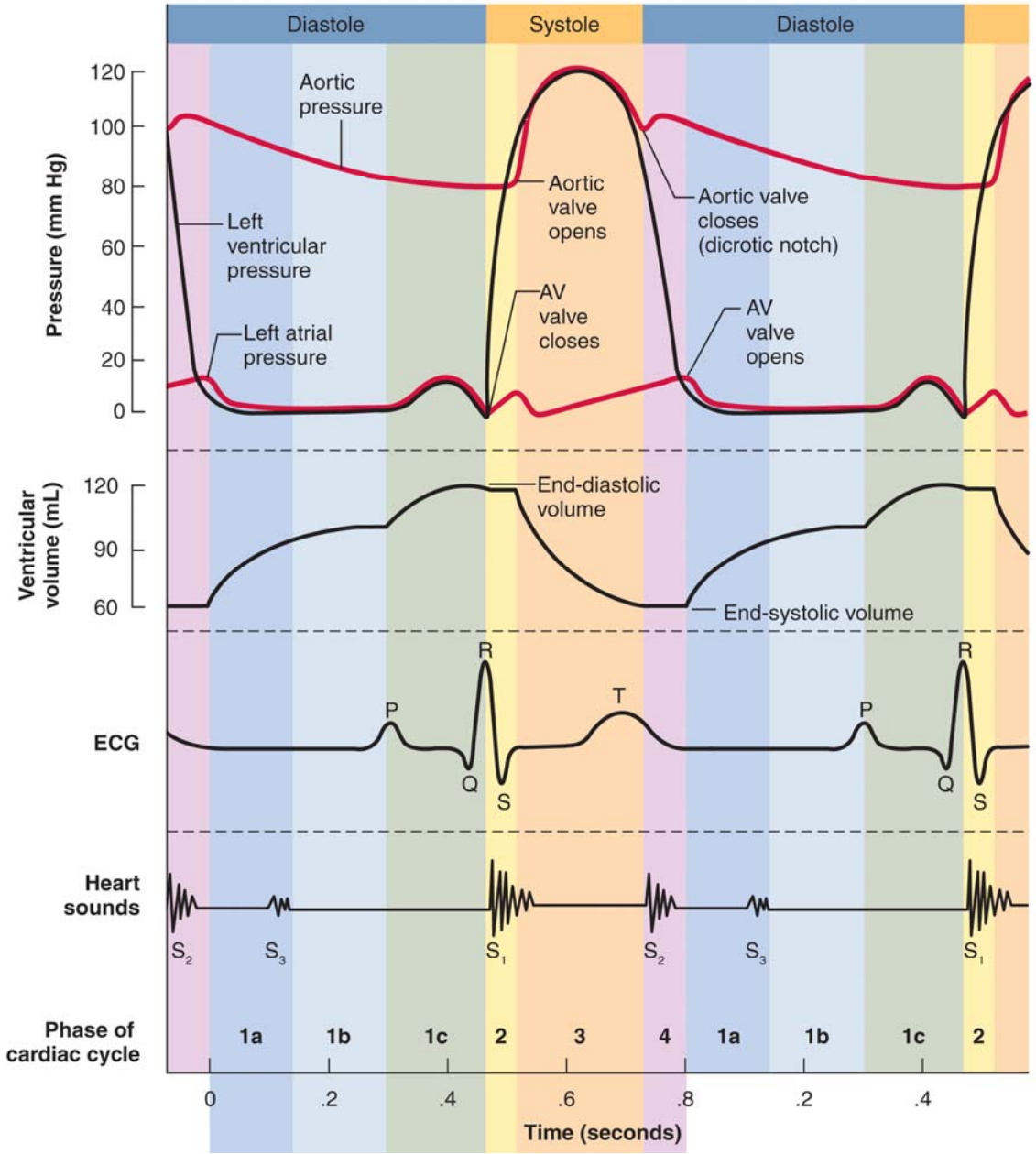

Semilunar valves open

Semilunar valves closed

(b)

# Summary of Cardiac Cycle Events





# Cardiac Output (CO)

*cardiac output = stroke volume x heart rate*

Volume of blood ejected by ventricle in 1 minute

CO = 70 ml / Beat x 75 Beat / Minutes = 5.25 L / Min

Cardiac Output May Be Changed By

chronotropic effects (time // related to the heart rate)

inotropic effects (related to the force of contraction)

