Cardiovascular Physiology

November 20, 2007

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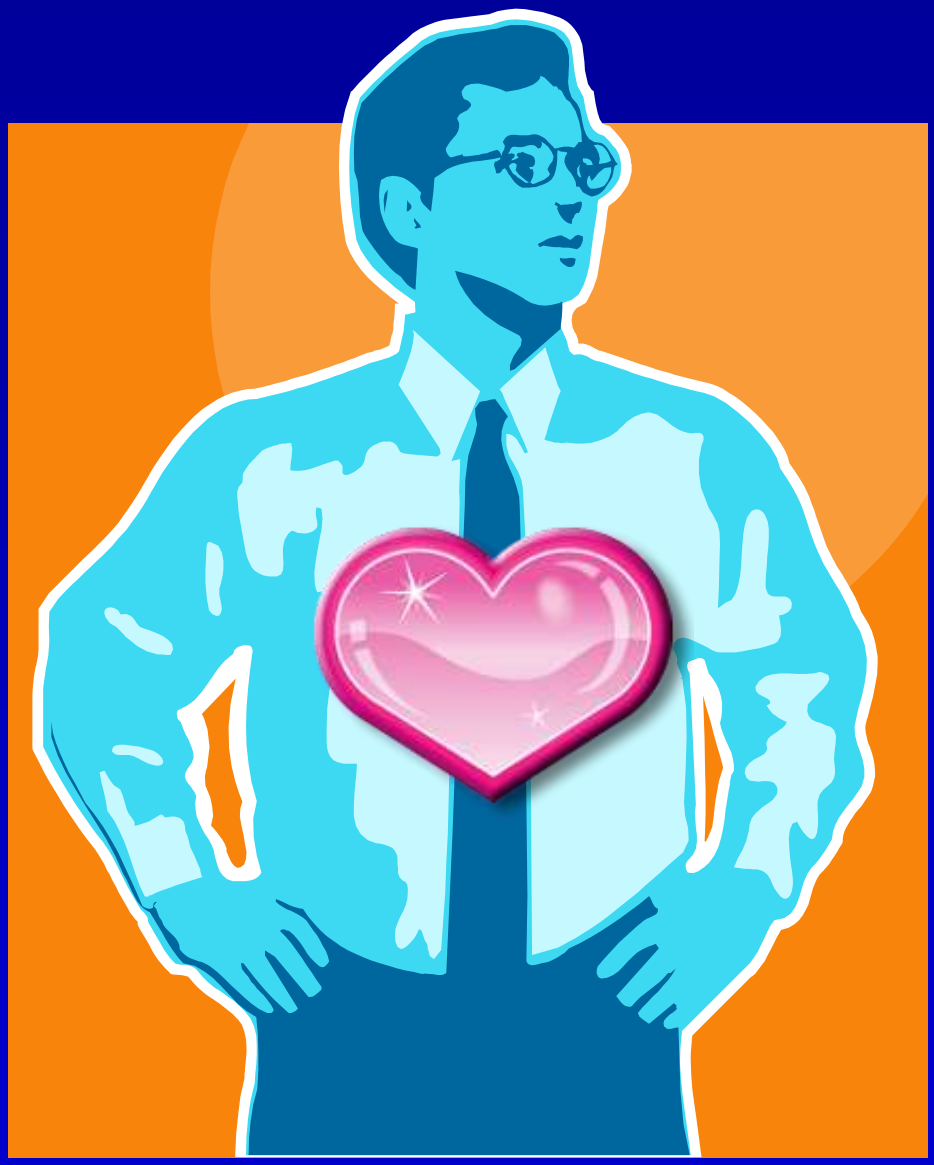
UTHSCSA and STXVHCS

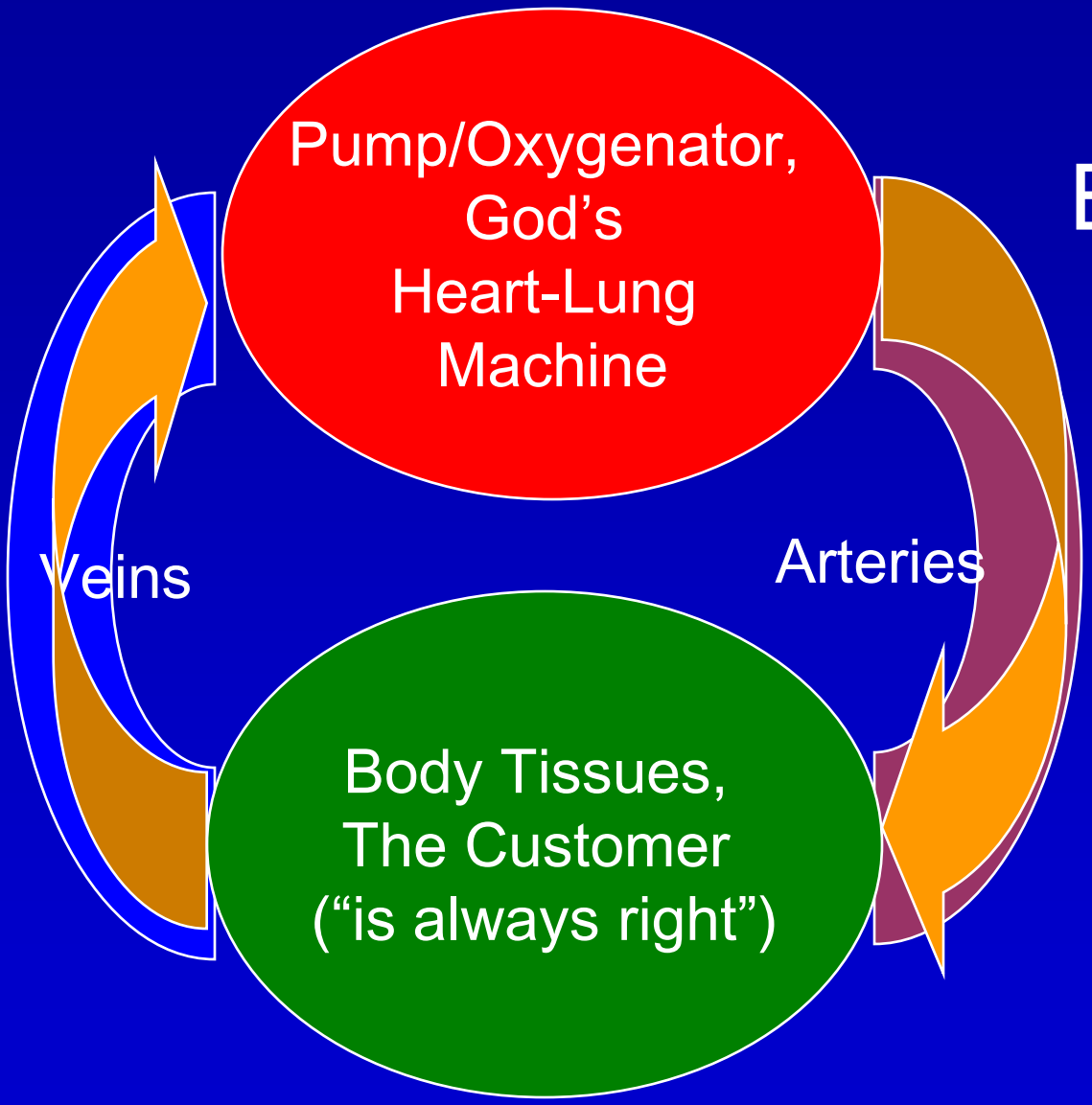
References: Internet, McGraw-Hill E-Books, Milnor, Braunwald

Big Picture

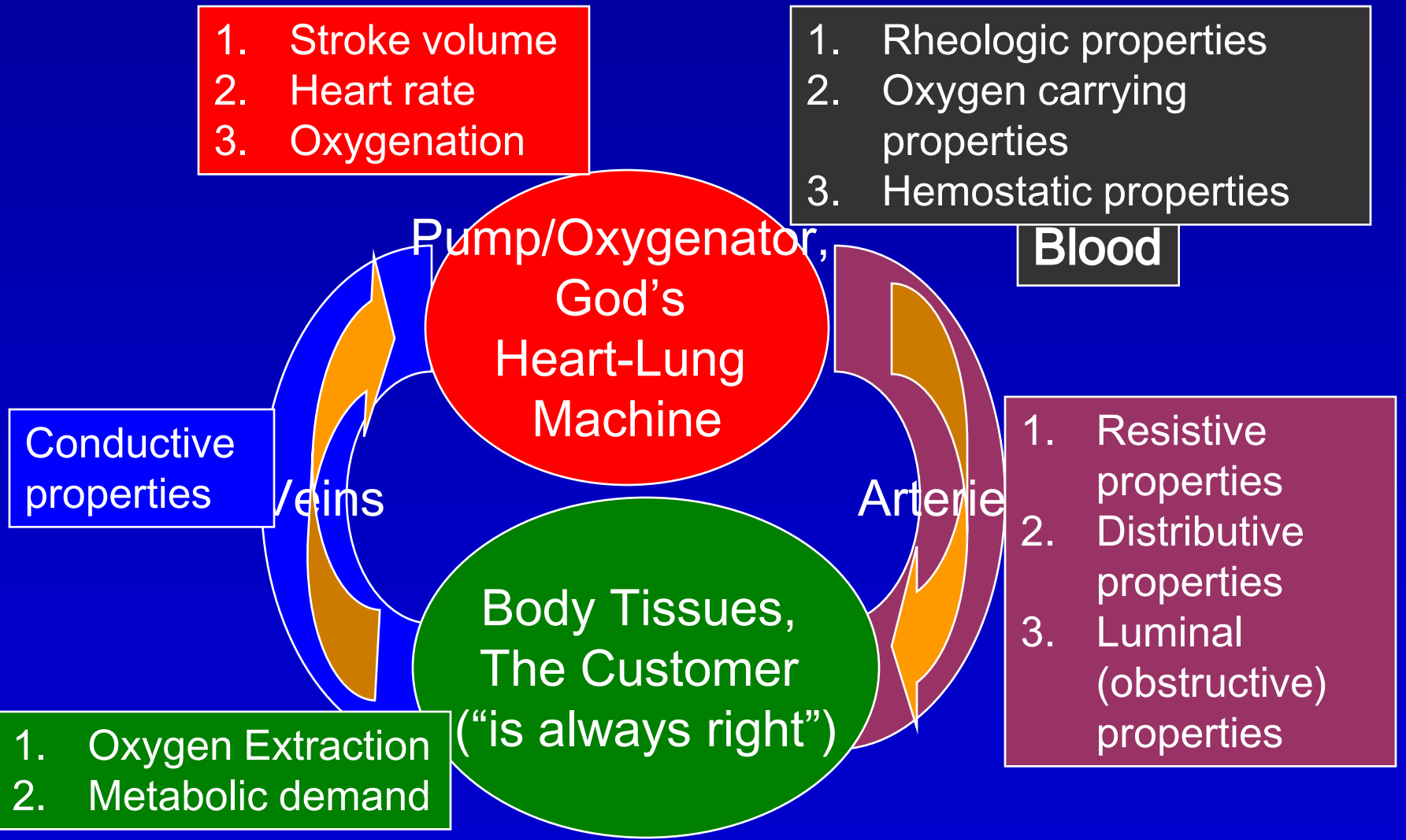
Cardiovascular system produces **flow** of blood in person



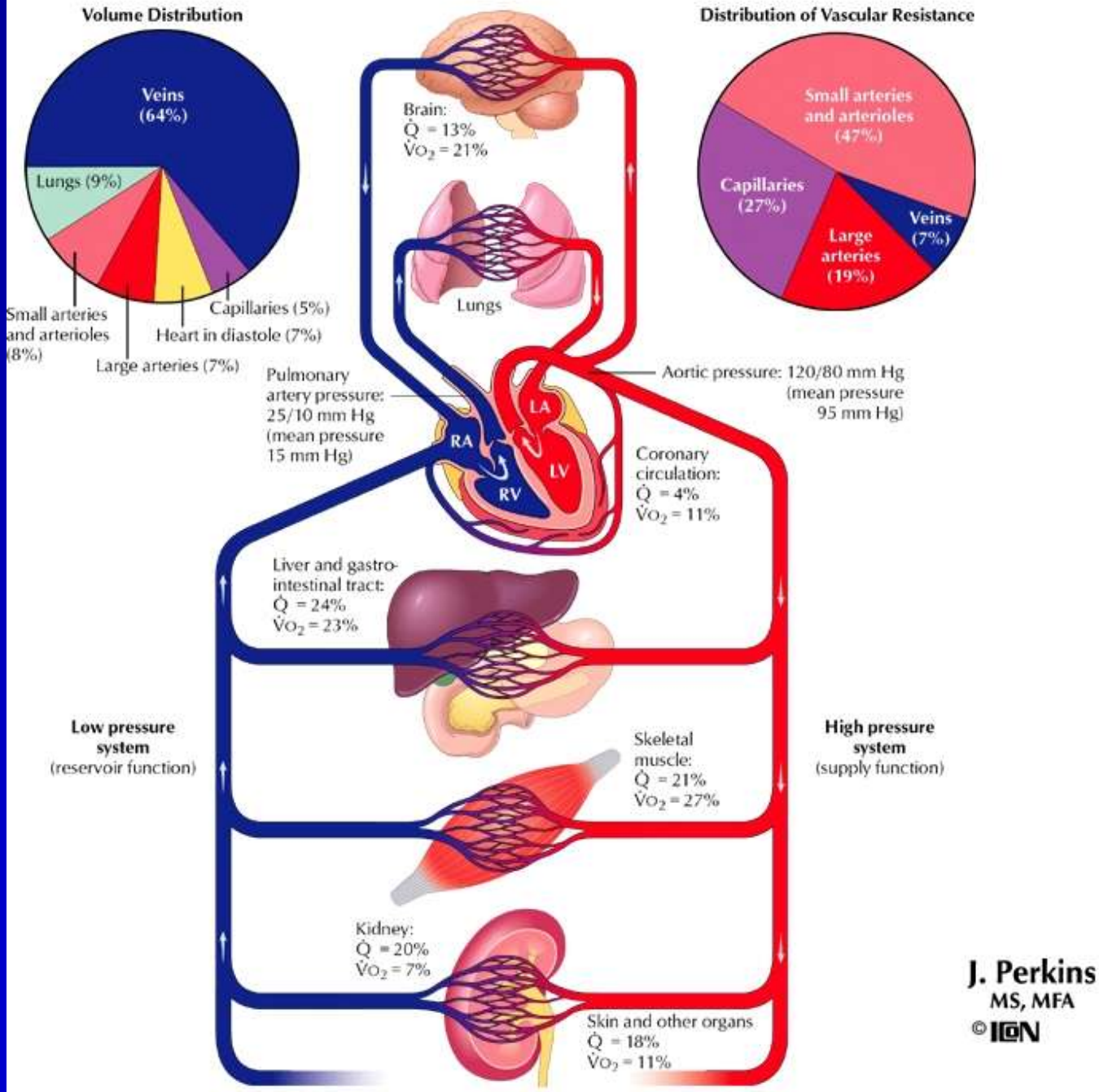
Big Picture – Blood Flow



Big Picture – Blood Flow



Overview of the Cardiovascular System



J. Perkins
MS, MFA

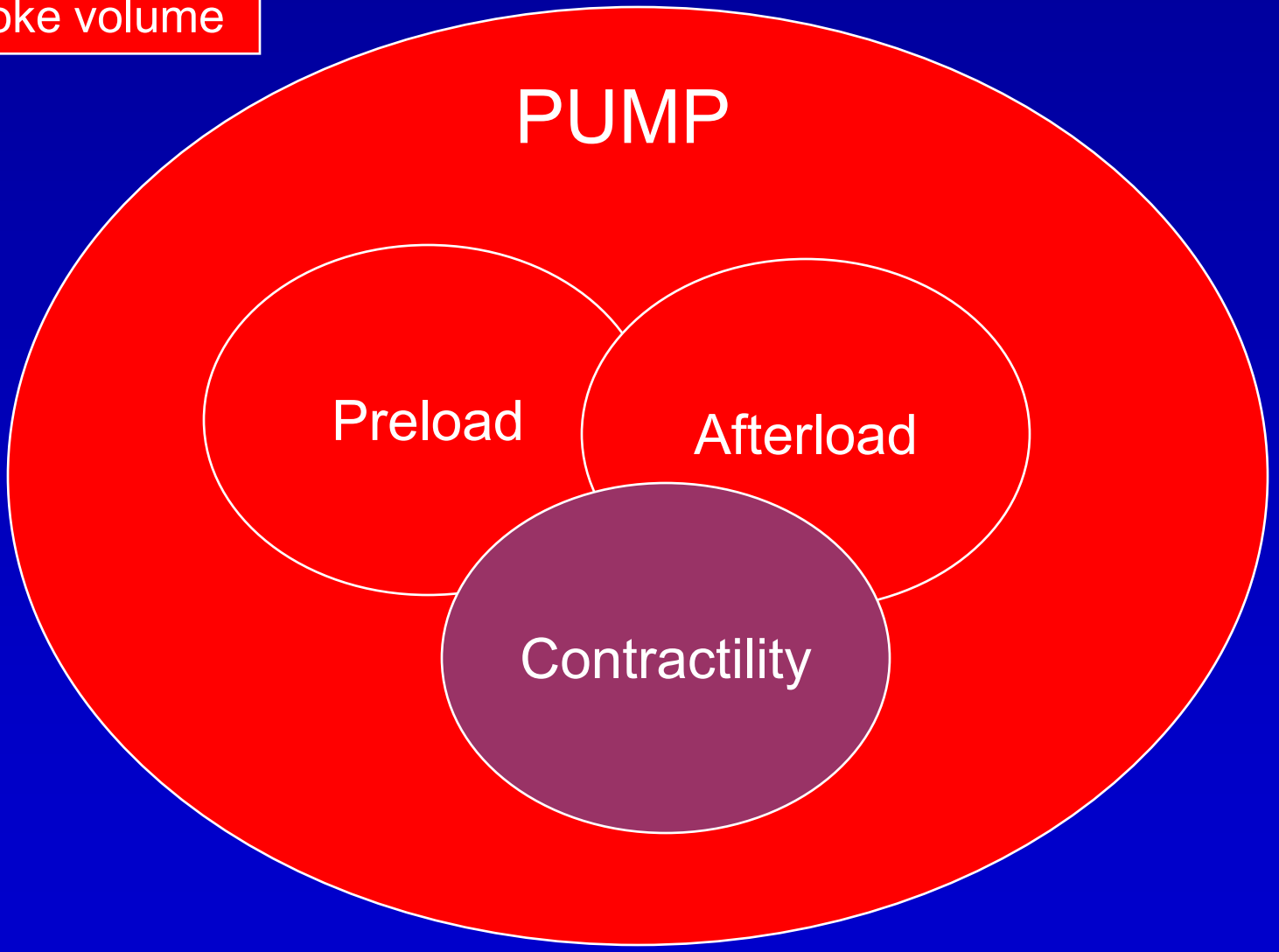
Narrower - Cardiopulmonary

1. Stroke volume
2. Heart rate
3. Oxygenation

Pump/Oxygenator, God's Heart-Lung Machine

Narrower Still – Cardiac and Systole

1. Stroke volume



Contractility is the "holy grail" of Cardiac Function Investigators

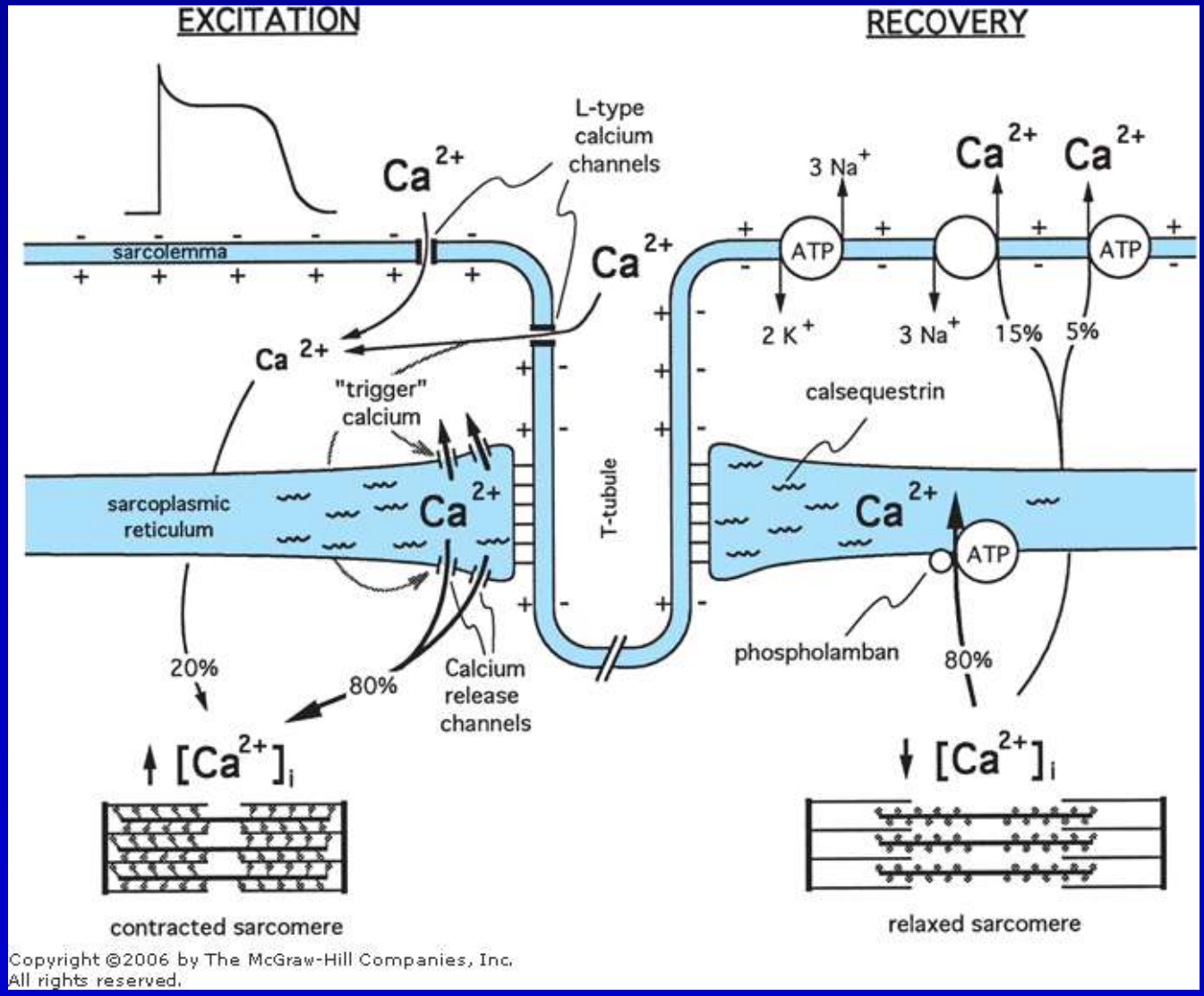
- LV Systolic Function – theory
  - Early work
  - Molecular work
  - Chamber work
- LV Systolic Function – assessment
  - Pressure
  - Volume
  - Time

TABLE 20–1 Uses of Cardiac Function Assessment

Diagnosis
Prognostication
Timing of intervention
Mechanism of therapy
Assessment of therapy
Detection of complications
Surrogate for clinical outcomes

Carroll JD and Hess OM. Ch 20, "Assessment of Normal and Abnormal Cardiac Function" Braunwald's Heart Disease, 7th ed. 2004.

Excitation – Contraction Coupling



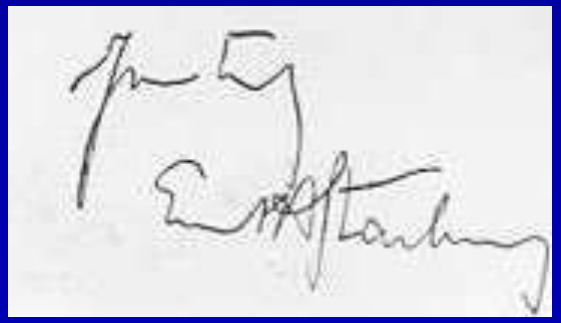
- Excitation-contraction coupling and sarcomere shortening.

Mohrman, DE et al. Cardiovascular Physiology. 1997. p. 37.

Otto Frank

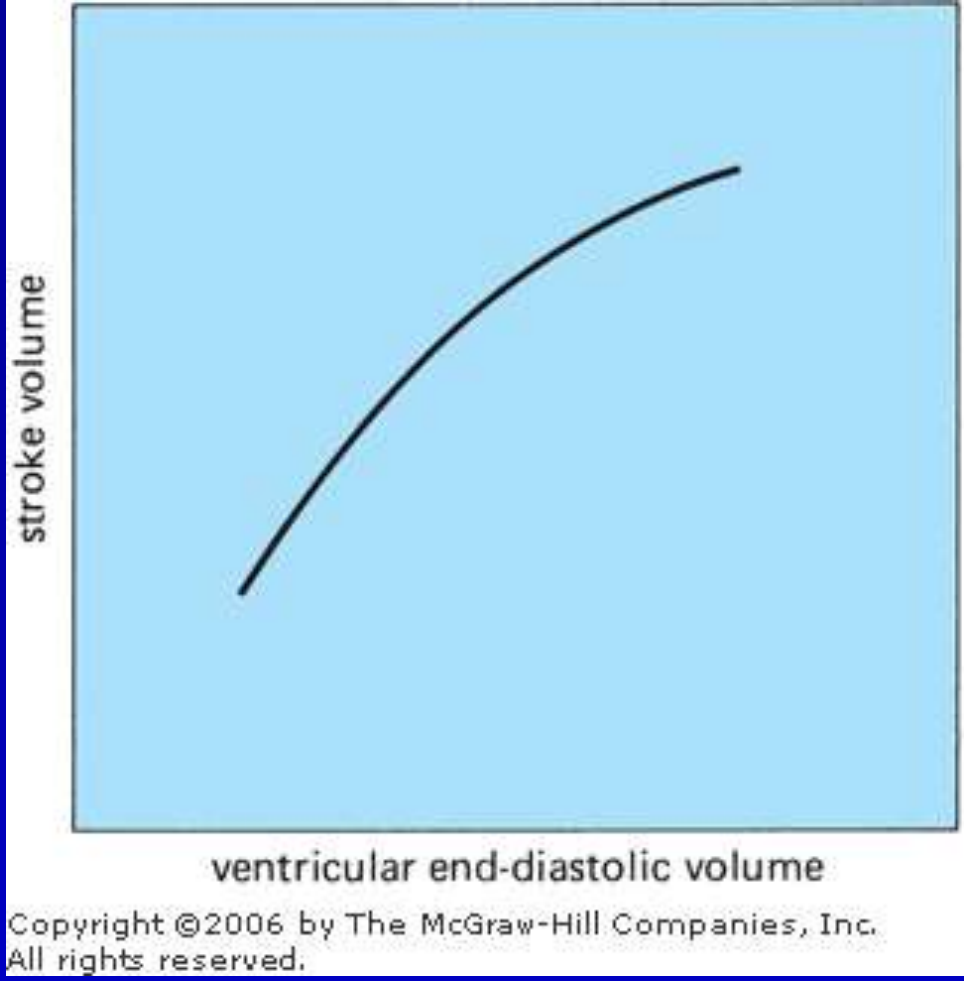
- **Otto Frank** (June 21, 1865 - 1944) was a German physiologist. He was educated at Munich, Kiel, Heidelberg, Glasgow and Strassburg. He is best known, along with Ernest Starling, for the Frank-Starling law of the heart.
- The law states that "Within physiological limits, the force of contraction is directly proportional to the initial length of the muscle fiber". (not the Otto Frank who was the father of Anne Frank)

Ernest Starling



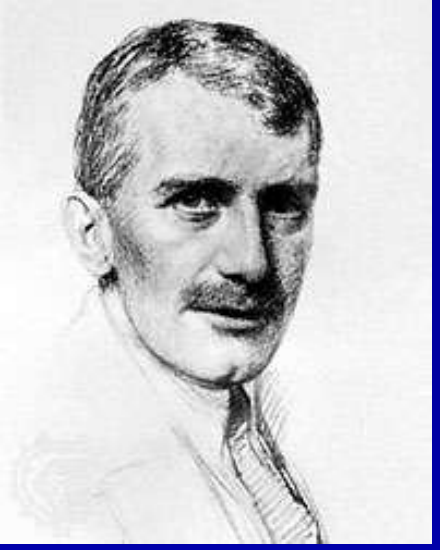
- **Ernest Starling** was an English physiologist born on April 17, 1866, in London, and died on May 2, 1927. He worked mainly at University College London, although he also worked for many years in Germany and France. His main collaborator in London was his brother-in-law, William Maddock Bayliss.
- Starling is most famous for developing the "Frank-Starling law of the heart", presented in 1915 and modified in 1919.
- Other major contributions to physiology included the Starling equation, describing fluid shifts in the body (1896)

The Frank-Starling Curve



- One of the most fundamental causes of variations in stroke volume was described by William Howell in 1884 and by Otto Frank in 1894 and formally stated by E. H. Starling in 1918. These investigators demonstrated that as cardiac filling increases during diastole, the volume ejected during systole also increases.

