Chapter 12:
Cardiovascular Physiology

Excitation-Contraction Coupling

The mechanism that couples excitation – an action potential in the plasma membrane of the muscle cell – and contraction of heart muscle

Figure 9-12

Passage of an action potential along the transverse tubule opens nearby voltage-gated calcium channels, the "ryanodine receptor," located on the sarcoplasmic reticulum, and

calcium ions released into the cytosol bind to troponin.

The calcium-troponin complex "pulls" tropomyosin off the myosin-binding site of actin, thus allowing the binding of the cross-bridge, followed by its flexing to slide the actin filament.

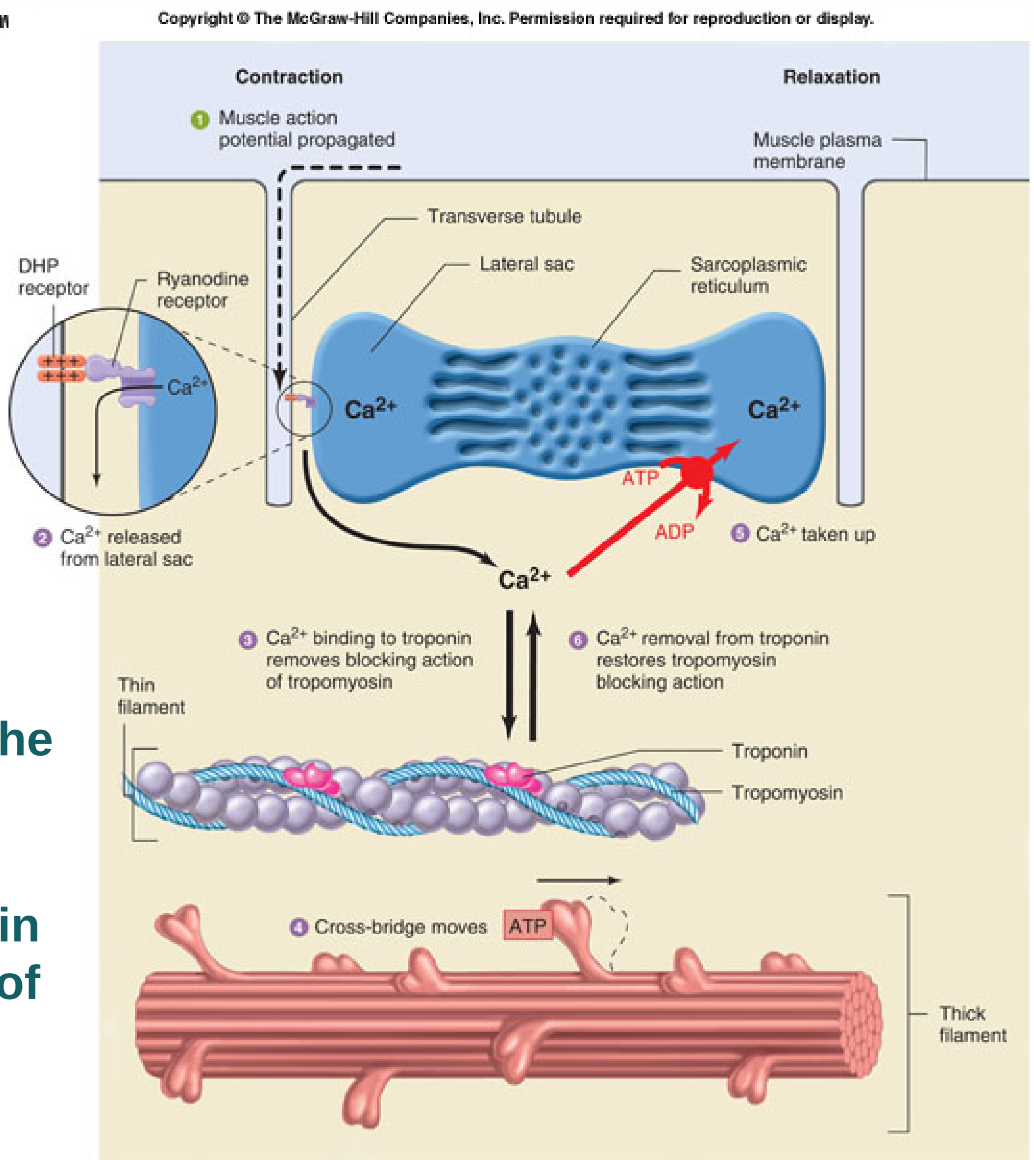

Figure 12-17

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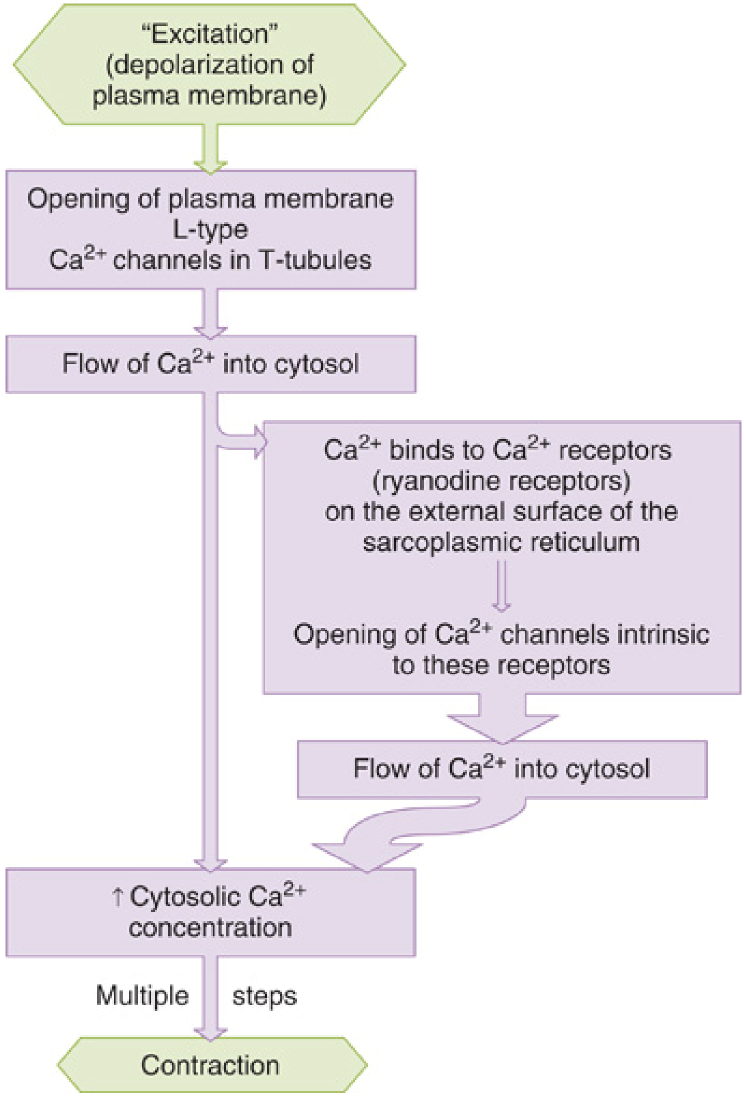
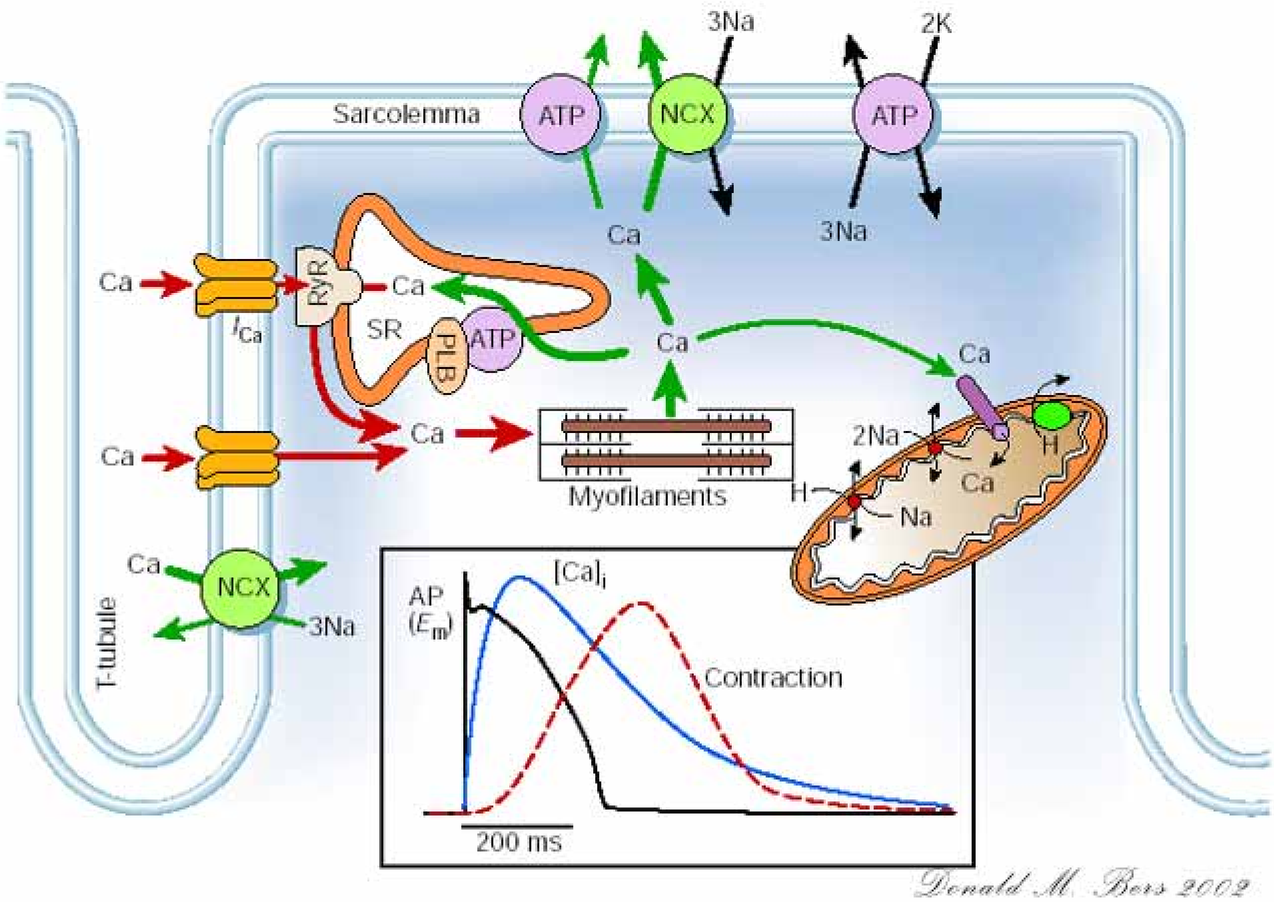
Calcium ions regulate the contraction of cardiac muscle:

the entry of extracellular calcium ions causes the release of calcium from the sarcoplasmic reticulum (calcium-induced calcium release), the source of about 95% of the calcium in the cytosol.



Excitation-contraction coupling in cardiac muscle

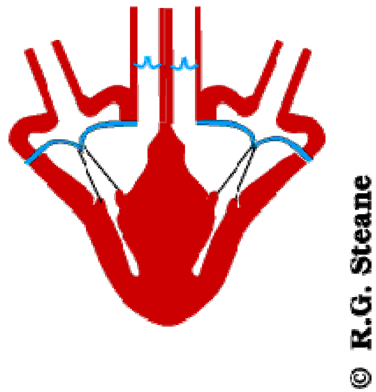
Click here to play the Cardiac EC Coupling Flash Animation



3Na
2K
Sarcolemma
ATP
NCX
ATP
3Na
Ca
Ca
RyR
Ca
I_{Ca}
SR
PLB
ATP
Ca
Ca
Ca
Ca
Myofilaments
2Na
H
Ca
H
Na
Ca
NCX
3Na
T-tubule
[Ca]i
AP
(E_m)
Contraction
200 ms
Donald M. Bers 2002

Cardiac cycle

- The cardiac events that occur from beginning of one heartbeat to the beginning of the next are called the cardiac cycle



Mechanical Events of the Cardiac Cycle

Click here to play the Mechanical Events of the Cardiac Cycle Flash Animation

What happens in the heart during each cardiac cycle?