# Cardiac Output

*cardiac output = stroke volume x heart rate*

- CO about 4 to 6 L/min at rest (test figure 5.25 L)
  - This means a RBC leaving the left ventricle will arrive back at the left ventricle in 1 minute (approximately 5 L of blood in circulation)
  - vigorous exercise increases CO during event
    - Fit person up to 21 L/min
    - World class athlete up to 35 L/min
- cardiac reserve – the difference between a person's maximum and resting Cardoac Output

# Cardiac Output

*cardiac output = stroke volume x heart rate*

- *Key Idea: At rest, CO is "regulated" so it stays about the same (5.25 L / min) /// Why?*
- *Therefore if stroke volume changes (increases) (e.g. over time due to conditioning) then HR should fall*
- *This means the heart is not working as hard /// therefore it may "last longer"!!!!*
  - SV increases with fitness /// decreases with disease and aging
  - to keep cardiac output constant as we increase in age, the heart rate increases as the stroke volume decreases

# The other factor that influence cardiac output

Three variables govern stroke volume:

- Preload (more preload = more SV = more blood ejected!)
- Afterload (blood pressure in aorta which resist ejection of blood from heart) /// as afterload increases there is more resistance to eject blood / result in less SV)
- Contractility = inotropic influence = as force of myocardiocyte contraction increases results in more SV

- Net affects seen:
  - increased preload or increasing the contractility of cardiocyte increases stroke volume
  - increased afterload causes decrease stroke volume

# Preload and Stroke Volume

- **Preload** – the amount of tension (caused by filling of the ventricles) in myocardium immediately before it begins to contract
  - increased preload causes increased force of contraction
  - exercise increases venous return and stretches myocardium
  - cardiocytes generate more tension (not like skeletal muscle / tension length relationship)
  - increased cardiac output matches increased venous return

- **Frank-Starling Law of the Heart** - SV$\propto$ EDV
  - stroke volume is proportional to the end diastolic volume
  - ventricles eject as much blood as they receive
  - the more they are stretched, the harder they contract // not like skeletal muscle

# Afterload and Stroke Volume

- Afterload – the blood pressure in the aorta and pulmonary trunk immediately distal to their semilunar valves
  - opposes the opening of aortic and pulmonary semilunar valves
  - limits stroke volume
- *Hypertension increases afterload and opposes ventricular ejection // overtime cause hypertrophy of heart // enlarged heart is very bad!*

# Role of Circulation, Afterload and Ventricular Failure

- Anything that *impedes arterial circulation* in either the systemic or pulmonary circuit may also increase afterload

- E.g. // lung diseases will restrict blood flow into pulmonary circulation // blood "backs up" or "builds up above the semilunar valve

- Cor pulmonale – right ventricular failure due to *obstructed pulmonary circulation*

  - These diseases restrict blood flow through lungs: emphysema, chronic bronchitis, and black lung disease

# Contractility and Stroke Volume

- contractility refers to how hard the myocardium contracts for any given preload

- positive inotropic agents that increase contractility
  - hypercalcemia can cause strong, prolonged contractions and even cardiac arrest in systole
  - catecholamines increase calcium levels
  - glucagon stimulates cAMP production
  - digitalis raises intracellular calcium levels and contraction strength

# Contractility and Stroke Volume (cont.)

- negative inotropic agents reduce contractility
  - hypocalcemia can cause weak, irregular heartbeat and cardiac arrest in diastole
  - hyperkalemia reduces strength of myocardial action potentials and the release of $Ca^{2+}$ into the sarcoplasm
  - vagus nerve has an effect on atria (the nodes) which reduces heart rate
  - However…..few vagus nerves innervate myocardiocytes in ventricles /// therefore vagus has no significant negative inotropic effect

# Heart Rate

- Heart rate varies throughout life
  - infants have HR of 120 bpm or more
  - young adult females avg. 72 - 80 bpm
  - young adult males avg. 64 to 72 bpm
  - heart rate rises again in the elderly
- Positive chronotropic agents – factors that raise the heart rate
- Negative chronotropic agents – factors that lower heart rate

# Chronotropic Effects of the Autonomic Nervous System

- autonomic nervous system
  - does not initiate the heartbeat,
  - but ANS modulates the rhythm and force

