Introduction to Cardiovascular Physiology

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Overview of the CV system

- Purposes
  - Distribute metabolites and O_2
  - Collect wastes and CO_2
  - Thermoregulation
  - Hormone distribution
- Components
  - Heart – the driving force
  - Arteries – distribution channels
  - Veins - collection channels
  - Capillaries – exchange points

Anatomy of the vasculature

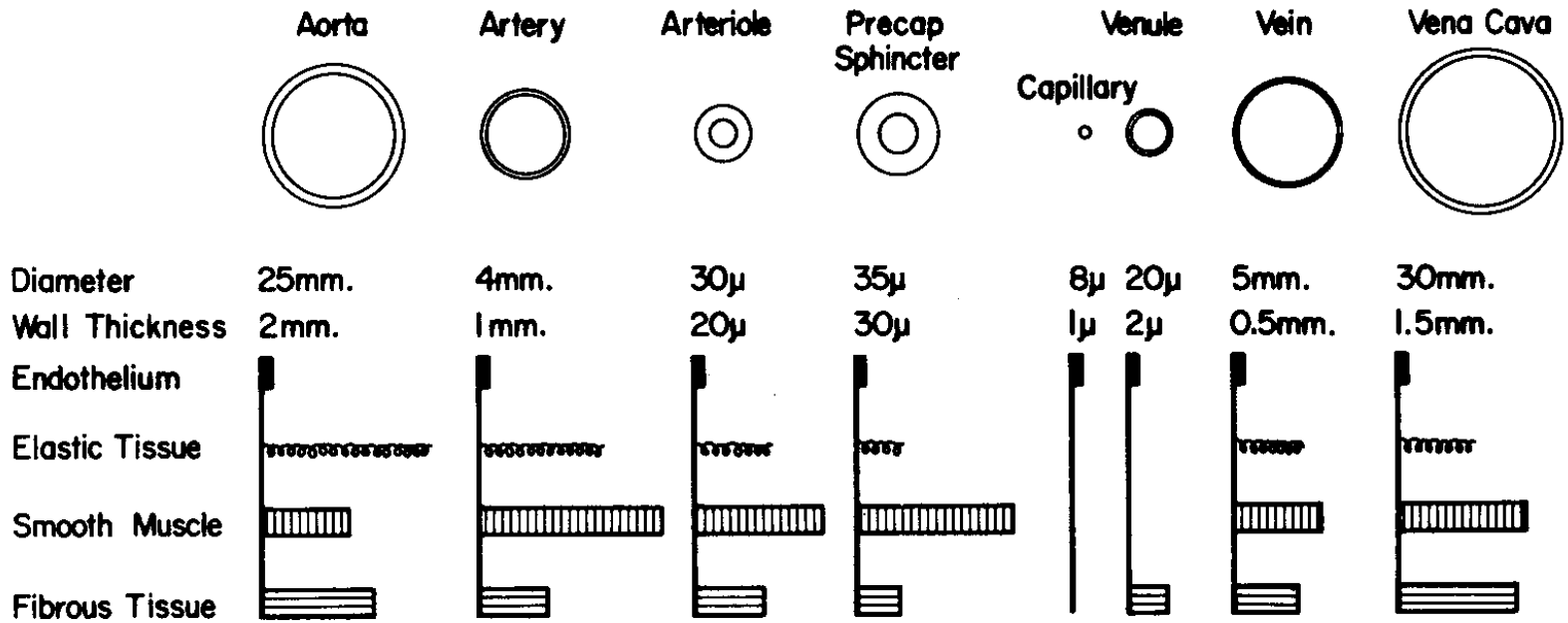
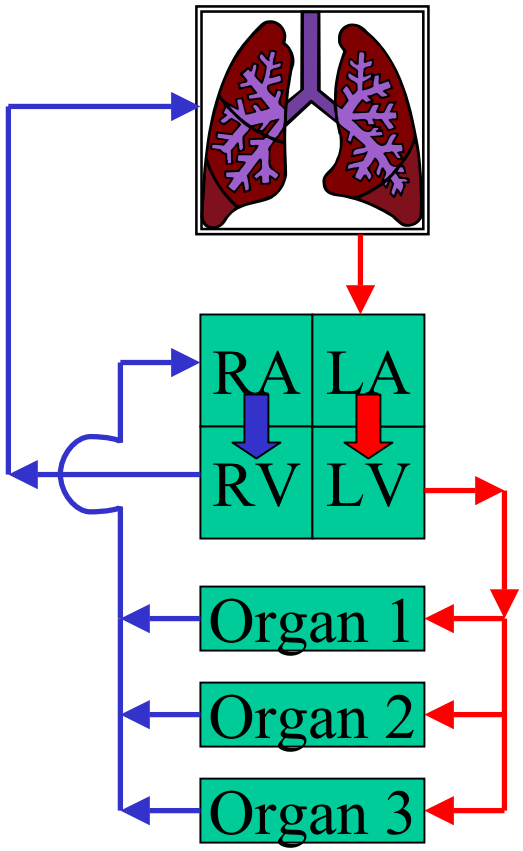


Fig. 1-1. Internal diameter, wall thickness, and relative amounts of the principal components of the vessel walls of the various blood vessels that compose the circulatory system. Cross sections of the vessels are not drawn to scale because of the huge range from aorta and venae cavae to capillary. (Redrawn from Burton, A. C.: Physiol. Rev. **34**:619, 1954.)

Parallel and series design



- A given volume of blood passes through a single organ
- Blood entering an organ has uniform composition
- Perfusion pressure is the same for each organ
- Blood flow to each organ can be controlled independently

Relationships among the vascular beds

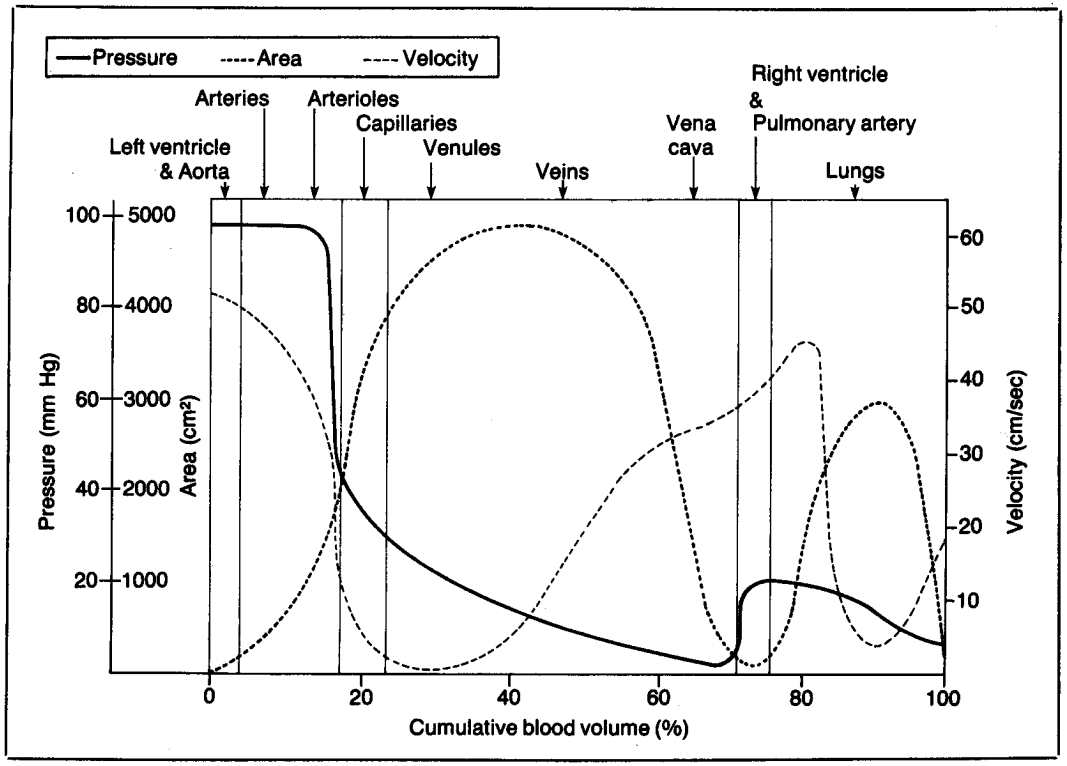


Figure 2-2. Relationships between velocity, area, volume, and pressure in various segments of the cardiovascular system. The same volume of blood must pass through each segment of the system per unit time; therefore, the velocity and area are inversely related. The resistance of the large vessels is minimal, so pressure loss also is minimal until the small arterioles are reached.