- Pressure
- Volume
- Valves
- Blood flow

Figure 12-19

Systole: ventricles contracting

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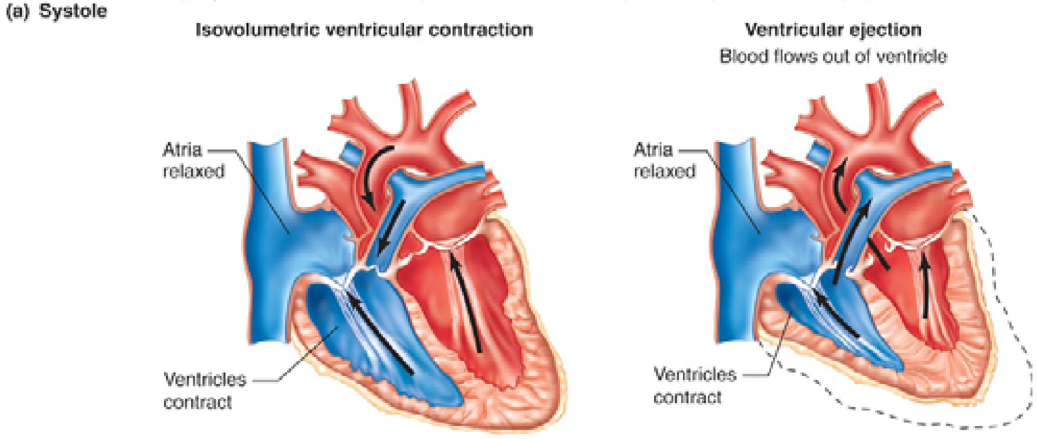

AV valves:	Closed	Closed
Aortic and pulmonary valves:	Closed	Open

Diastole: ventricles relaxed

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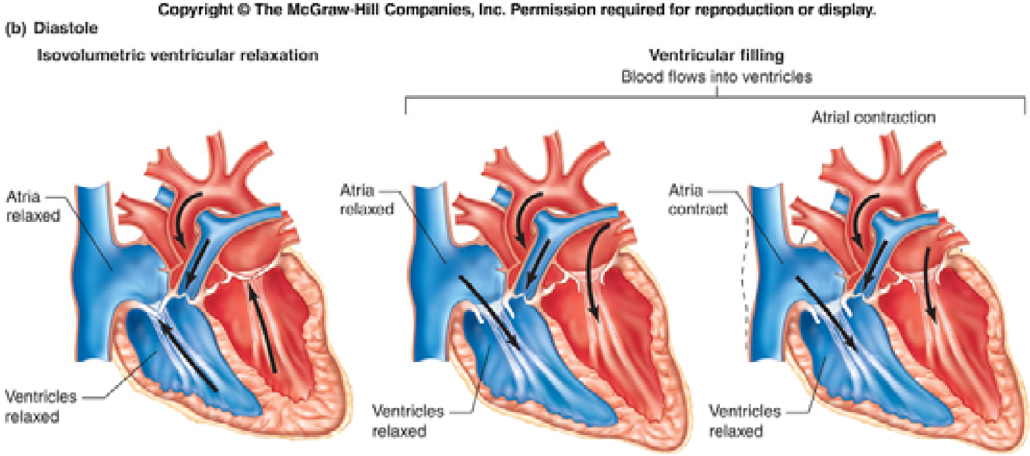
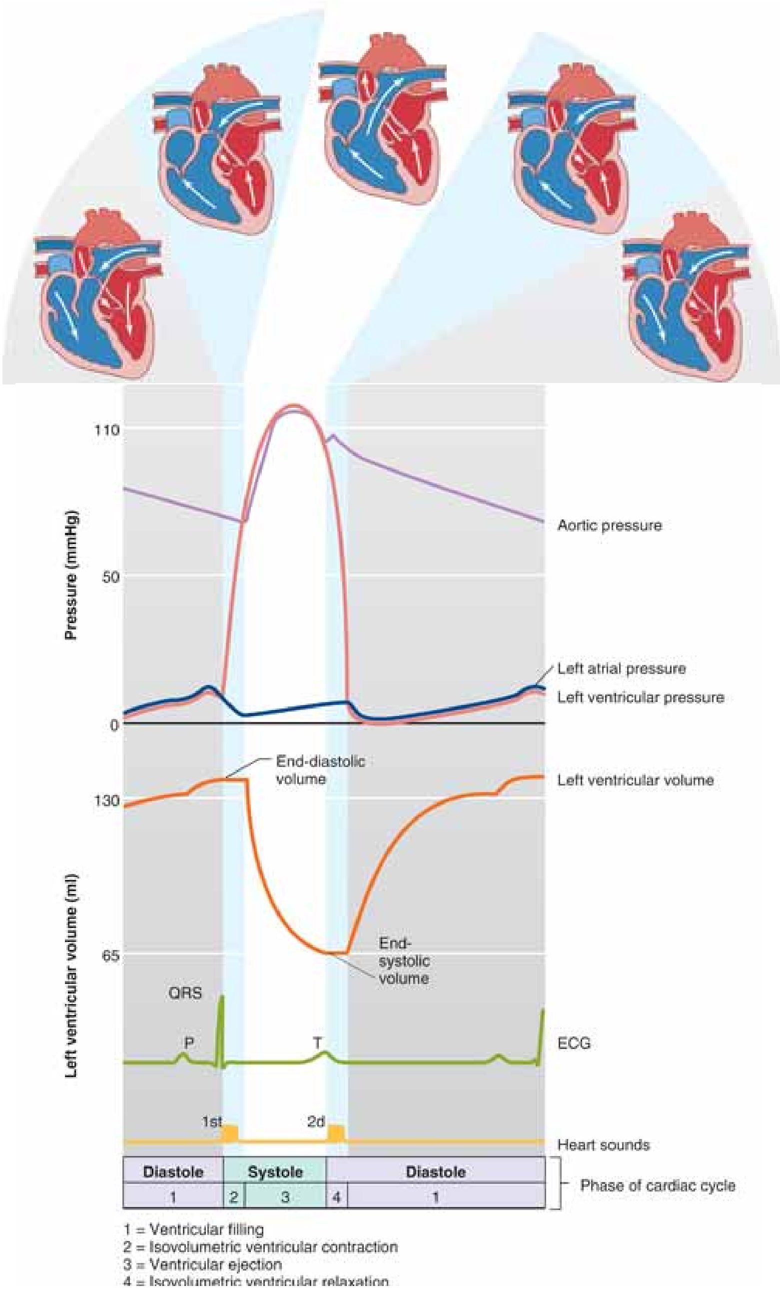


AV valves:	Closed	Open	Open
Aortic and pulmonary valves:	Closed	Closed	Closed

Figure 12-20

Summary of events in the left atrium, left ventricle, and aorta during the cardiac cycle



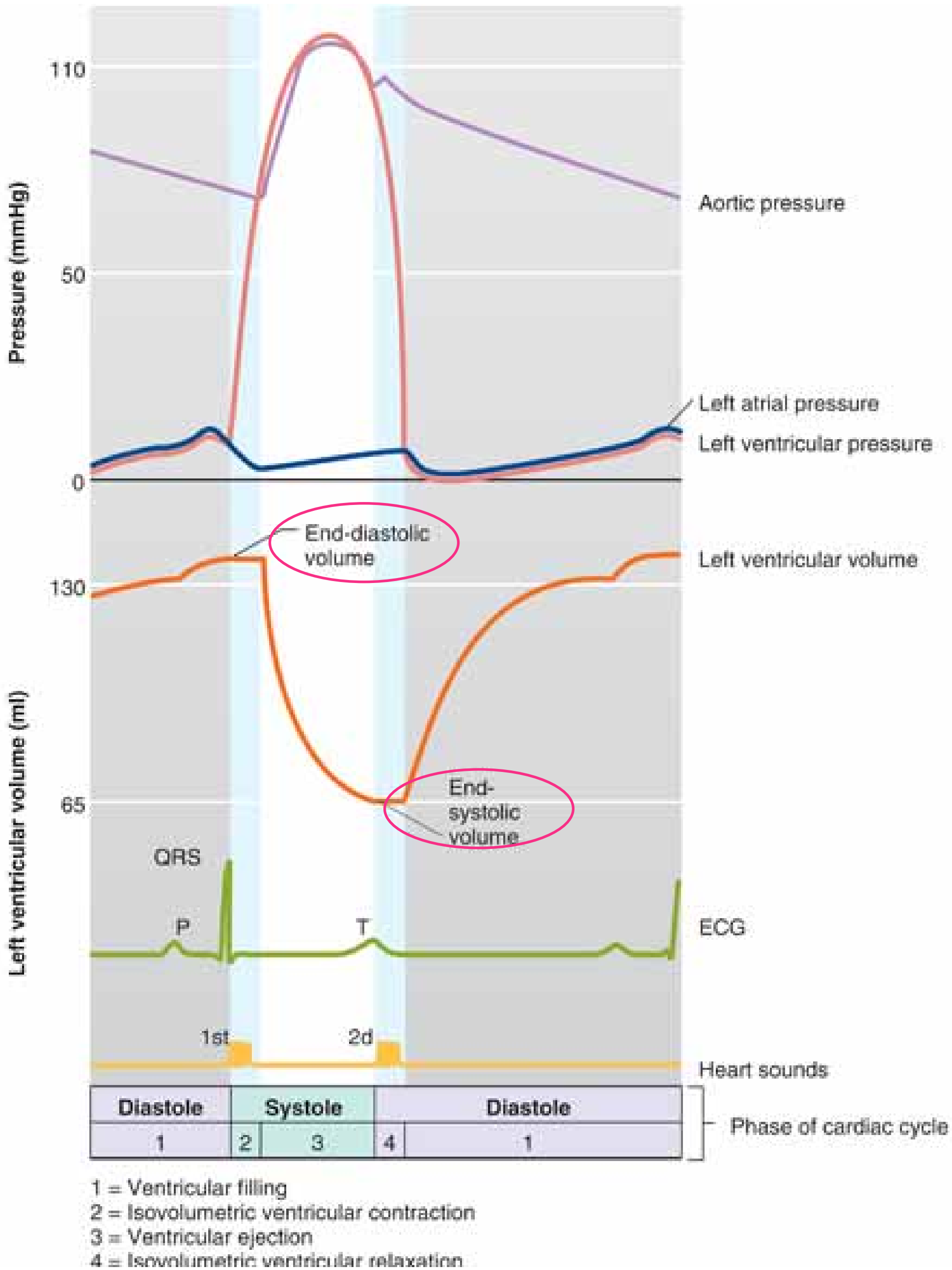

110
50
0
Pressure (mmHg)
Aortic pressure
Left atrial pressure
Left ventricular pressure
End-diastolic volume
130
65
Left ventricular volume (ml)
Left ventricular volume
End-systolic volume
QRS
P
T
ECG
1st
2d
Heart sounds
Diastole
Systole
Diastole
1
2
3
4
1
Phase of cardiac cycle
1 = Ventricular filling
2 = Isovolumetric ventricular contraction
3 = Ventricular ejection
4 = Isovolumetric ventricular relaxation

Figure 12-21

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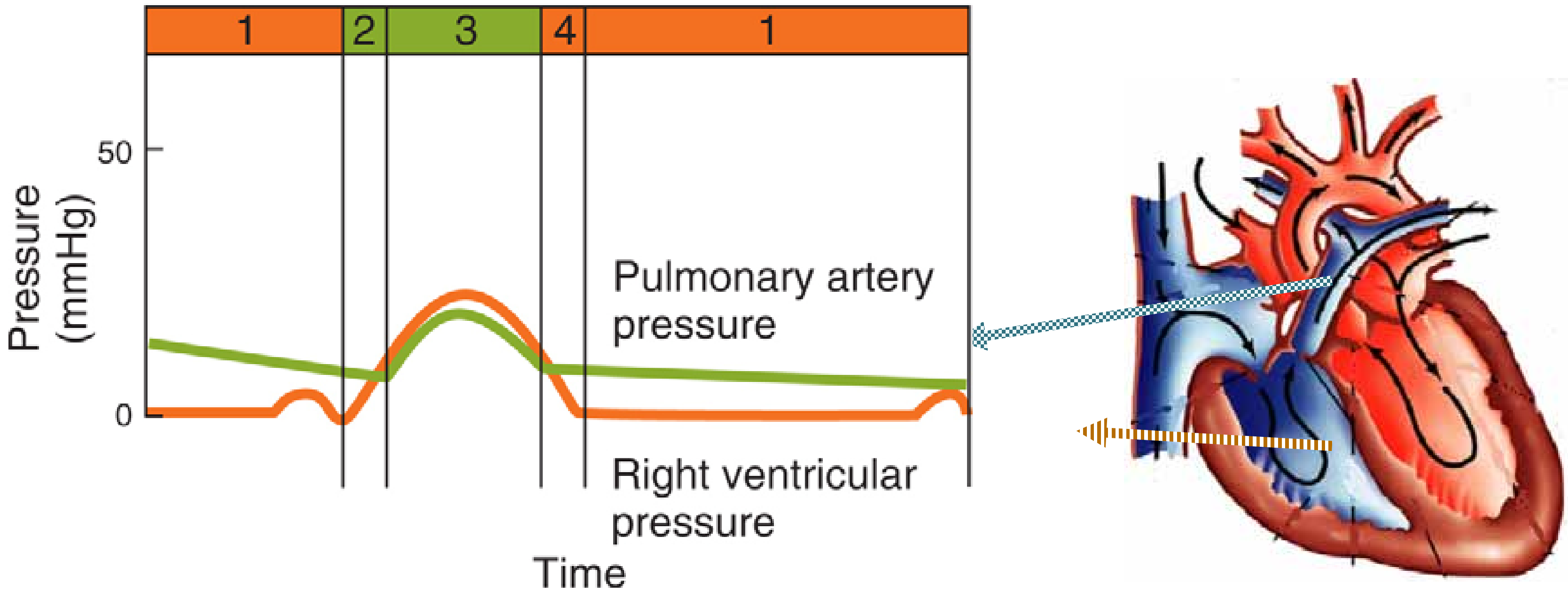
1 = Ventricular filling
2 = Isovolumetric ventricular contraction
3 = Ventricular ejection
4 = Isovolumetric ventricular relaxation



Pressure changes in the right heart during a contraction cycle.