- cardiostimulatory effect
  - some neurons of the cardiac center transmit signals to the heart by way of sympathetic pathways

- cardioinhibitory effect
  - others transmit parasympathetic signals by way of the vagus nerve

## Chronotropic Effects of the Autonomic Nervous System (cont.)

- Sympathetic postganglionic fibers are adrenergic
  - they release norepinephrine // binds to β-adrenergic receptors in the heart
  - activates c-AMP second-messenger system in *cardiocytes (and nodal cells) --- result in 3 important events*
    - leads to the opening of slow $Ca^{2+}$ channels in plasma membrane / fibers contract more quickly
    - Opens calcium channels in sarcoplasmic reticulum / fibers contract more quickly
    - cAMP accelerates the uptake of $Ca^{2+}$ by the sarcoplasmic reticulum // fibers relax more quickly
    - Net result is ability to accelerate heart rate up to 240 bpm!

# Chronotropic Effects May Reduce Stroke Volume

*By accelerating the rate of contraction (how fast calcium is added to sarcoplasm) and then accelerating the reuptake of calcium into sarcoplasmic reticulum to increase rate of relaxation --- heart rate is increased!*

- Sympathetic NS (norepinephrine) able to increase the heart rate as high as 240 bpm

– Note: at these high heart rates / diastole becomes too brief for complete filling of the ventricles!!!!

– So at 240 bpm both stroke volume and cardiac output are reduced

## Chronotropic Effects of the Autonomic Nervous System

- parasympathetic (vagus nerves) are cholinergic fibers // inhibitory effects on the SA and AV nodes
  - acetylcholine (ACh) binds to muscarinic receptors (cAMP mediated)
  - opens $K^+$ gates in the nodal cells
  - as $K^+$ leaves the cells, they become hyperpolarized and fire less frequently
  - heart slows down
  - parasympathetics effect on the heart is faster than sympathetics

## Chronotropic Effects of the Autonomic Nervous System (cont.)

- Vagal Tone (parasympathetic tone)
  - the heart has a intrinsic “natural” firing rate of 100 bpm
  - vagal tone – holds down this natural heart rate to 70 – 80 bpm at rest
  - Caused by steady background firing rate of the vagus nerves

# Chronotropic Chemicals

- chemicals affect heart rate //  in addition to the neurotransmitters from cardiac nerves
  - blood born adrenal catecholamines (NE and epinephrine) are potent cardiac stimulants

- **drugs may also stimulate heart**
  - **nicotine** stimulates catecholamine secretion
  - **thyroid hormone** increases number adrenergic receptors on heart so more responsive to sympathetic stimulation
  - **caffeine** inhibits cAMP breakdown ///  therefore can prolong the adrenergic effect

# Chronotropic Chemicals - Electrolytes

- Electrolyte : $K^+$ has greatest chronotropic effect
  - hyperkalemia (higher than normal concentration in blood)
    - Result / $K^+$ diffuses into cardiocytes / excess $K^+$ cytoplasm
    - Membrane voltage elevated which inhibits repolarization
    - Myocardium becomes less excitable
    - heart rate slows and becomes irregular
    - May arrest in dyastole
  - hypokalemia (lower than normal concentration in blood)
    - $K^+$ diffuses out of the cardiocytes
    - cells hyperpolarized / membrane potential more negative
    - require increased stimulation to reach threshold / harder to stimulate heart
  - Potassium imbalances are very dangerous and require emergency medical treatment!

# Chronotropic Chemicals - Electrolytes

- Electrolyte : $Ca^{2+}$ also affect heart rate
  - **hypercalcemia** – excess of $Ca^{2+}$
    - decreases heart rate and contraction strength
    - Slow heart rate
  - **hypocalcemia** – deficiency of $Ca^{2+}$
    - increases heart rate
    - More of an affect on contraction strength
    - Rare condition
    - *Greater effect is on nerve fibers causing action potential in somatic nerve fibers going to skeletal muscles (like diaphragm) / death from respiratory arrest!*

Increased end-diastolic volume (stretches the heart)

Positive inotropic agents such as increased sympathetic stimulation; catecholamines, glucagon, or thyroid hormones in the blood; increased $Ca^{2+}$ in extracellular fluid