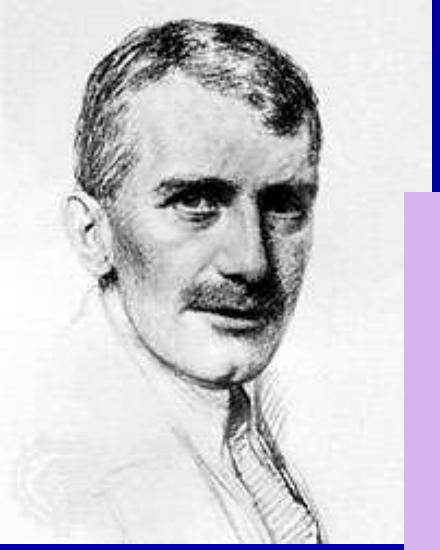
Mohrman, DE et al. Cardiovascular Physiology. 1997. p. 57.



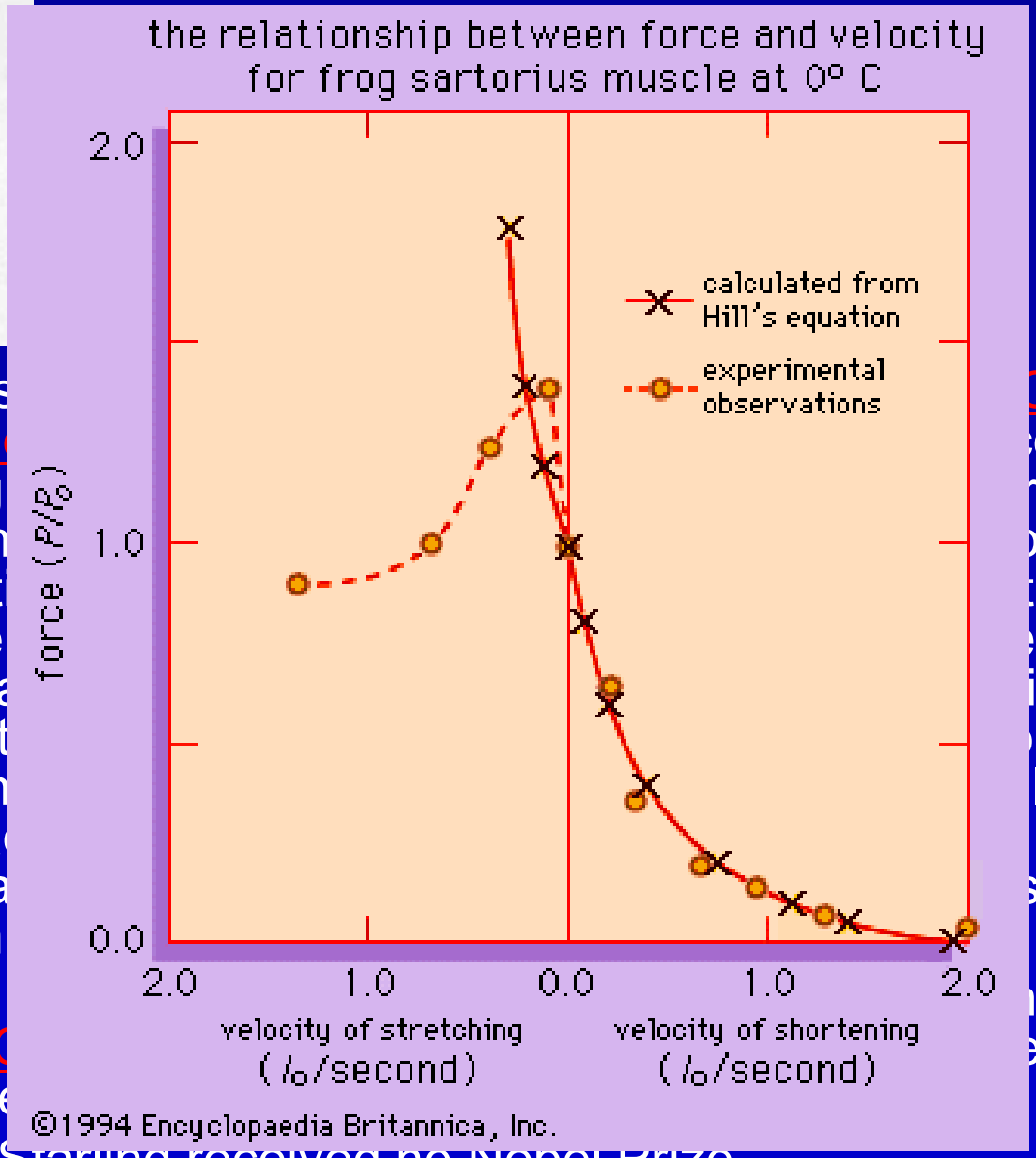
A. V. Hill

- Archibald Vivian Hill, September 26, 1886 to June 3, 1977

- British physiologist and biophysicist who received (with Otto Meyerhof) the 1922 Nobel Prize for Physiology or Medicine for discoveries concerning the production of heat in muscles. His research helped establish the origin of muscular force in the breakdown of carbohydrates with formation of lactic acid in the absence of oxygen. At the University of Cambridge (1911-14) Hill began his investigations of the physiological thermodynamics of muscle and nerve tissue. Working with a straplike (sartorius) thigh muscle in the frog, he was able to demonstrate that oxygen is needed only for the recovery, not the contractile, phase of muscular activity, laying the foundation for the discovery of the series of biochemical reactions carried out in muscle cells that results in contraction.
- In 1923 he succeeded Ernest Starling as professor of physiology at University College, London, a post he held until his retirement in 1951. He continued as an active researcher until 1966.
- Frank and Starling received no Nobel Prize.



A. V. Hill



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  contraction
- In 1923 he … ysiology at
  University C… ement in 1951.
  He continue
- Frank and Starling received no Nobel Prize.

Milnor – Hemodynamics, 2nd ed., 1989, Chapter 10, "Cardiac Dynamics"

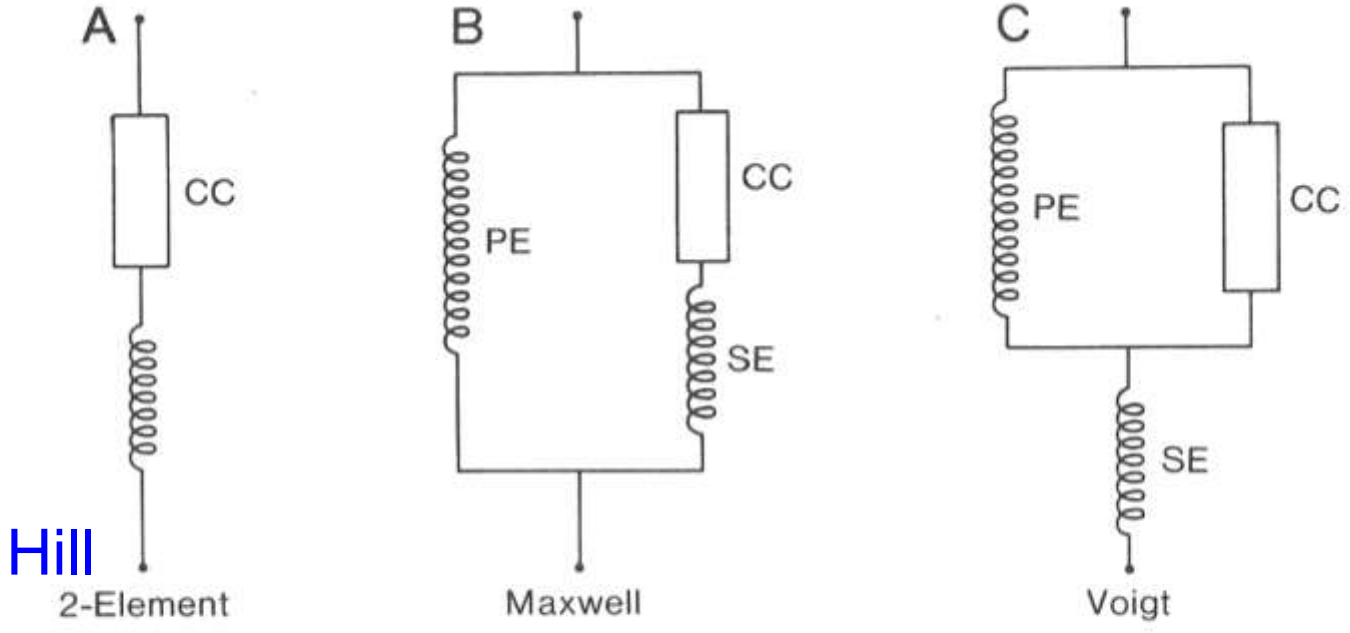


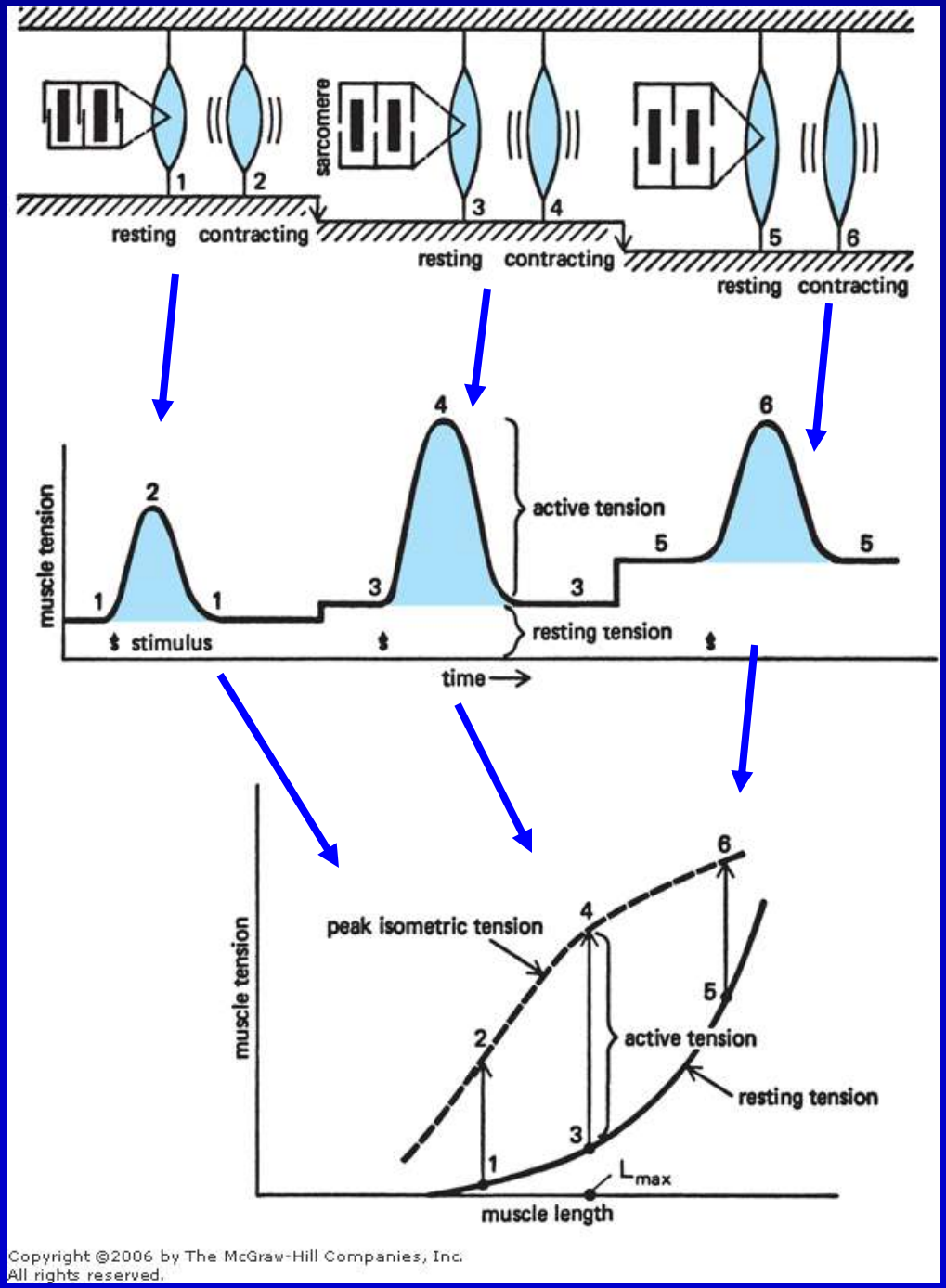
Fig. 10.4. Theoretic models of cardiac muscle. *CC*, contractile component; *SE*, series elastic element; *PE*, parallel elastic element. *SE* is purely elastic, though nonlinear. In the three-element models, contractile component is assumed to be freely extensible, but in the two-element model it must maintain a constant length while bearing the resting force (preload). In resting state, preload is carried entirely by *PE* in the Maxwell model, but by *PE* and *SE* in Voigt model.

The concept of series elasticity has not proved to be appropriate.

Length – Tension Relationships

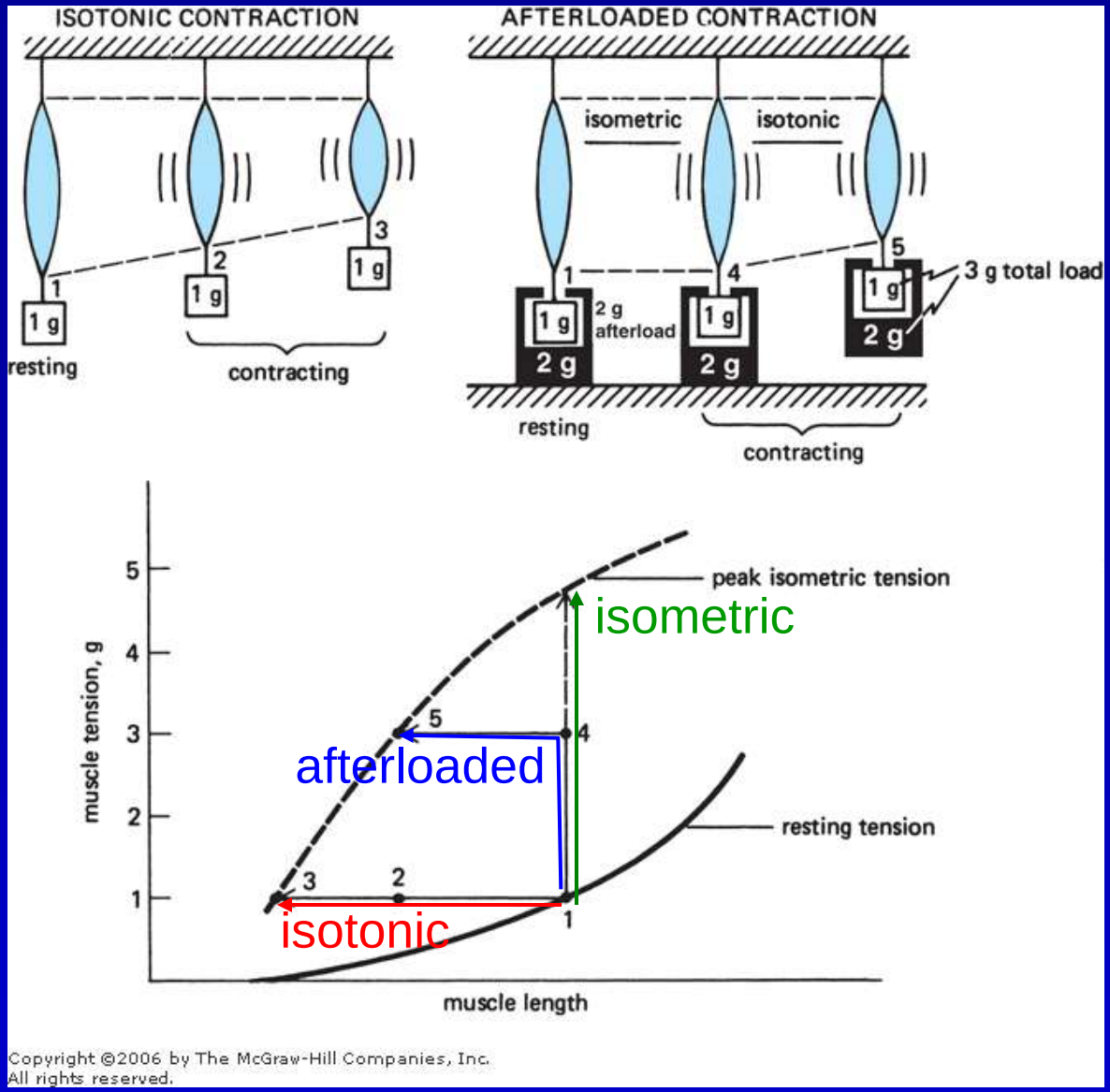
- Isometric contractions and the effect of muscle length on resting tension and active tension development.
- Any intervention that increases the peak isometric tension that a muscle can develop at a fixed length is said to increase cardiac muscle **contractility**. Such an agent is said to have a positive **inotropic** effect on the heart.

Mohrman, DE et al. Cardiovascular Physiology. 1997. p. 40.



Length – Tension Relationships

- Isometric
- Isotonic
- Afterloaded



Mohrman, DE et al. Cardiovascular Physiology. 1997. p. 42.

Milnor – Hemodynamics, 2nd ed., 1989, Chapter 10, "Cardiac Dynamics"

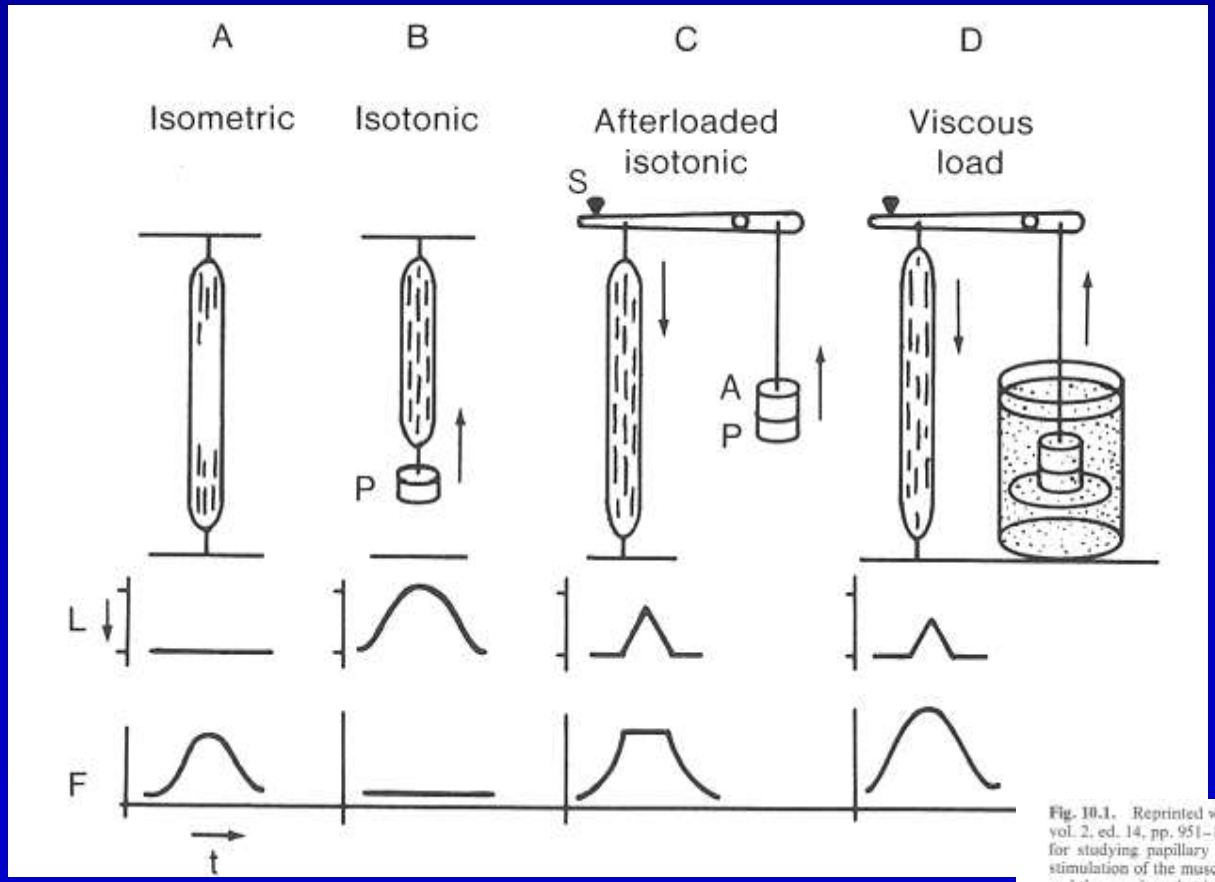
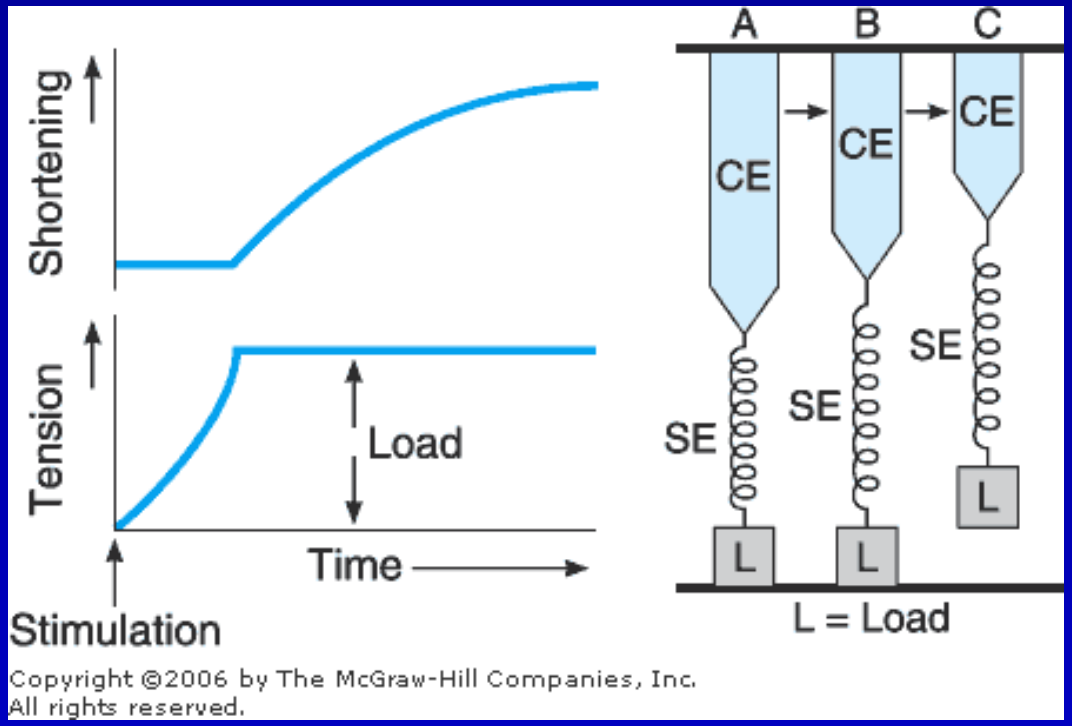


Fig. 10.1. Reprinted with permission from W. R. Milnor. In *Medical Physiology*, edited by V. B. Mountcastle, vol. 2, ed. 14, pp. 951–1125. C. V. Mosby, St. Louis, 1980. Diagram of four different experimental arrangements for studying papillary muscles *in vitro* (*above*) and the changes in length (*L*) and force (*F*) developed on stimulation of the muscle (*below*). **A,** isometric contraction. Muscle is stretched to a preselected resting length and then anchored at both ends. On stimulation, muscle develops force but cannot shorten. **B,** isotonic contraction. Upper end of muscle is anchored, and selected weight (preload, *P*) is attached to lower end. Force remains constant (equal to weight of preload) during activation and muscle shortens. **C,** isotonic afterload. Lower end of muscle is anchored and upper end is attached to a lever, with preload on opposite end of lever. A "stop" (*S*) is placed against lever, so that muscle cannot be stretched further, and an additional weight (afterload, *A*) is then added. On stimulation, muscle maintains a constant length until it develops force equal to the combined preload and afterload, then begins to shorten. **D,** viscous afterload. Preload, stop, and afterload are attached as for isotonic afterload, but a wide, thin disc of negligible weight is also added, and entire "load" is immersed in a container filled with viscous fluid. When muscle has developed force equal to preload and afterload and begins to shorten, it must develop additional force to pull plate through viscous fluid. Moving load against this "viscous resistance" is roughly analogous to ventricular ejection of blood into arterial system.