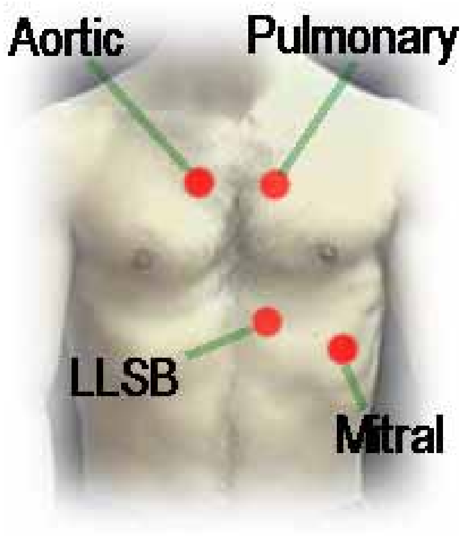
Role of atria and ventricles during each cardiac cycle

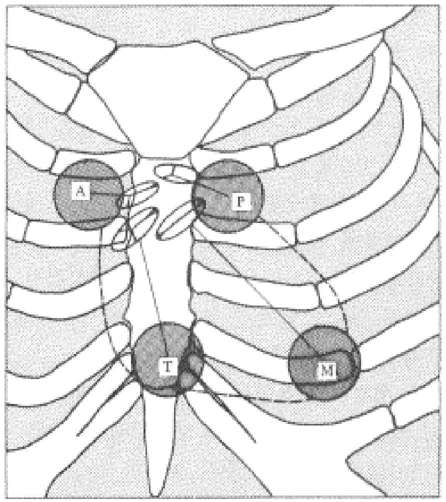
- Atria———primer pump
- Ventricles———major source of power

Heart Sounds

- 1st sound
  - soft low-pitched lub
  - associated with closure of the AV valves
  - Marks the onset of systole
- 2nd sound
  - louder dup
  - associated with closure of the PA and aortic valves
  - Occurs at the onset of diastole

Chest surface areas for auscultation of normal heart sounds

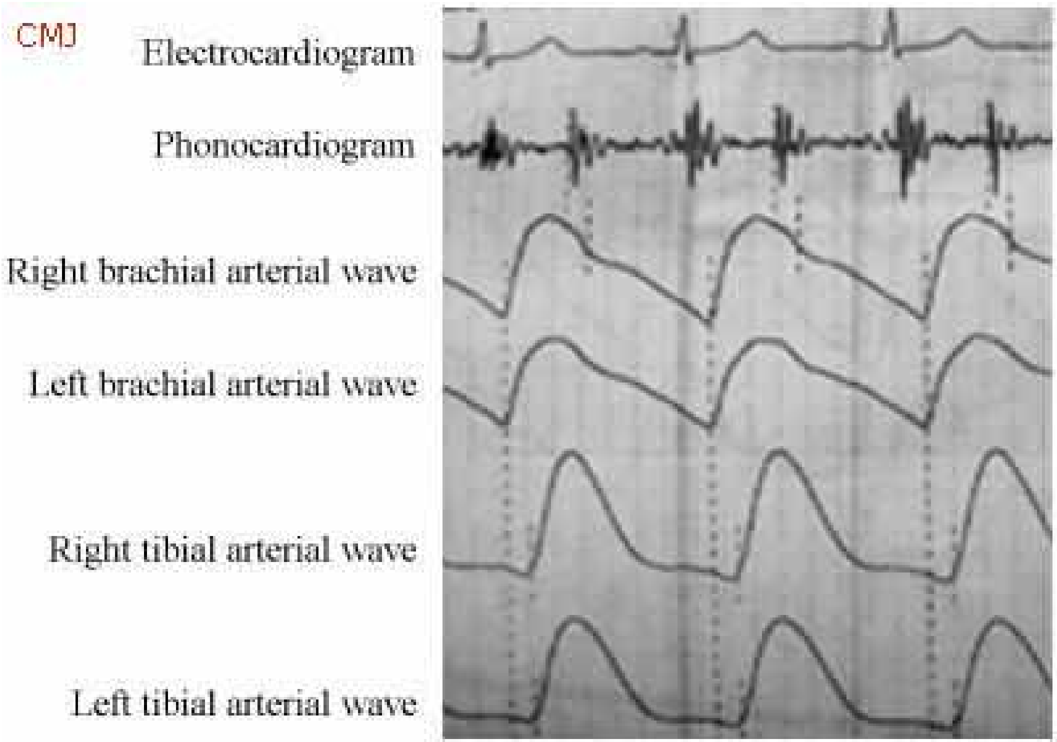


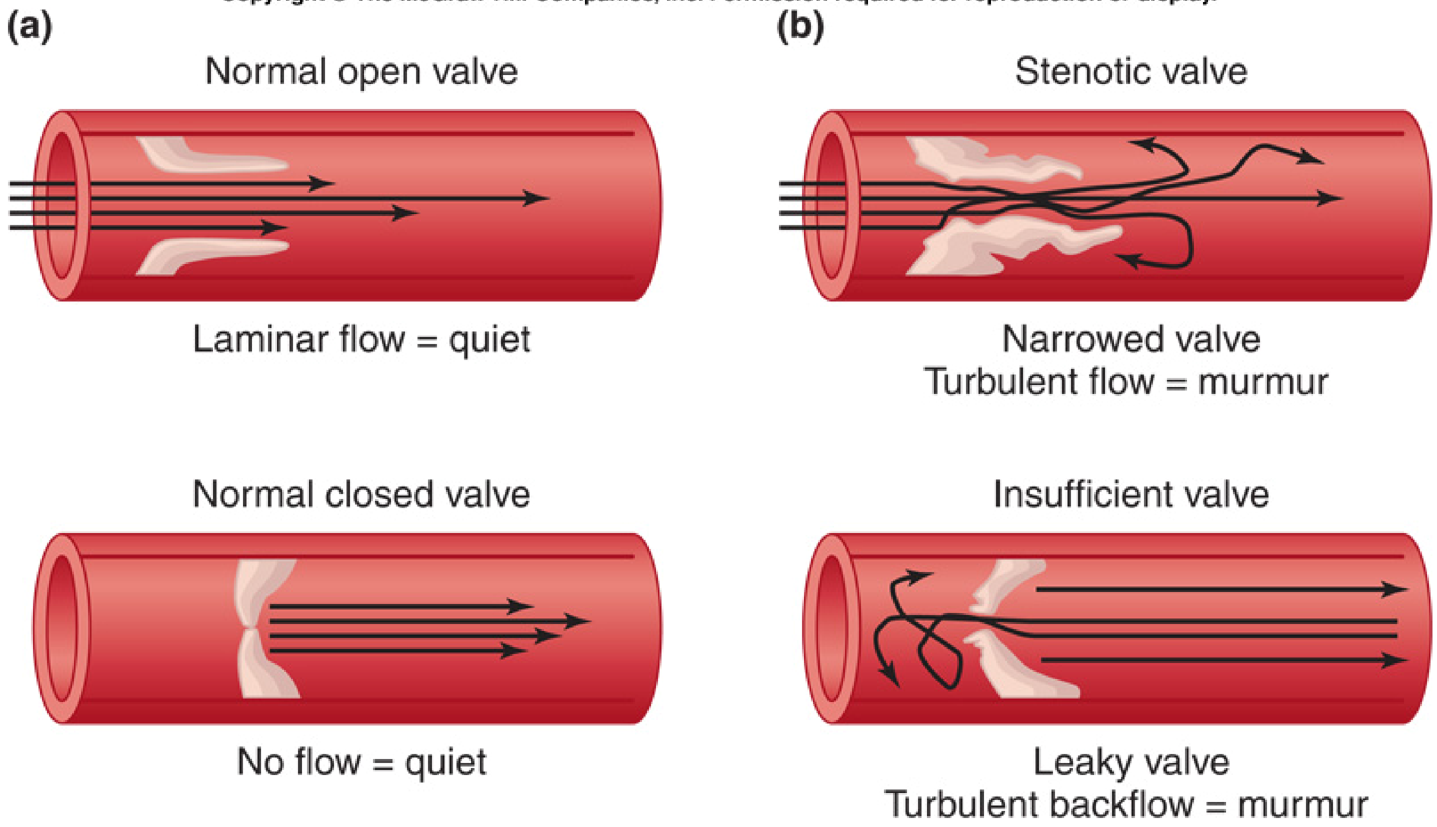


Four traditional value areas
– Aortic space: 2RIS
– Pulmonic valve: 2LIS
– Tricuspid valve: 4ICS LLSB
– Mitral valve: Apex

RIS--right intercostal space
LIS—left intercostal space
ICS--intercostal space
LLSB--left lower sternal border

Phonocardiogram





Heart valve defects causing turbulent blood flow and murmurs

Acute rheumatic fever

Mitral stenosis -- Accentuated first sound

Mitral stenosis – Presystolic murmur

Mitral regurgitation -- systolic murmur

Aortic insufficiency -- Loud systolic ejection murmur, third sound

Evaluation of Heart Pumping

1. Stroke volume (SV): volume

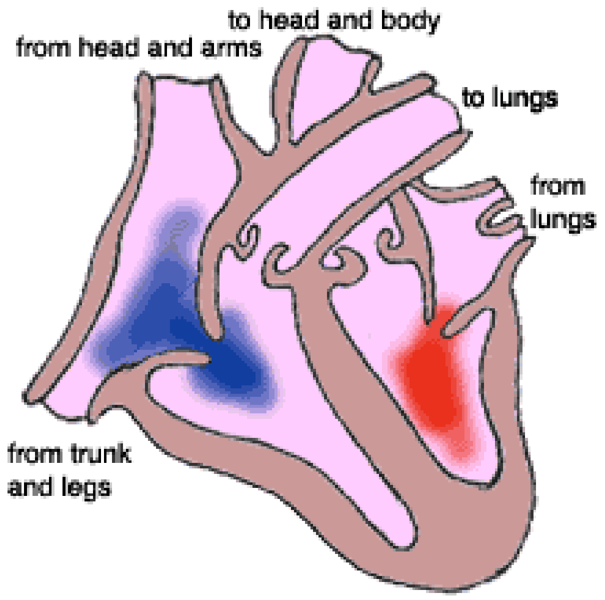
   of blood pumped per beat

   SV = EDV - ESV

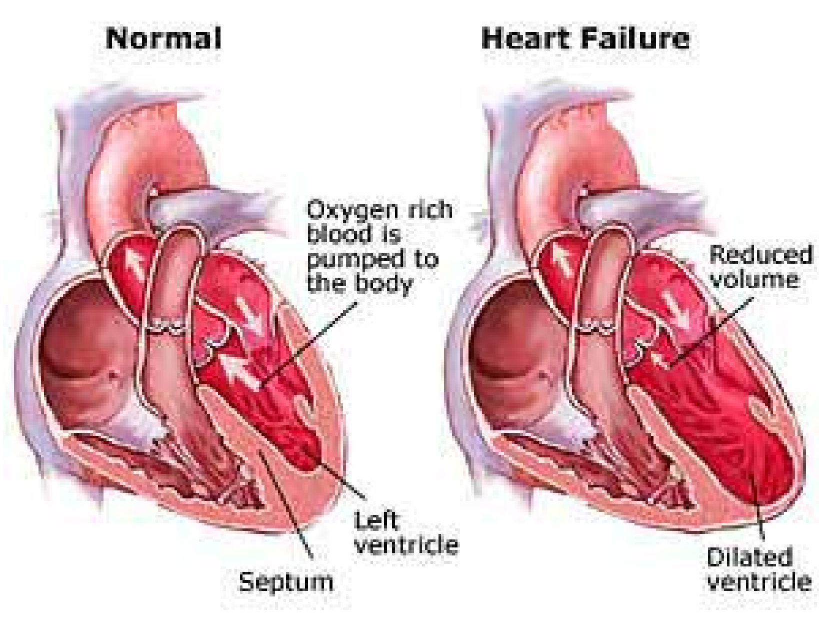
   EDV: end-diastolic volume

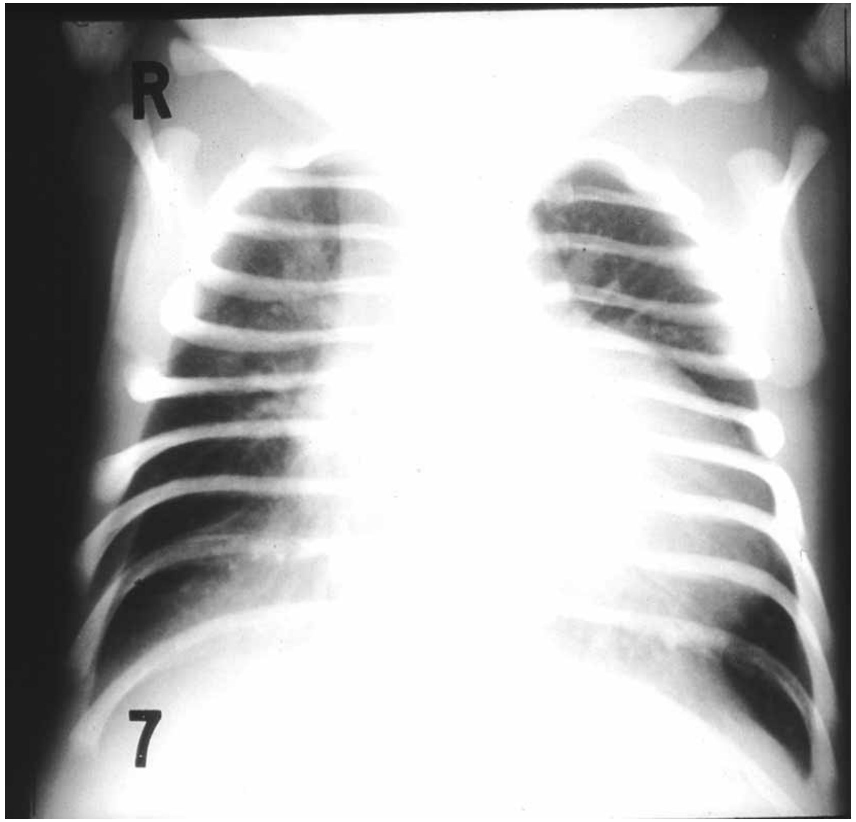
   ESV: end-systolic volume

   ~70ml (60~80ml)



Stroke volume for evaluation?