Decreased arterial blood pressure during diastole

Increased PRELOAD

Increased CONTRACTILITY

Decreased AFTERLOAD

Within limits, cardiac muscle fibers contract more forcefully with stretching (Frank–Starling law of the heart)

Positive inotropic agents increase force of contraction at all physiological levels of stretch

Semilunar valves open sooner when blood pressure in aorta and pulmonary artery is lower

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Increased STROKE VOLUME

Increased CARDIAC OUTPUT

Increased HEART RATE

Increased sympathetic stimulation and decreased parasympathetic stimulation

Catecholamine or thyroid hormones in the blood; moderate increase in extracellular $Ca^{2+}$

Infants and senior citizens; females; low physical fitness; increased body temperature

NERVOUS SYSTEM
Cardiovascular center in medulla oblongata receives input from cerebral cortex, limbic system, proprioceptors, baroreceptors, and chemoreceptors

CHEMICALS

OTHER FACTORS

# Heart Function Terms

- Pulse pressure – surge of pressure produced by each heart beat that can be felt by palpating a superficial artery with the fingertips

- Tachycardia - resting adult heart rate above 100 bpm
  - stress, anxiety, drugs, heart disease, or fever
  - loss of blood or damage to myocardium

- Bradycardia - resting adult heart rate of less than 60 bpm
  - in sleep, low body temperature, and endurance trained athletes

# Exercise and Cardiac Output

- *exercise makes the heart work harder // stroke volume increases // heart rate can be slower and still reach target cardiac output // increase cardiac reserve*

- Exercise stimulate proprioceptors in skeletal muscles that send signal to cardiac center

  - at beginning of exercise, signals from joints and muscles reach the cardiac center

    - sympathetic output from cardiac center increases cardiac output

  - increased muscular activity /// increases venous return

    - increases preload /// results in an increase cardiac output

  - *increase in both heart rate and stroke volume can both cause increases in cardiac output*

# Exercise and Cardiac Output

- exercise produces ventricular hypertrophy
  - increased stroke volume allows heart to beat more slowly at rest
  - athletes with increased cardiac reserve can tolerate more exertion than a sedentary person

# Valvular Insufficiencies

- valvular insufficiency (incompetence) // any failure of a valve to prevent reflux (regurgitation) the backward flow of blood

- valvular stenosis – cusps are stiffened and opening is constricted by scar tissue

    - result of **rheumatic fever** autoimmune attack on the mitral and aortic valves

    - heart overworks and may become enlarged

# Valvular Insufficiencies

- heart murmur – abnormal heart sound produced by regurgitation of blood through incompetent valves

- mitral valve prolapse – insufficiency in which one or both mitral valve cusps bulge into atria during ventricular contraction
    - hereditary in 1 out of 40 people
    - may cause chest pain and shortness of breath

# Congestive Heart Failure

- results from the failure of either ventricle to eject blood effectively

- One ventricle ejects proper amount of blood while the other ventricle ejects less blood