- Flow is constant in each segment, so velocity and area are inversely related
- Pressure loss occurs mainly at the small arterioles, the resistance vessels
- The veins contain most of the blood

Properties of arteries

- Elastic arteries
  - Consists of the Aorta and its large branches
  - Fairly distensible because of high elastin content
  - Diastolic elastic recoil provides potential energy for flow when the heart is not contracting
- Muscular arteries
  - Most of the named arteries
  - Contain increased smooth muscle
  - Large lumen-to-wall ratio

Properties of the microcirculation

- Consists of arterioles, capillaries, and venules
- Arterioles
  - Reduced lumen-to-wall ratio
  - Controlling point for flow
  - Convert pulsatile to steady flow
- Capillaries
  - Exchange point between blood and interstitial fluid
  - Mechanisms of exchange include:
    - Diffusion
    - Bulk flow
    - Vesicular transport

Equations of exchange

- Diffusion is described by:

$$Q = DA\frac{dc}{dx}$$

where Q is flow, A is area, D is the diffusion coefficient, and dc/dx is the concentration gradient. D incorporates such constants as solubility, temperature, and molecular size.

- Bulk flow is described by the Starling equation:

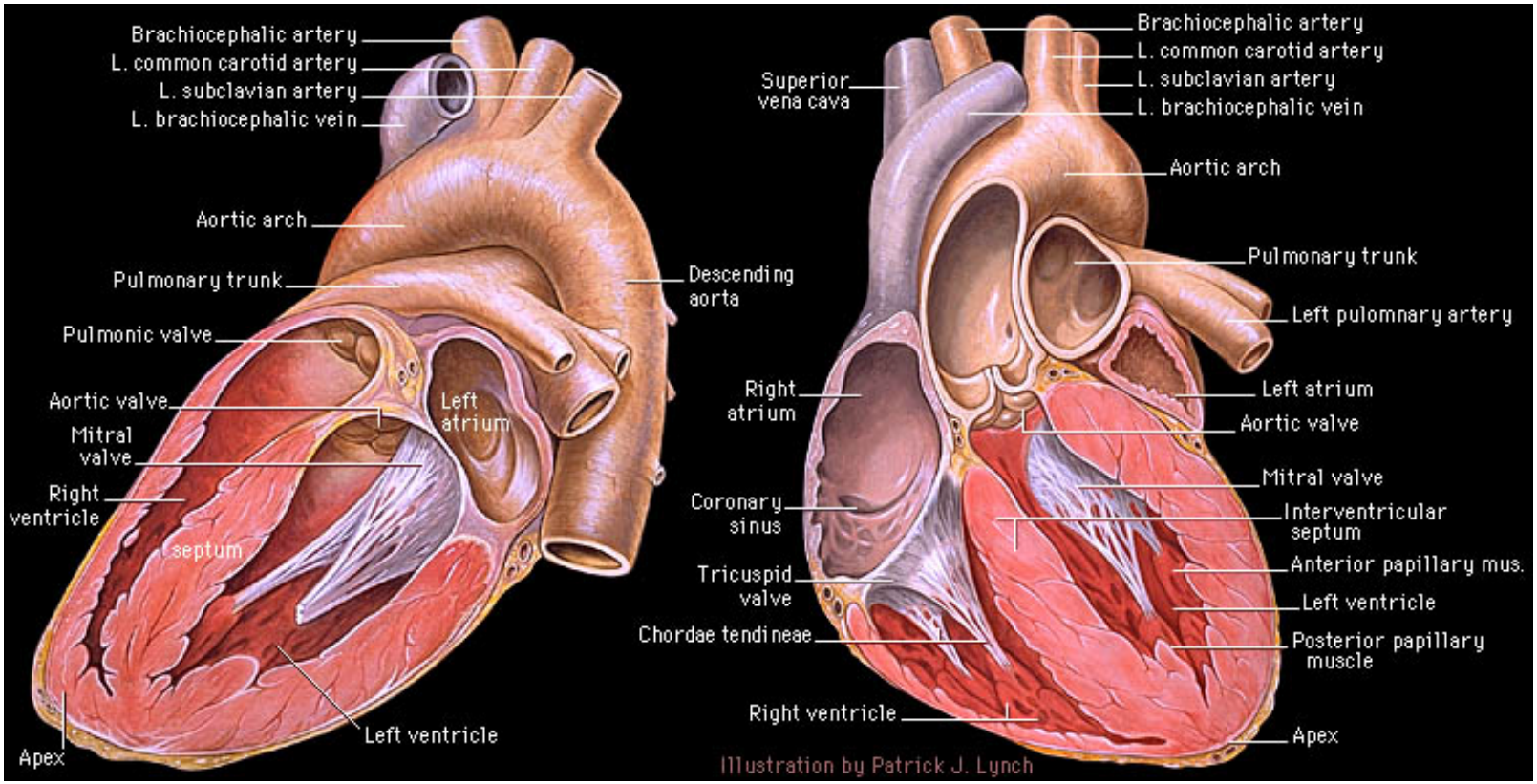
$$Q = k(\Delta P - \Delta \pi)$$

where Q is the flow of water, ΔP is the hydrostatic pressure difference, Δπ is the osmotic pressure difference, and k is the hydrostatic permitivity constant.

Veins and lymphatics

- Veins
  - Thin-walled, smaller amounts of smooth muscle or elastin
  - Slow flow, large cross-sectional area
  - Acts a conduits and reservoirs
  - Venoconstriction raises ventricular filling, cardiac output
- Lymphatics
  - Drains the interstitium
    - Only route for of returning interstitial proteins
  - Low flow (~2L/day)

Cardiac anatomy



- The myocardial syncytium
  - All atrial cells are coupled, all ventricular cells are coupled, the AV node links the two
  - Connections between cells are known as intercalated disks
- Electrical activation leads to contraction (EC coupling)

Cardiac cellular anatomy

- Basic units is a sarcomere (Z line to Z line)
  - Think filaments of myosin in the A band
  - Thin filaments of actin in the I band
- Sarcoplasmic reticulum
  - Holds Ca^{2+}
  - Forms cisternae
  - Approximation to T tubules (sacrolemmal invaginations) known as a dyad