- Cat papillary muscle –
- 10 mm long and 0.7 mm diameter
- Length-Tension Analysis

Early LV Systolic Function Theory



- Model for contraction of afterloaded muscles. **A:** Rest. **B:** Partial contraction of the contractile element of the muscle (CE), with stretching of the series elastic element (SE) but no shortening. **C:** Complete contraction, with shortening. (Reproduced, with permission, from Sonnenblick EH in: *The Myocardial Cell: Structure, Function and Modification.* Briller SA, Conn HL [editors]. Univ Pennsylvania Press, 1966.)

Milnor – Hemodynamics, 2nd ed., 1989, Chapter 10, "Cardiac Dynamics"

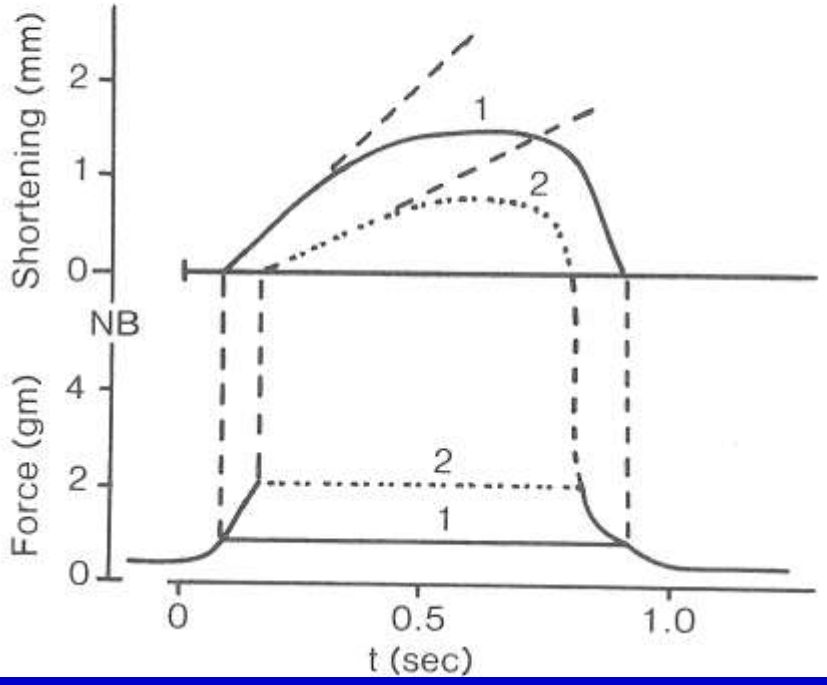


Fig. 10.2. Modified from Sonnenblick, 1962. Isotonic afterloaded contractions in the papillary muscle of the cat heart. *Ordinates, above,* change in length (shortening); *below,* force. *Abscissa,* time after stimulation. Responses to two different afterloads are shown—1 g (*continuous line*), and 2 g (*dotted line*). Preload 0.4 g in both cases. Slope of *dashed lines* in *upper panel* is the early velocity of shortening, which is slower with the greater load.

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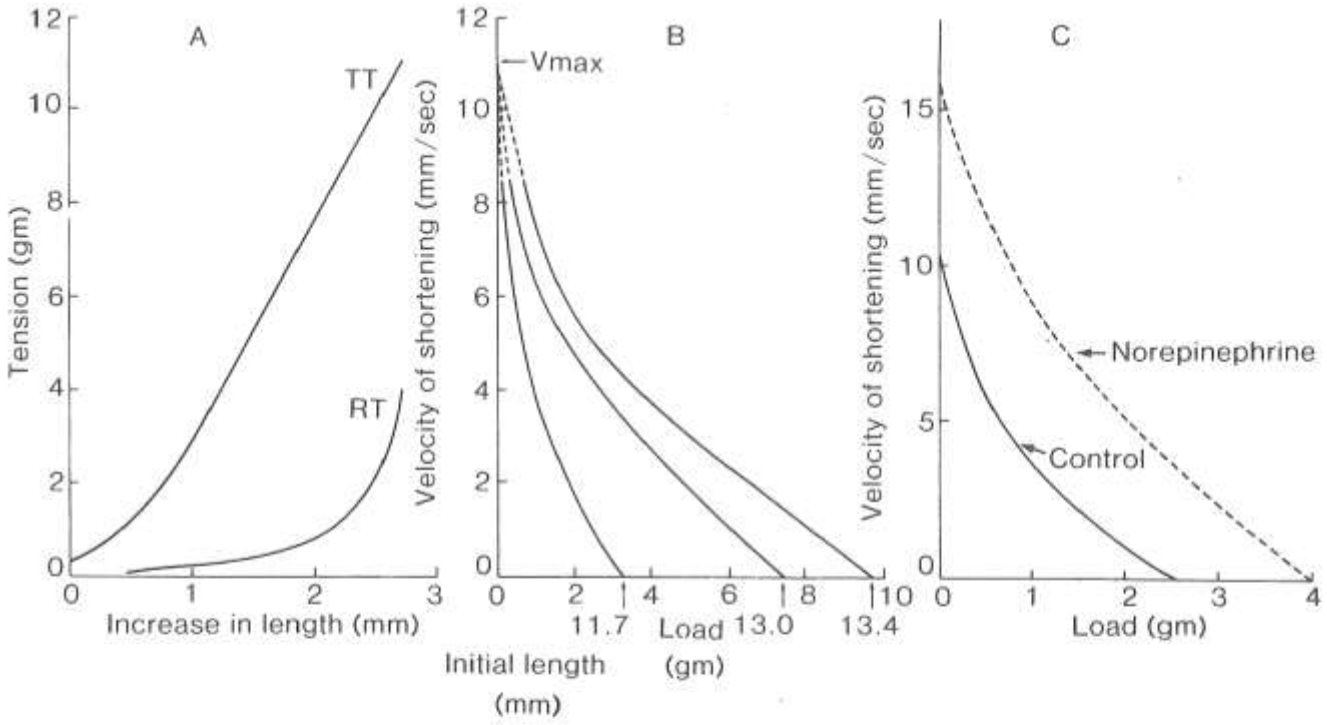
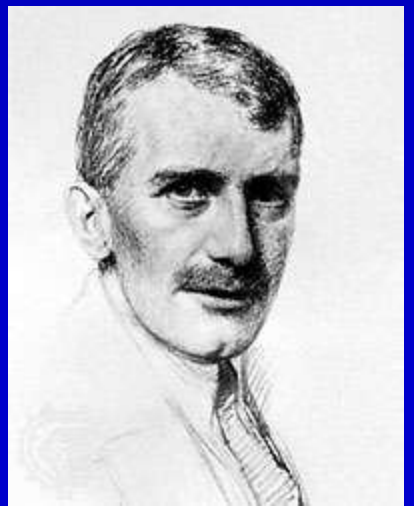


Fig. 10.3. Modified from Sonnenblick, 1966. Length-tension-velocity relations in isolated papillary muscle of cat heart. **A,** resting tension (*RT*) and total developed tension (*TT*); both increase with increasing initial length. Active tension (not shown here) is difference between *TT* and *RT*. **B,** force-velocity curves for three different initial muscle lengths. From *left* to *right*, *first arrow* indicates curve for initial muscle length of 11.7 mm; *second arrow*, 13.0 mm; *third arrow*, 13.4 mm. Velocity of shortening falls as load increases in all three instances. The load at which no shortening occurs (P_0, the point where curves intersect abscissa, indicating velocity = 0) becomes greater as initial length is increased. Maximum unloaded velocity (v_{max}) is determined by extrapolating curves to intercept ordinate (load = 0). Early investigations suggested that v_{max} is independent of initial length, as shown here, but that is not always the case. **C,** effect of norepinephrine on force-velocity curve. Both v_{max} and P_0 are greater after the administration of norepinephrine than in the control state.

V_{max} – maximum velocity of shortening, unloaded velocity

A.V.Hill (1938) skeletal muscle



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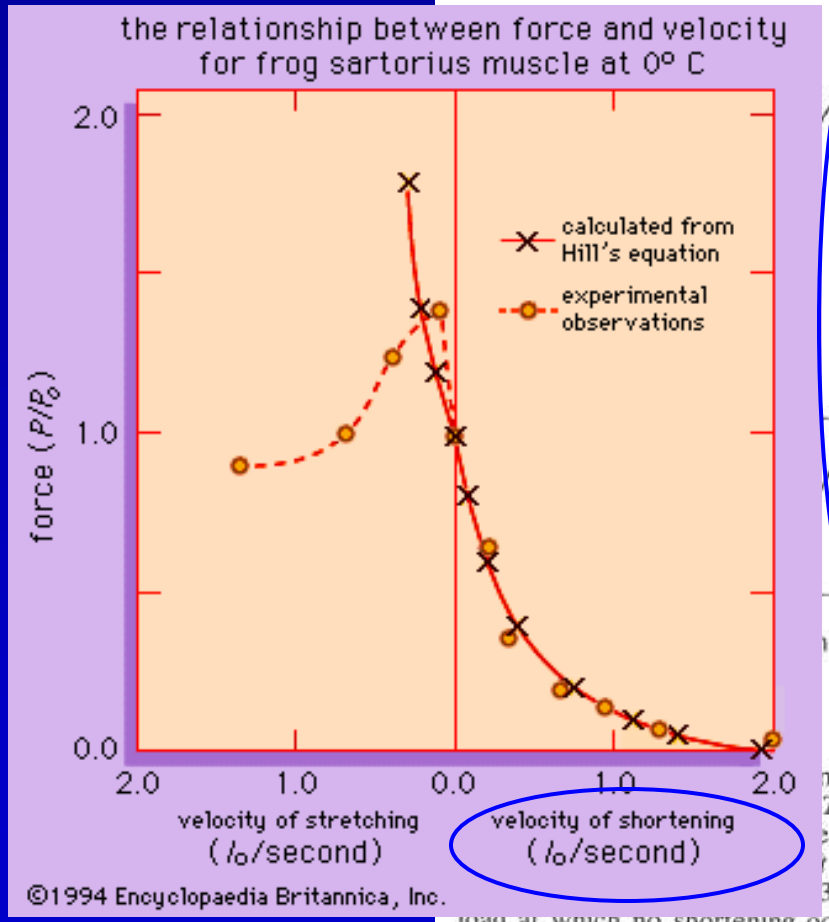

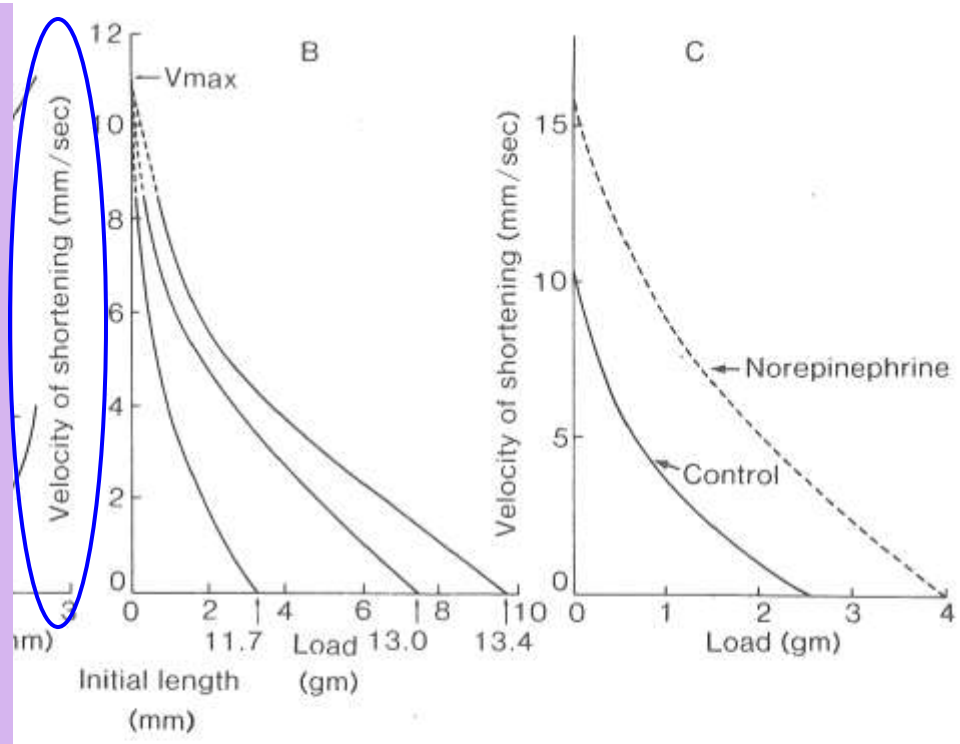

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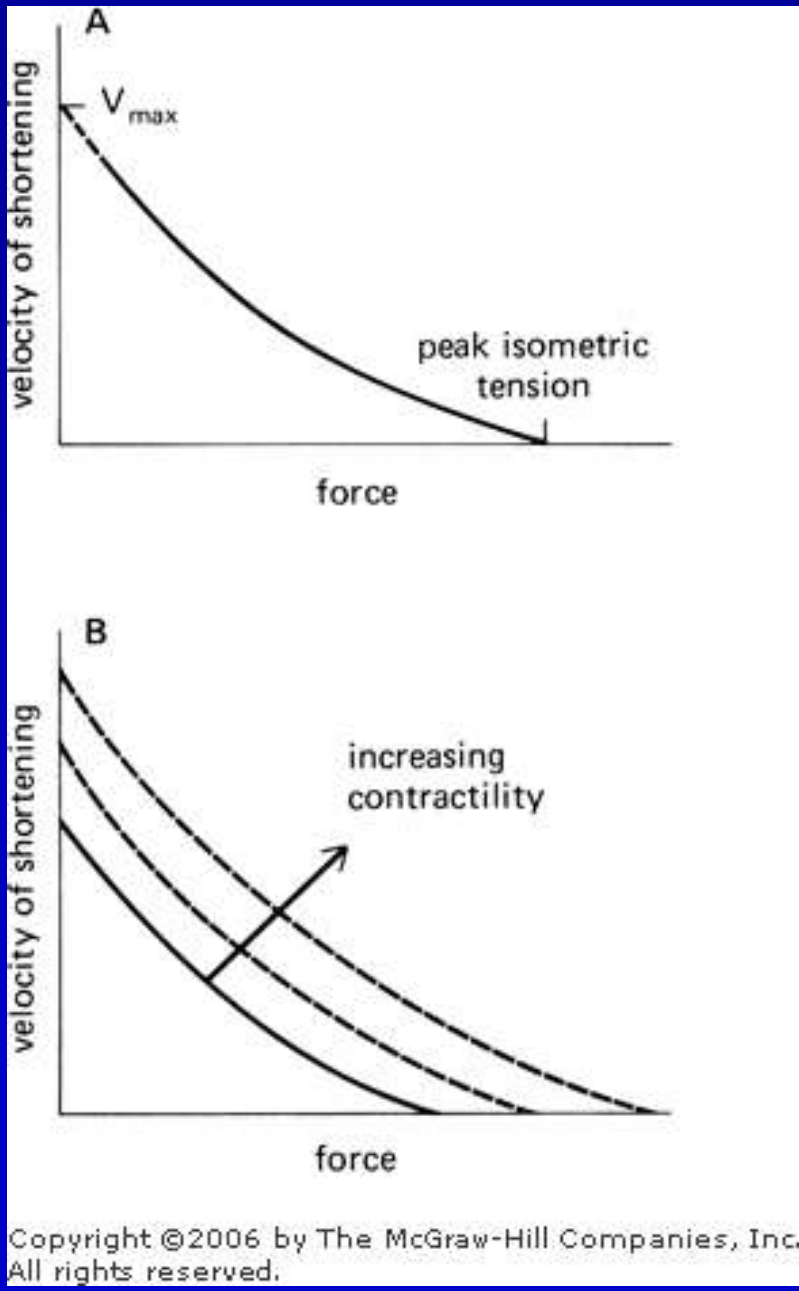
Force-Velocity Relationship

- Measure peak velocity of shortening of the preparation during **isotonic** contractions against several different total loads
- Construct a line, extrapolate to zero force to find V_{max}
- The V_{max} point has been shown to be closely correlated with the actin-myosin ATPase activity of the muscle and is thought to indicate the maximum possible rate of interaction between thick and thin filaments within the sarcomere



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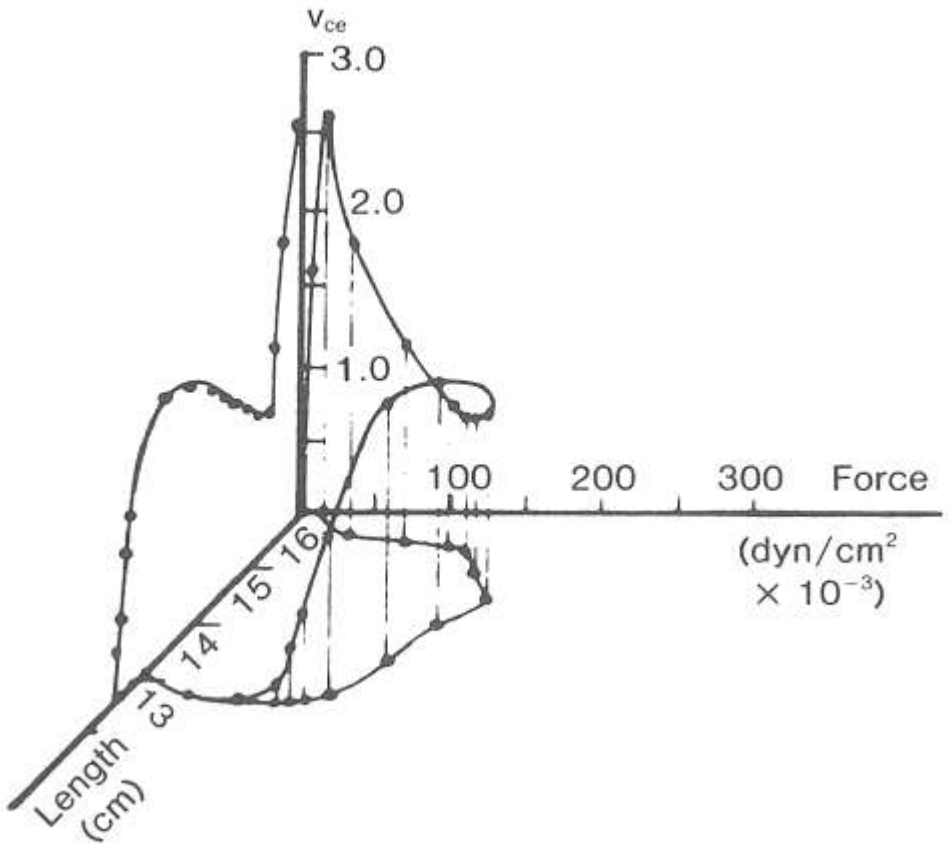


Fig. 10.8. Reprinted with permission from A. A. Bove and P. R. Lynch. *Journal of Applied Physiology* **29:** 884–888, 1970. Force, length, and contractile element velocity in the left ventricle of an anesthetized dog. Ventricular volume measured by biplane cineradiography. Points are plotted at intervals of 14.8 msec, showing the sequence of events for one cardiac cycle. Force in 10^{-3} dyn/cm^2, length (circumference) in cm, and v_{ce} in circumferences per sec. The tracing lies in the back plane of the figure during isovolumic contraction, moves out to vary in three dimensions during ejection, and moves in the bottom plane during diastole.

Contractility

- What the muscle is capable of doing
- The potential for contraction that the muscle possesses in its resting state by virtue of local physicochemical conditions
- Actual performance of the muscle in a given setting is subject to the limitations imposed by external mechanical conditions on the ability of the muscle to respond
- Conceptional definition: “The ability to shorten and develop force that is conferred on muscle cells by their physicochemical state.”
- Operational definition: Nonexistent – presumably would include at the very least the measurement of force, length, velocity, and time, all expressed in some kind of multidimensional matrix
- “Index” of contractility: an outward and visible sign of the inward condition of the myocardium

Milnor – Hemodynamics, 2nd ed., 1989, Chapter 10, "Cardiac Dynamics"

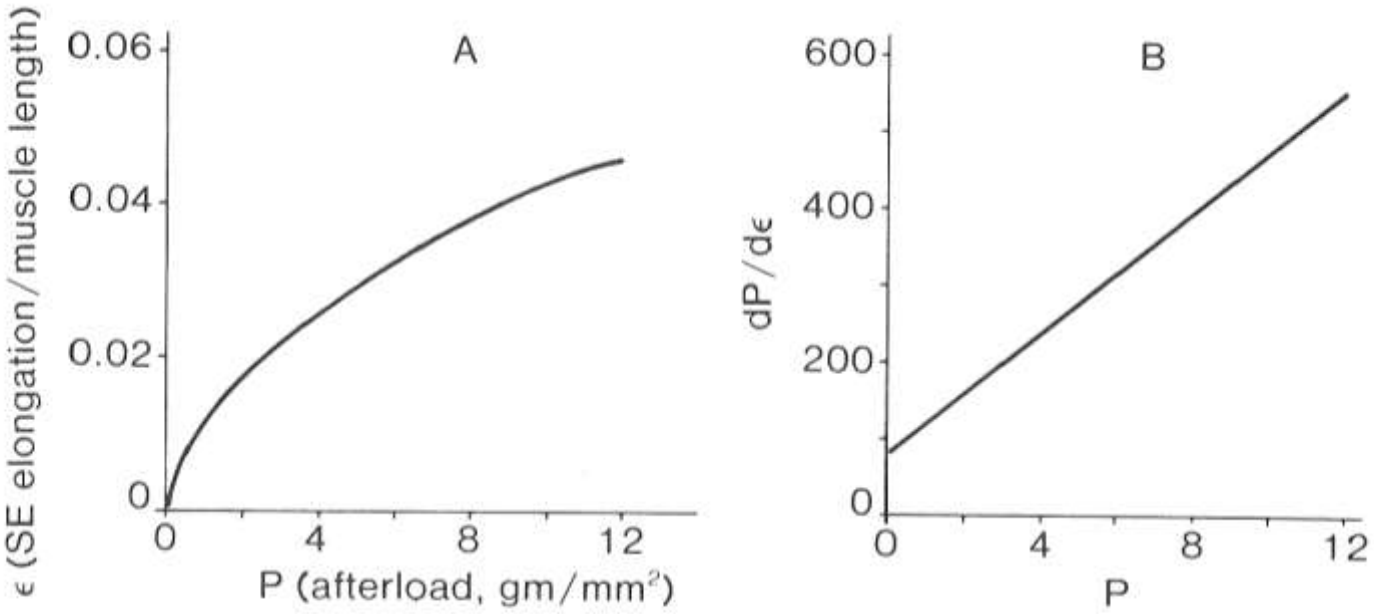
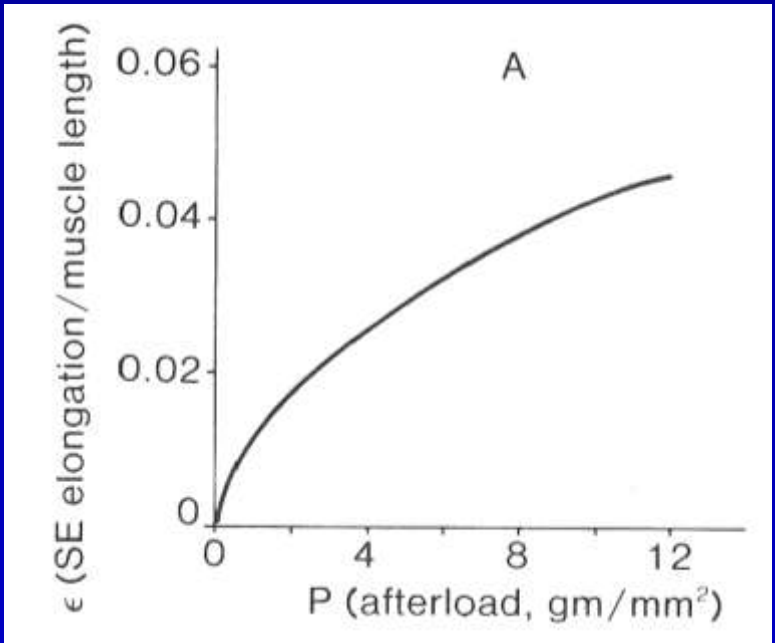


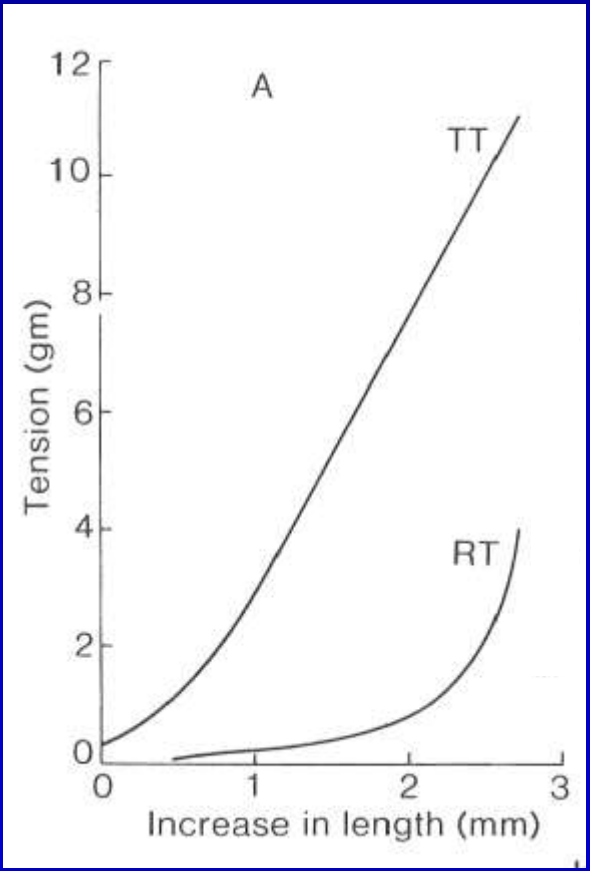
Fig. 10.5. From data reported by Parmley and Sonnenblick, 1967. Stress-strain relationships measured by quick-release method on cat papillary muscle. *Abscissa*, stress (P), the afterload per unit muscle cross section, g/mm². *Ordinates*, *left*, strain (ε), ratio of change in length to postrelease length; *right*, $dP/d\varepsilon$, gm/mm². Cross-sectional area of muscle, 0.98 mm²; average length, 6.4 mm; preload, 0.5 gm. Results of this experiment fit the equation $dP/d\varepsilon = KP + C$, where the dimensionless constant $K = 40$, and $C = 80$ g/mm².