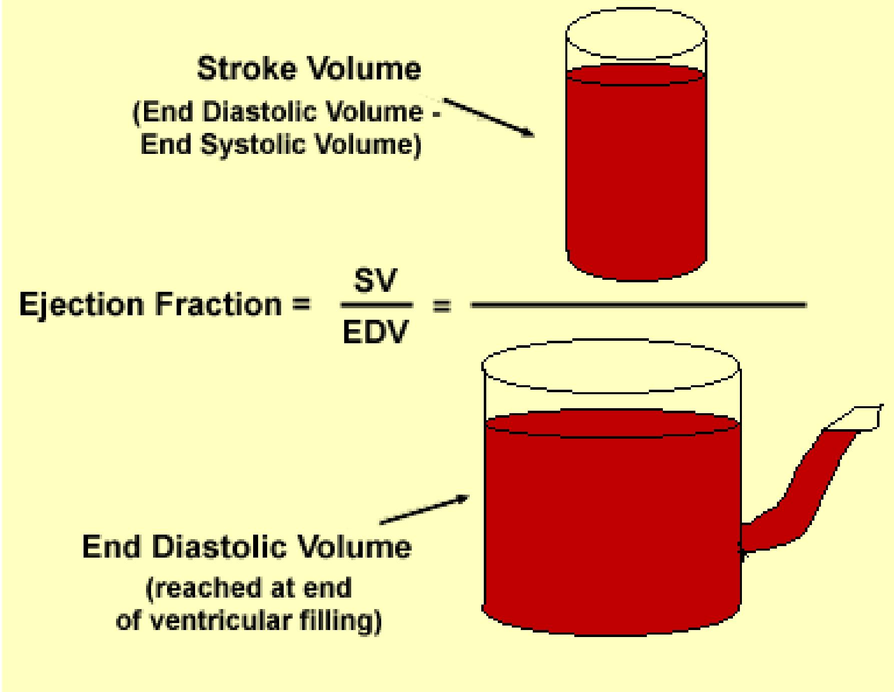


heart enlargement

2. Ejection fraction (EF)

EF=(SV/EDV) x 100%

55~65%

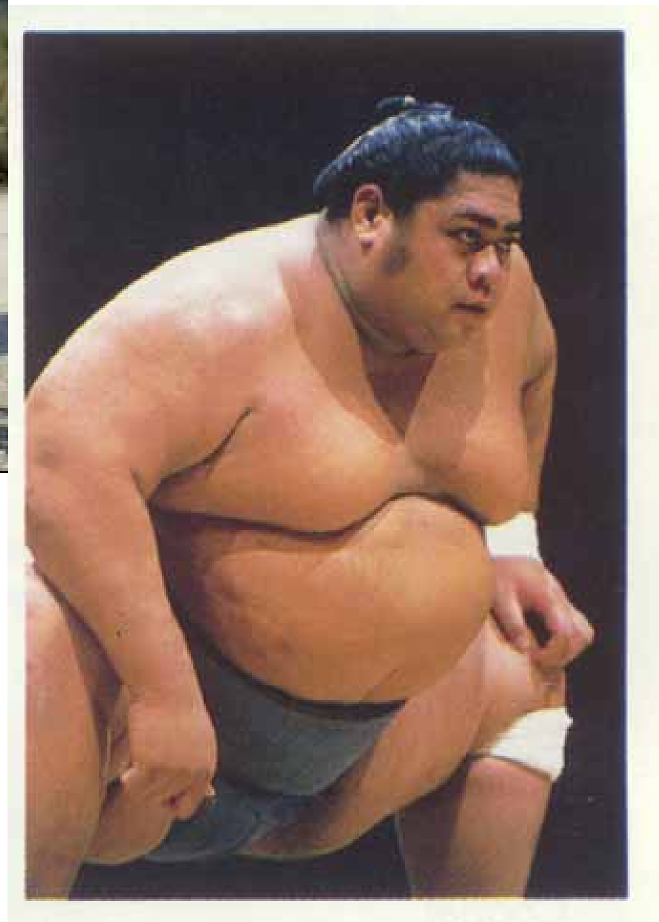


Calculation of Ejection Fraction

3. Cardiac output (CO): the total volume of blood pumped by each ventricle per minute

CO=SV x heart rate (HR)

5 L/min (4.5~6.0 L/min)



What parameters for comparison of people in different size?

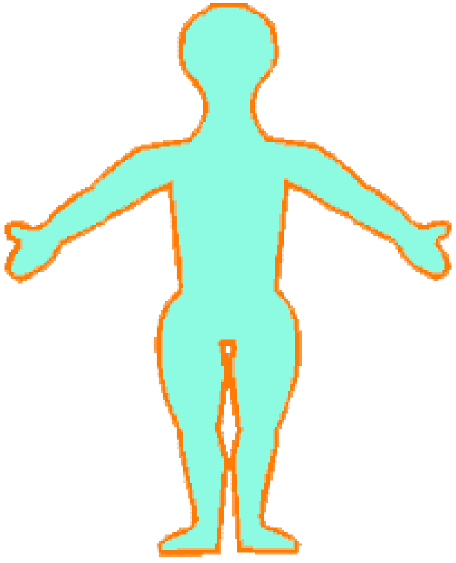
4. Cardiac index (CI):

cardiac output per

square meter of body

surface area

3.0~ 3.5 L/min•m^2



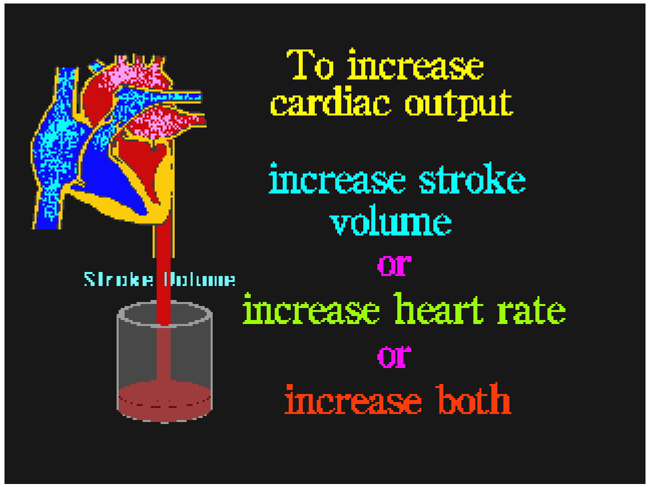
Body surface area = 2.0 m^2
CO = 5 L/min
CI = 2.5 L/min/m^2

Body surface area = 1.5 m^2
CO = 3.75 L/min
CI = 2.5 L/min/m^2

5. Cardiac reserve: the maximum percentage that the cardiac output can increase above the normal level

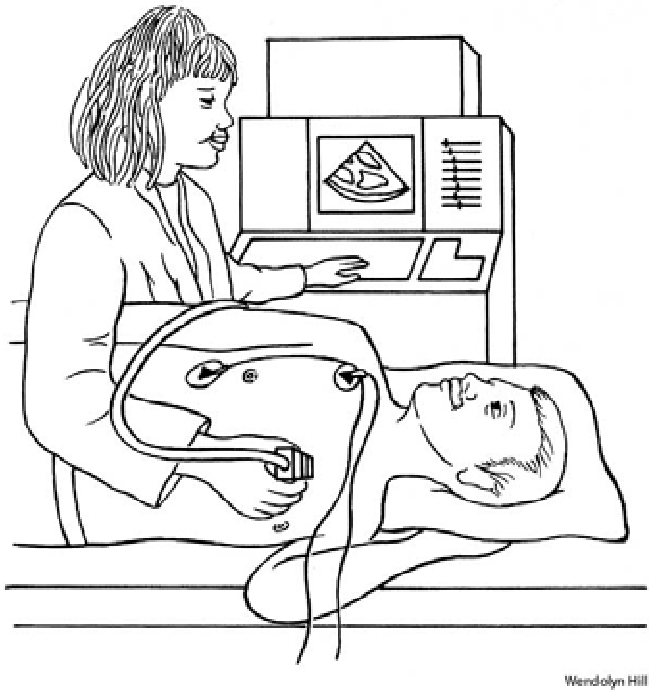
In the normal young adult the cardiac reserve is 300 to 400 percent

Achieved by an increase in either stroke volume (SV) or heart rate (HR) or both

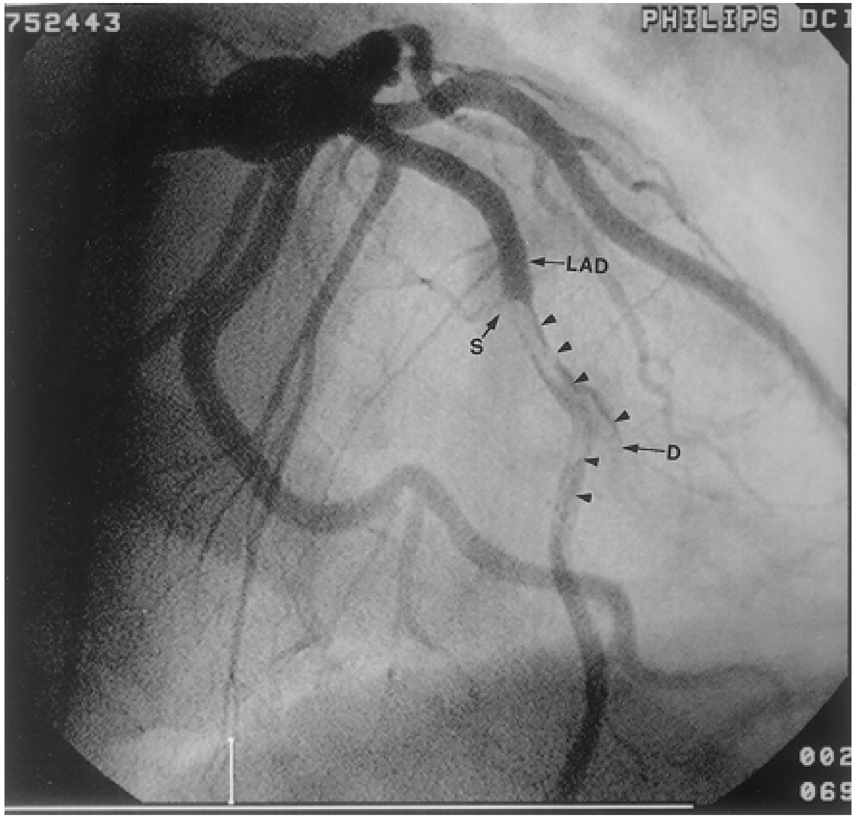


Measurement of Cardiac Function

- Echocardiography



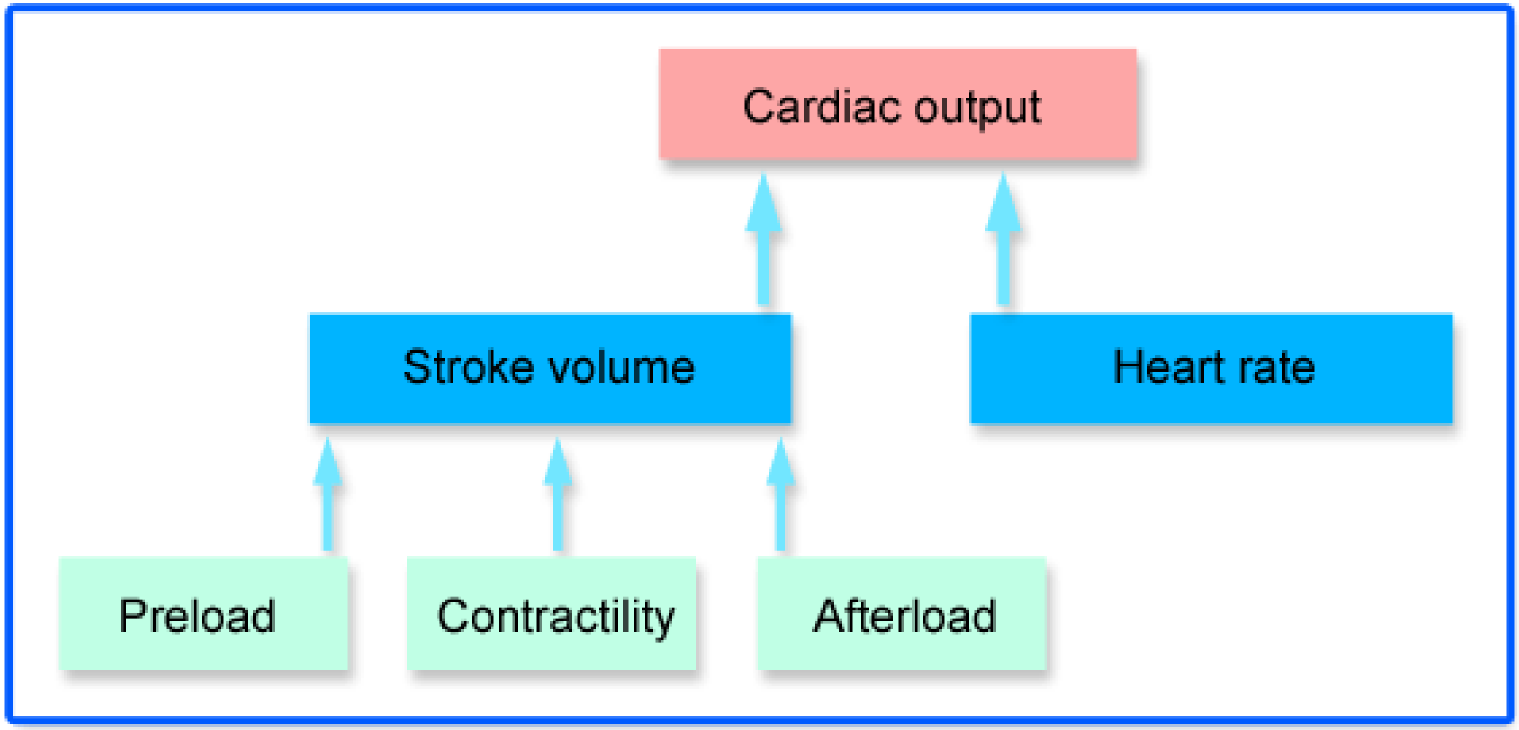
- Cardiac angiography



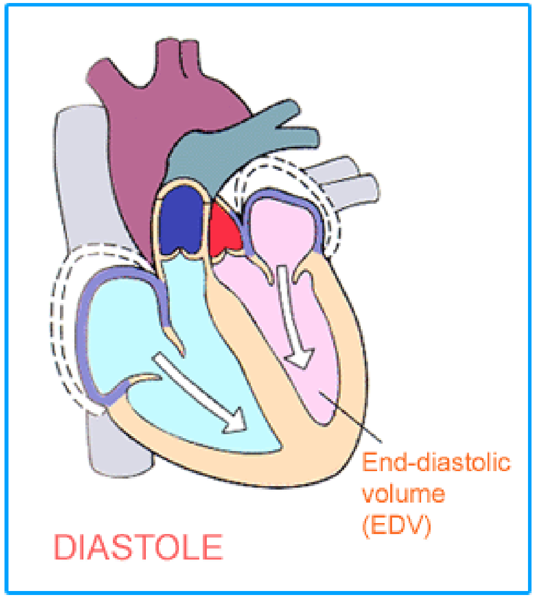
Coronary Angiography from a 56-year-old man presented with unstable angina and acute pulmonary edema