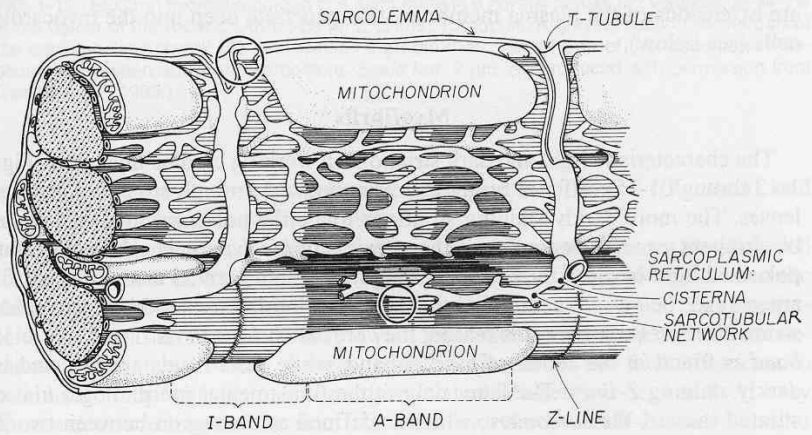
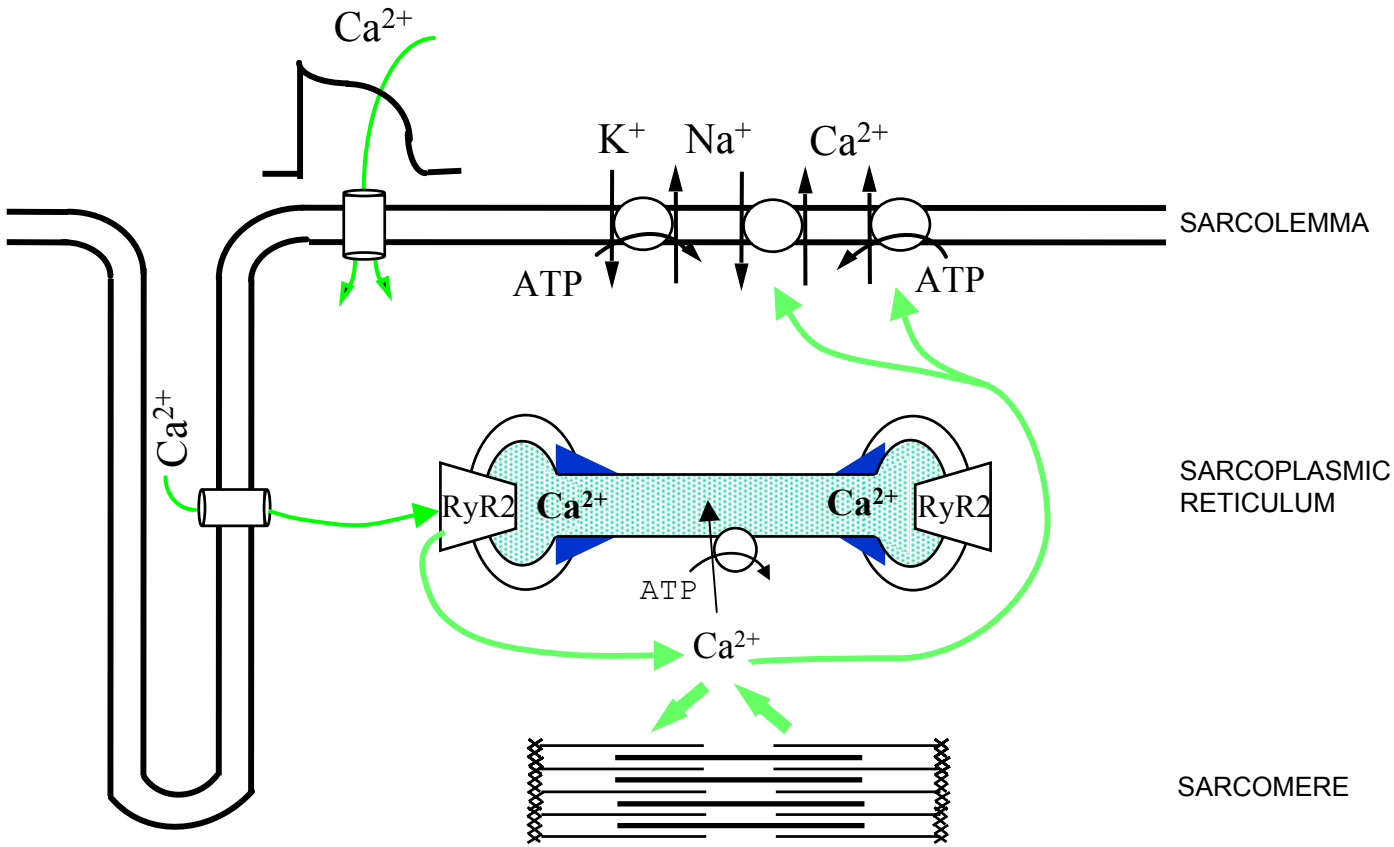


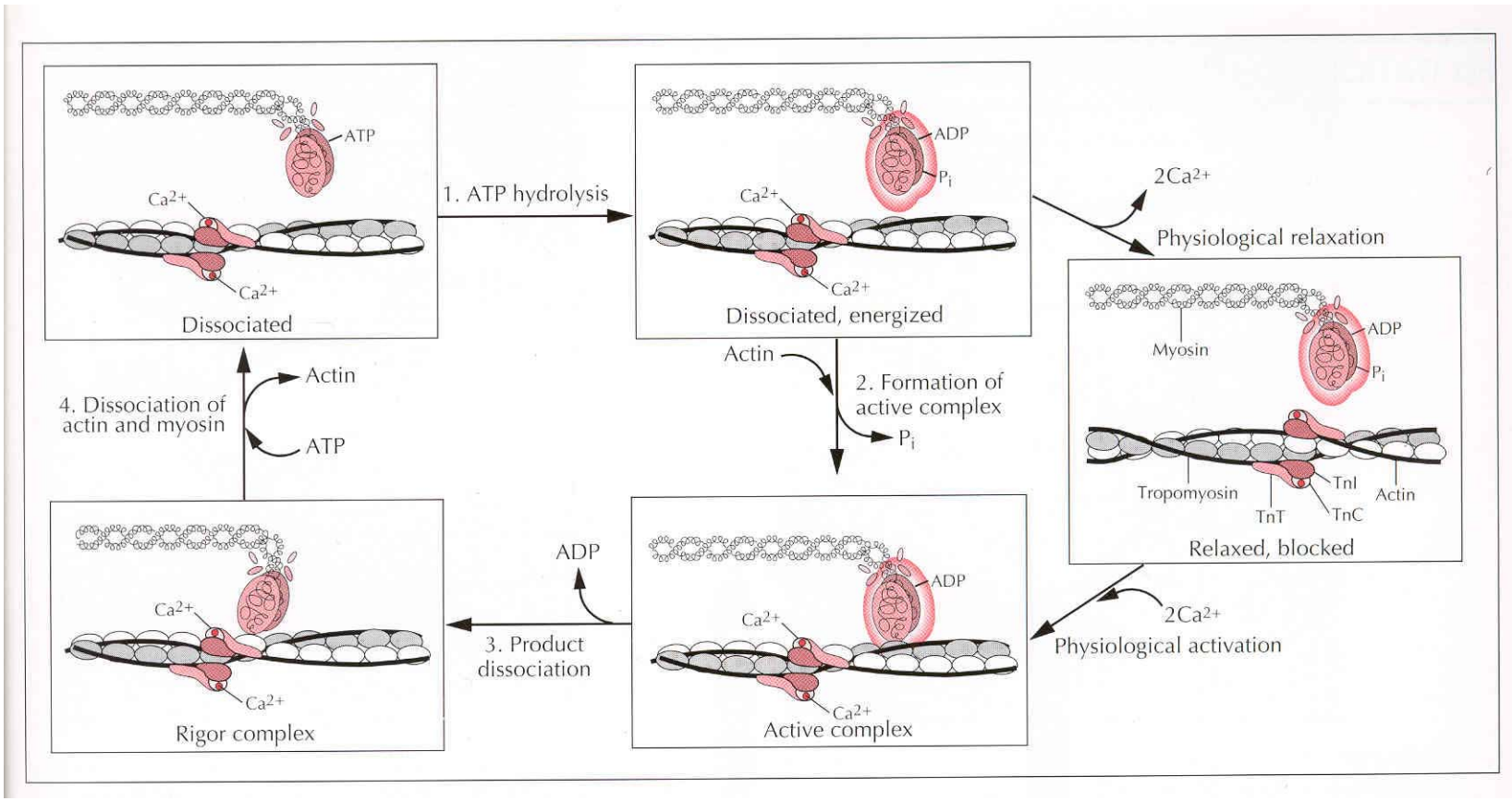
FIG. 1-14. Ultrastructure of the working myocardial cell. Contractile proteins are arranged in a regular array of thick and thin filaments (seen in cross section at the *left*). The A-band represents the region of the sarcomere occupied by the thick filaments into which thin filaments extend from either side. The I-band is the region of the sarcomere occupied only by thin filaments; these extend toward the center of the sarcomere from the Z-lines, which bisect each I-band. The sarcomere, the functional unit of the contractile apparatus, is defined as the region between successive Z-lines and contains two half-I-bands and one A-band. The sarcoplasmic reticulum, a membrane network that surrounds the contractile proteins, consists of the sarcotubular network at the center of the sarcomere and the cisternae, which abut on the t-tubules and the sarcolemma. The transverse tubular system (t-tubule) is lined by a membrane that is continuous with the sarcolemma, so that the lumen of the t-tubules carries the extracellular space toward the center of the myocardial cell. Mitochondria are shown in the central sarcomere and in cross section at the *left*. (From Katz, 1975, copyright © 1975, Massachusetts Medical Society. All rights reserved.)