- The ventricle which ejects less blood is the failing ventricle

- usually due to a heart weakened by

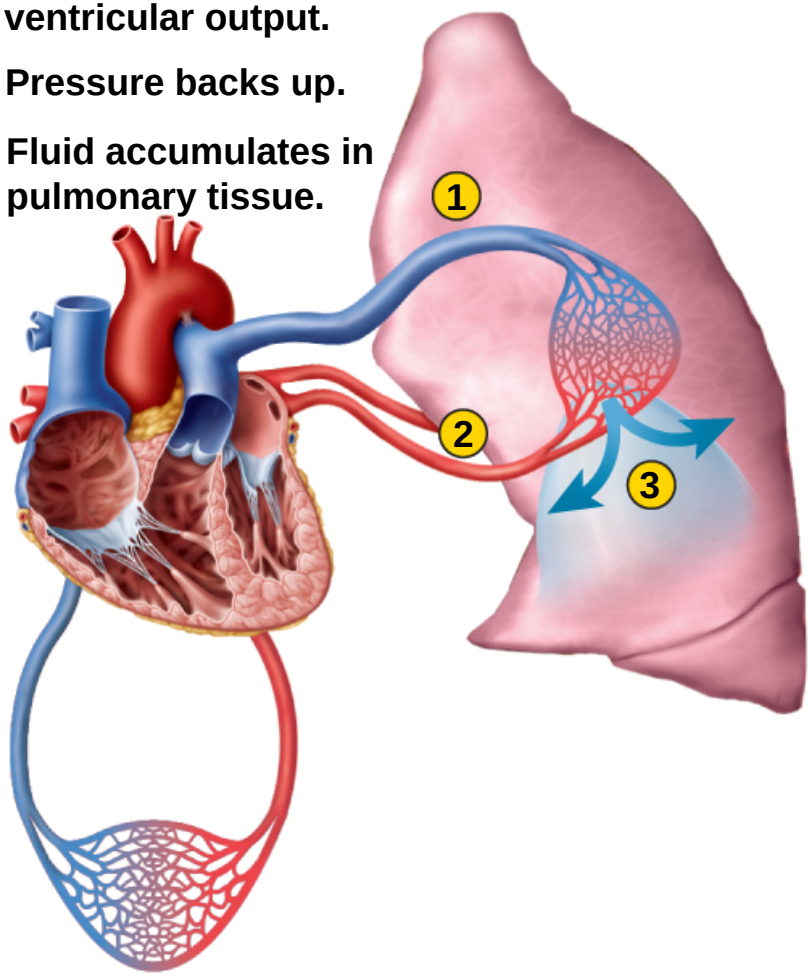
  - myocardial infarction
  - chronic hypertension
  - valvular insufficiency
  - congenital defects in heart structure.

# Congestive Heart Failure // Left Ventricular Failure

- Left ventricle ejects less blood (e.g. Rt V ejects 70 ml and Lt V ejects 50 ml)
- Rt. Ventricle is ejecting 20 ml more blood than Lt. ventricle during each cardiac cycle
- extra “20 ml” most go somewhere // it accumulates in the lung interstitial space // pulmonary edema
- shortness of breath or sense of suffocation

# Unbalanced Ventricular Output

1. **Right ventricular output exceeds left ventricular output.**
2. **Pressure backs up.**
3. **Fluid accumulates in pulmonary tissue.**




**(a) Pulmonary edema**

Left ventricular failure results in pulmonary edema

Note:

Cor pulmonale will also results in pulmonary edema

Due to lung emphysema and other disease states which cause restriction (fibrosis) in lung tissue

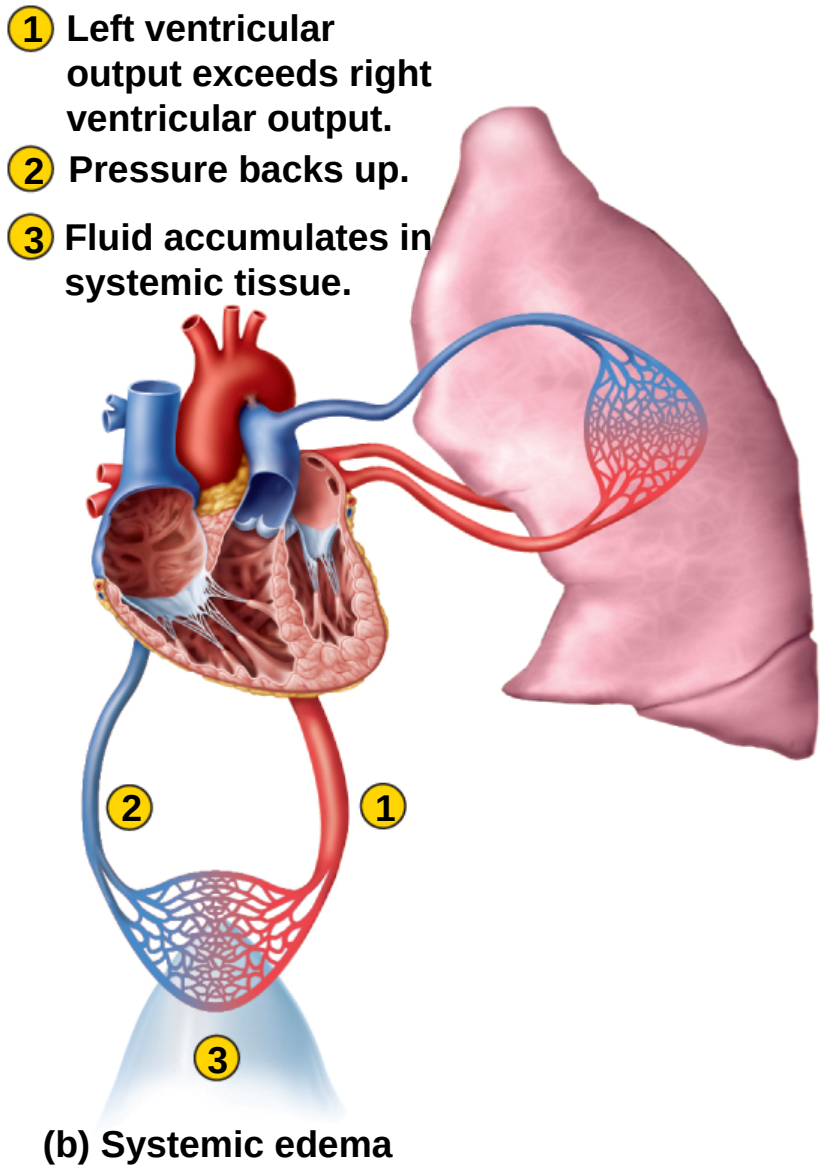
Enlarged right heart // these condition will contribute to right heart failure