Rerkpattanapipat P, et al. Circulation. 1999;99:2965

Regulation of heart pumping



Regulation of stroke volume

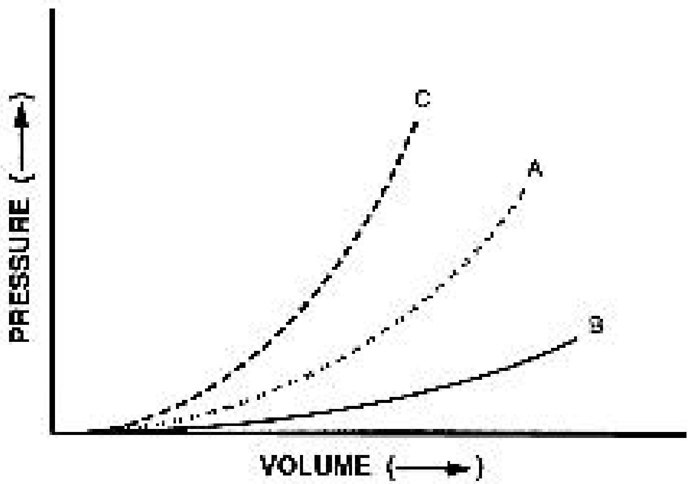


1. Preload – Frank-Starling mechanism

Preload of ventricles:

end-diastolic volume (EDV)

end-diastolic pressure (EDP)



Frank-Starling mechanism

(Intrinsic regulation or heterometric regulation)

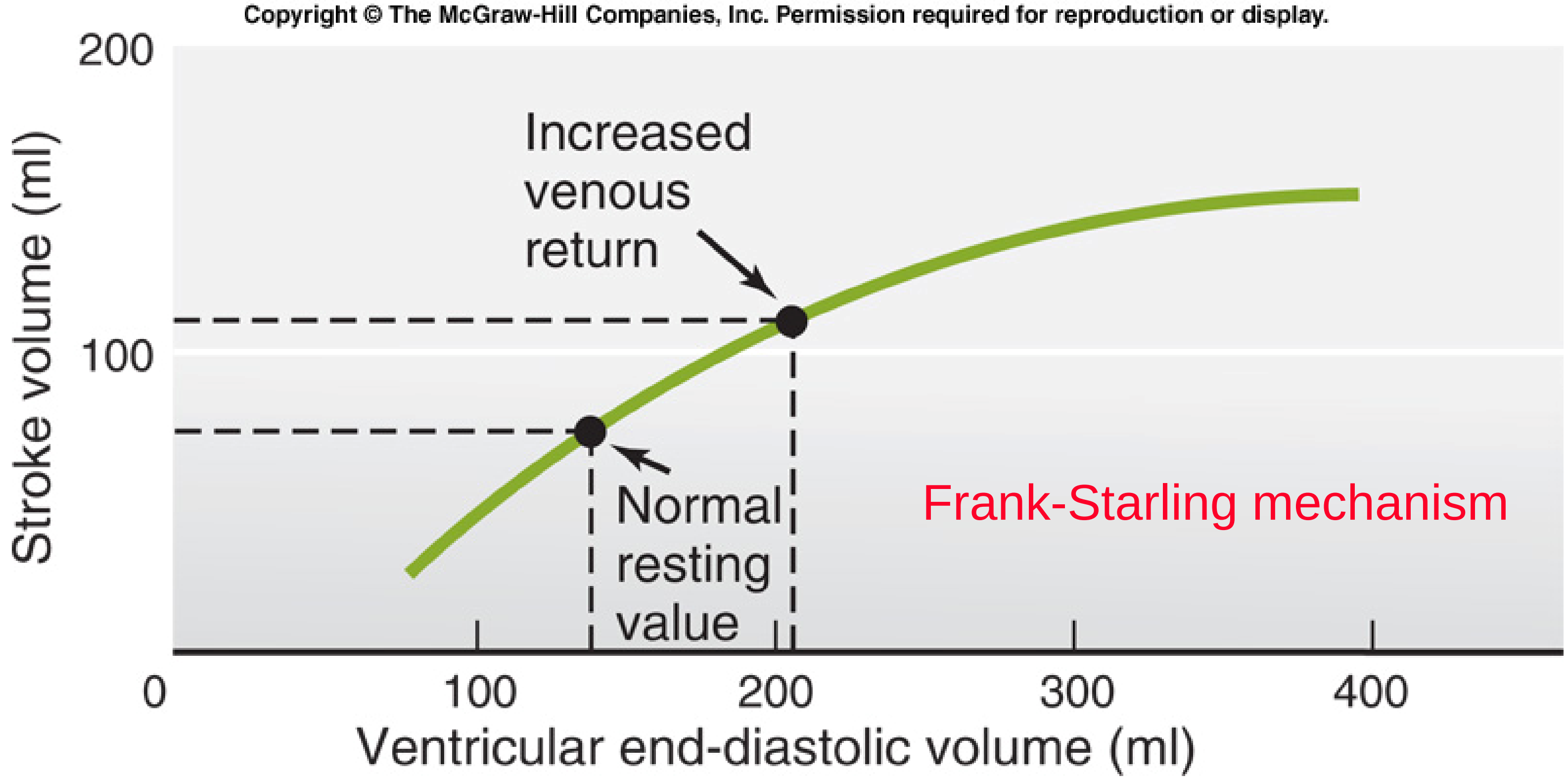
The fundamental principle of cardiac behavior which states that the force of contraction of the cardiac muscle is proportional to its initial length

Significance:

Precise regulation of SV

Figure 12-25

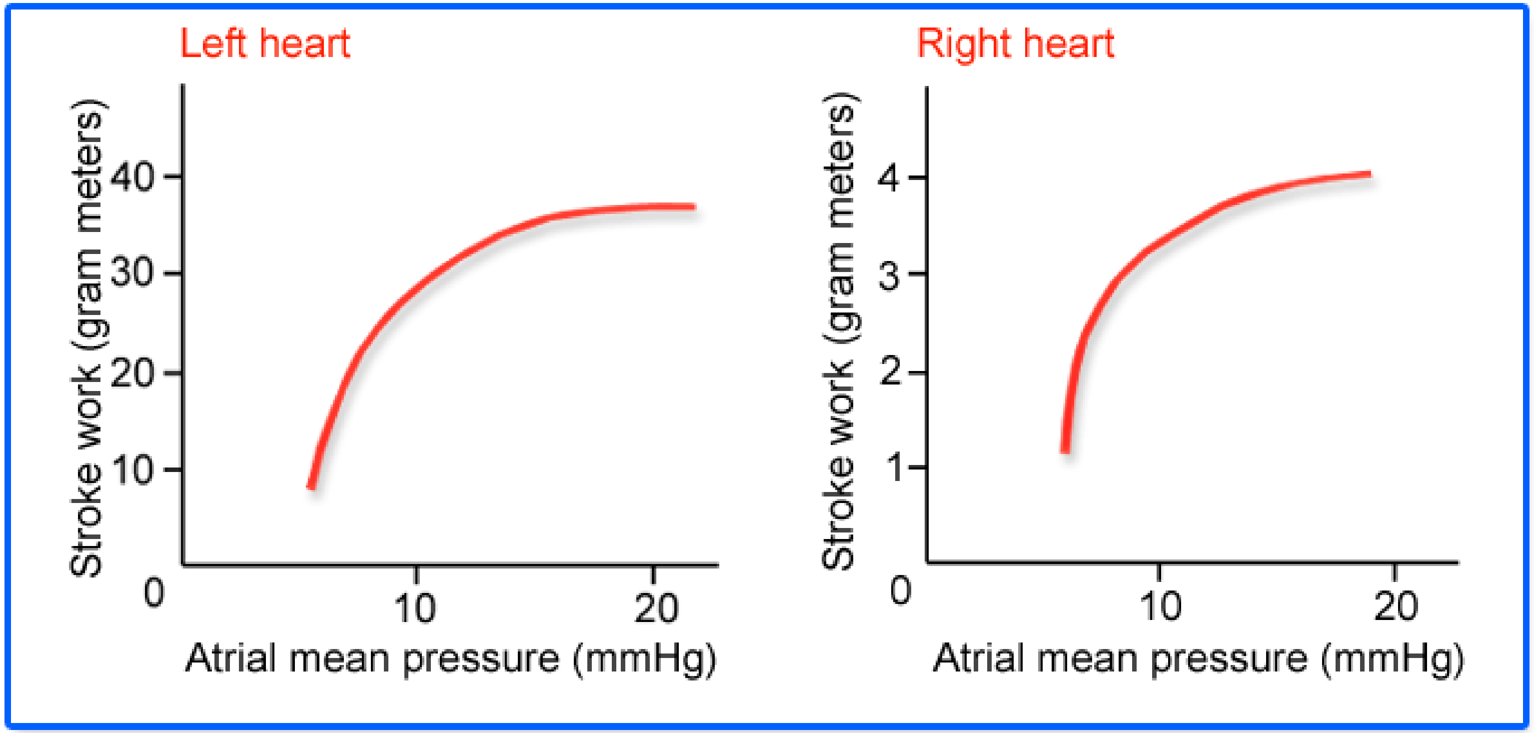
Control of stroke volume



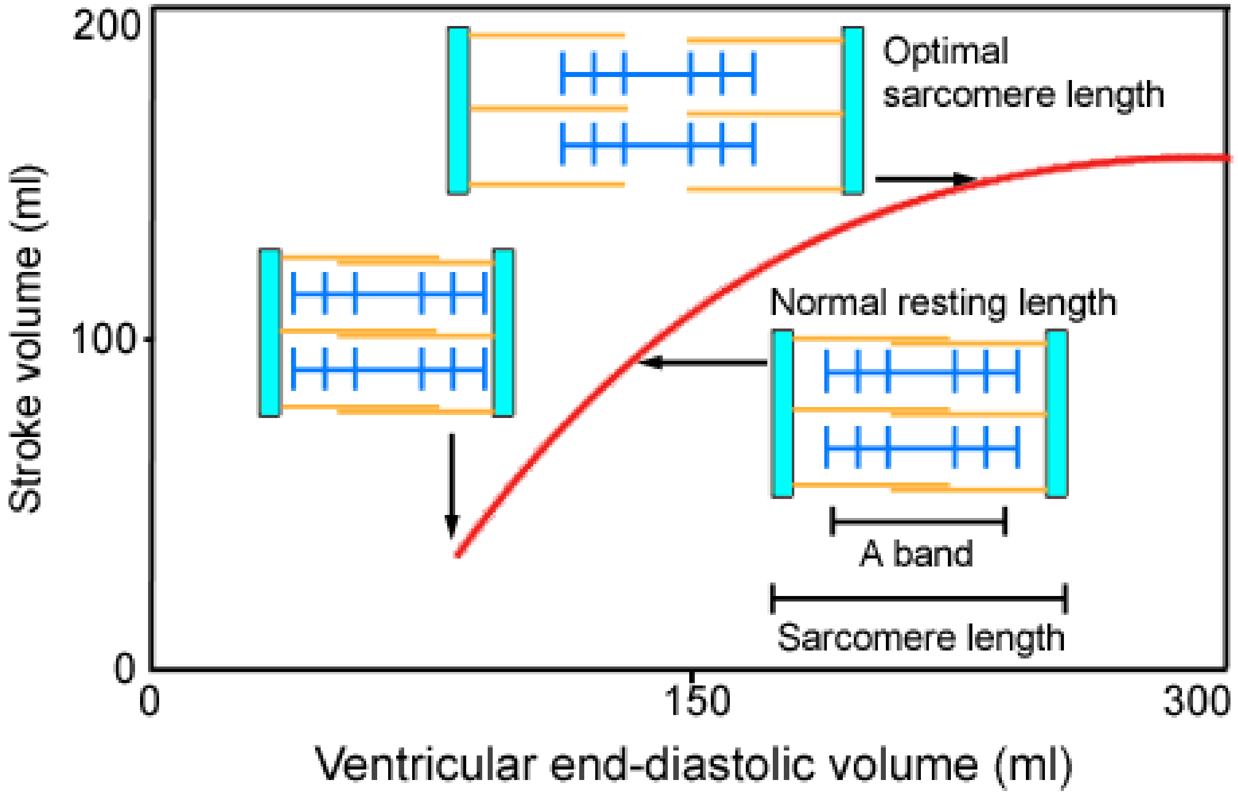
To increase the heart's stroke volume:

fill it more fully with blood. The increased stretch of the ventricle will align its actin and myosin in a more optimal pattern of overlap.

Ventricular function curve (Frank-Starling curve)



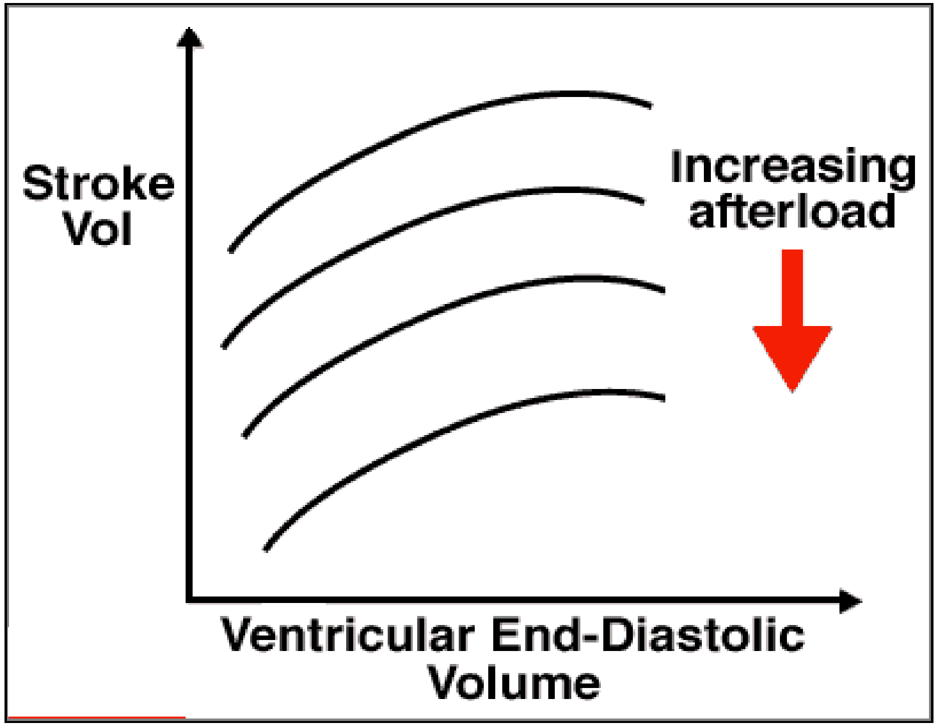
Ventricular function curve (Frank-Starling curve)