Ca^{2+} induced Ca^{2+} release

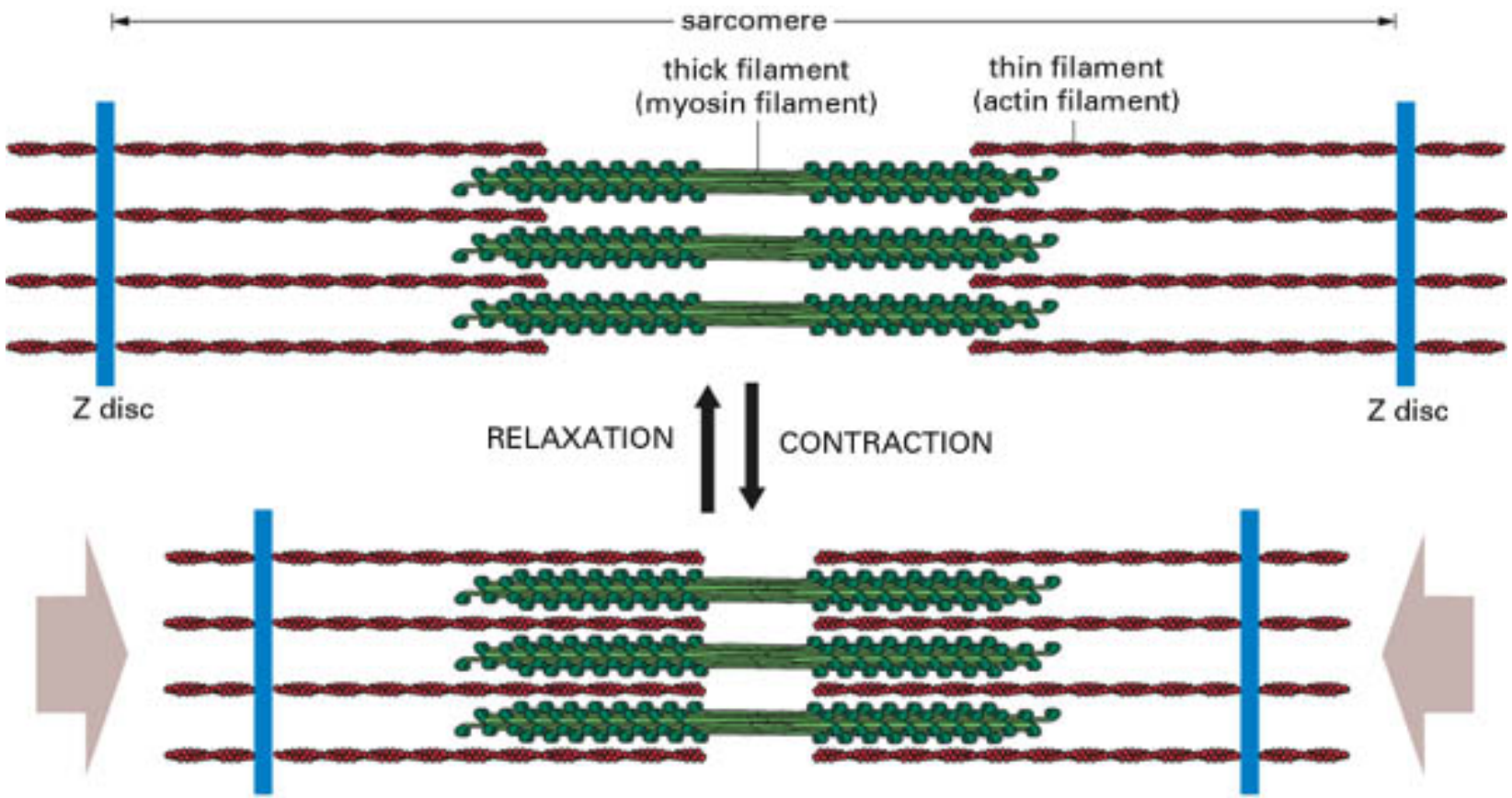


- Ca^{2+} enters from sacrolemmal Ca^{2+} channels, diffuses to the SR Ca^{2+} release channel (ryanodine receptor), and causes a large Ca^{2+} release.
- SR Ca^{2+} release raises intracellular Ca^{2+} from 10^{-7} M to 10^{-5} M, enough to cause Ca^{2+} binding to troponin, displacing tropomyosin, causing actin-myosin cross bridge cycling

The sliding filament hypothesis



Sliding filaments 2



Length-tension (Frank-Starling Effect)

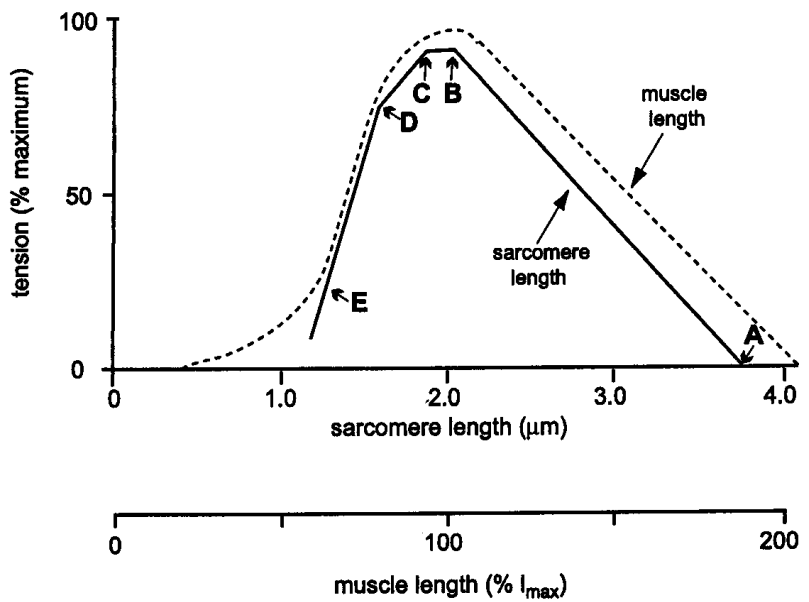
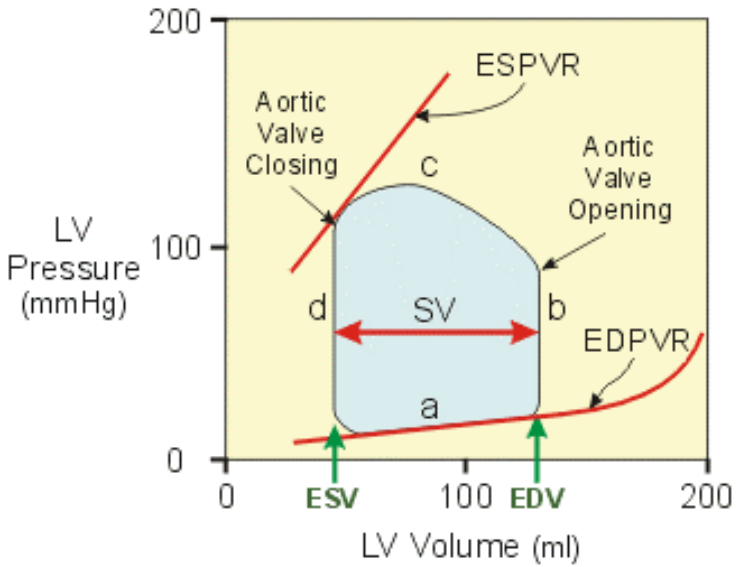