Stress-strain curve is approximately exponential in shape

Data obtained from quick-release method; Stress – afterload per unit muscle cross section – g/mm2; Strain – ratio of change in length to postrelease length

Stress-Strain and Length-Tension





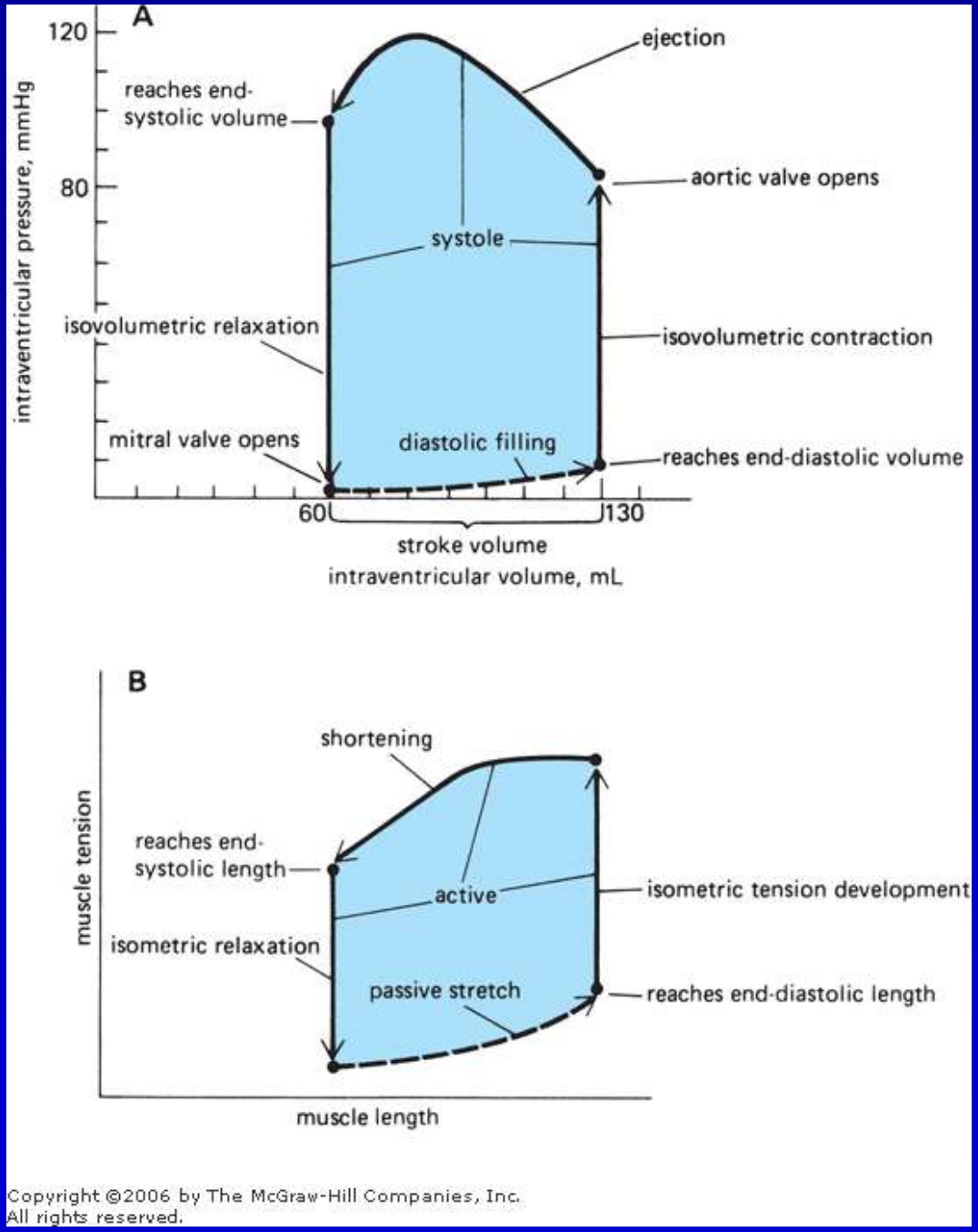
- Stress is like tension, strain is like length

Correspondence Between Length-Tension and Pressure-Volume

Chamber property

Vs

Muscle fiber property



Mohrman, DE et al. Cardiovascular Physiology. 1997. p. 56.

Milnor – Hemodynamics, 2nd ed., 1989, Chapter 10, "Cardiac Dynamics"

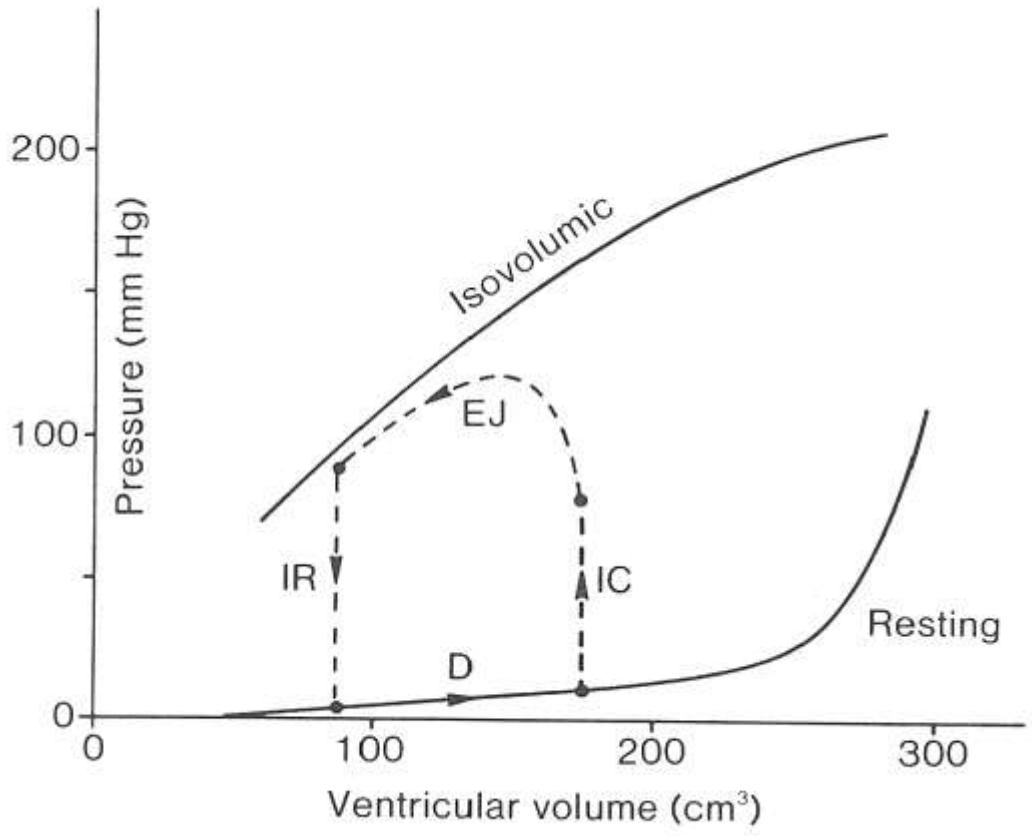
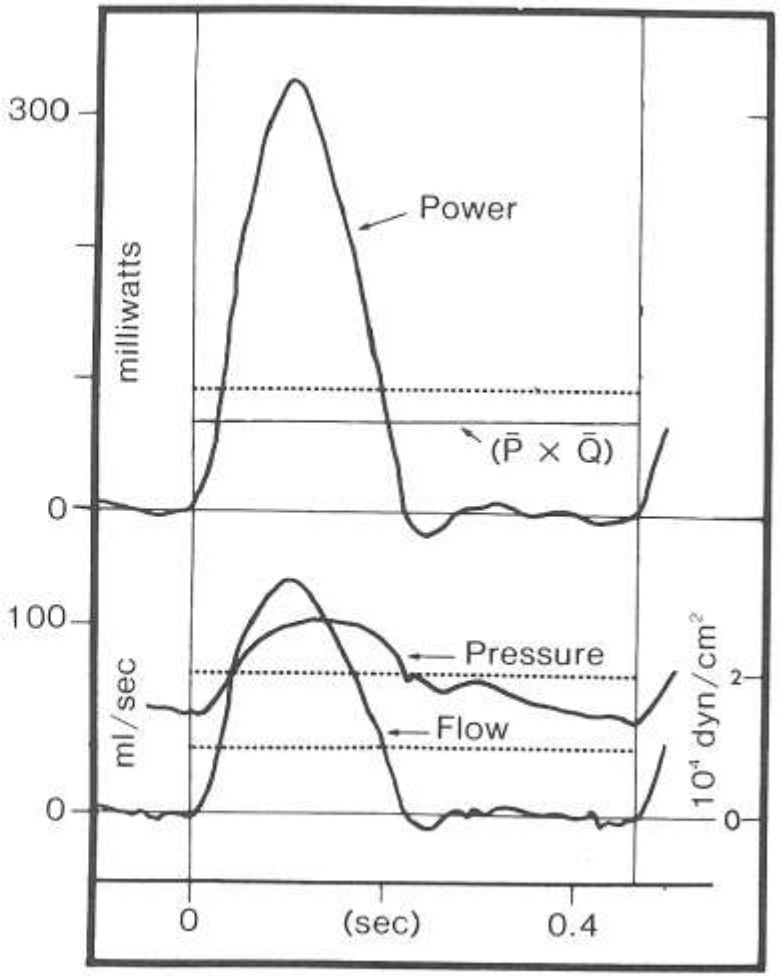


Fig. 10.6. Diagram of pressure and volume in human left ventricle. *Lower continuous line,* resting or diastolic relationships. *Upper continuous lines,* pressure maxima reached from indicated resting volume under isovolumic conditions. *Dashed line,* sequence in typical normal beat. *D*, diastole; *IC*, isovolumic contraction period; *EJ*, ejection; *IR*, isovolumic relaxation.

Milnor – Hemodynamics, 2nd ed., 1989, Chapter 10, "Cardiac Dynamics"

Fig. 10.11. Pulsatile pressure, flow, and their product, hydraulic power, in the main pulmonary artery of an unanesthetized dog. Power was recorded by multiplying pressure and flow at every instant with an electronic multiplier. *Abscissa,* time (sec). *Above,* power supplied by the right ventricle (omitting kinetic energy). *Below,* pressure (*scale on right* in 10^4 dyn/cm^2) and flow (*scale on left,* ml/sec). Averages of the three curves over one cardiac cycle are shown by *dashed lines.* Mean pressure ($\bar{P}$) multiplied by mean flow ($\bar{Q}$) is indicated by *solid line* in *upper panel.* Difference between $\bar{P}\bar{Q}$ product and the true average power is the extra energy entailed in pulsations (see text).



Milnor – Hemodynamics, 2nd ed., 1989, Chapter 10, "Cardiac Dynamics"

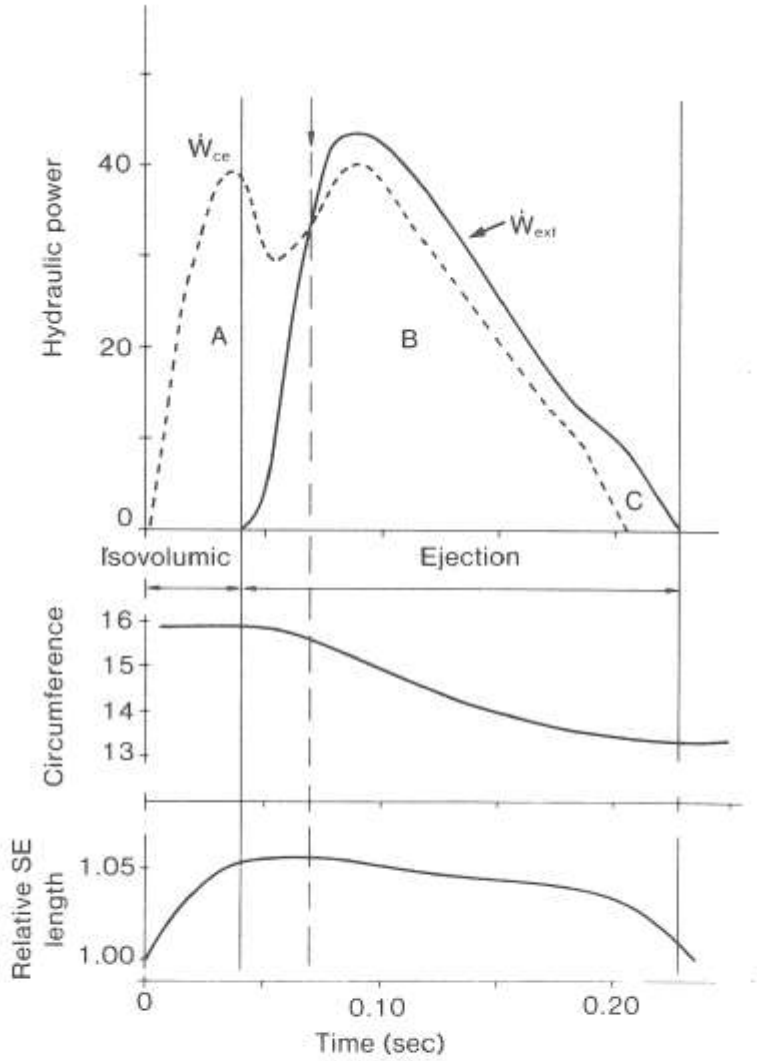
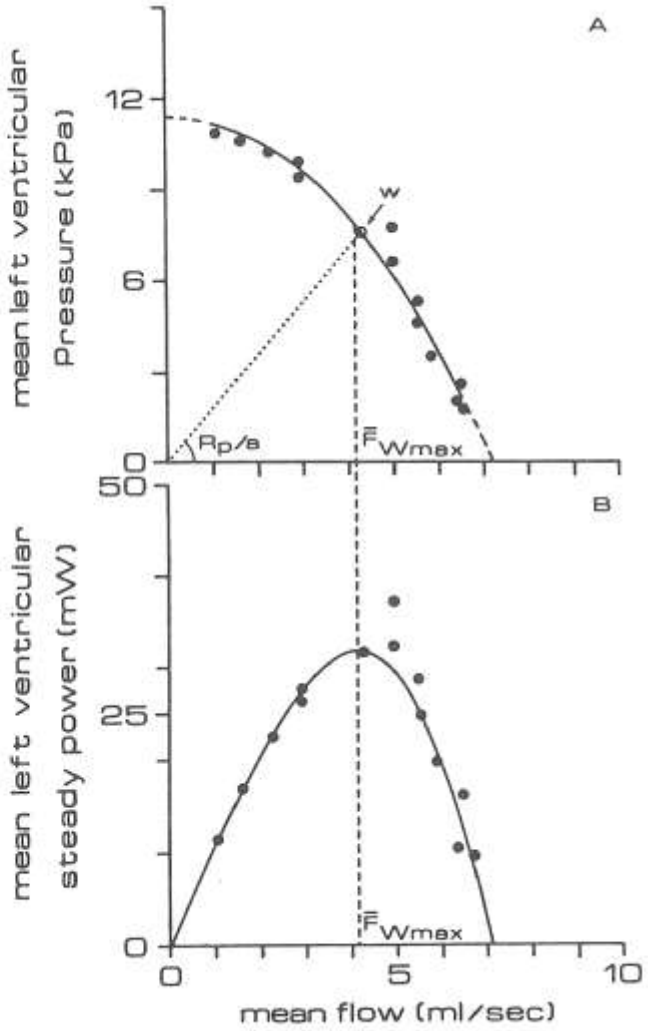


Fig. 10.13. Nichols, Walker, and Milnor, unpublished data. Hydraulic power of the left ventricle in a conscious, resting dog. A spherical shell model was assumed for the ventricular cavity and a Voigt model with $K = 30$ for the muscle fibers. *Abscissa*, time (sec). *Upper panel*, hydraulic power expended externally (W_{ext}, *continuous line*) and contractile component power (W_{ce}, *dashed line*) (10^6 dyn cm/sec). *Center panel*, ventricular circumference (cm); *bottom panel*, relative change in length of the series elastic element. *Arrow* and *vertical dashed line* show the instant of peak wall force. Area *A* is the work done by the contractile element in stretching the *SE*, *B* the work it does in moving blood out of the chamber, and *C* the elastic energy returned by the *SE* as it recoils to its original length in the latter part of diastole, contributing to the ejection of blood. End-diastolic volume, 68 cm^3; stroke volume, 27 cm^3; weight of animal, 21 kg.

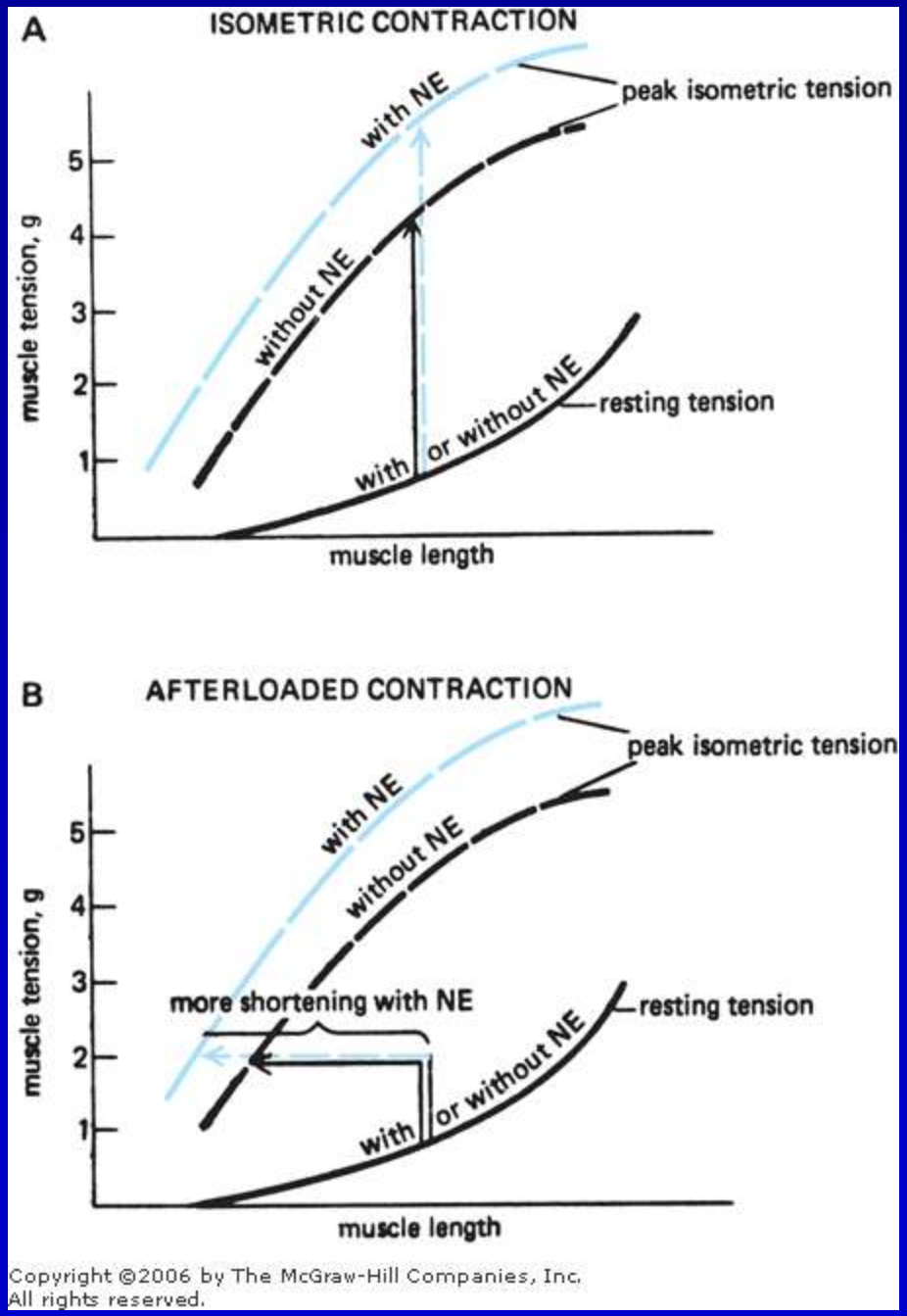
Milnor – Hemodynamics, 2nd ed., 1989, Chapter 10, "Cardiac Dynamics"

Fig. 10.14. Reprinted with permission from Van den Horn *et al.*, 1986. Left ventricular function in isolated feline heart. *Abscissa,* ventricular output (flow, ml/sec). *Ordinates:* above, left ventricular pressure (kPa, 1 Pa = 1 N/m²); below, steady-flow power (mW). Constant end-diastolic volume, heart rate, and inotropic state. Ventricular afterload varied by adjusting mechanical resistance to outflow. **A.** Pump function graph, showing inverse relation between pressure and flow. *W*, working point, the pressure and flow when ventricle pumped normally into aorta. *Dotted line,* peripheral resistance at working point. **B.** Steady power (external work per unit time, product of pressure and flow) for each point in **A**. $\bar{F}_{max}$, mean flow at maximum power.

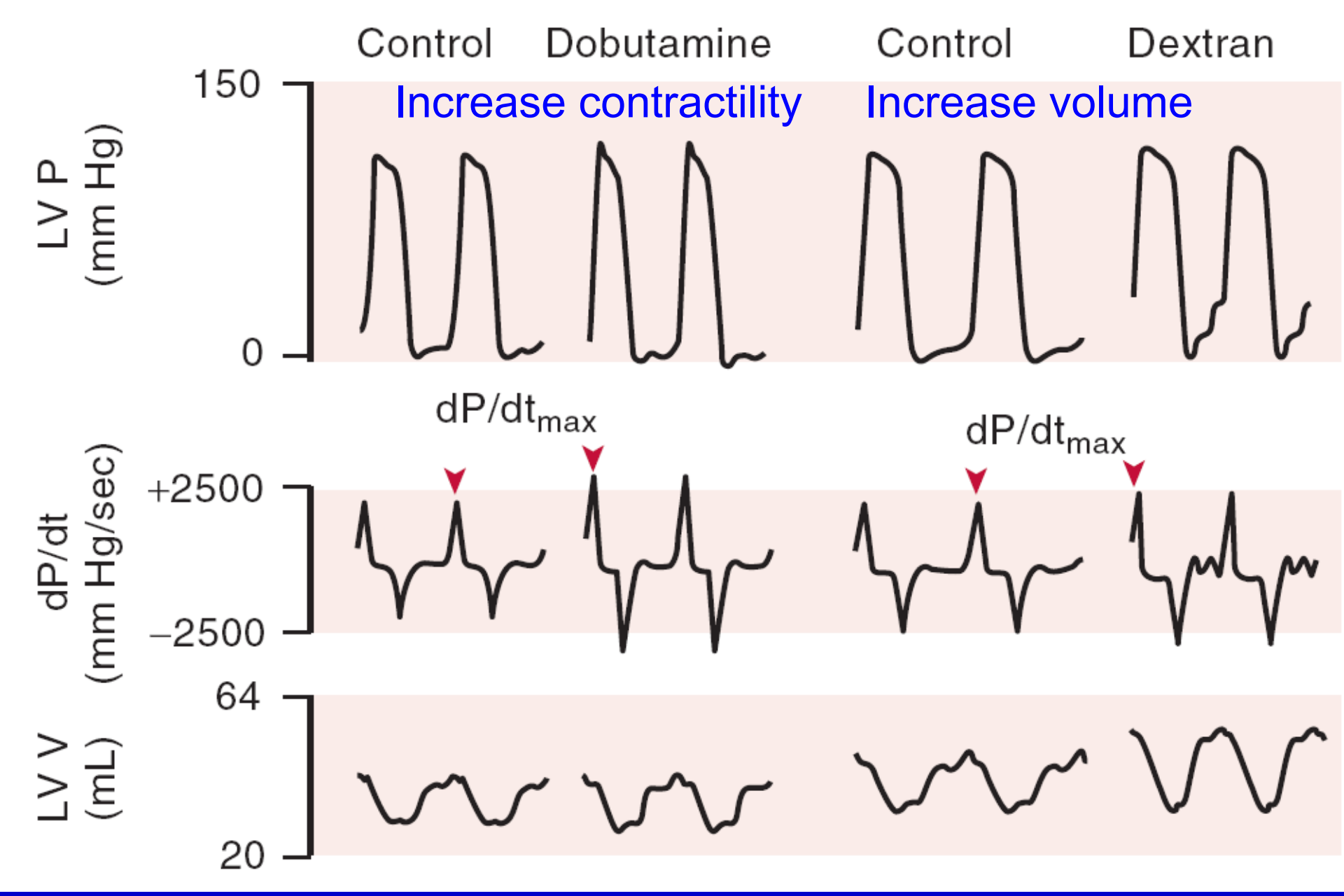


Length – Tension Relationships

- Effect of norepinephrine (NE) on isometric (**A**) and afterloaded (**B**) contractions of cardiac muscle



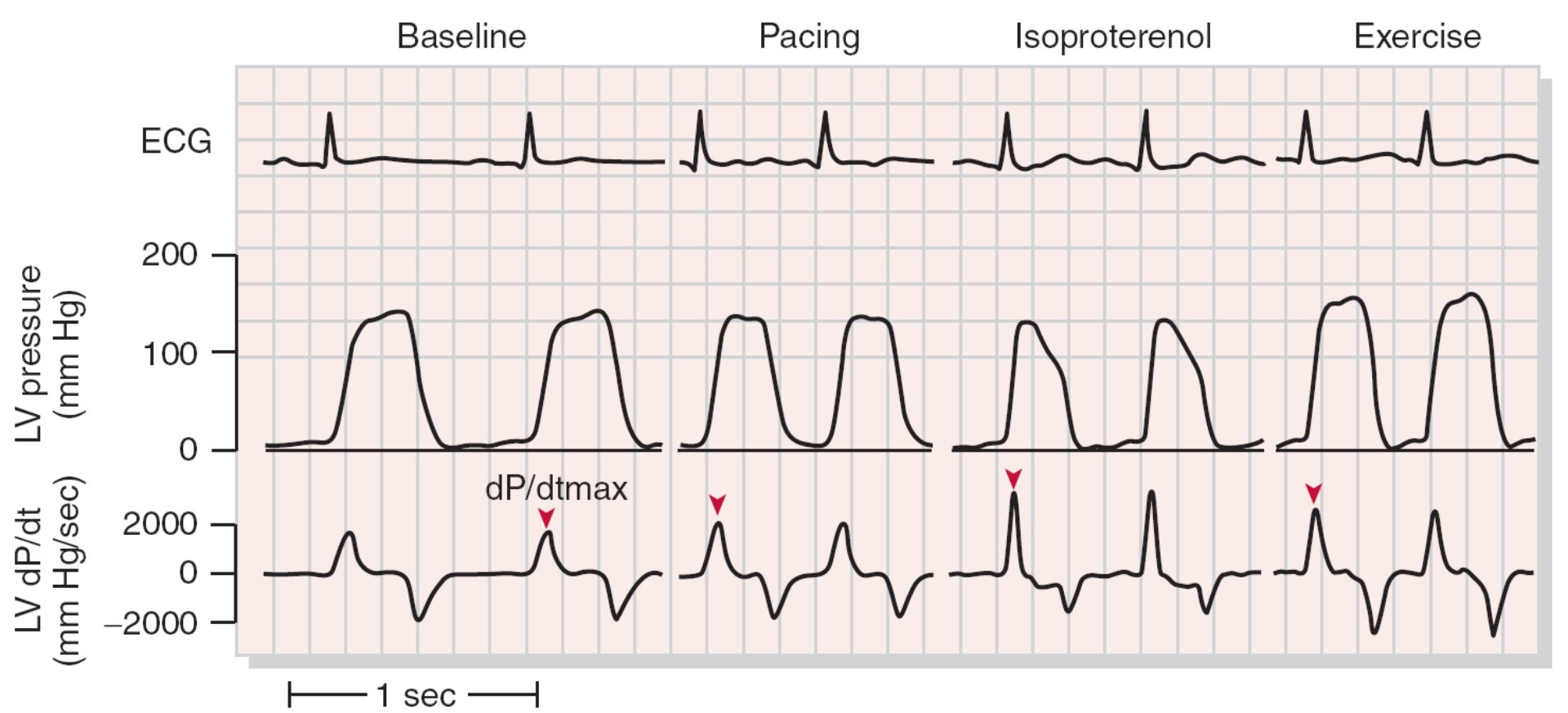
Mohrman, DE et al. Cardiovascular Physiology. 1997. p. 44.