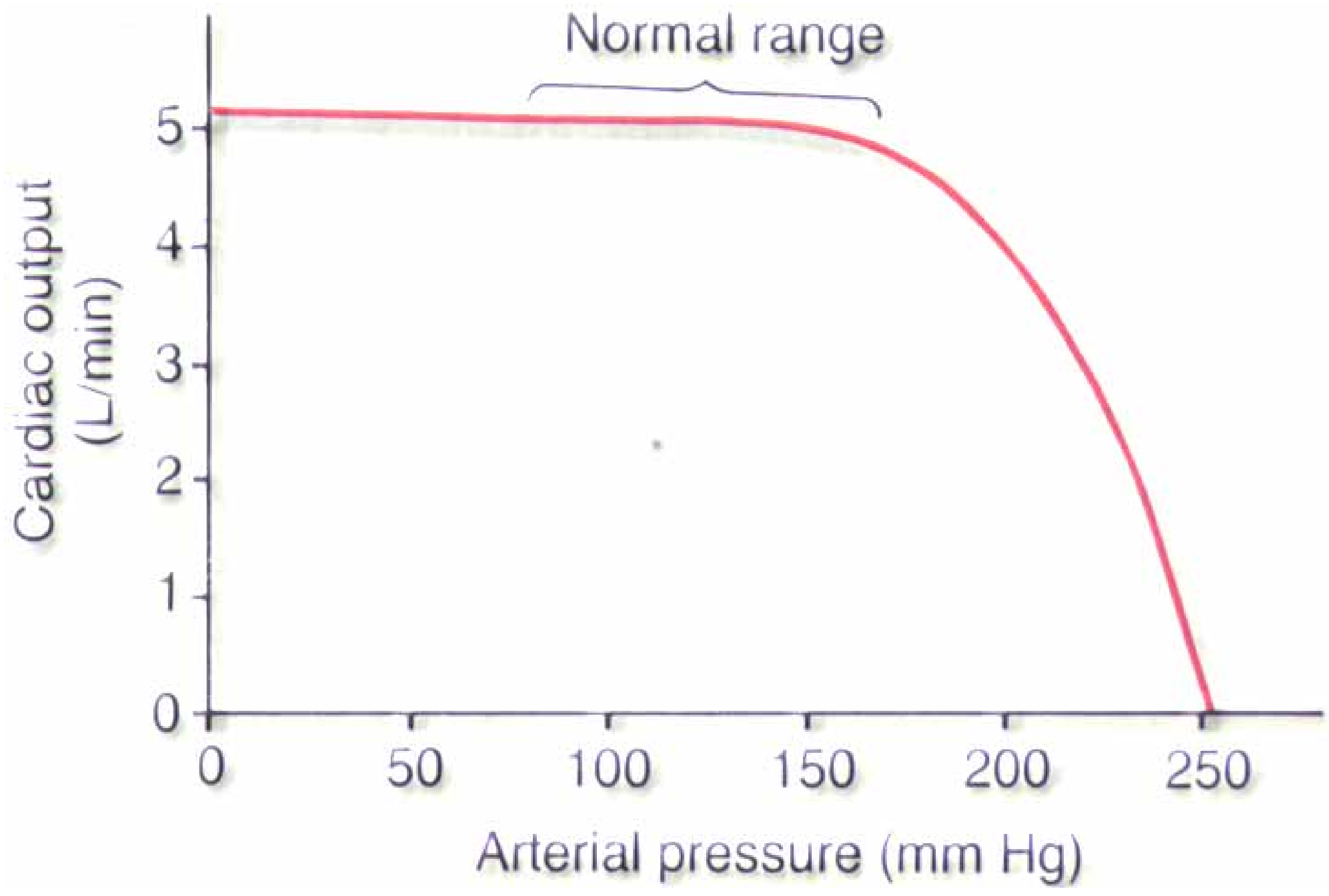


Factors affecting preload (EDV)

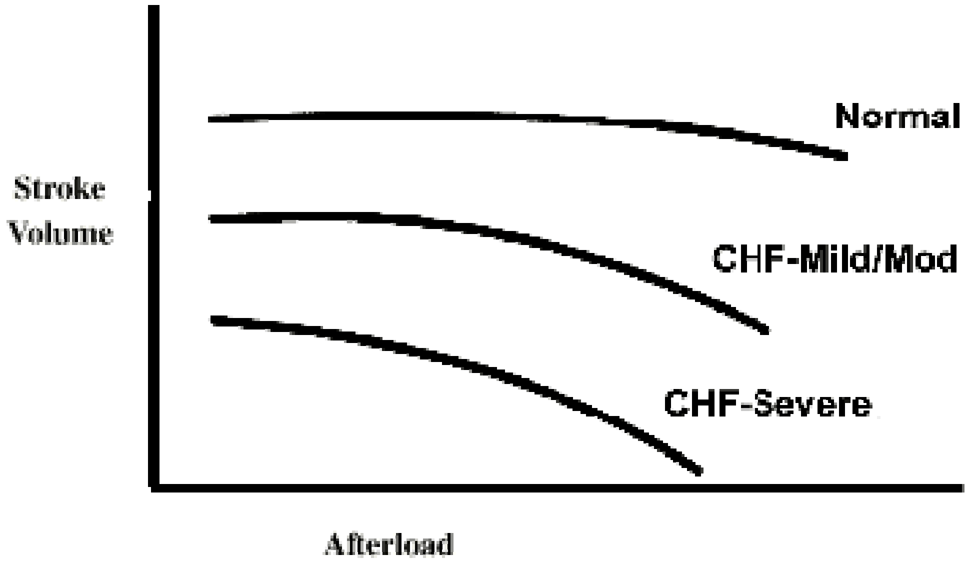
- (1) Venous return
  - Filling time
  - Venous return rate
  - Compliance
- (2) Residual blood in ventricles after ejection

2. Afterload (Usually measured as arterial pressure)





Normal range
Cardiac output (L/min)
0
1
2
3
4
5
0
50
100
150
200
250
Arterial pressure (mm Hg)



- Afterload has very little effect on the normal ventricle
- However, as systolic failure develops even small increases in afterload have significant effects on compromised ventricular systolic function
- Conversely, small reductions in afterload in a failing ventricle can have significant beneficial effects on impaired contractility

3. Myocardial contractility (Inotropic state)

Homometric regulation

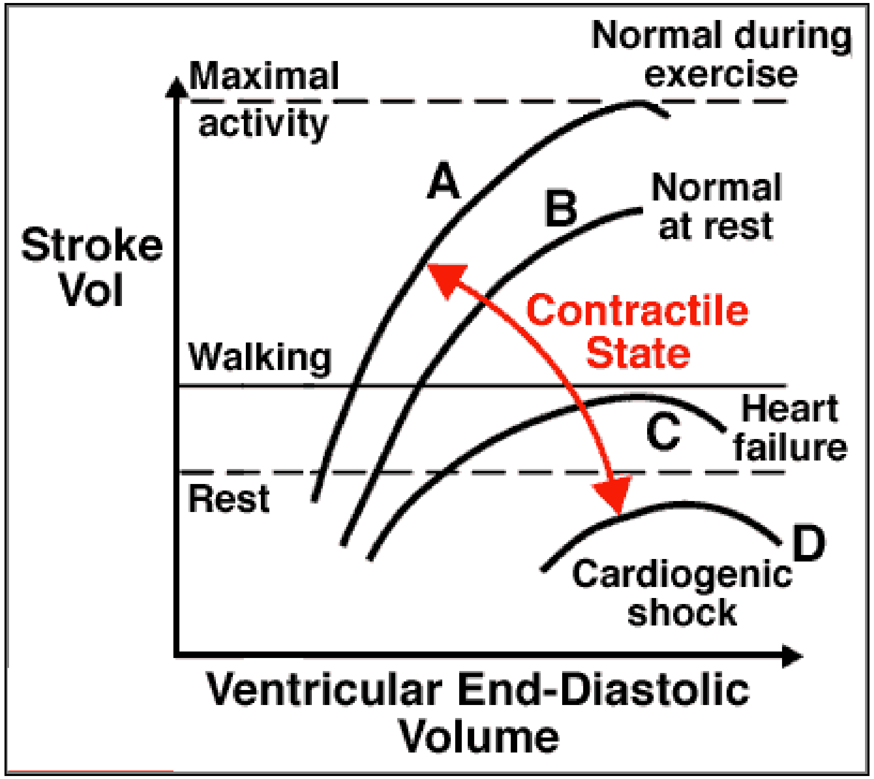


Figure 12-26

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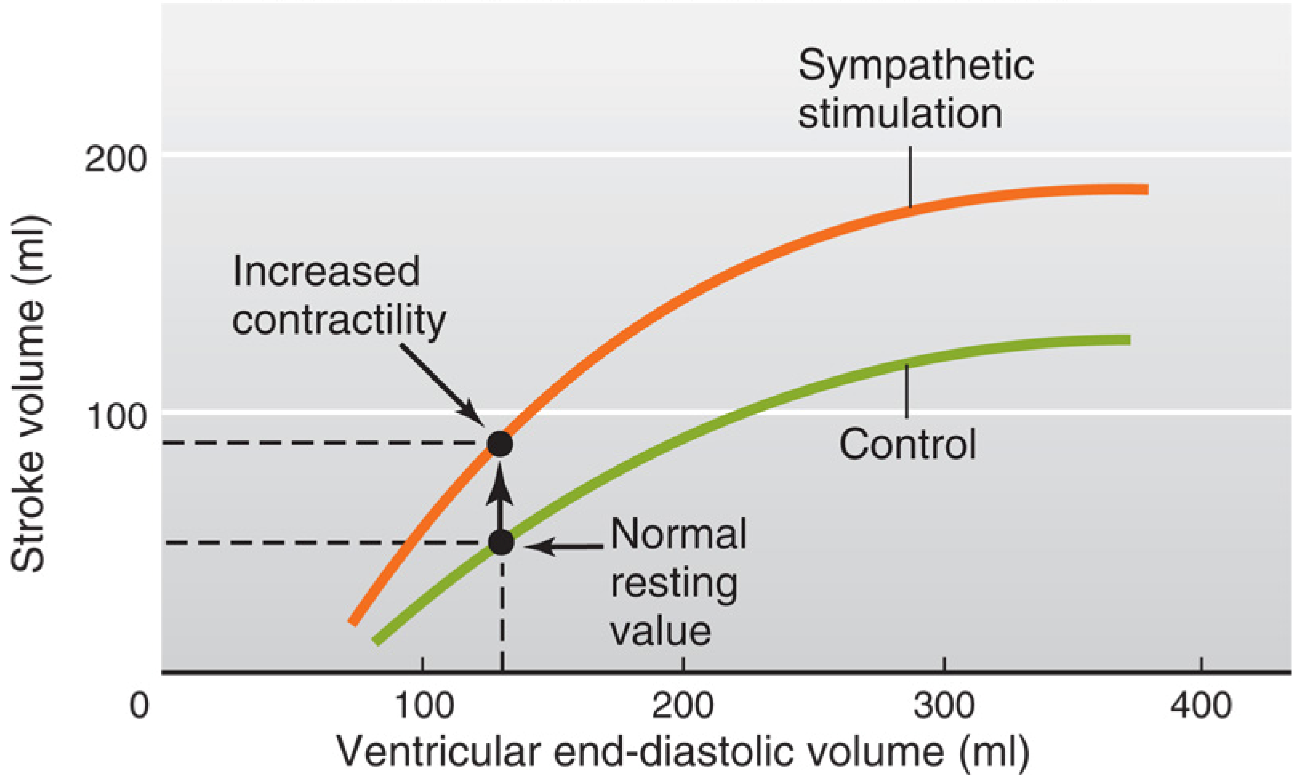

To further increase the stroke volume:

fill it more fully with blood

AND

deliver sympathetic signals (norepinephrine and epinephrine); it will also relax more rapidly, allowing more time to refill.