# Congestive Heart Failure // Rt. Ventricular Failure

- Right ventricle ejects less blood (e.g. Lt V ejects 70 ml and Rt V ejects 50 ml)
- Left ventricle ejects extra 20 ml of blood per cardiac cycle
- Rt ventricle can not receive the total volume so extra 20 ml filters into the systemic interstitial space // systemic edema - seen primarily in the legs
- enlargement of the liver, ascites (pooling of fluid in abdominal cavity), distension of jugular veins, swelling of the fingers, ankles, and feet

- *Note: Either condition will lead eventually to total heart failure*

# Unbalanced Ventricular Output

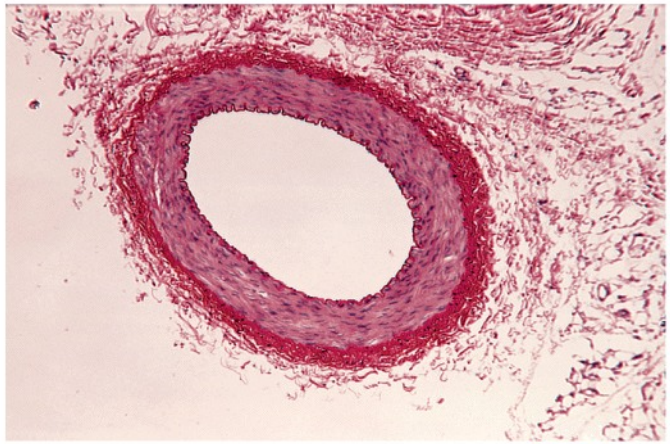



(b) Systemic edema

Right ventricular failure results in systemic (peripheral) edema

# Pathology in Heart's Arteries

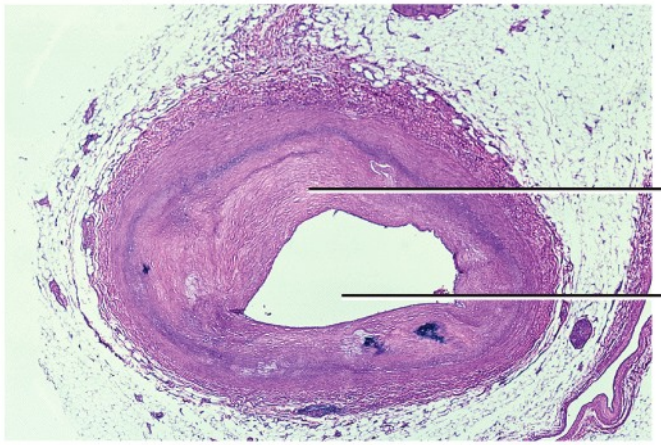
Chuck Brown/Photo Researchers, Inc.