Carroll JD and Hess OM. Ch 20, "Assessment of Normal and Abnormal Cardiac Function" Braunwald's Heart Disease, 7th ed. 2004.

Treppe, or Staircase Phenomenon

- **Changes in heart rate** influence cardiac contractility
- A small amount of extracellular Ca2+ enters the cell during the plateau phase of each action potential
- As HR increases, more Ca2+ enters the cells per minute
- There is a buildup of intracellular Ca2+ and a greater amount of Ca2+ is released into the sarcoplasm with each action potential
- Thus, a sudden increase in rate is followed by a progressive increase in contractile force to a higher plateau
- This behavior is called the ***staircase phenomenon*** **(or treppe)**
- Changes in contractility produced by this intrinsic mechanism are sometimes referred to as ***homeometric autoregulation***
- The importance of such rate-dependent modulation of contractility in normal ventricular function is not clear at present
- Bowditch phenomenon is another name (Milnor, p. 280)



Increase in dP/dtmax during increases in contractility produced by pacing tachycardia, isoproterenol, and exercise

Carroll JD and Hess OM. Ch 20, “Assessment of Normal and Abnormal Cardiac Function” Braunwald’s Heart Disease, 7th ed. 2004.

Milnor – Hemodynamics, 2nd ed., 1989, Chapter 10, "Cardiac Dynamics"

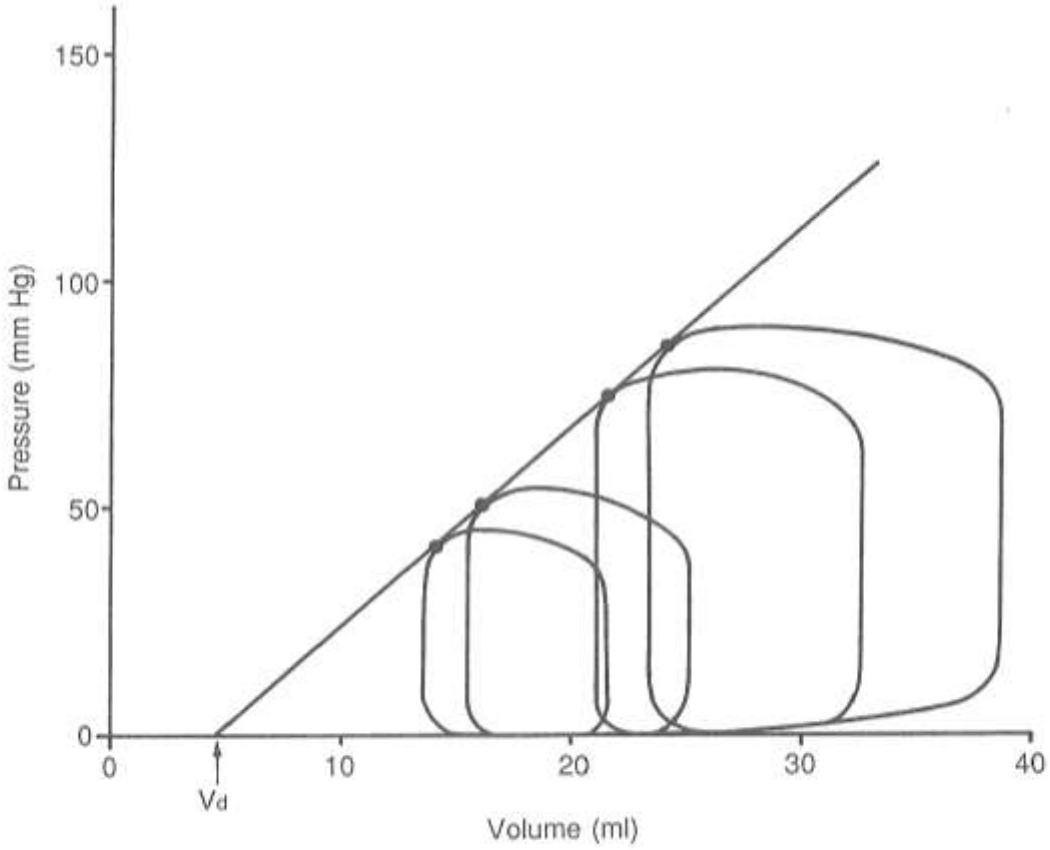
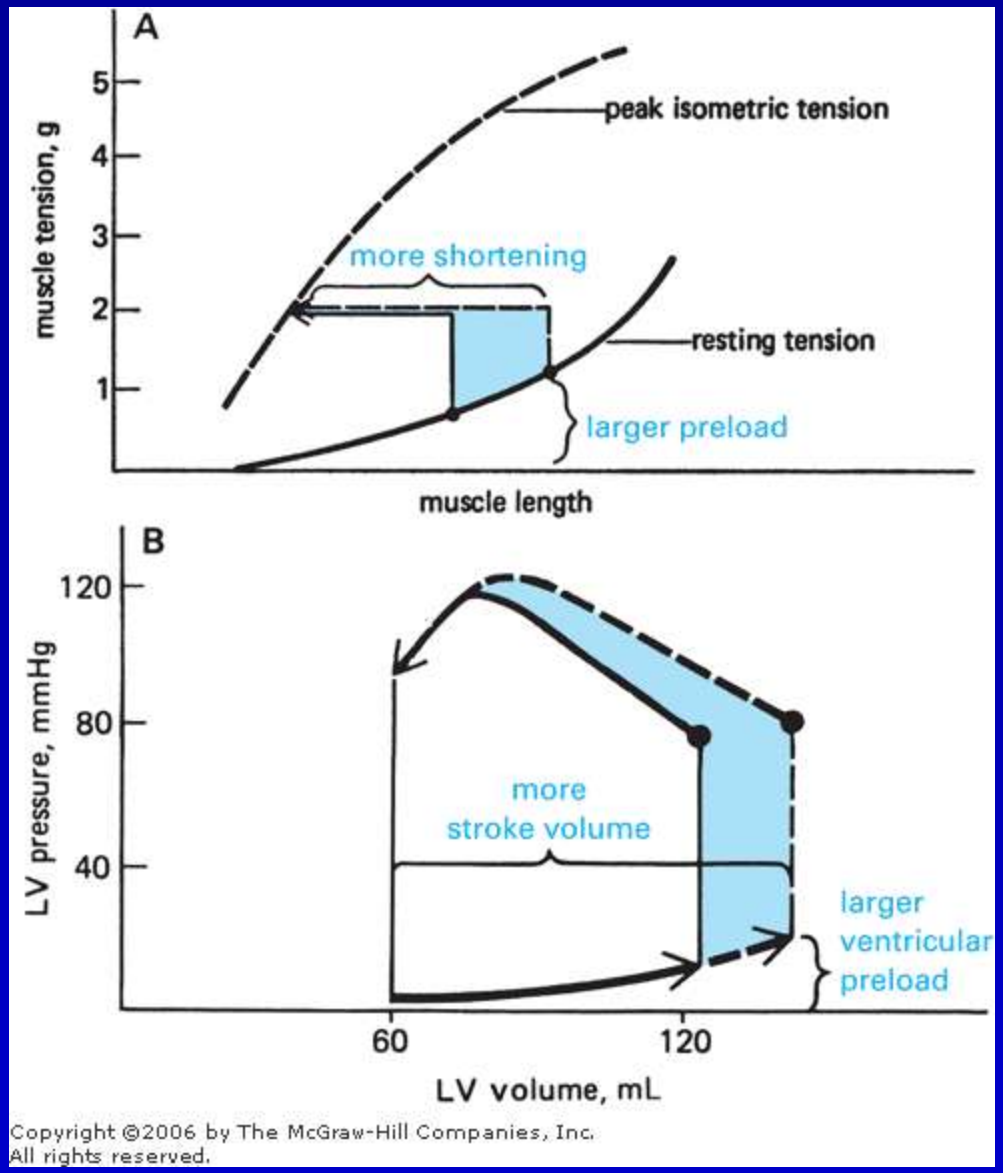


Fig. 10.10. From data in Maughan *et al.*, 1984. Left ventricular pressures (*ordinate*) and volumes (*abscissa*) in isolated canine heart pumping into a constant, artificial arterial resistance and impedance. Four beats are shown, each starting from a different end-diastolic volume. End-systolic points in each case tend to fall on a straight line, which intercepts the volume axis at V_d.

Preload Effects on fiber shortening and on stroke volume

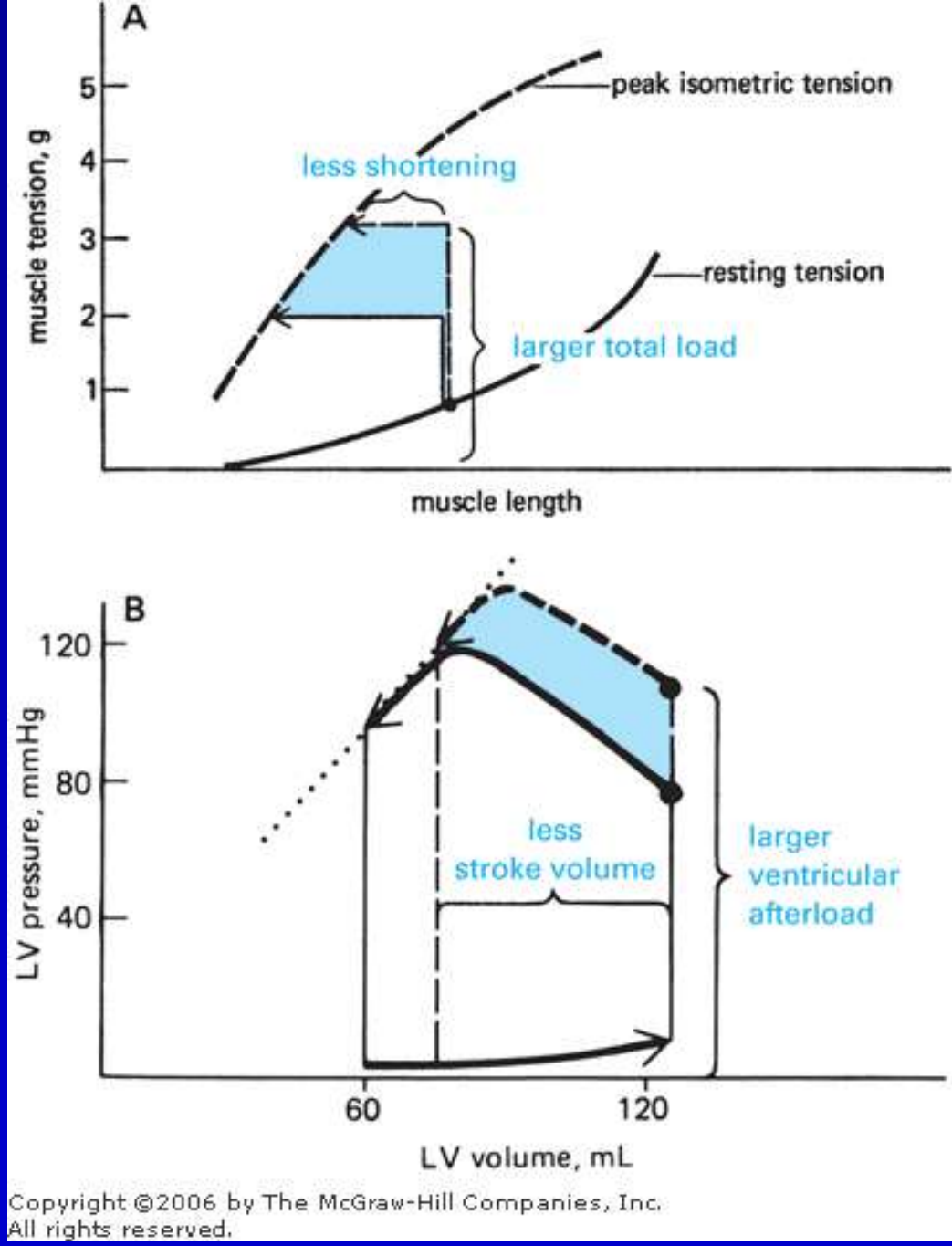
Effect of changes in preload on cardiac muscle shortening during after-loaded contractions **A** and on ventricular stroke volume **B**.



Mohrman, DE et al. Cardiovascular Physiology. 1997. p. 58.

Afterload Effects on fiber shortening and on stroke volume

Effect of changes in afterload on cardiac muscle shortening during afterloaded contractions **A** and on ventricular stroke volume **B**.



Mohrman, DE et al. Cardiovascular Physiology. 1997. p. 59.

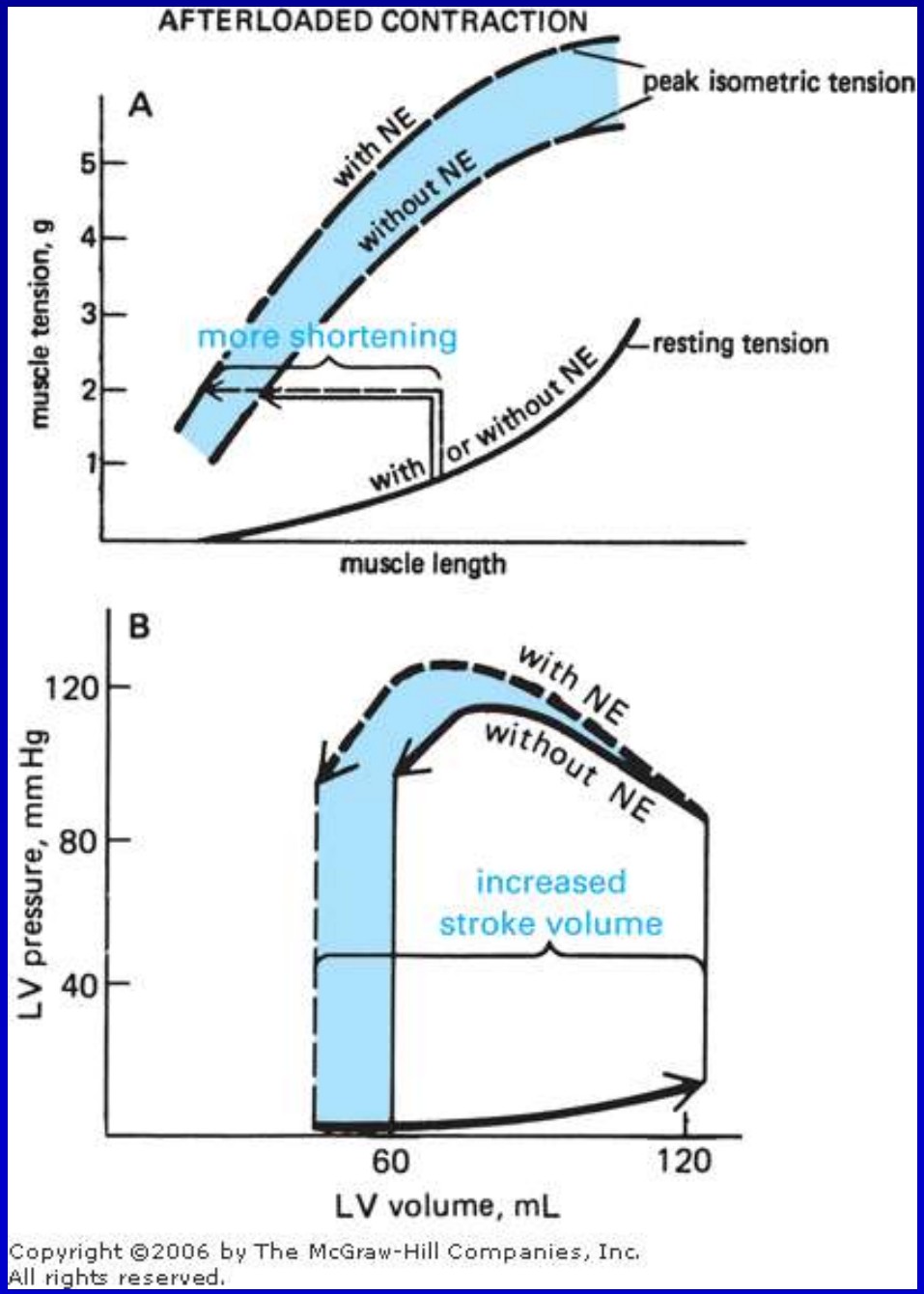
Contractility Effects on fiber shortening and on stroke volume

Effect of norepinephrine (NE) on cardiac muscle shortening during afterloaded contractions **A** and on ventricular stroke volume **B**.

The Vmax value is commonly used as an index of the state of contractility of isolated cardiac muscle. Myocardial contractility cannot be directly measured in patients.

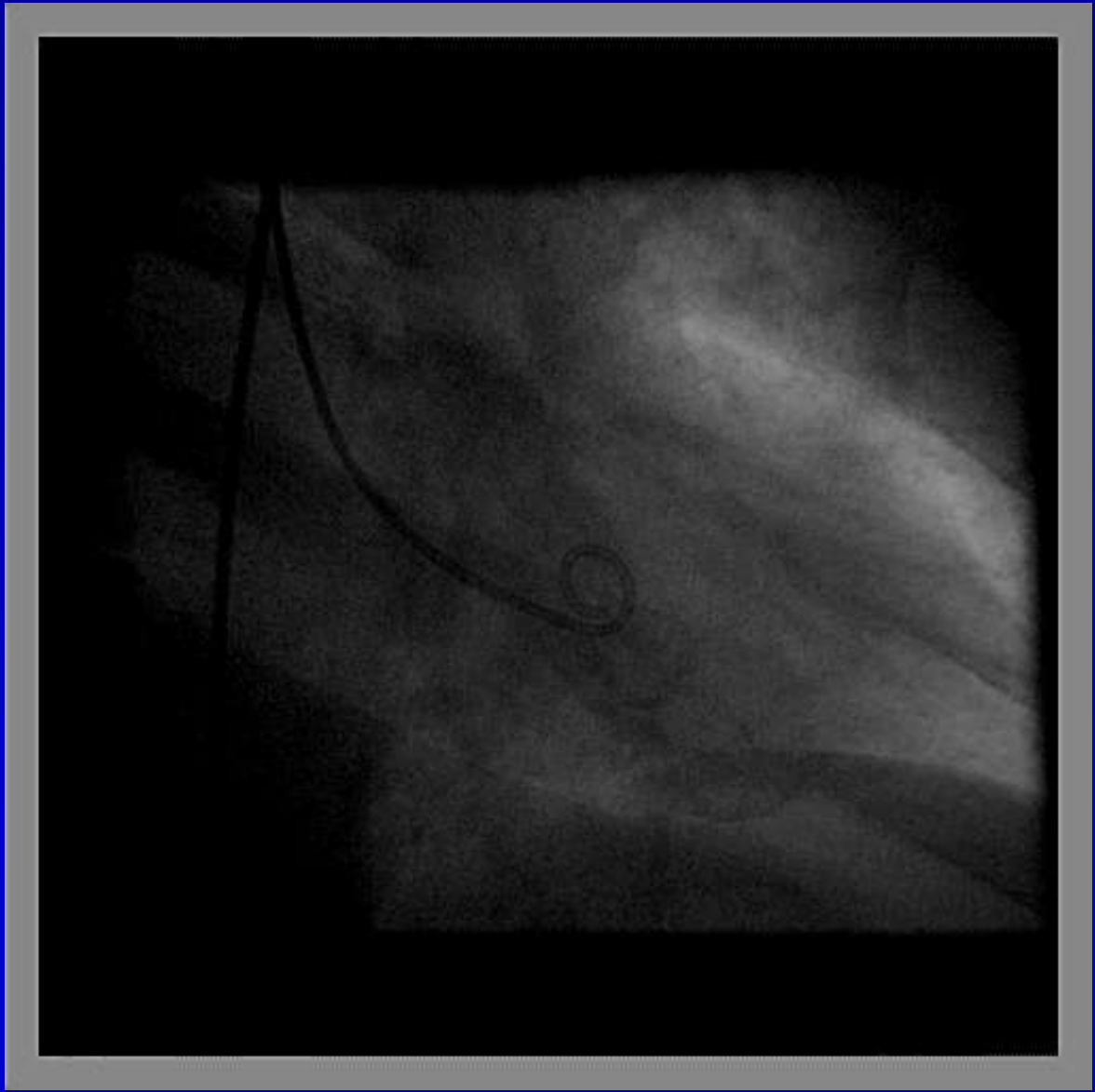
The maximum rate of pressure development (*dP/dt*max) during the isovolumetric contraction may be used as an index of contractility on the grounds that, in isolated cardiac muscle preparations, changes in contractility and Vmax cause changes in the rate of tension development in an isometric contraction.

Decreases in left ventricular *dP/dt*max below the normal values of 1500 to 2000 mmHg/s indicate that myocardial contractility is below normal.



Mohrman, DE et al. Cardiovascular Physiology. 1997. p. 60.

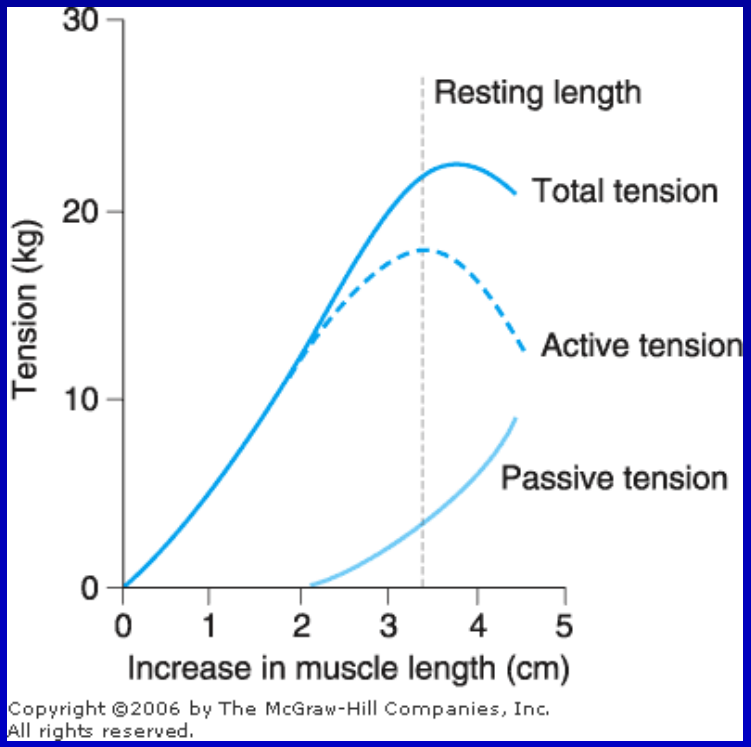
Observing the Squeeze

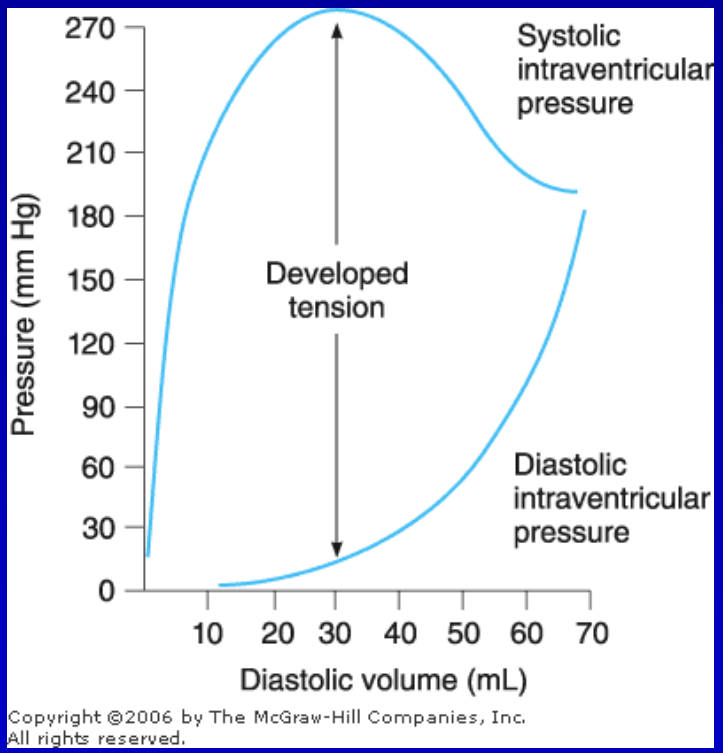


"energy of contraction is proportional to the initial length of the cardiac muscle fiber."

The relation between SV and EDV is called the Frank–Starling curve

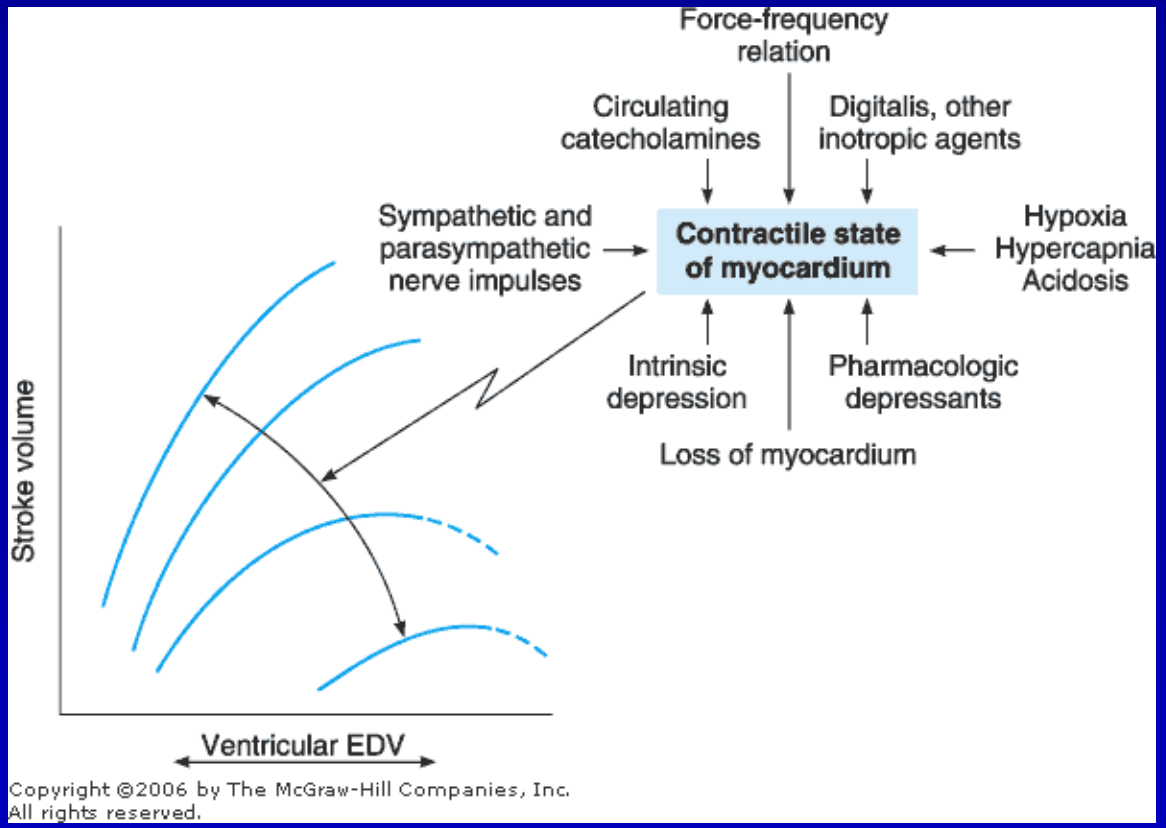
Starling's law of the heart or the Frank–Starling law.