FIG. 8-11. Length–tension curve for a small group of sarcomeres in a frog semitendinosus muscle (*solid line*) compared with that for the whole muscle shown in Fig. 8-10 (*dashed line*). Sarcomere length is shown as the upper abscissa; muscle length is below. At a sarcomere length of 3.65 μm (*A*), no tension is developed. Tension rises to a maximum as the sarcomere shortens to a length of approximately 2.2 μm (*A* → *B*). As sarcomere length decreases to below approximately 2.0 μm (*B* → *C*), tension remains constant. When sarcomere length decreases below 2.0 μm, tension begins to decrease (*C* → *D*). At sarcomere lengths below approximately 1.65 μm (*D* → *E*), tension declines very rapidly. Contraction bands appear at these extremely short sarcomeres.

- Length of a fiber determines force generation
- The major determinate of length in the heart is chamber volume
- The ascending limb results from length-dependent changes in EC coupling
- The descending limb derives mostly from the number of thick and thin filament cross bridge interactions

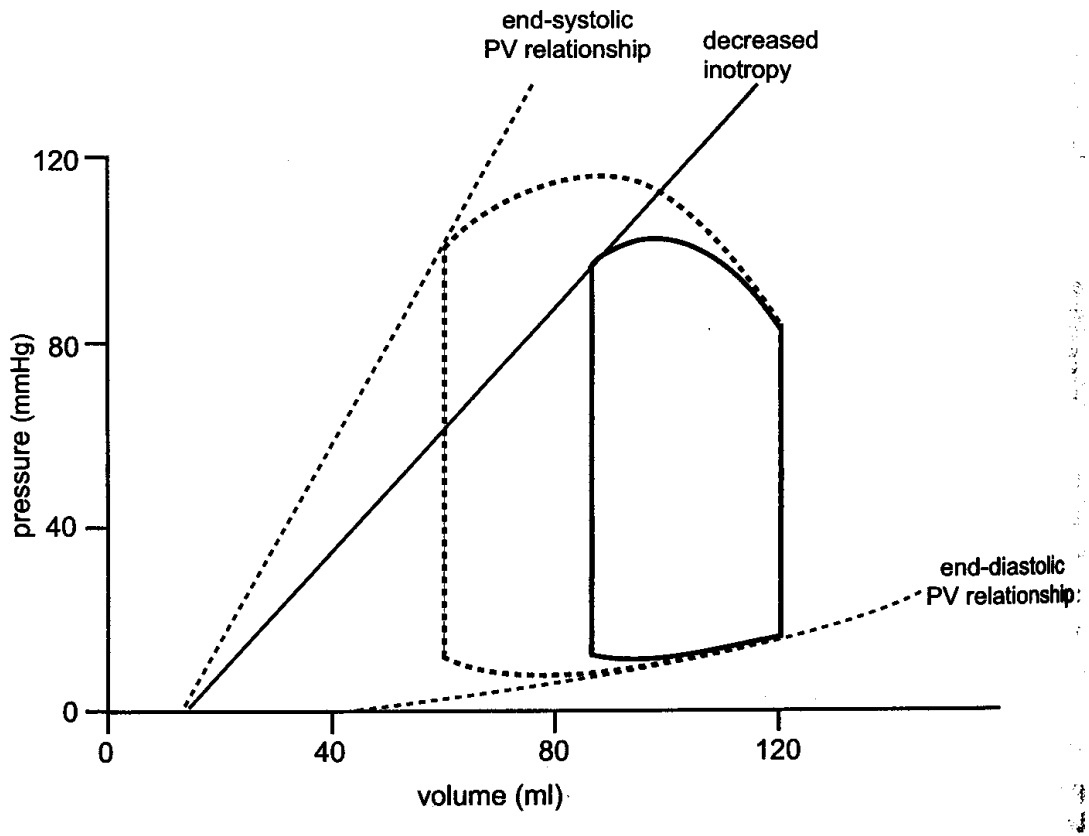
Pressure-volume loops

- Determinants of cardiac output (stroke volume x heart rate)
  - Preload or ventricular end diastolic volume
  - Afterload or Aortic pressure
  - Contractility or modulation of active force generation (ESPVR, inotropy)
  - Ventricular compliance (EDPVR, lusitropy)
  - Heart rate



ESV= end systolic volume;
EDV = end-diastolic volume;
SV = stroke volume

PV loop in heart failure



Myocardial work

- Most myocardial work is potential work

$$W = \int PdV$$

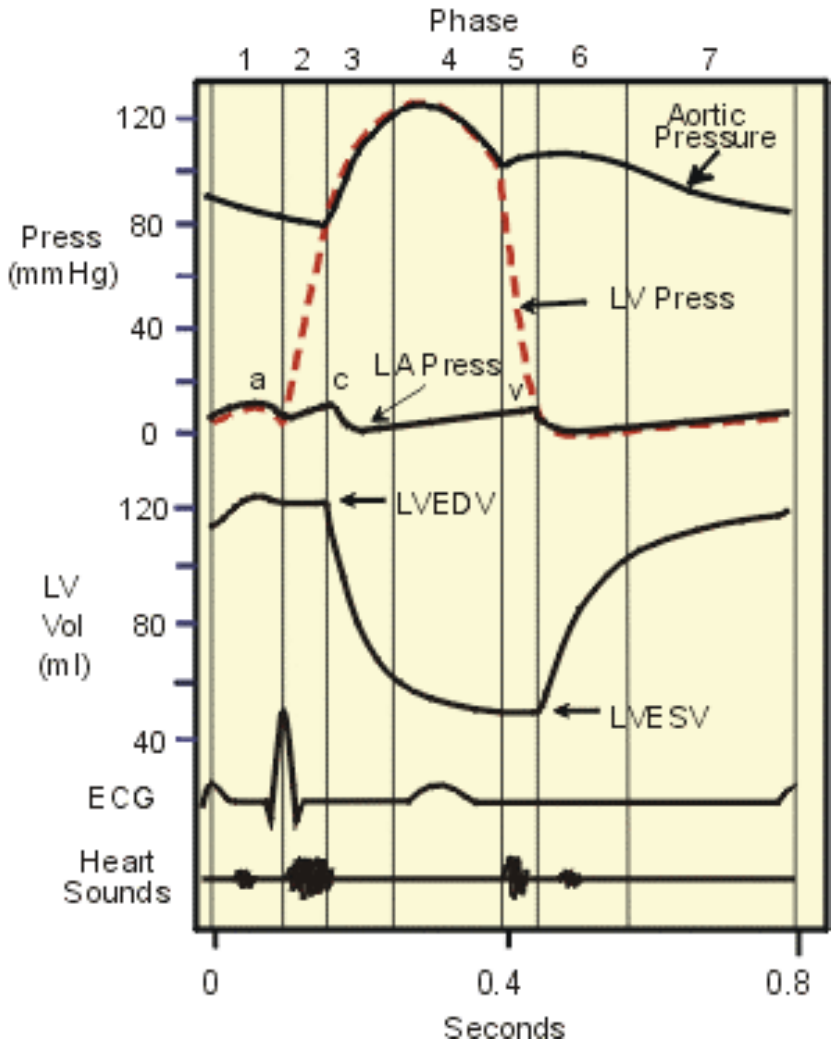
- Myocardial O_2 consumption is a function of myocardial wall tension, contractility, and heart rate
- The law of Laplace:

$$T = \mathrm{Pr}/2$$

where T is tension, P is pressure, and r is the radius.