LM 16x

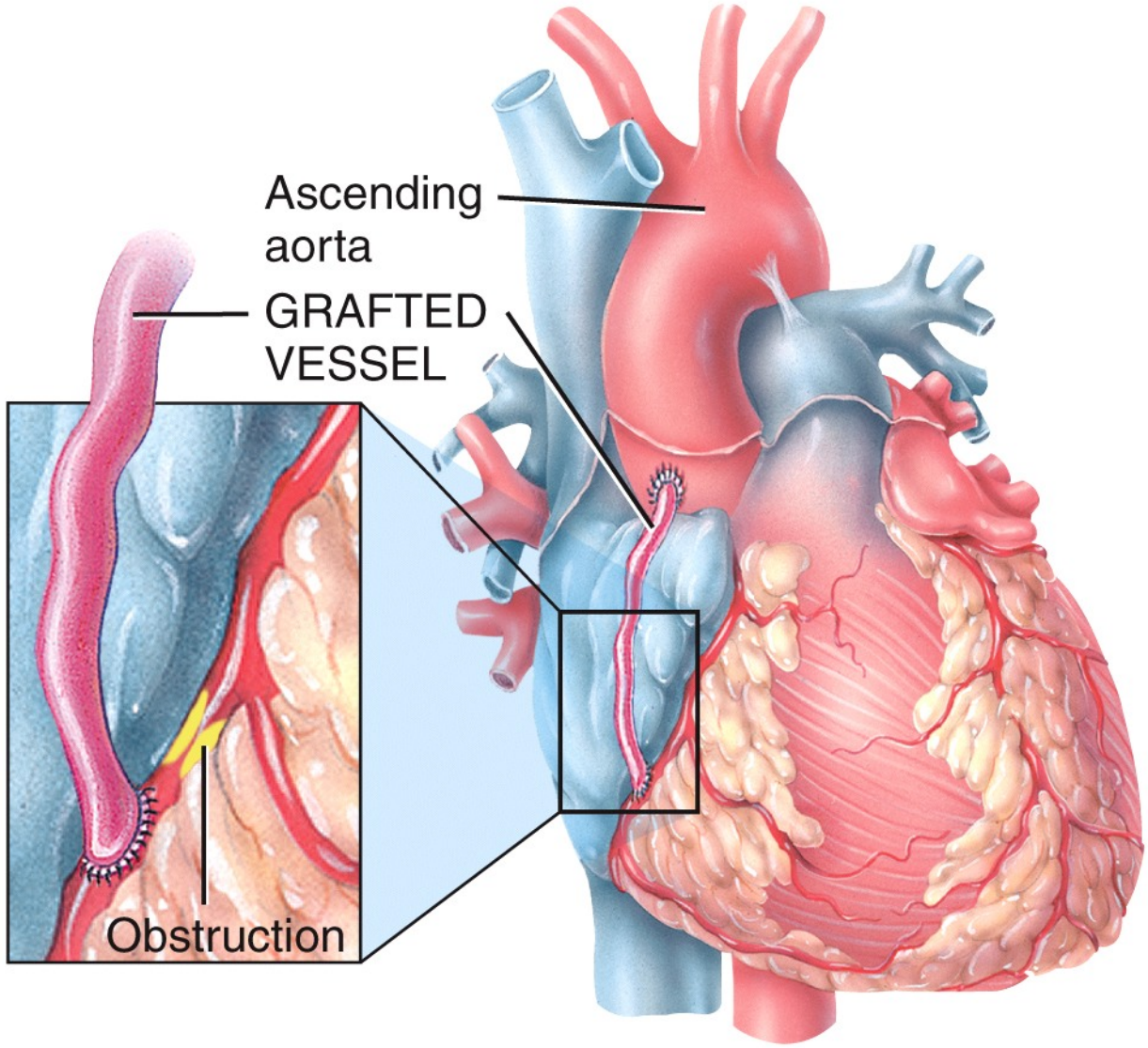
Normal artery

Carolina Biological Supply Company/Phototake

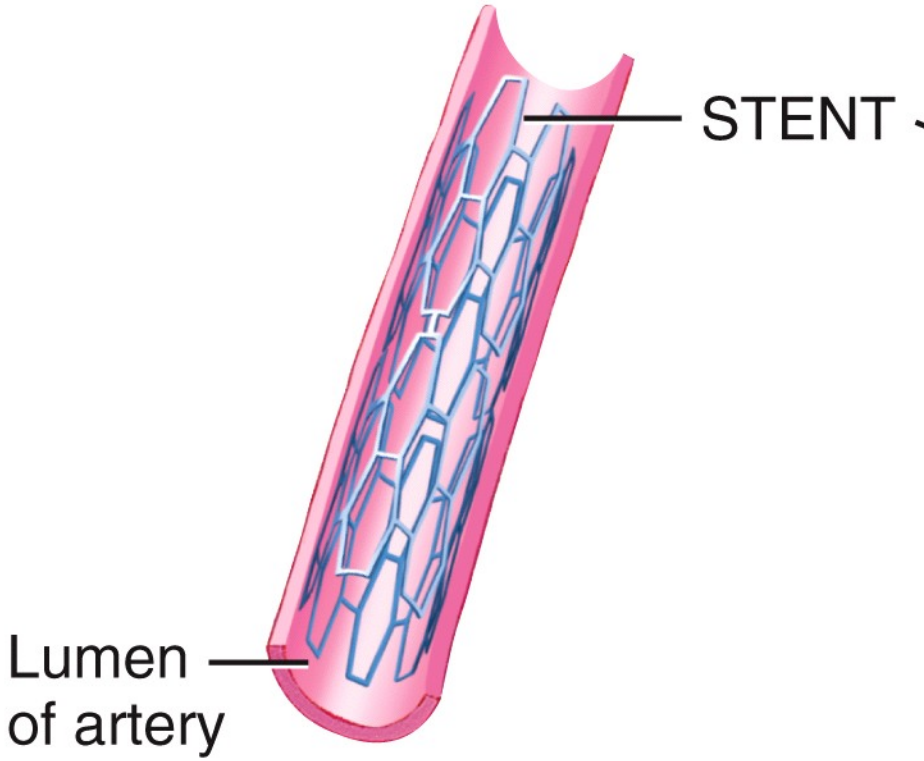



LM 20x

Obstructed artery