Figure 12-27

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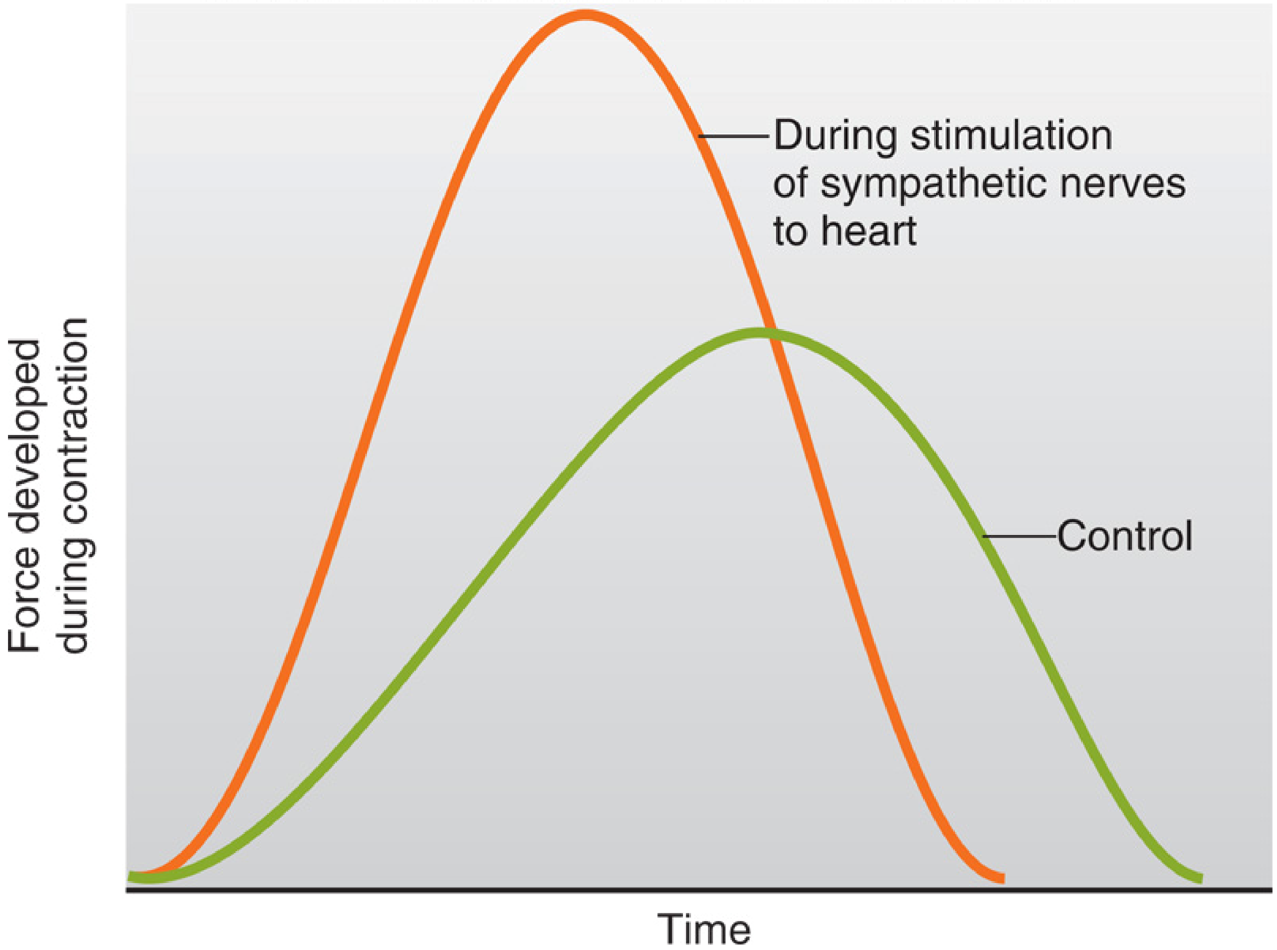
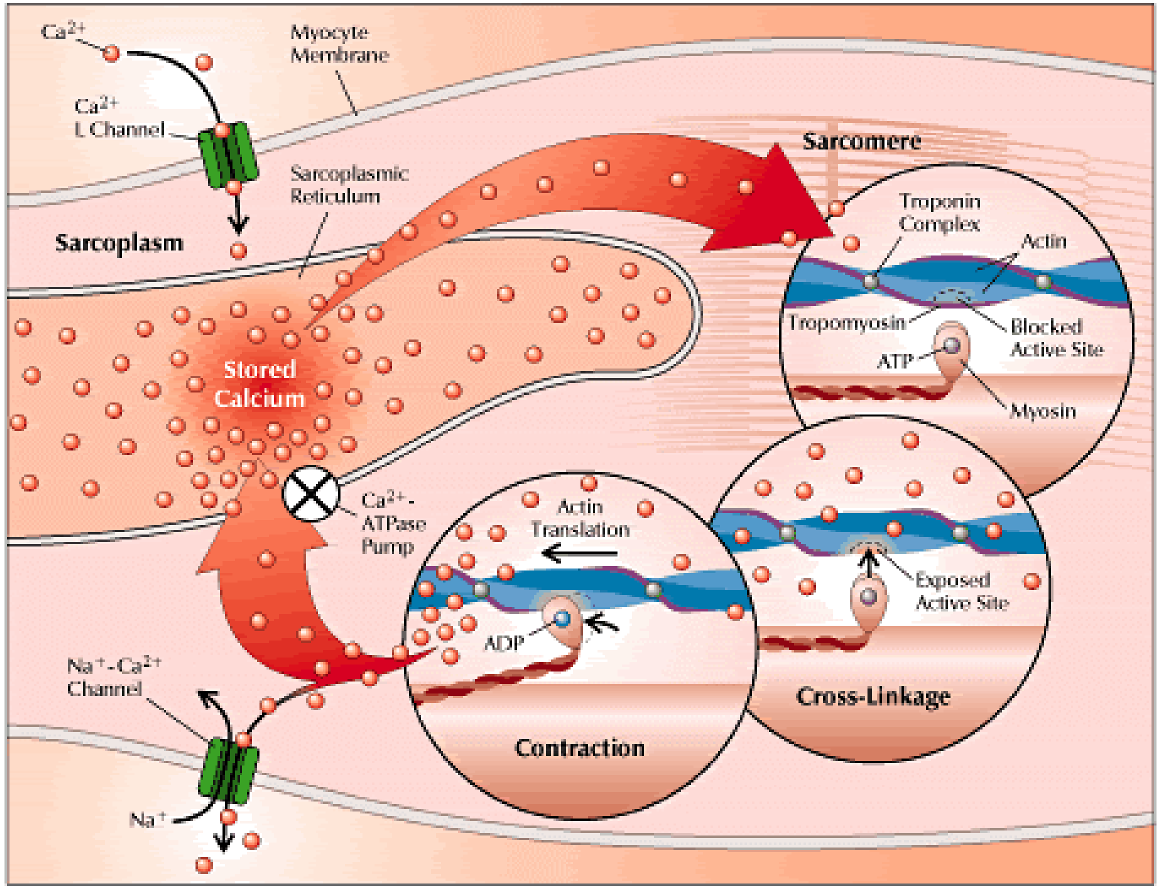
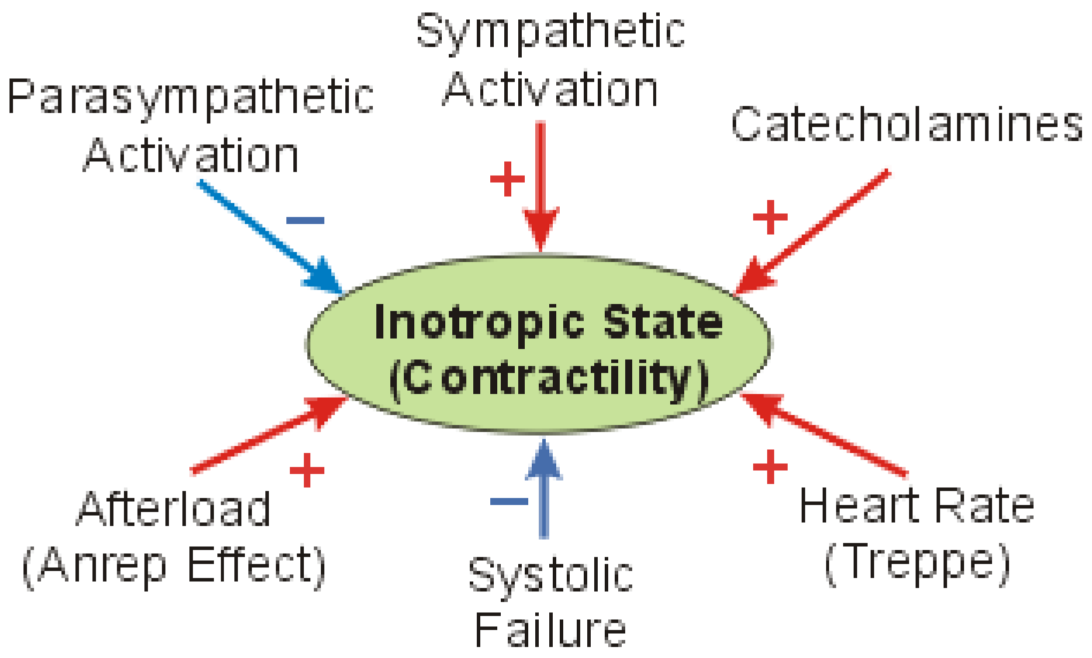


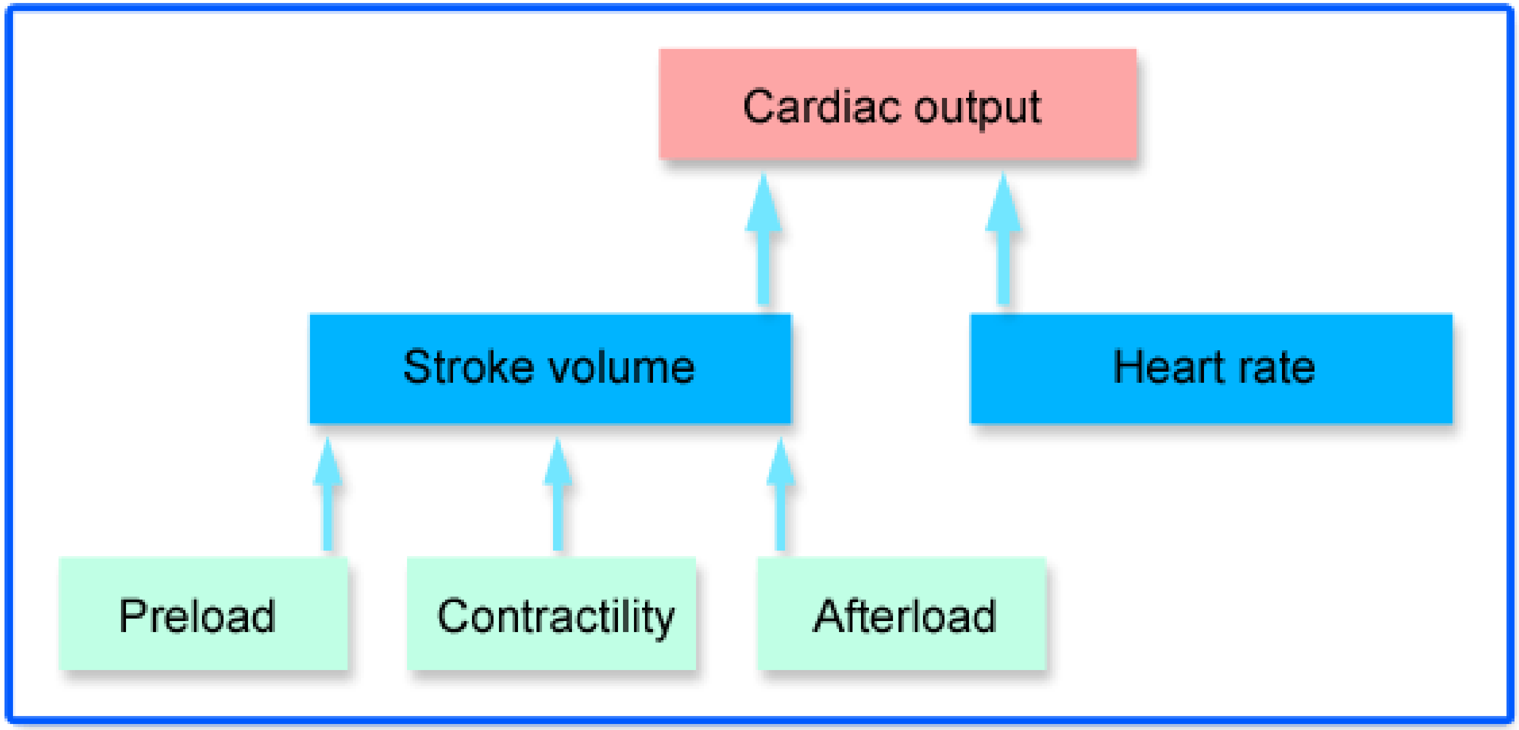
Sympathetic signals (norepinephrine and epinephrine) cause a stronger and more rapid contraction *and* a more rapid relaxation.



Ca2+
Myocyte Membrane
Ca2+ L Channel
Sarcomere
Sarcoplasmic Reticulum
Sarcoplasm
Troponin Complex
Actin
Tropomyosin
Blocked Active Site
ATP
Stored Calcium
Myosin
Ca2+-ATPase Pump
Actin Translation
Exposed Active Site
ADP
Na+-Ca2+ Channel
Cross-Linkage
Contraction
Na+

Factors regulating contractility

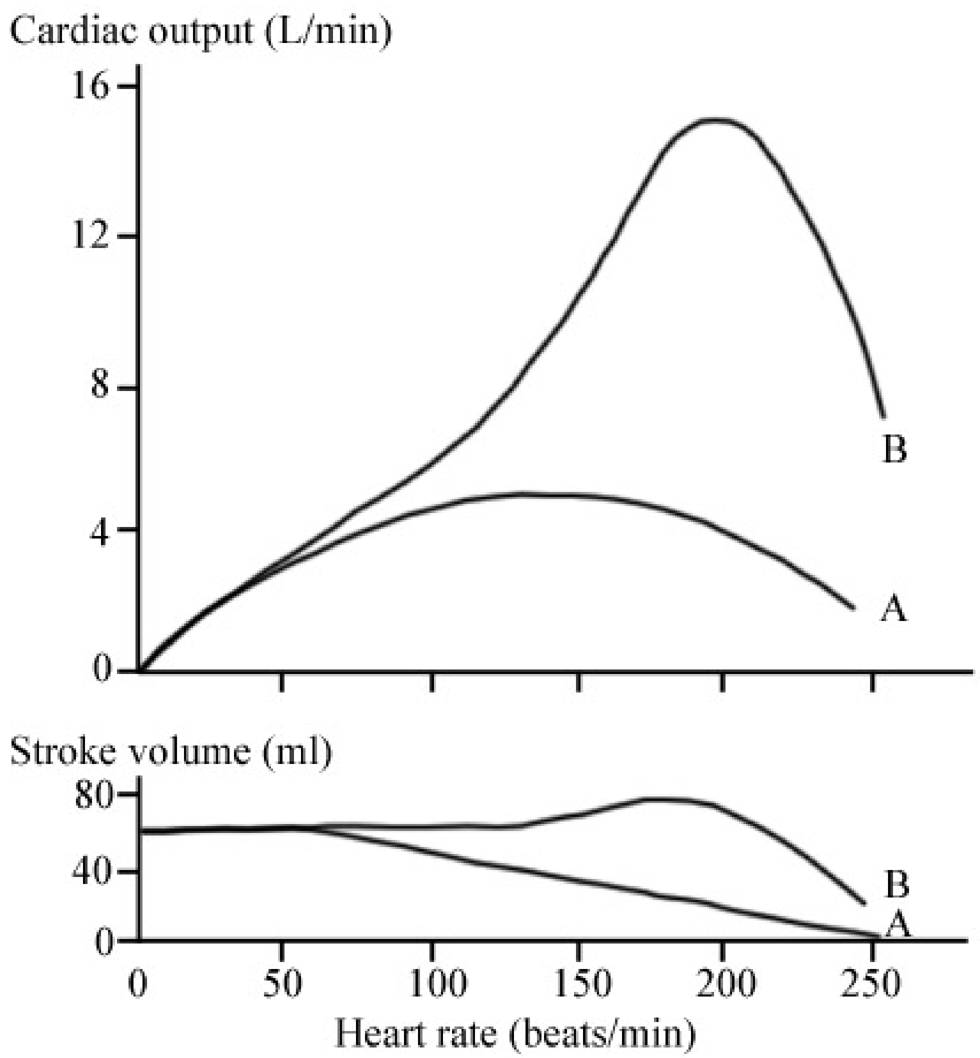



Cardiac output
Stroke volume
Heart rate
Preload
Contractility
Afterload

Regulation of heart rate

- HR↑→CO↑ (CO = SV x HR)
- HR↑→Contractility↑ (Treppe effect)
- HR↑→ diastolic filling time ↓