  - Larger ventricles have higher wall tension and O_2 utilization to produce the same pressure as smaller ones

The cardiac cycle



- Systole
  - Phase 1: atrial contraction
  - Phase 2: Isovolumetric contraction
    - Interval between ventricular systole and semilunar valve opening
  - Phases 3 & 4: rapid and reduced ejection (55-60%)
- Diastole
  - Phase 5: Isovolumetric relaxation
    - Begins with closure of the semilunar valves
  - Phase 6: Rapid filling
    - Opening of the AV valves
  - Phase 7:Diastasis

Hemodynamics

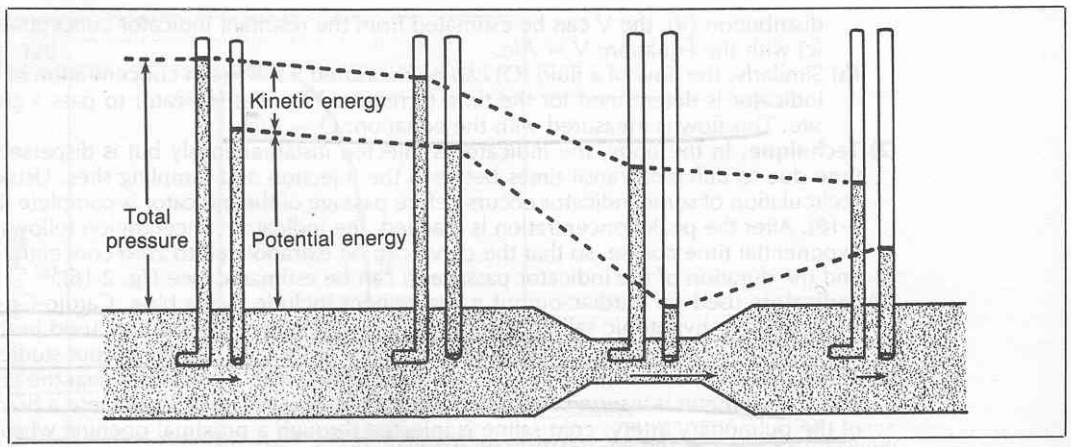


Figure 2-19. System of pitot tubes indicating the variation in total pressure, potential energy, and kinetic energy with change in flow velocity. The *arrows* represent the relative velocities in the segments of the system. The *narrow section*, a high resistance segment, causes a large pressure drop. An increased flow velocity decreases lateral pressure (increases kinetic energy) and is termed a Bernoulli effect.

- Flow is a function of a pressure gradient and represents the conversion of potential to kinetic energy
- Laminar flow is described by Poiseuille's Law:

$$Q = \frac{\pi r^4 \Delta P}{8 \eta l}$$

Where ΔP is the pressure gradient, r is the radius, η is the viscosity, and l is the length of the tube.

Arterial pressure

- Rearranging Hook's Law gives:

$$dP = \frac{EdV}{V}$$

  where E is the elastic constant (similar to Young's modulus of elasticity), dP is the pulse pressure, dV is the net systolic arterial uptake ($\propto$ stroke volume), and V is the mean arterial volume

- Physiological determinants of ABP include:
  - Heart rate
    - Raises V by decreasing runoff time
  - Stroke volume
    - $\uparrow$ SV $\Rightarrow \uparrow$ V, mean ABP, dP, dV
  - Increased peripheral vascular resistance
    - Raises V by decreasing runoff
  - Elastic constant generally increases with age

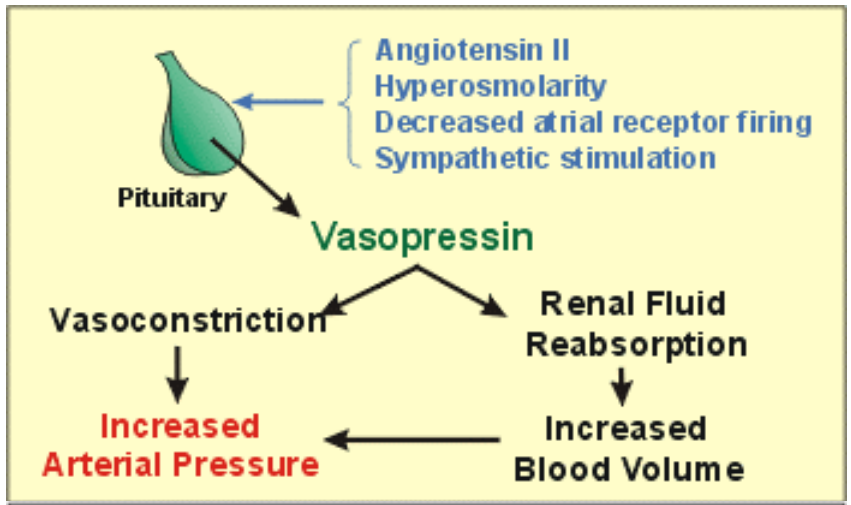
Venous return

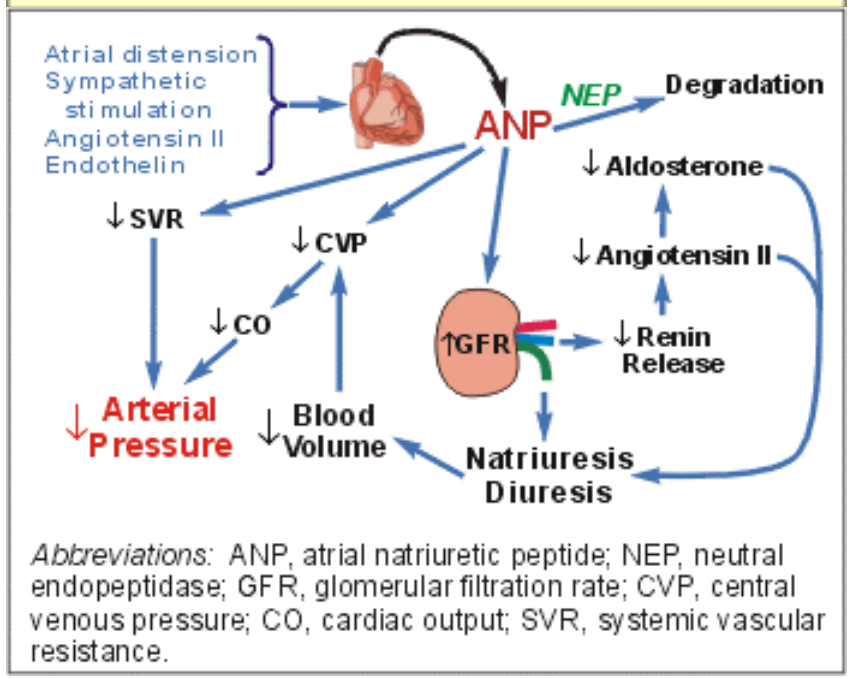
- Low resistance, low pressure, high distensibility segment
- Contain 70-80% of circulating blood volume

- Factors affecting venous return
  - Gravity
    - Supine to erect transition shifts ~ 500 mL of blood to the leg veins, decreasing cardiac output and ABP
  - Valves – prevent retrograde flow in dependent veins
  - Muscle activity – compresses veins to enhance return
  - Respiration – Negative intrathoracic pressure enhances venous return

CV regulation

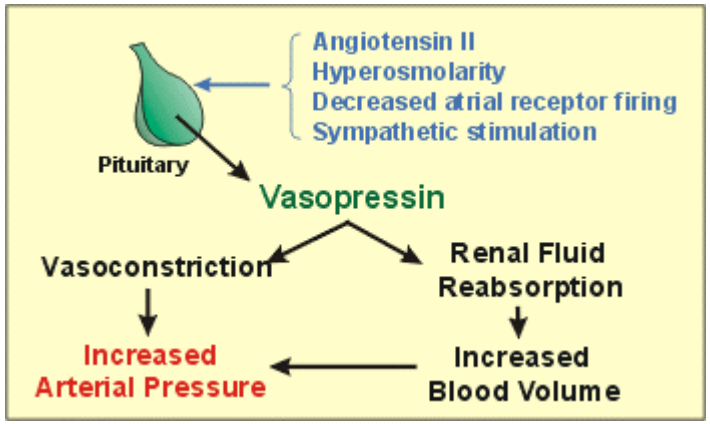
- Control of blood volume
  - Neural
    - Baroreceptors and antidiuretic hormone (ADH)
    - Atrial tissue and natriuretic peptides
  - Endocrine
    - ADH release in response to increased osmolarity
    - Renin-angiotensin-aldosterone system