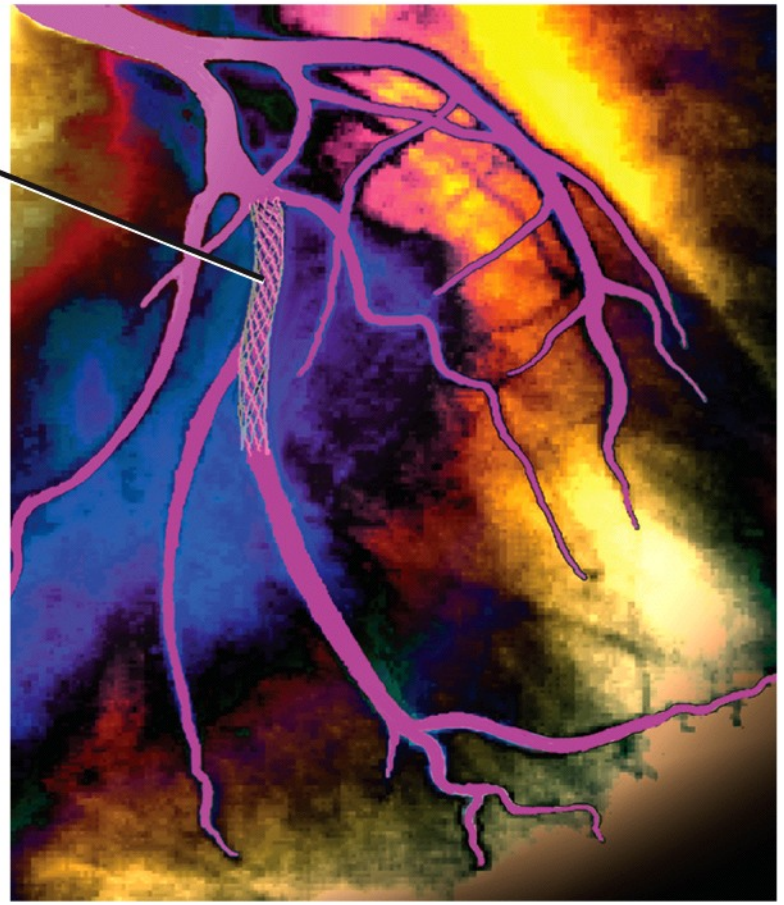



(a) Coronary artery bypass grafting (CABG)




(c) Stent in an artery





(d) Angiogram showing a stent in the circumflex artery