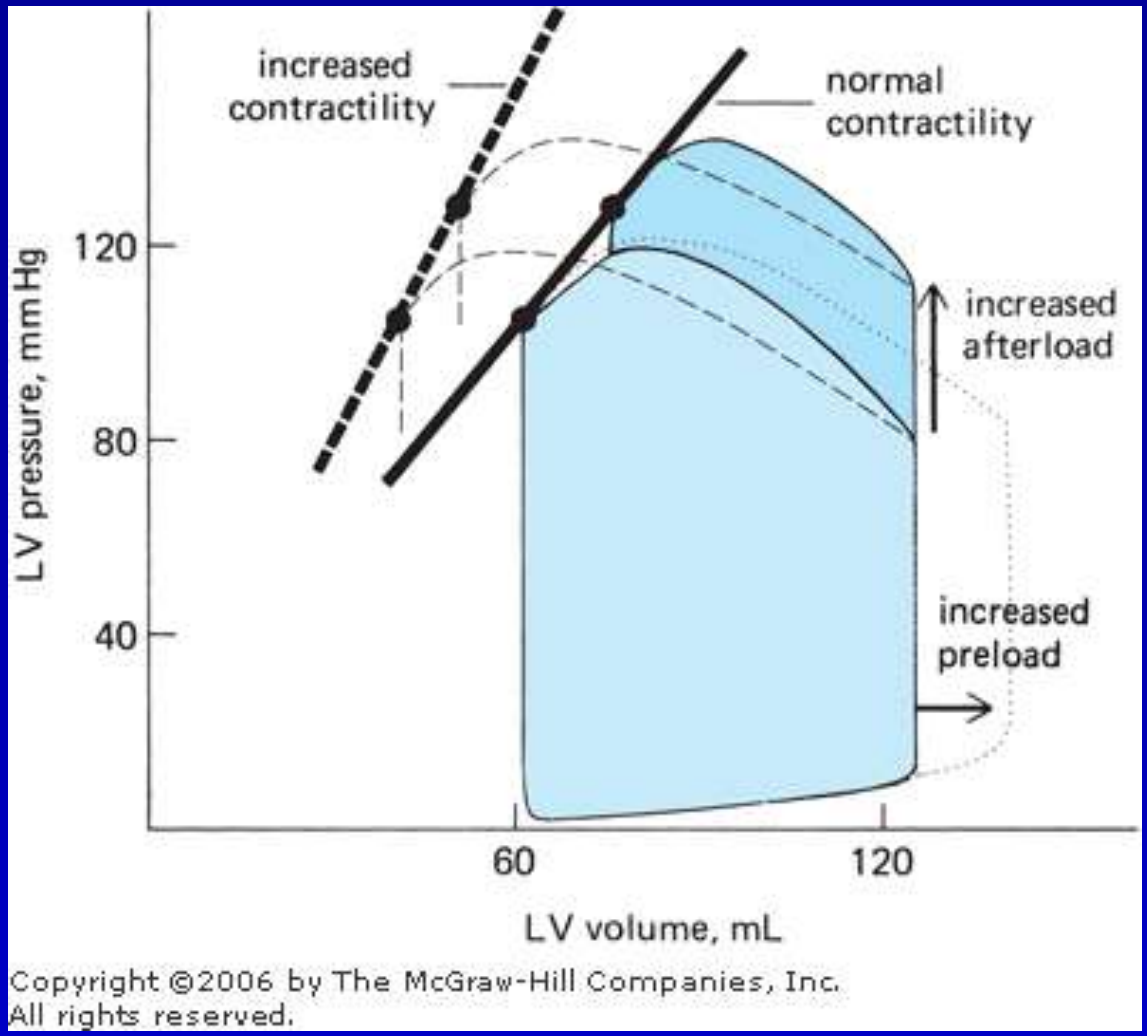
A. Length–tension relationship for the human triceps muscle. The passive tension curve measures the tension exerted by this skeletal muscle at each length when it is not stimulated. The total tension curve represents the tension developed when the muscle contracts isometrically in response to a maximal stimulus. The active tension is the difference between the two.
B. Length–tension relationship for cardiac muscle. The values are for canine heart

Contractility and the Frank-Starling Curve



- Effect of changes in myocardial contractility on the Frank–Starling curve. The curve shifts downward and to the right as contractility is decreased. The major factors influencing contractility are summarized on the right. The dashed lines indicate portions of the ventricular function curves where maximum contractility has been exceeded; i.e., they identify points on the "descending limb "of the Frank–Starling curve. EDV, end-diastolic volume. (Reproduced, with permission, from Braunwald E, Ross J, Sonnenblick EH: Mechanisms of contraction of the normal and failing heart. N Engl J Med 1967;277:794. Courtesy of Little, Brown, Inc.)

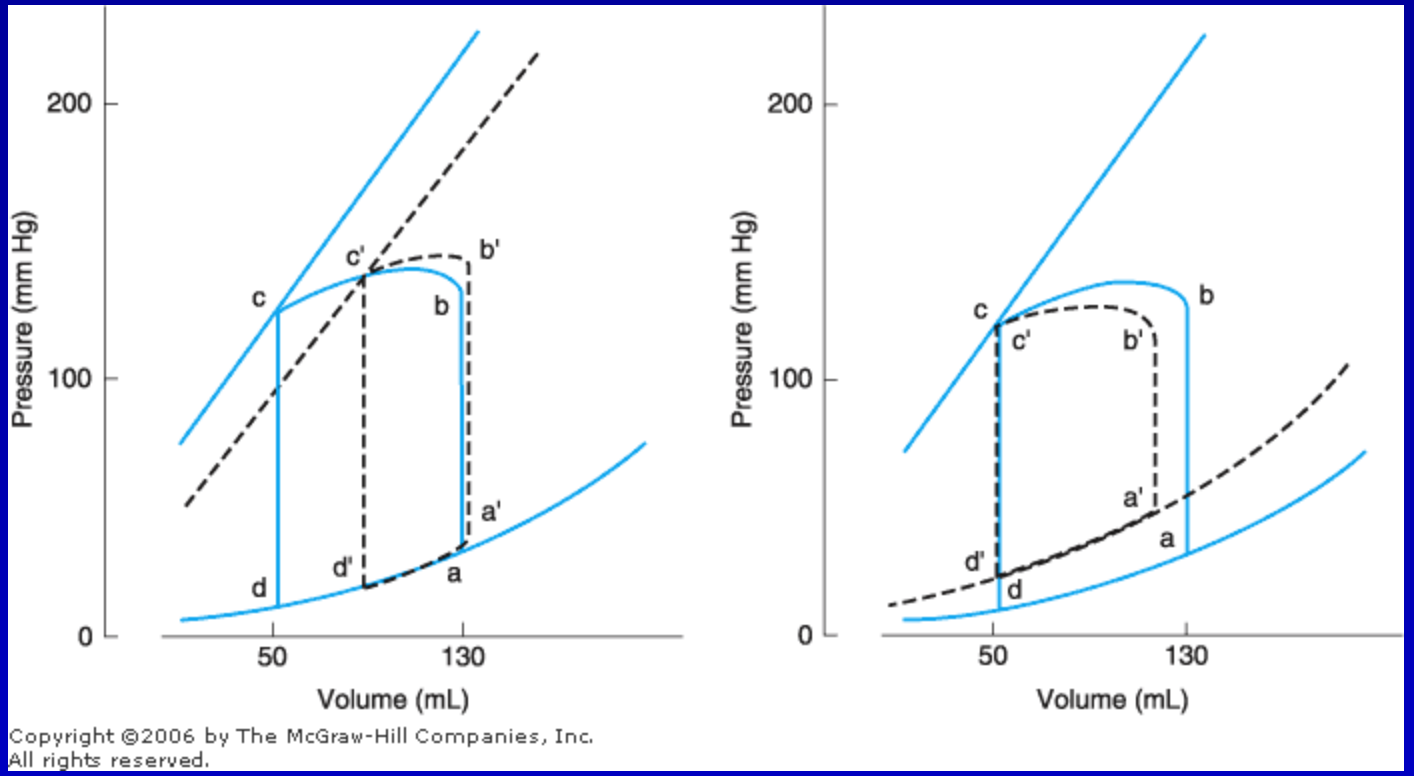
ESPVR – End-Systolic Pressure-Volume Relation



- The effect of increased contractility upon the left ventricular end-systolic pressure-volume relationship.

Mohrman, DE et al. Cardiovascular Physiology. 1997. p. 69.

Pressure-Volume Loops



- Effect of systolic and diastolic dysfunction on the pressure–volume loop of the left ventricle. **Left:** Systolic dysfunction shifts the isovolumic pressure–volume curve (see Figure 29–2) to the right, decreasing the stroke volume from b–c to b'–c'. **Right:** Diastolic dysfunction increases end-diastolic volume and shifts the diastolic pressure-volume relationship upward and to the left. This reduces the stroke volume from b–c to b'–c'. (Reproduced, with permission, from McPhee SJ, Lingappa VR, Ganong WF [editors]: *Pathophysiology of Disease,* 4th ed. McGraw-Hill, 2003.)

Indices of Contractility

- Pressure: peak positive dP/dt, or dP/dt/P
- Tension-time index (area under the systolic portion of the aortic pressure curve)
- Maximum acceleration of blood ejected
- Ventricular function curves (end-diastolic volume vs stroke work) – (stroke work is the integral of the instantaneous hydraulic power over one cardiac cycle – or the area of the pressure volume loop)
- Peak of time-varying elastance (Emax) slope of the ESPVR
- Stroke volume
- Ejection fraction

TABLE 20–2 Definitions of Terms Used to Describe Systolic and Diastolic Function

Term	Definition
Preload	Distending force of the ventricular wall, which is highest at end-diastole and is responsible for sarcomere length at the beginning of systolic contraction
Afterload	Resisting force of the ventricular wall during systolic ejection, which is necessary to overcome peripheral vascular resistance or impedance; measures of afterload are peak-systolic, mean-systolic, or end-systolic wall stress
Contractility	Intrinsic ability of the myocardium to generate force at a certain rate and time (controlled for loading conditions)
Cardiac output	Stroke volume multiplied by heart rate
Stroke work	Mean systolic blood pressure multiplied by stroke volume
Stroke force	Stroke work per ejection time
Stress	Force per area
Wall stress	Pressure multiplied by radius, divided by wall thickness × 2
Compliance or distensibility	Change in volume per change in pressure (dV/dP)
Elastance	Slope of the end-systolic pressure-volume relation
Elasticity	Property of a material to restore its initial length or geometry after distending force has been removed
Strain	Length change in percent of initial length; two definitions are used: LaGrangian strain $e = (l - l_o)l_o$ and natural strain $e = \ln(l/lo)$
Stiffness	Pressure per volume change (dP/dV). *Ventricular stiffness* is a measure for changes of the ventricle as a whole; *myocardial stiffness* is a measure for changes of the myocardium itself. Ventricular properties are characterized by instantaneous pressure-volume relations, whereas myocardial properties are best described by stress-strain relations.
Creep	Time-dependent lengthening of a material in the presence of a constant force
Stress relaxation	Time-dependent decrease of stress in the presence of a constant length
Viscoelasticity	Resistance of a material to length changes (strain) or the velocity of length changes (strain rate)

Carroll JD and Hess OM. Ch 20, "Assessment of Normal and Abnormal Cardiac Function" Braunwald's Heart Disease, 7th ed. 2004.

TABLE 20–4 Characteristics of Selected Indices of Global Ventricular Function

Index	Sensitive to Inotropic Changes	Dependence On Preload	Dependence On Afterload	Dependence On Ventricular Volume or Mass	Ease of Application
Ejection fraction; fractional shortening	++	++	+++	++	++++
End-systolic volume or dimension	+	0	+++	++	++++
VCF	+++	0	+++	++	+++
Afterload-corrected VCF	+++	0	0	0	+
ESPVR	++++	0	0	+++	+
End-systolic stiffness	++++	0	0	0	+
Preload recruitable stroke work	+++	0	0	++	+
Left ventricular dP/dt	++++	++	++	++	++

ESPVR = slope of end-systolic pressure-volume relation; VCF = velocity of circumferential fiber shortening; dP/dt = rate of ventricular pressure rise.
Adapted from Carabello B: Evolution of the study of left ventricular function: Everything old is new again. Circulation 105:2701, 2002.

Carroll JD and Hess OM. Ch 20, "Assessment of Normal and Abnormal Cardiac Function" Braunwald's Heart Disease, 7th ed. 2004.

TABLE 20–8 Age-Related Differences in LV and Arterial Coupling in Patients with Dilated Cardiomyopathy

Parameters	Young Patients <35 yr	Intermediate-Aged Patients 35-50 yr	Older Patients >50 yr
Maximum + dP/dt (mm Hg/sec)	1011 ± 160	1170 ± 159	1147 ± 374
Stroke work (g-m/m^2)	19 ± 10	20 ± 10	19 ± 10
Pulse pressure (mm Hg)	26 ± 8	30 ± 11	38 ± 10
Pulse wave velocity (m/sec)	4.7 ± 0.4	6.5 ± 0.9	7.9 ± 0.6
Systemic vascular resistance (dyn-sec · cm^{-5})	1872 ± 789	2373 ± 762	2440 ± 770
Arterial compliance (ml/mm Hg)	1.33 ± 0.63	0.72 ± 0.40	0.51 ± 0.17

LV = left ventricular.

Adapted from Carroll JD, Shroff S, Arand P, et al: Arterial mechanical properties in dilated cardiomyopathy. J Clin Invest 87:1002-1009, 1991.

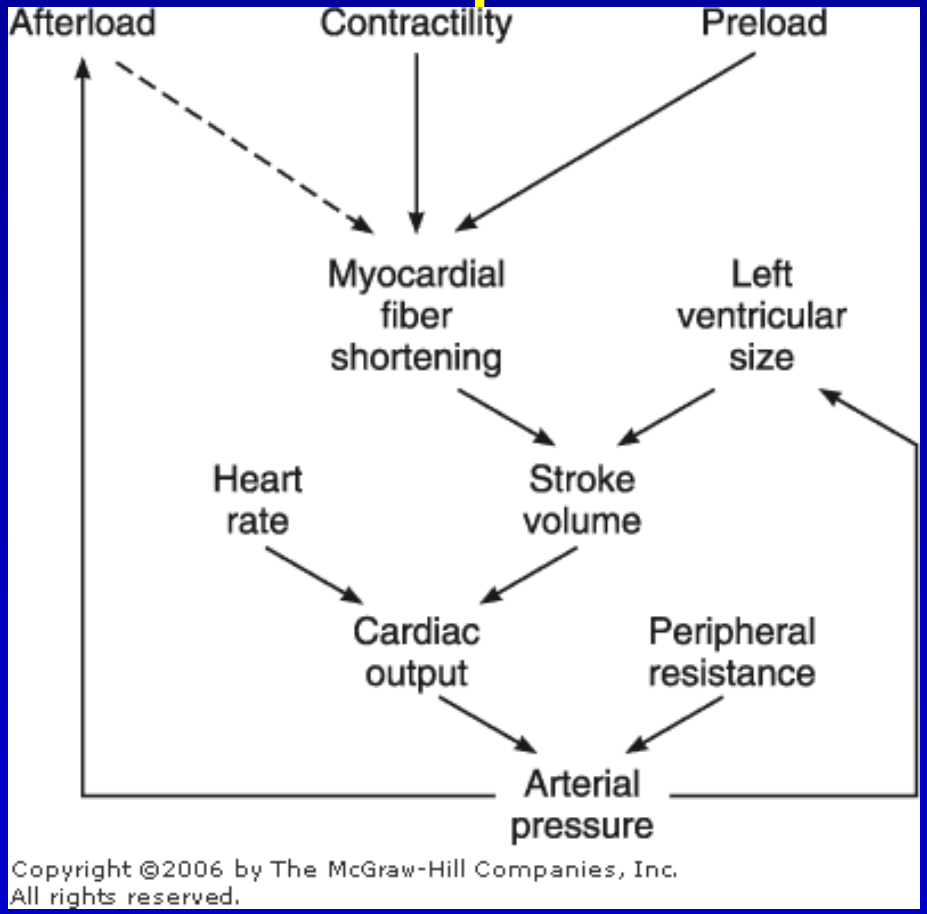
Carroll JD and Hess OM. Ch 20, "Assessment of Normal and Abnormal Cardiac Function" Braunwald's Heart Disease, 7th ed. 2004.

Effects of Various Conditions on Cardiac Output

	Condition or Factor[a]
No change	Sleep
	Moderate changes in environmental temperature
Increase	Anxiety and excitement (50–100%)
	Eating (30%)
	Exercise (up to 700%)
	High environmental temperature
	Pregnancy
	Epinephrine
Decrease	Sitting or standing from lying position (20–30%)
	Rapid arrhythmias
	Heart disease

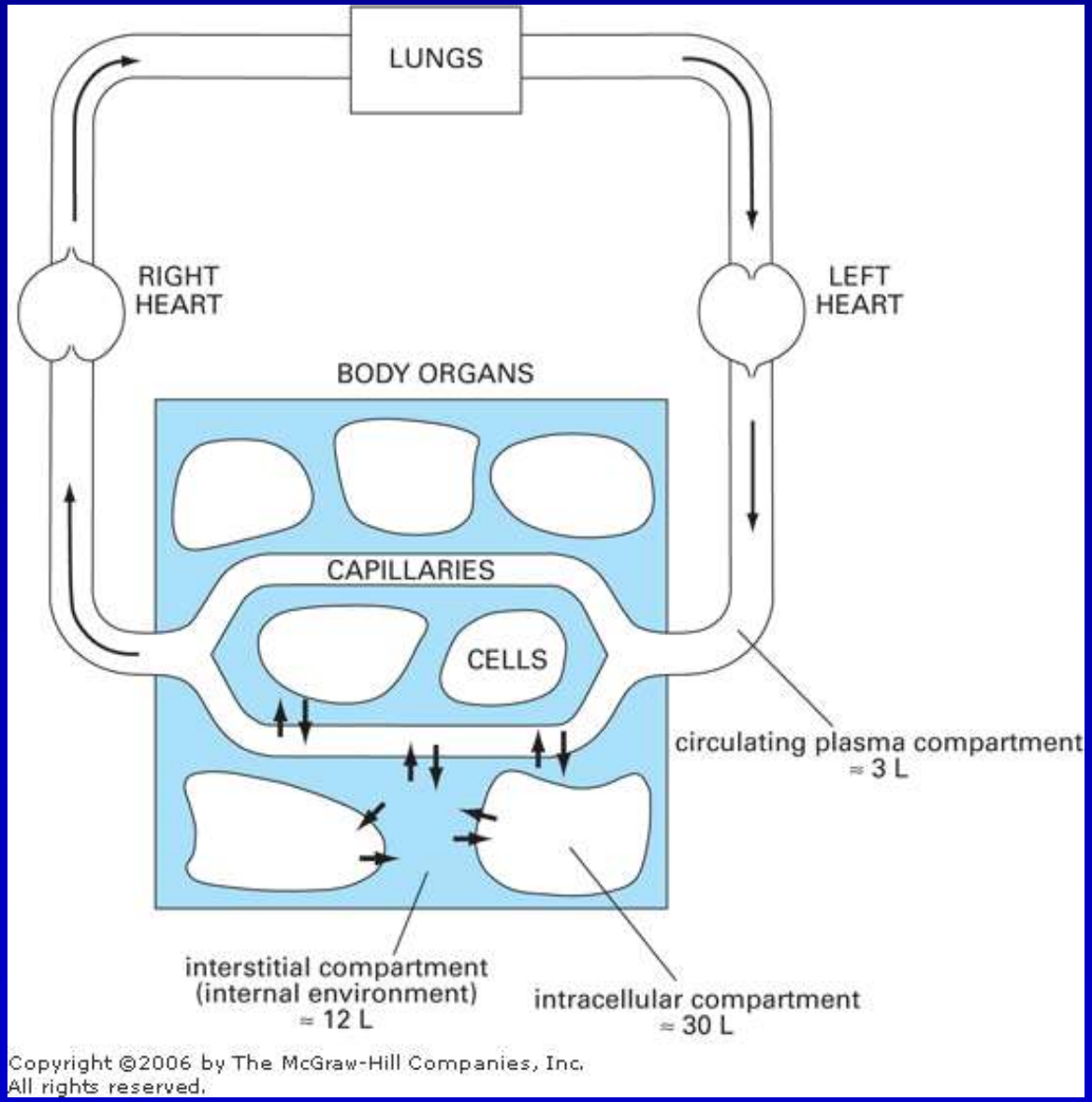
[a]Approximate percent changes are shown in parentheses.

Components Regulating Cardiac Output



Interactions between the components that regulate cardiac output and arterial pressure. Solid arrows indicate increases, and the dashed arrow indicates a decrease.

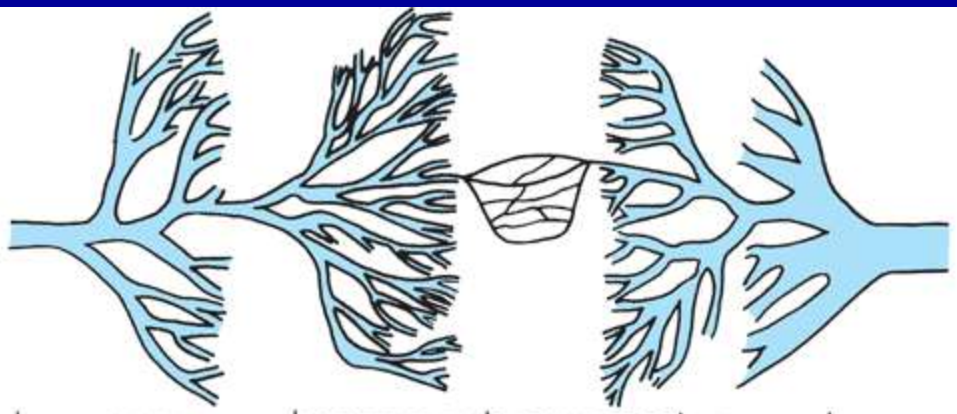
Fluid Distribution in the Body



Major body fluid compartments with average volumes indicated for a 70-kg human. Total body water is about 60% of body weight.

Mohrman, DE et al. Cardiovascular Physiology. 1997. from p. 2.

Vascular Properties

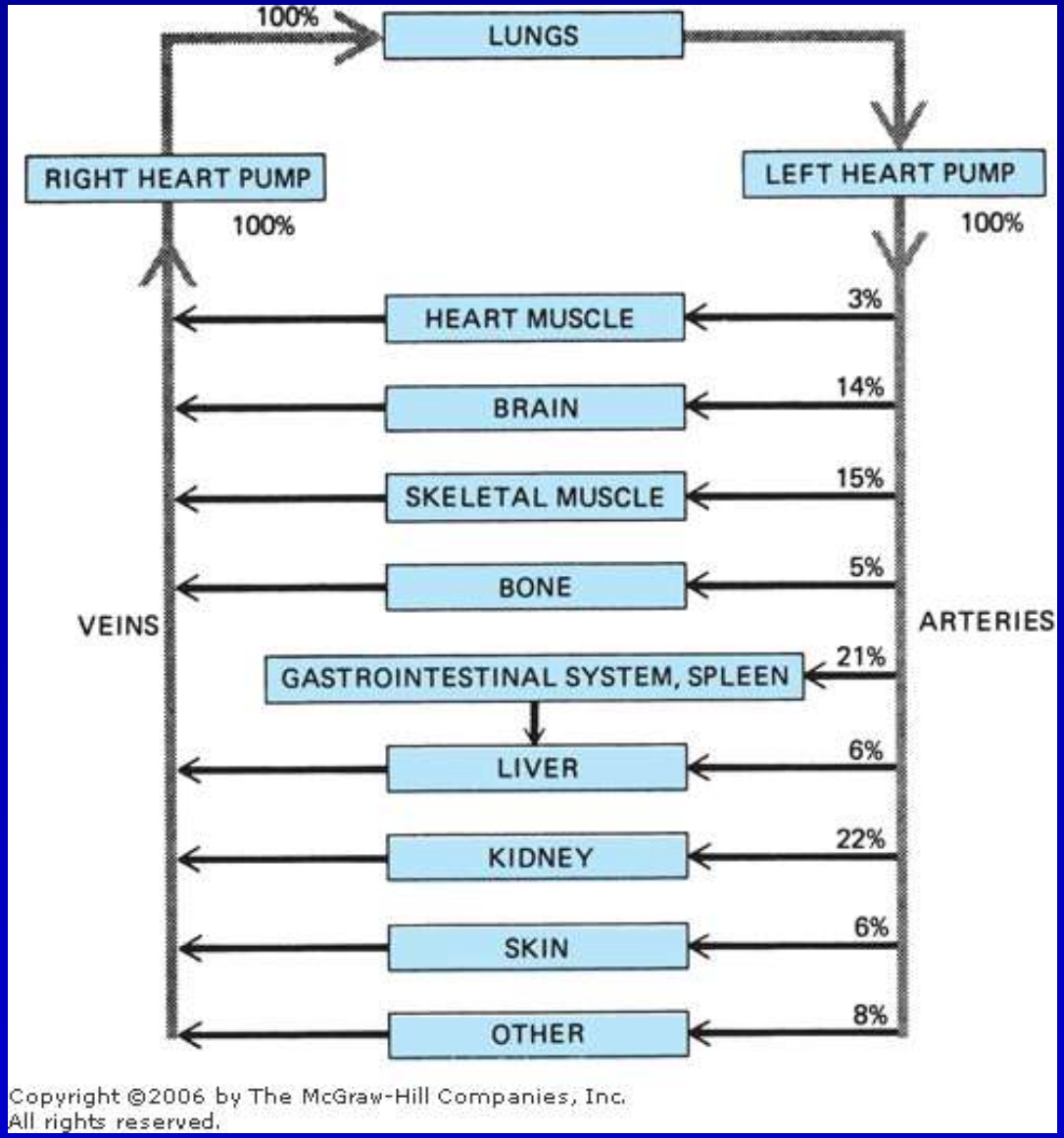


	ARTERIES		ARTERIOLES	CAPILLARIES	VENULES	VEINS	
	Aorta						Venae cavae
internal diameter	2.5 cm	0.4 cm	30 μm	5μm	70 μm	0.5 cm	3 cm
wall thickness	2 mm	1 mm	20 μm	1 μm	7μm	0.5 mm	1.5 mm
number	1	160	5×10^7	10^{10}	10^8	200	2
total cross-sectional area	4.5 cm^2	20 cm^2	400 cm^2	4500 cm^2	4000 cm^2	40 cm^2	18 cm^2

- Structural characteristics of the peripheral vascular system.