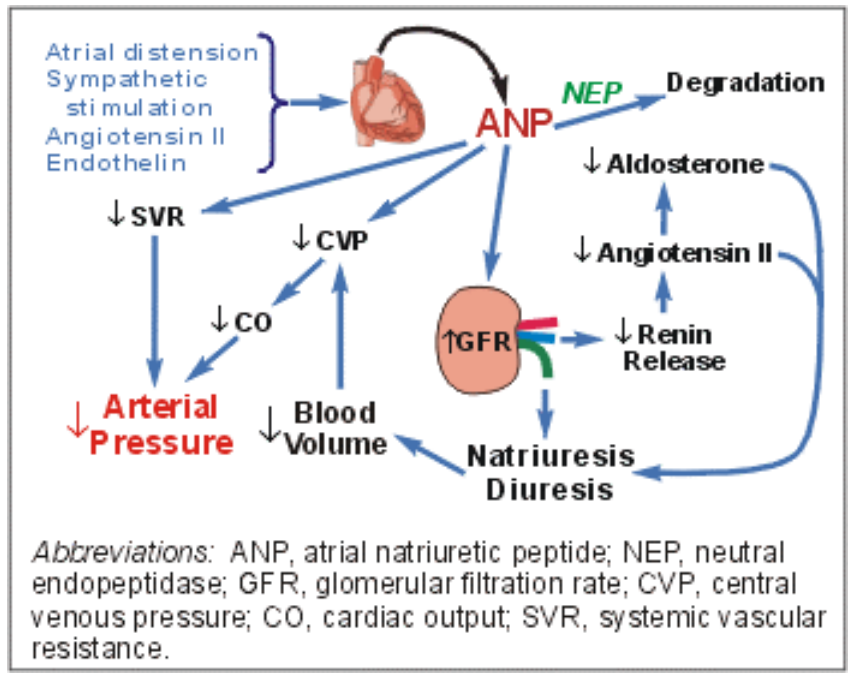


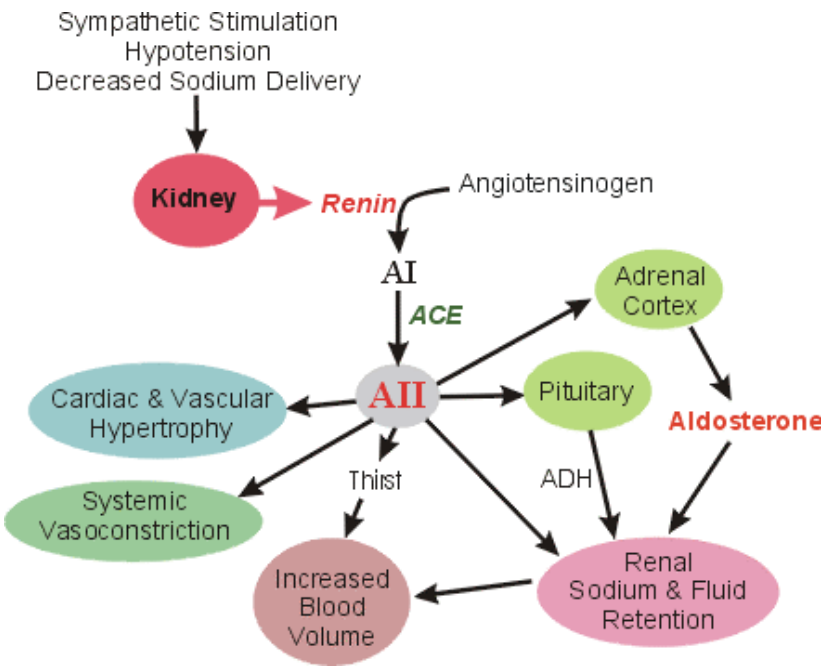


Abbreviations: ANP, atrial natriuretic peptide; NEP, neutral endopeptidase; GFR, glomerular filtration rate; CVP, central venous pressure; CO, cardiac output; SVR, systemic vascular resistance.

Control of blood volume







Control of arterial pressure

- Baroreceptors
  - Located in the carotid sinus and aortic arch
  - Receptor potential varies with mean and pulse pressures
  - Efferent pathway is the vagus (X) and glossopharyngeal (IX) nerves

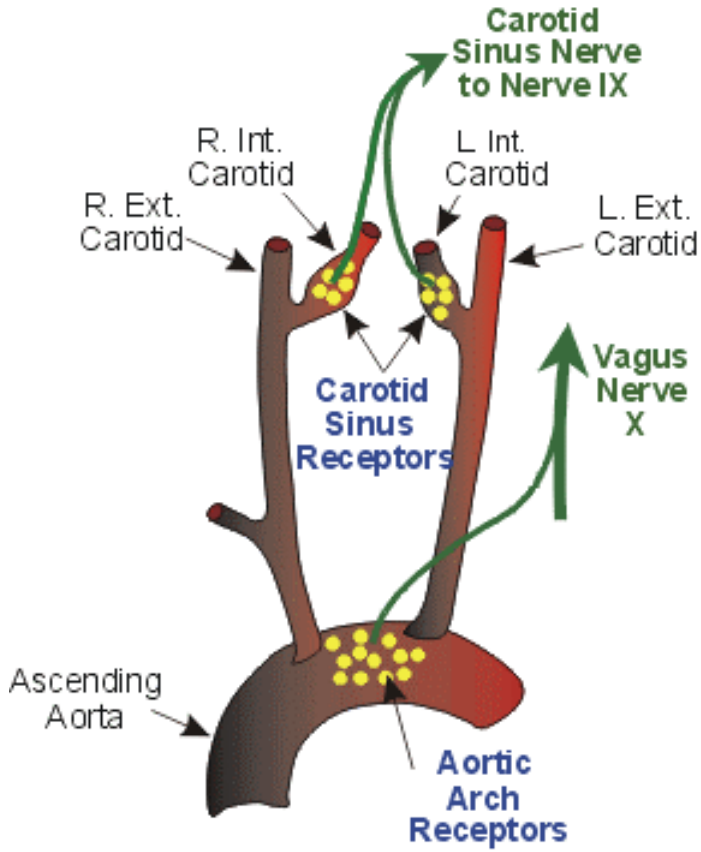
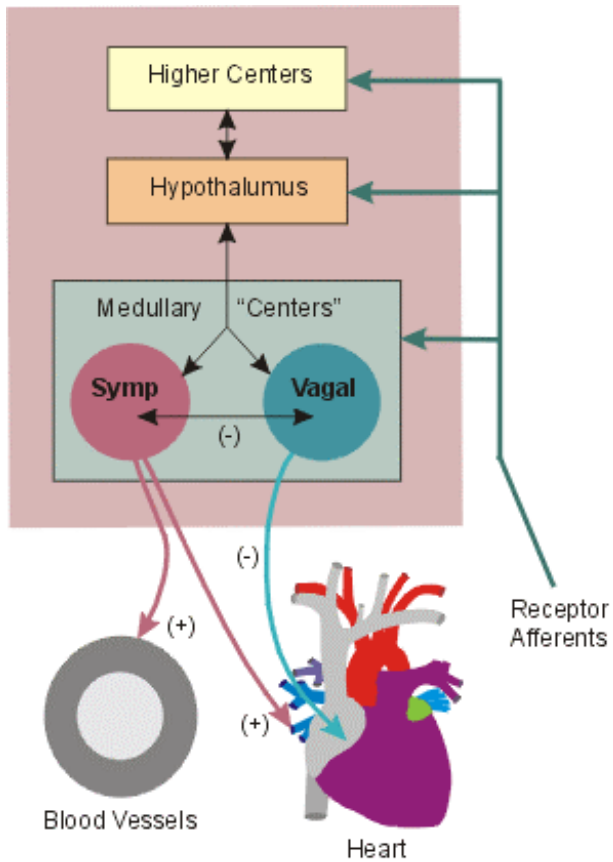