- ⊙ 40~180 /min，HR↑→CO↑
- ⊙ >180 /min，or <40/min，CO↓



A: resting
B: exercise

Control of heart rate

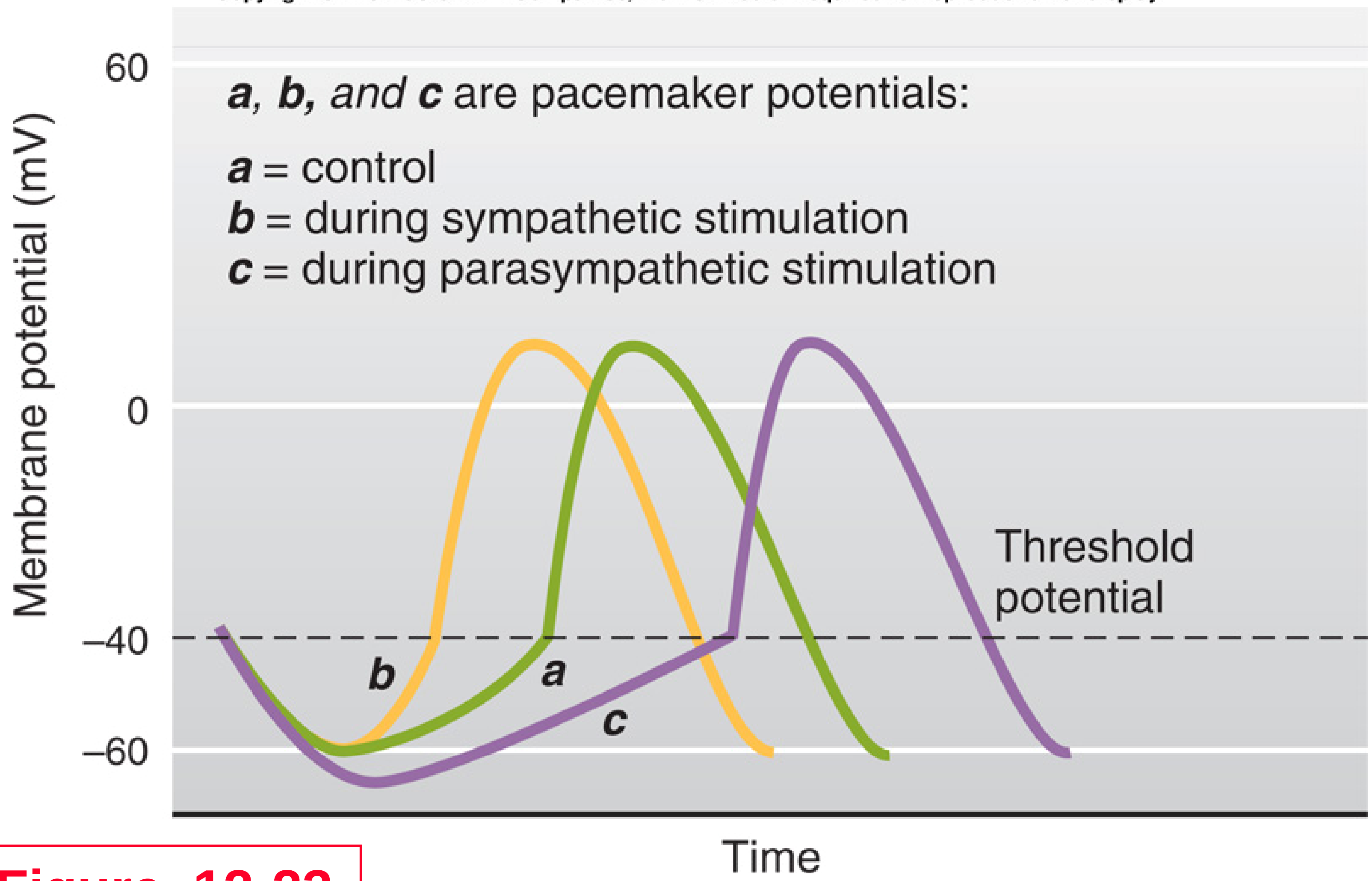
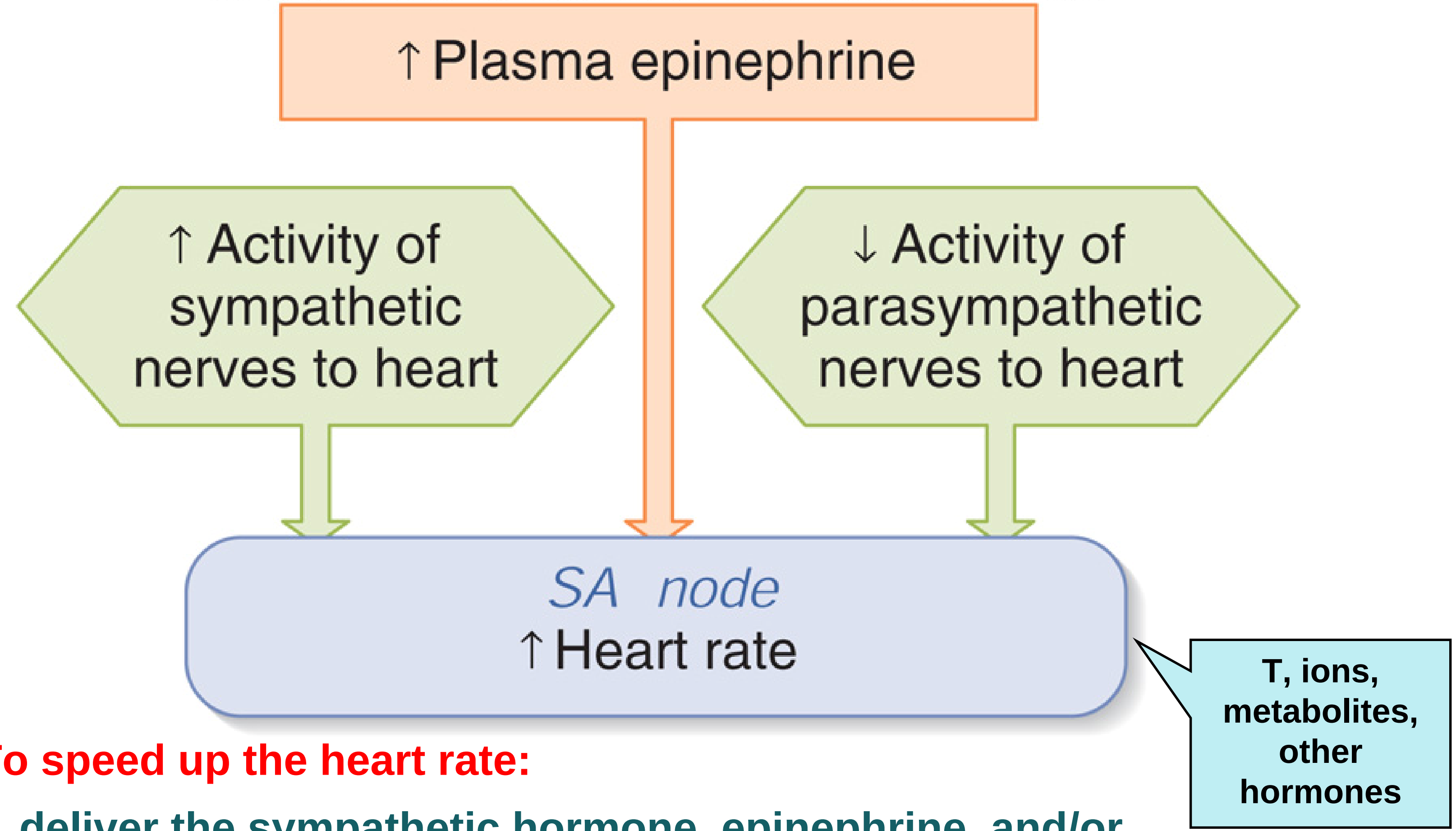


Figure 12-23

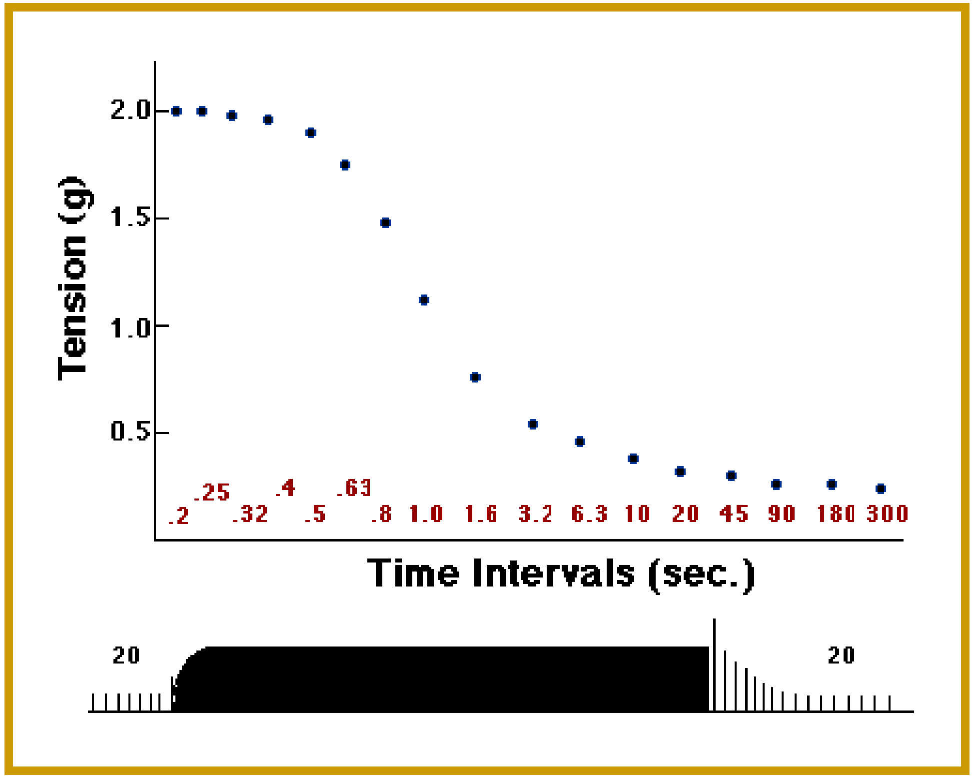
Figure 12-24



To speed up the heart rate:

- **deliver the sympathetic hormone, epinephrine, and/or**
- **release more sympathetic neurotransmitter (norepinephrine), and/or**
- **reduce release of parasympathetic neurotransmitter (acetylcholine).**

Staircase phenomenon (Treppe effect , Force-frequency relationship)



Increase in rate of contraction (heart rate) causes increase in contractility

TABLE 12–3 Effects of Autonomic Nerves on the Heart

AREA AFFECTED	SYMPATHETIC NERVES	PARASYMPATHETIC NERVES
SA node	Increased heart rate	Decreased heart rate
AV node	Increased conduction rate	Decreased conduction rate
Atrial muscle	Increased contractility	Decreased contractility
Ventricular muscle	Increased contractility	No significant effect

To increase SV, increase:
end-diastolic volume, norepinephrine delivery from sympathetic neurons, and epinephrine delivery from the adrenal medulla.

To increase HR, increase:
norepinephrine delivery from sympathetic neurons, and epinephrine delivery from adrenal medulla (reduce parasympathetic).

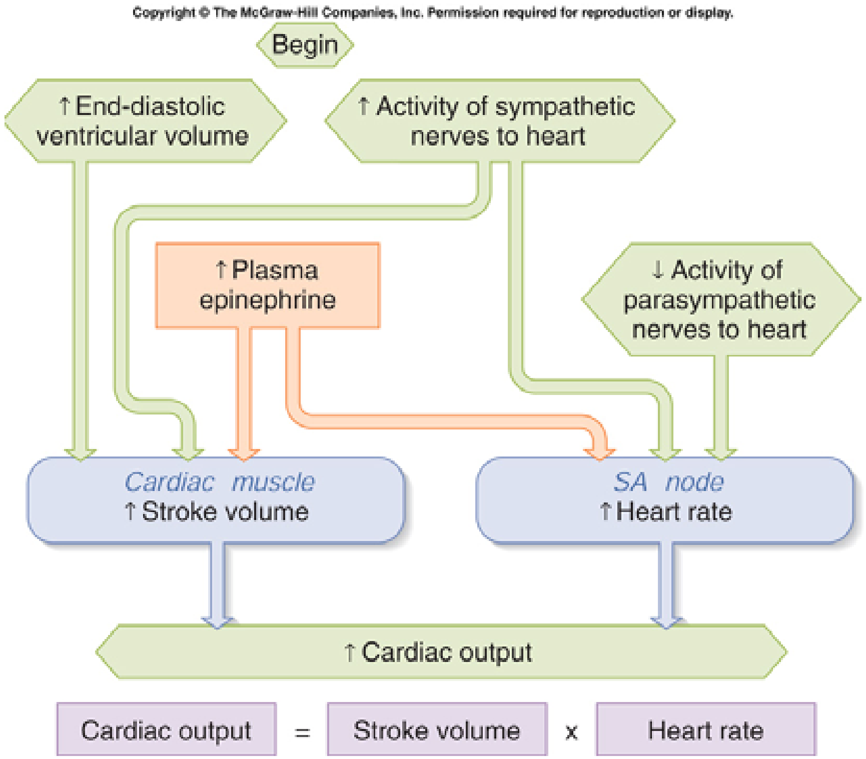


Figure 12-28

It is not possible, under normal circumstances, to increase one but not the other of these determinants of cardiac output.

The End.