Mohrman, DE et al. Cardiovascular Physiology. 1997. p. 93.

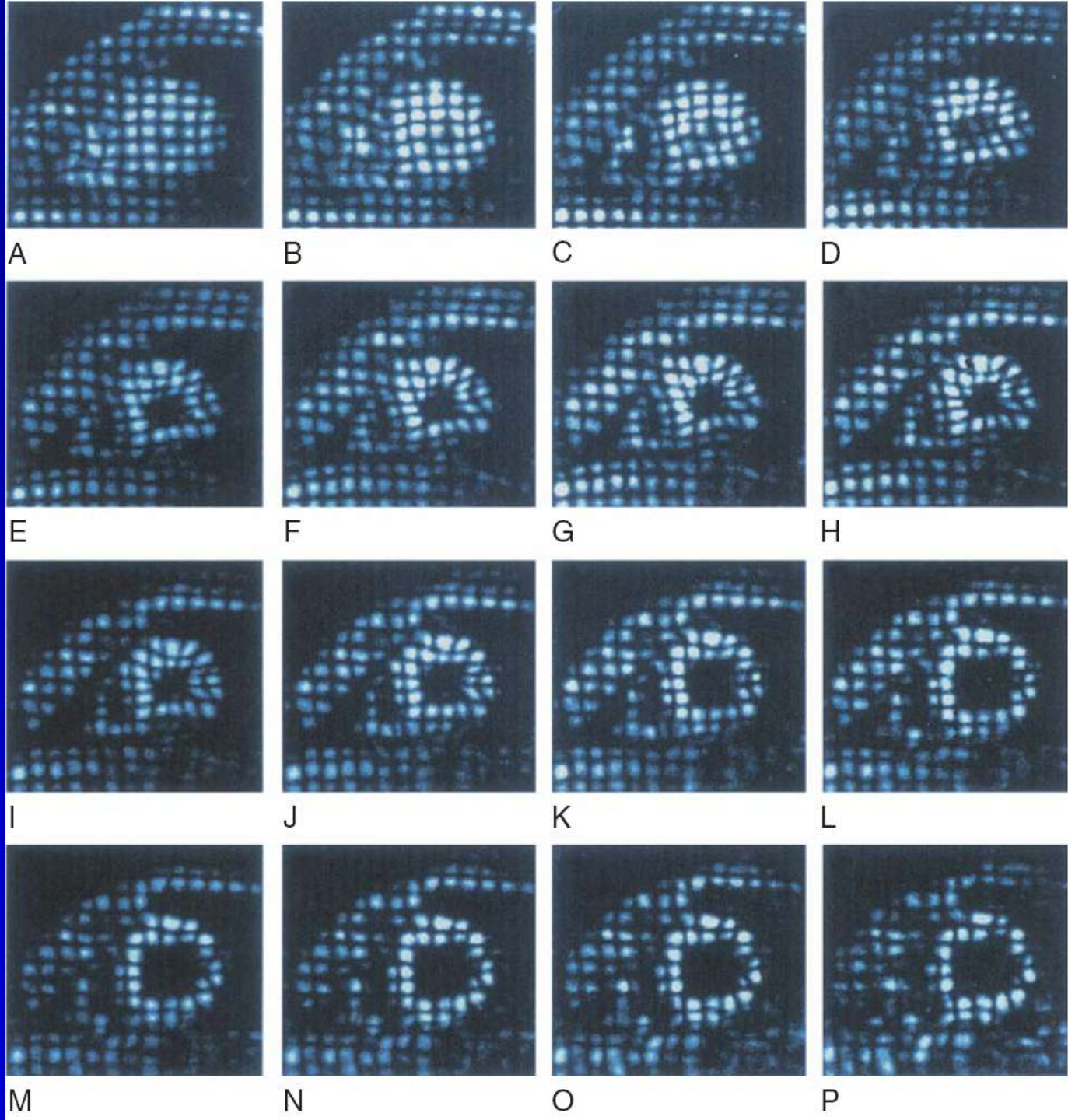
Distribution of Cardiac Output



Cardiovascular circuitry indicating the percentage distribution of cardiac output to various organ systems in a resting individual

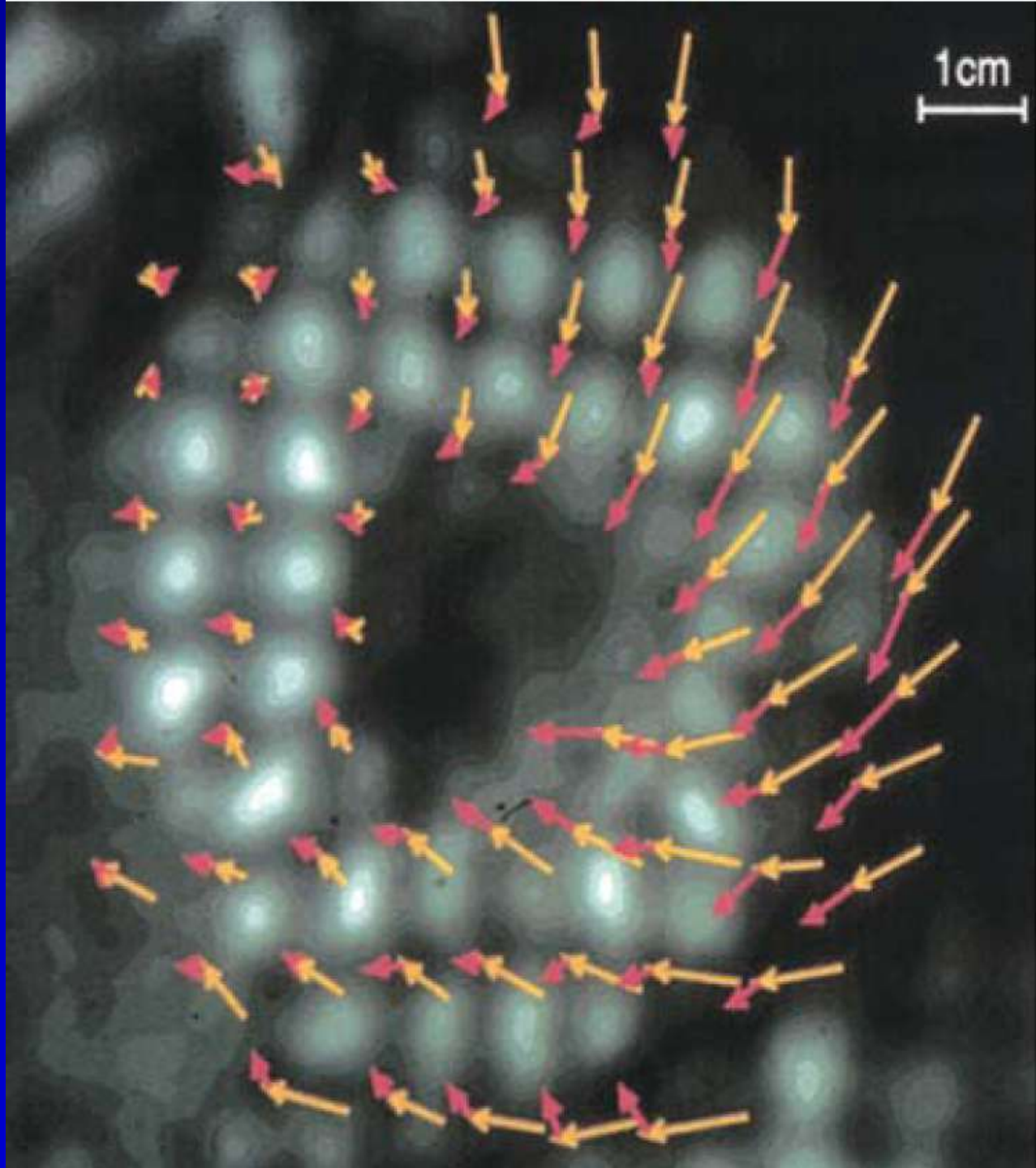
Mohrman, DE et al. Cardiovascular Physiology. 1997. p. 5.

Normal patient
Apex to base



Carroll JD and Hess OM. Ch 20, "Assessment of Normal and Abnormal Cardiac Function" Braunwald's Heart Disease, 7th ed. 2004.

Base of the heart
End-systolic image and local trajectories



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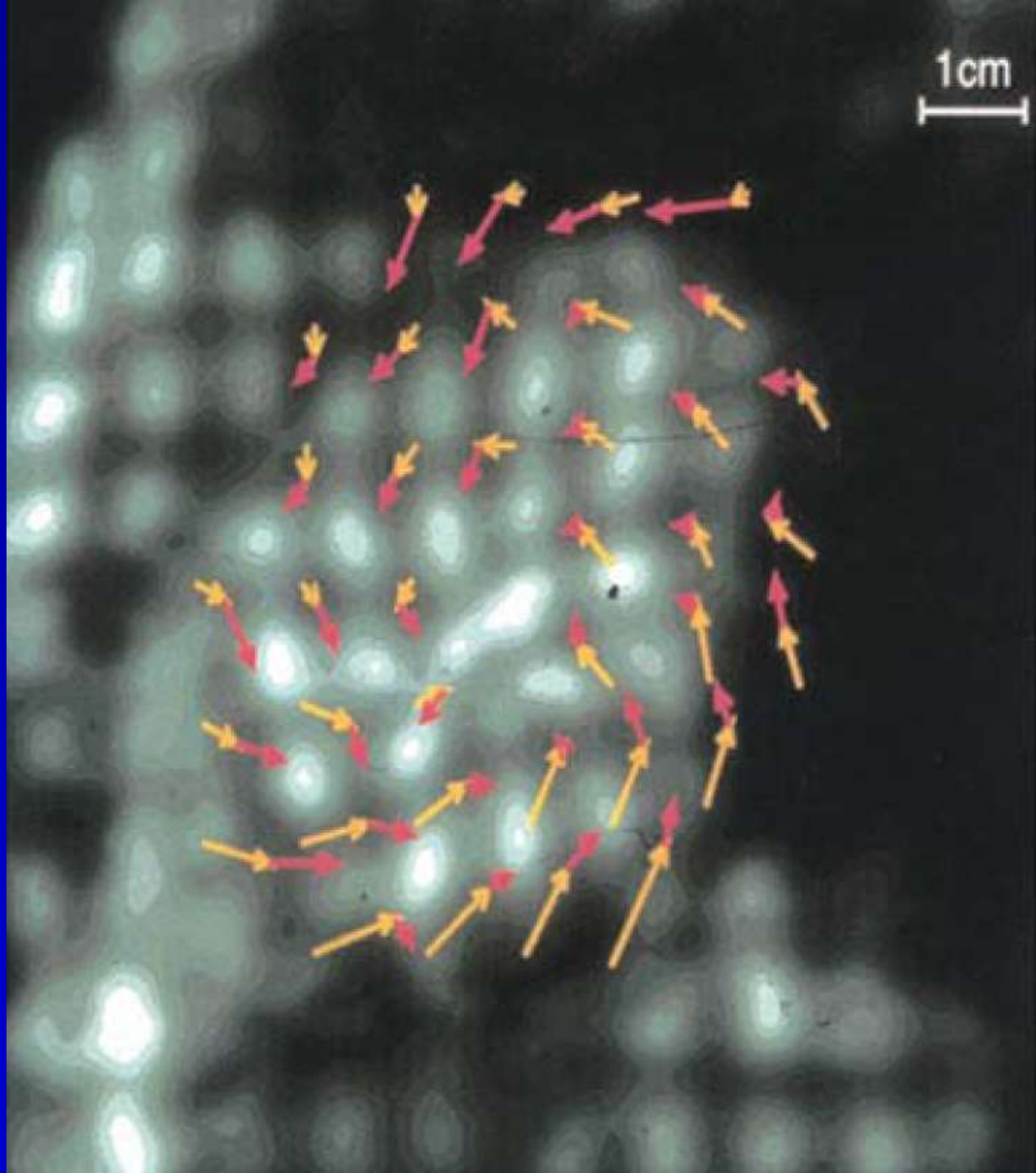
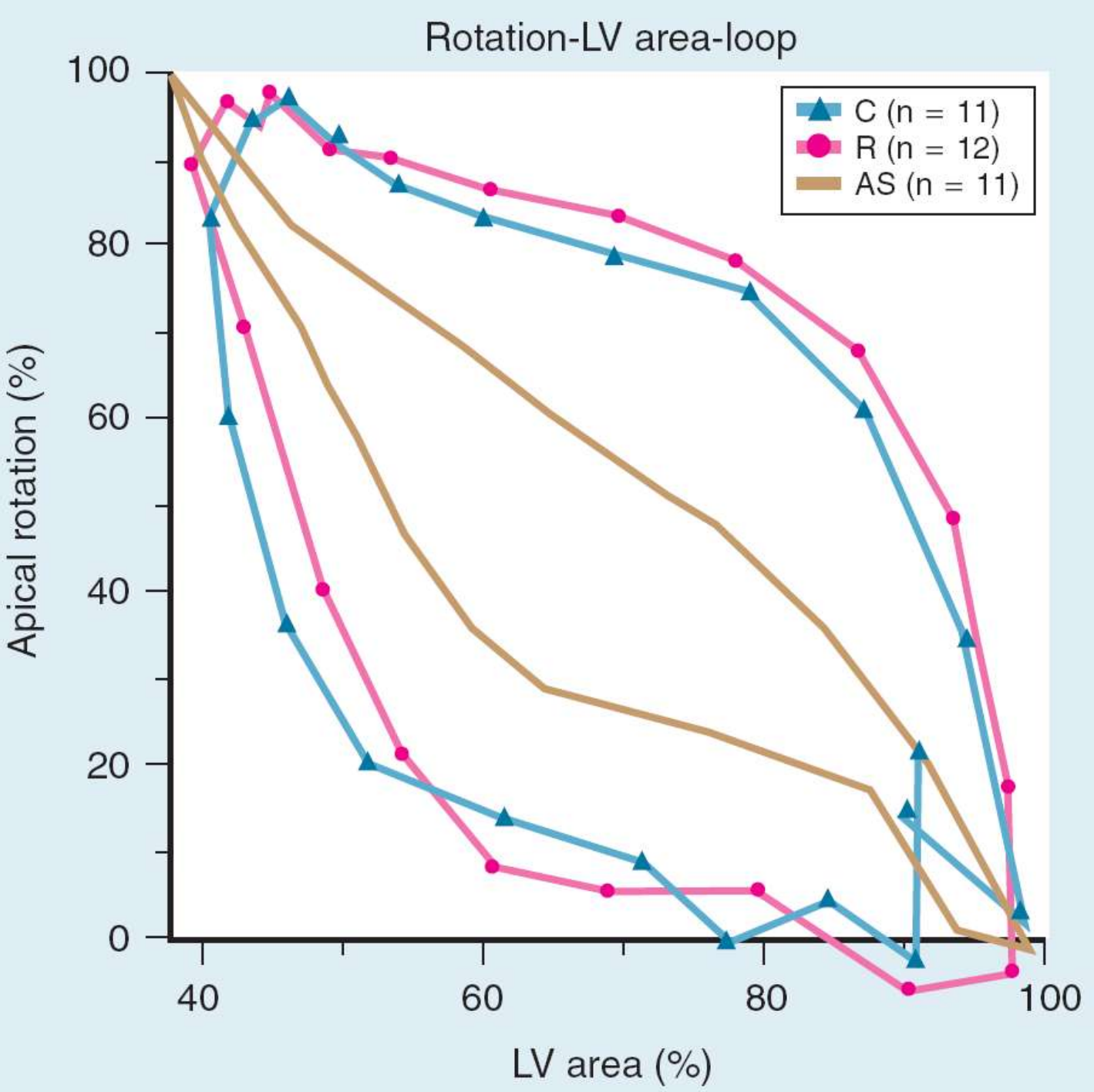
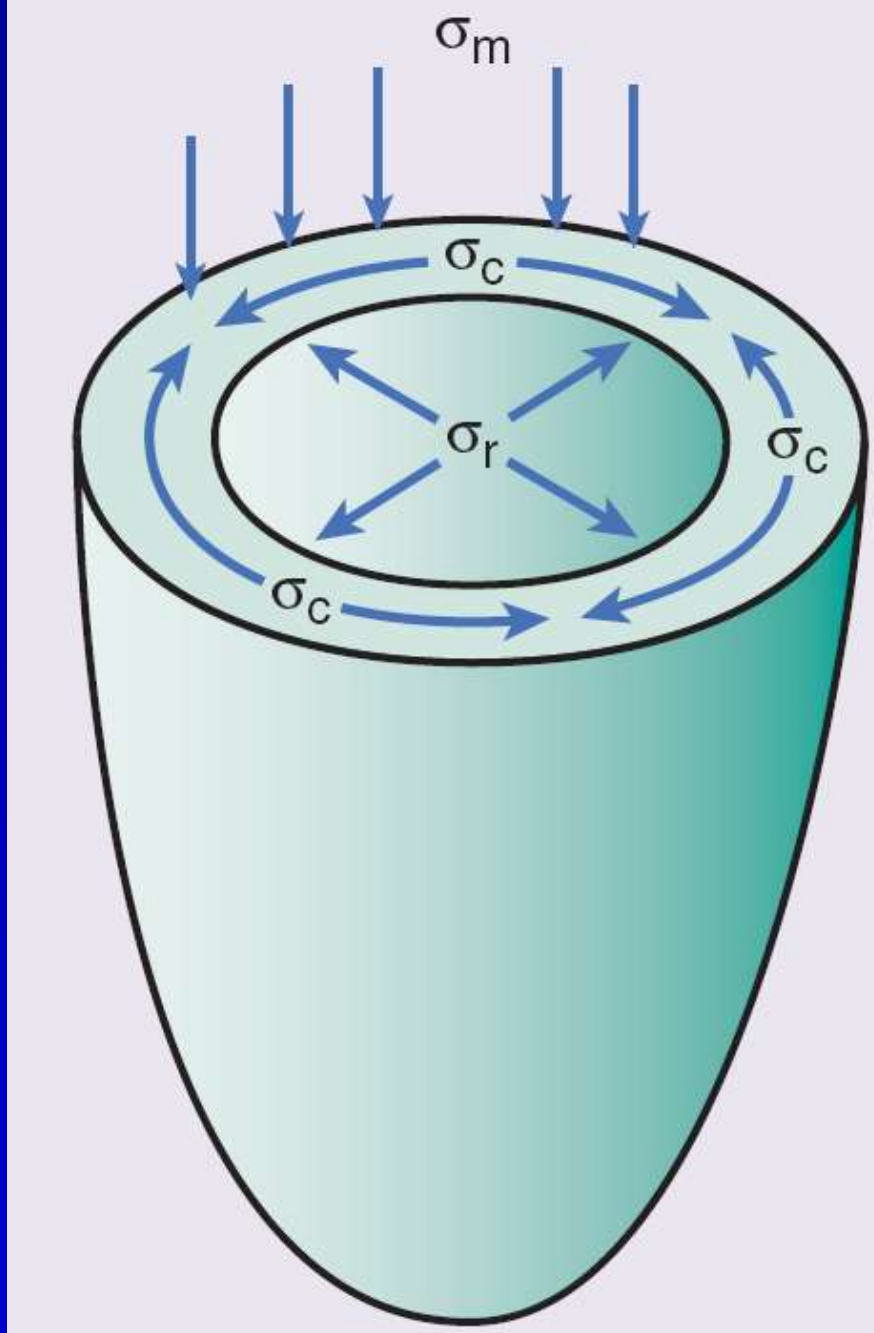
Apex of the heart



Carroll JD and Hess OM. Ch 20, "Assessment of Normal and Abnormal Cardiac Function" Braunwald's Heart Disease, 7th ed. 2004.



Carroll JD and Hess OM. Ch 20, "Assessment of Normal and Abnormal Cardiac Function" Braunwald's Heart Disease, 7th ed. 2004.