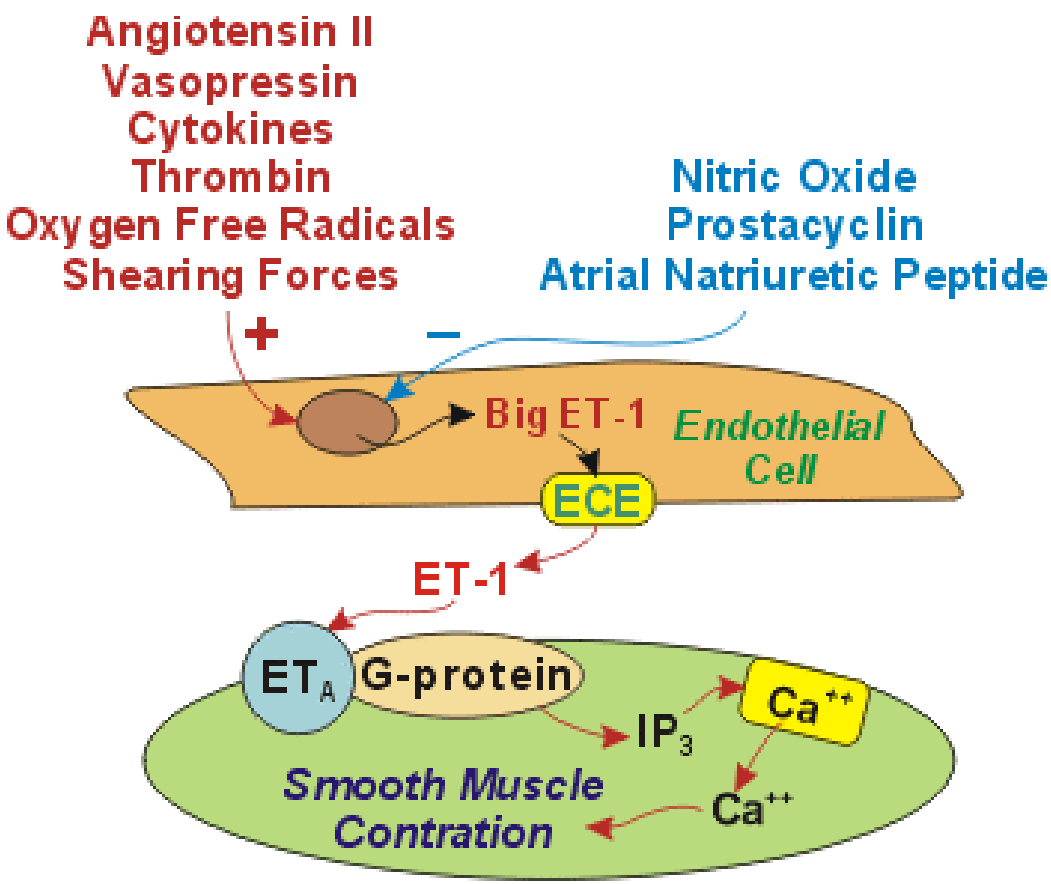
Figure 1. Location and innervation of arterial baroreceptors.

Control of arterial pressure (cont)

- CNS centers
  - Hypothalamus
  - Medulla
- Autonomic
  - Sympathetic
    - Postganglionic adrenergic fibers ⇒ vasoconstriction, ↑ chronotropy, ↑ lusitropy, and ↑ inotropy
    - Postganglionic cholinergic fibers ⇒ skeletal muscle vasodilation
  - Parasympathetic
    - Largely opposes sympathetic actions



Local control of flow



Coupling the heart and vasculature

Vascular function curve

$$CO = \frac{P_{ms} - P_{ra}}{R(1 + c_v / c_a)}$$

Where P_{ms}, P_{ra}, R, c_v, and c_a are the mean systemic pressure, right atria pressure, total peripheral resistance, arterial and venous capacitance, respectively.

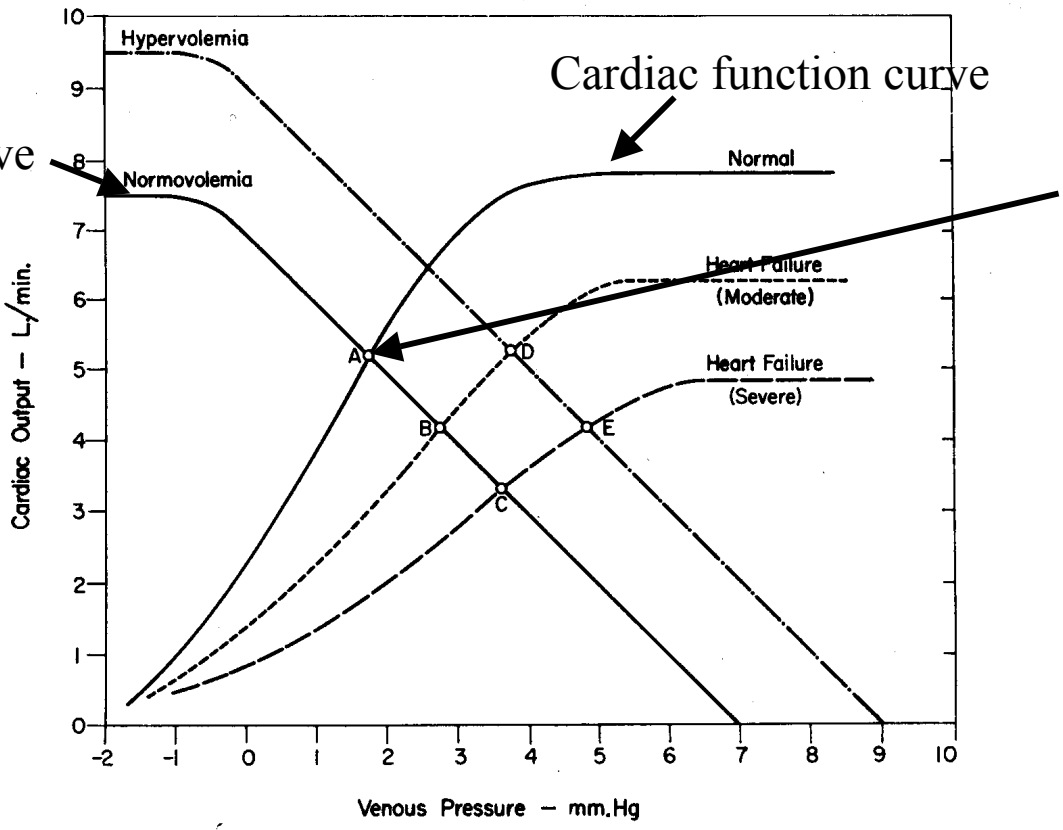


Fig. 9-14. With moderate or severe heart failure, the cardiac function curves are shifted to the right. With no change in blood volume, cardiac output decreases and venous pressure rises (from control equilibrium point *A* to point *B* or point *C*). With the increase in blood volume that usually occurs in heart failure, the vascular function curve is shifted to the right. Hence venous pressure may be elevated with no reduction in cardiac output (point *D*) or (in severe heart failure) with some diminution in cardiac output (point *E*).

References

1. Katz A.M., Physiology of the Heart, Lippincott Williams & Wilkins, New York, 2001.
2. Berne and Levy, Cardiovascular Physiology, 7th Edition, Mosby, St. Louis, 1996.