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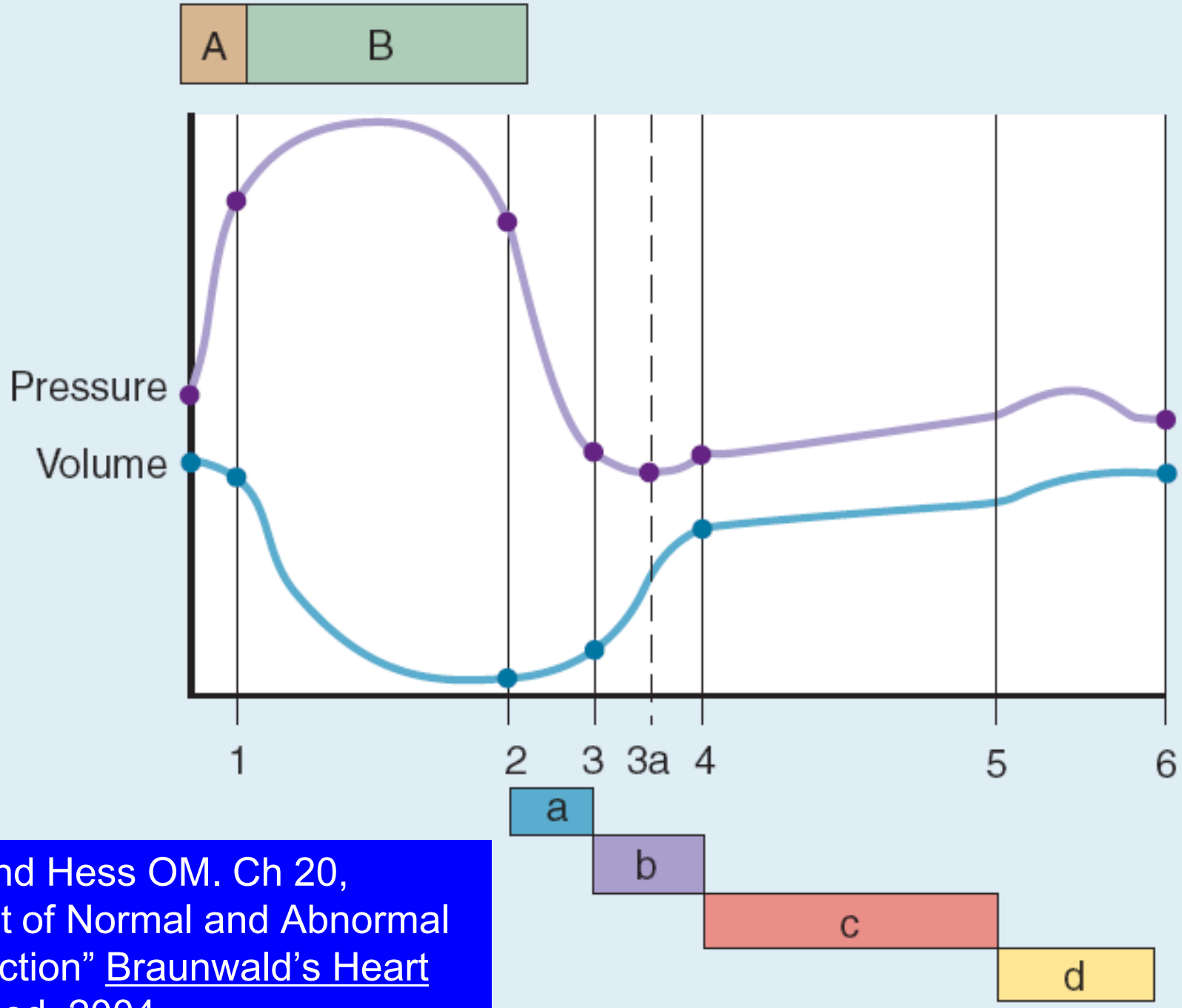
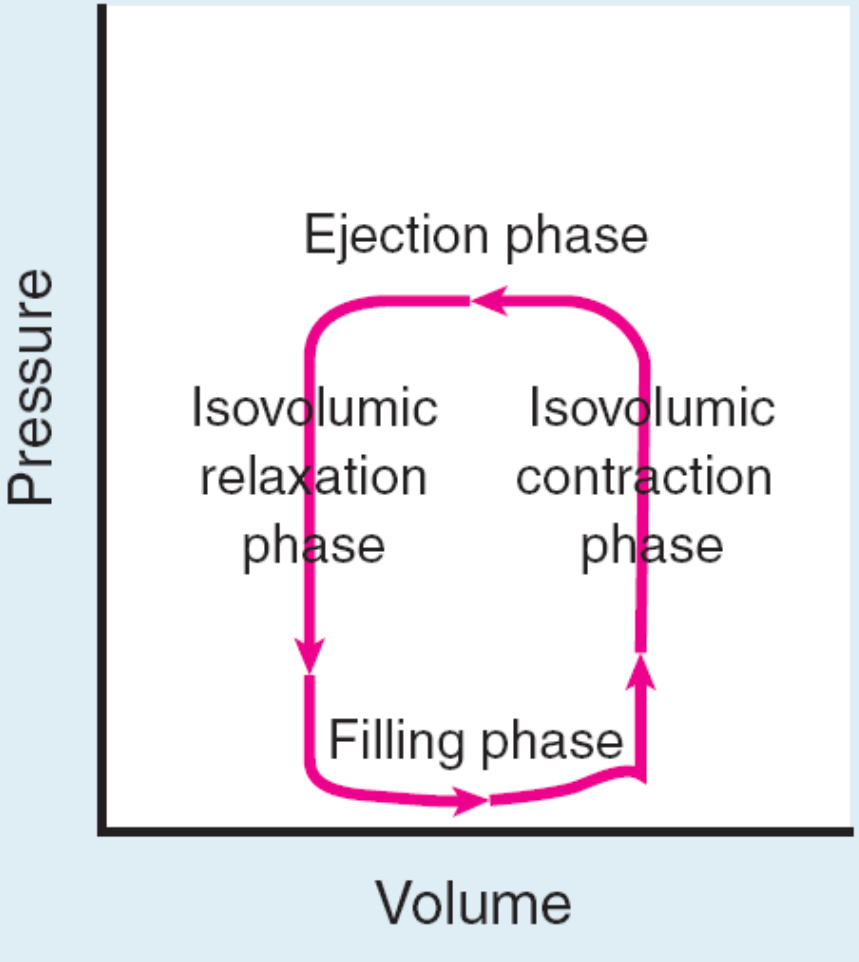
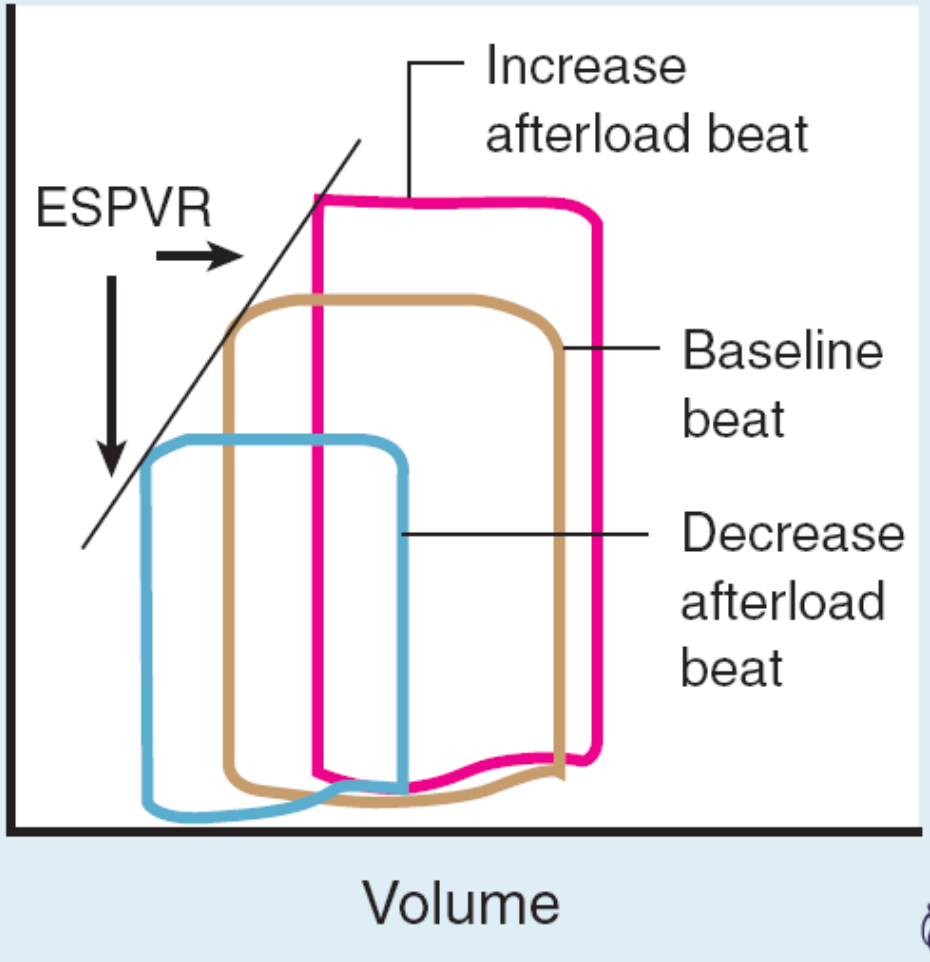
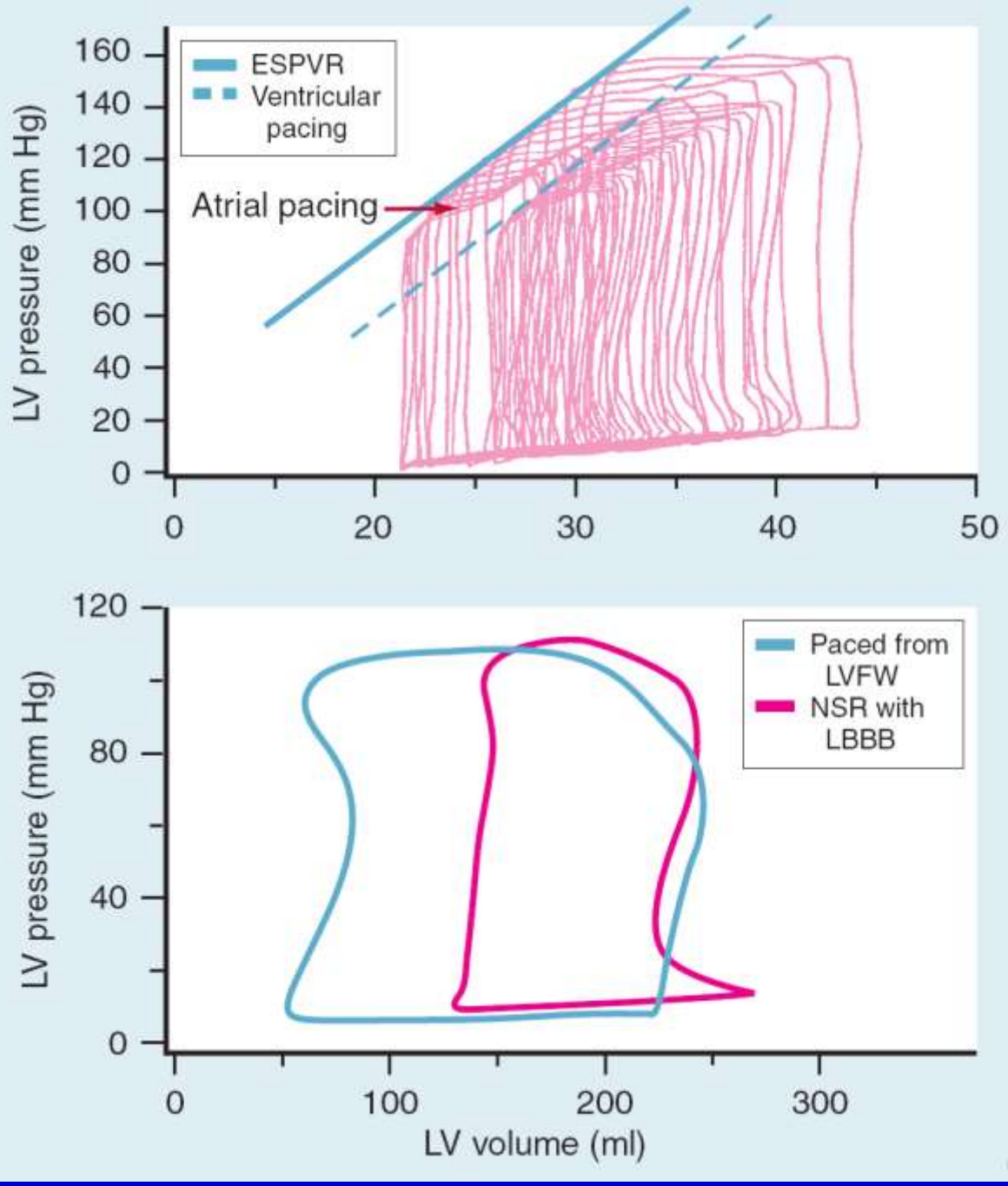


Carroll JD and Hess OM. Ch 20, "Assessment of Normal and Abnormal Cardiac Function" Braunwald's Heart Disease, 7th ed. 2004.

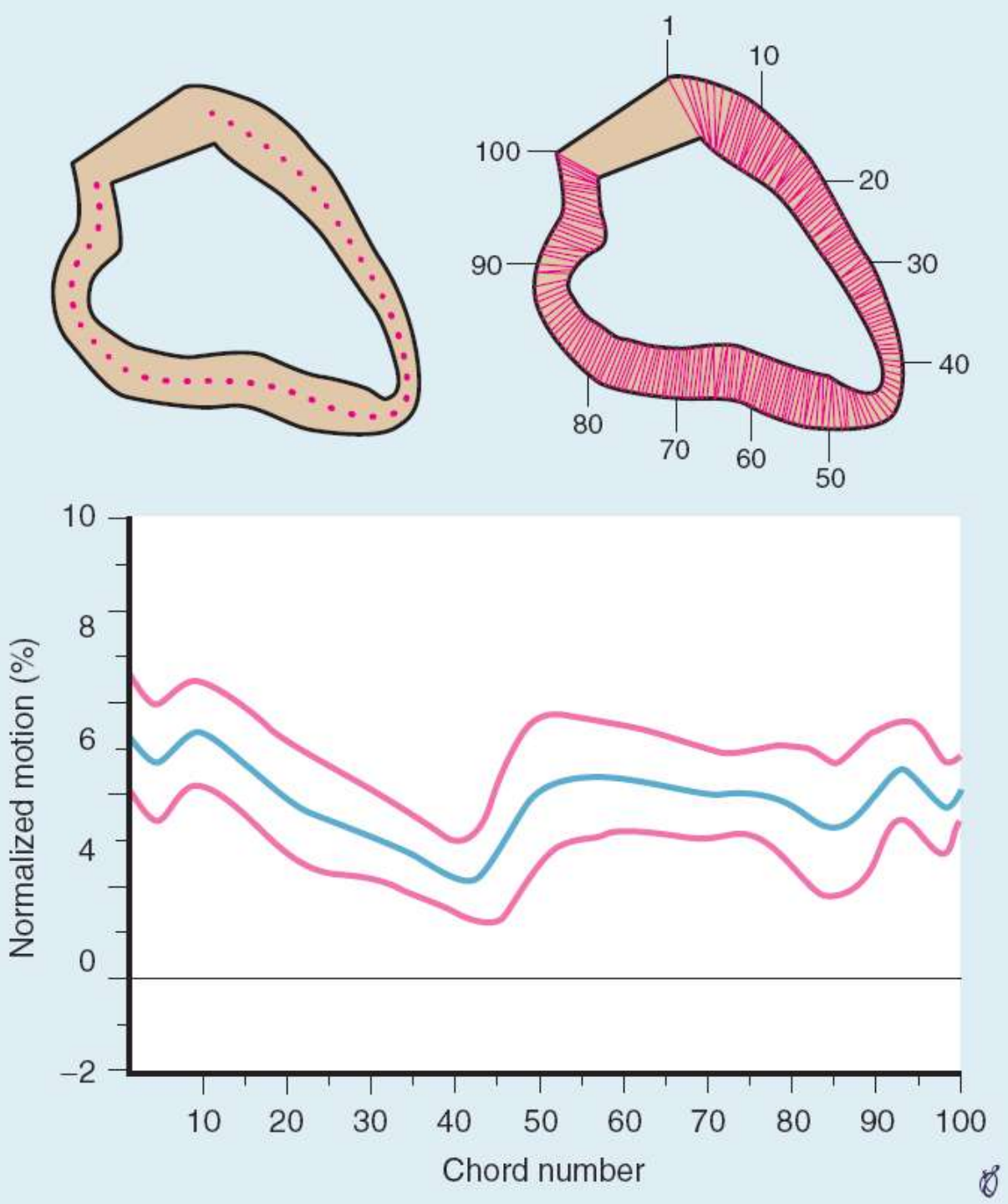




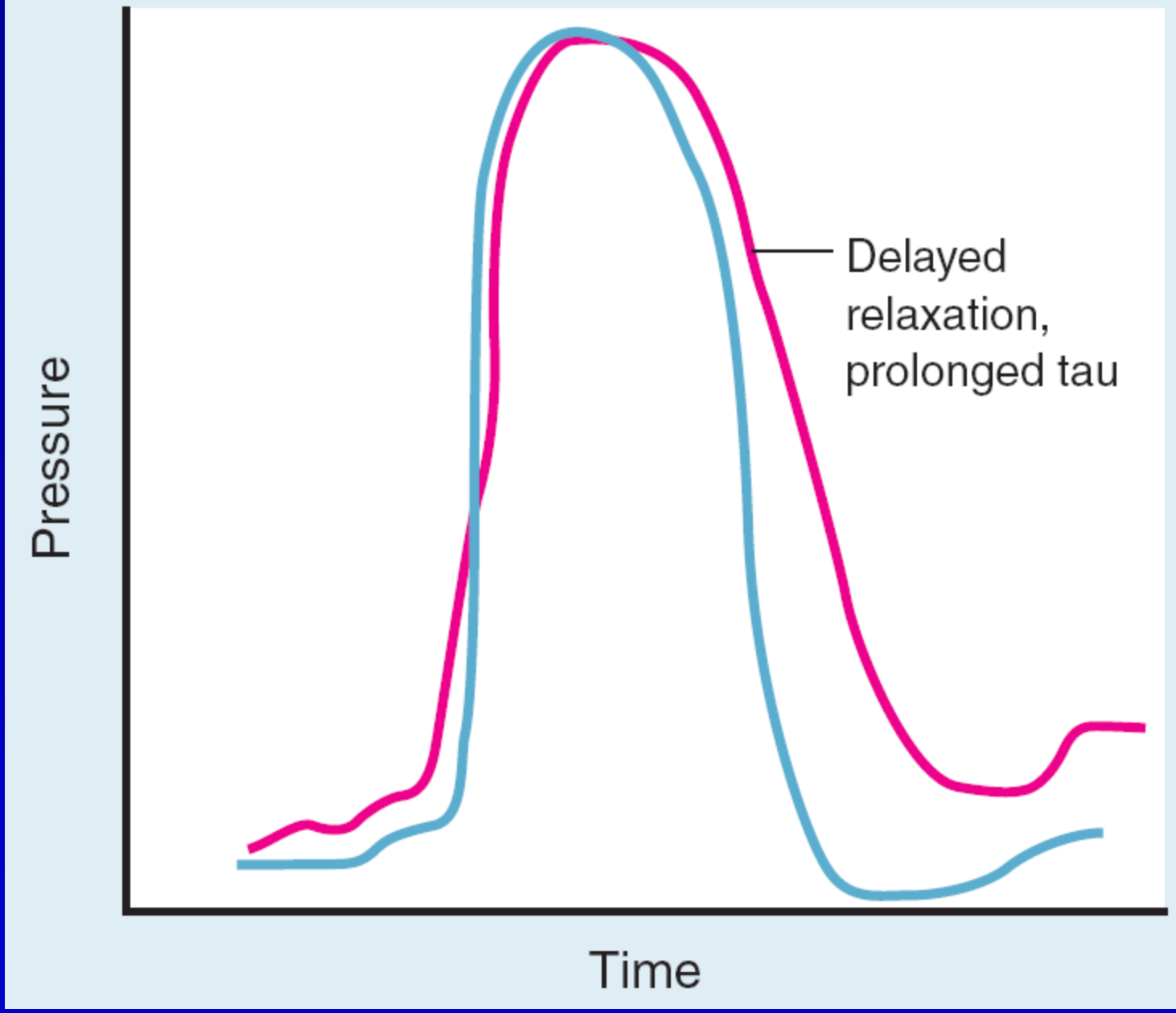
Carroll JD and Hess OM. Ch 20, "Assessment of Normal and Abnormal Cardiac Function" Braunwald's Heart Disease, 7th ed. 2004.



Carroll JD and Hess OM. Ch 20, "Assessment of Normal and Abnormal Cardiac Function" Braunwald's Heart Disease, 7th ed. 2004.



Carroll JD and Hess OM. Ch 20, "Assessment of Normal and Abnormal Cardiac Function" Braunwald's Heart Disease, 7th ed. 2004.



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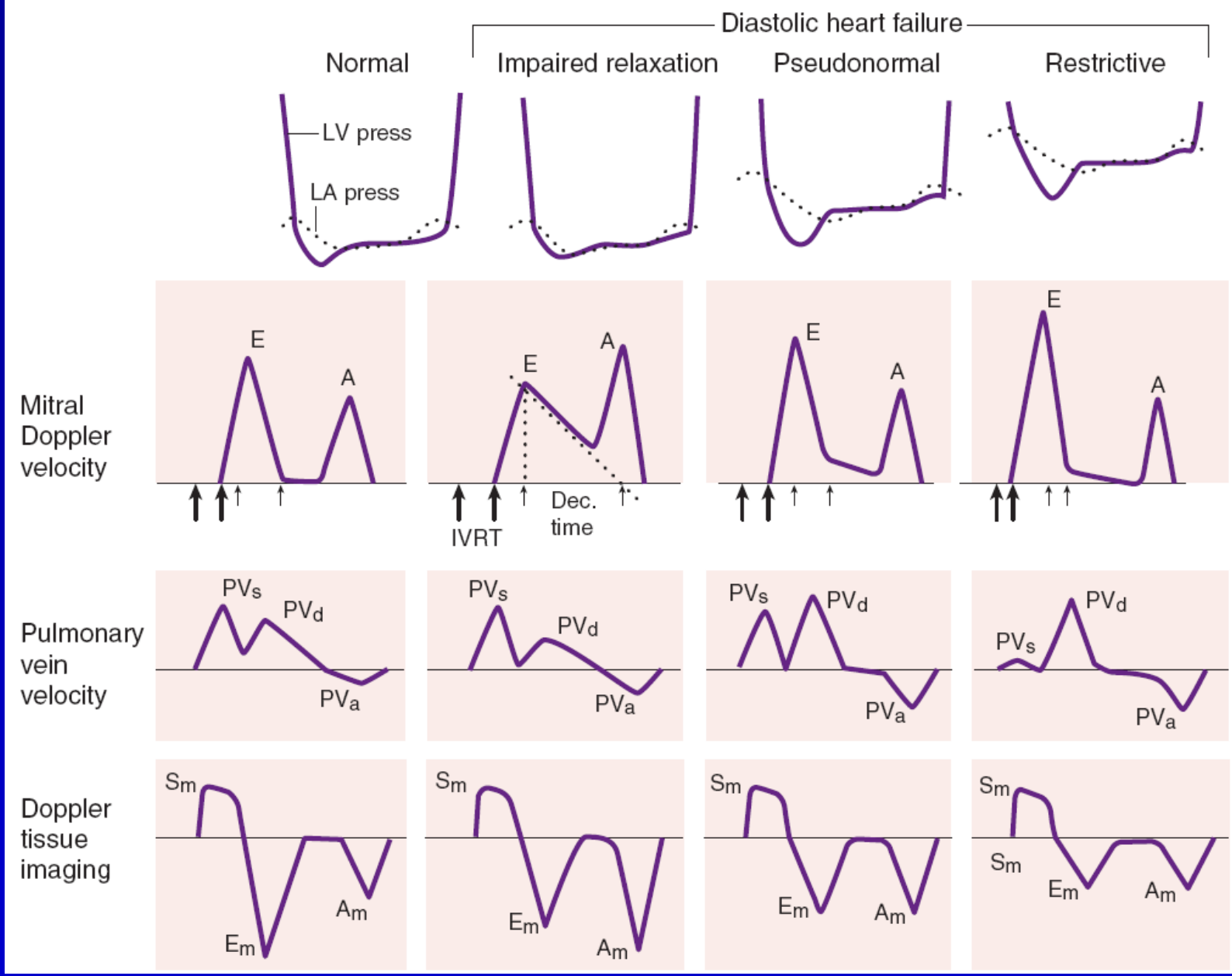
Summary

- Contractility is not well defined
- Contractility cannot be measured
- Indices of contractility are quite imperfect
- The LV ejection fraction interpreted in the physiologic context of HR and preload and afterload and milieu is my personal favorite



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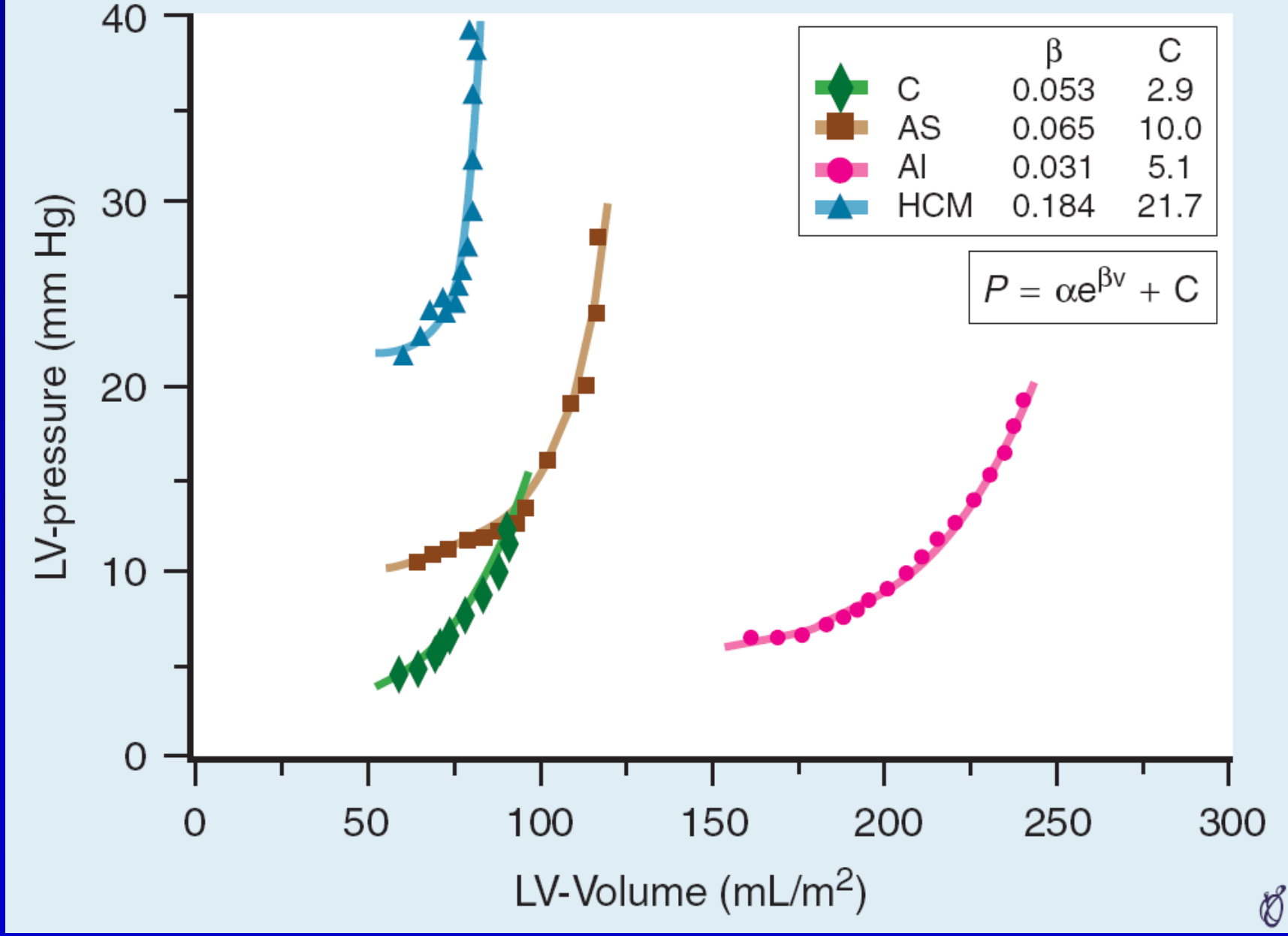

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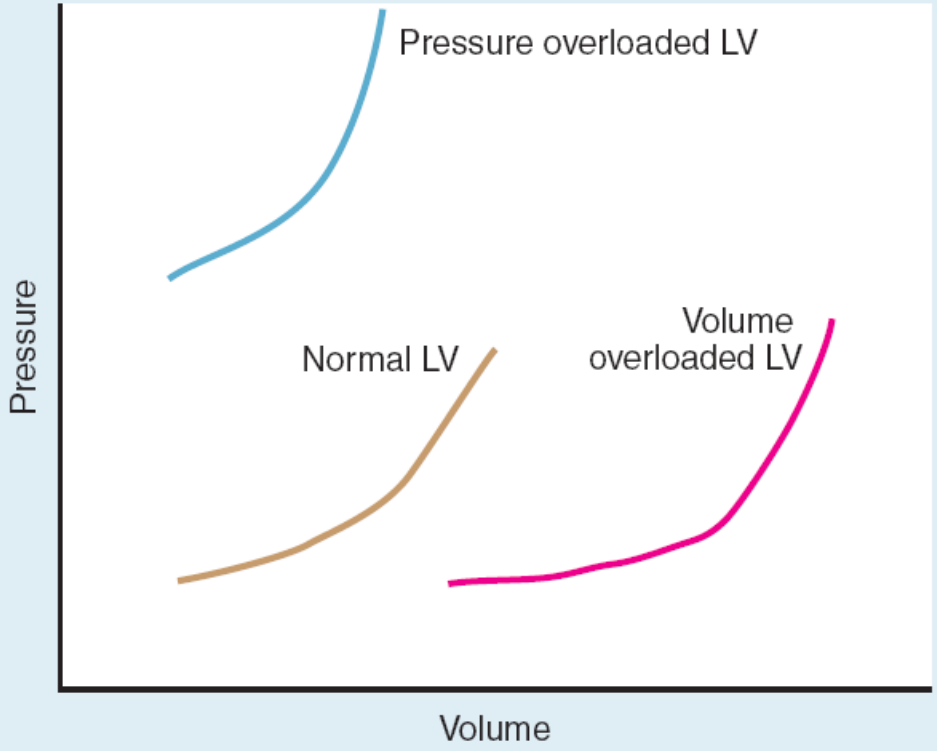

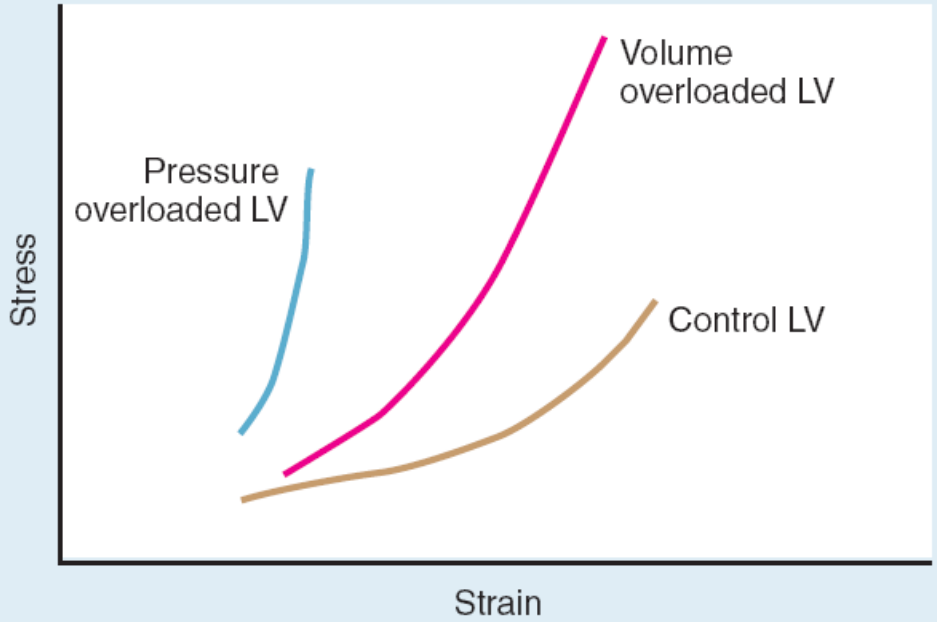

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TABLE 20–3 Two Pathways of Ventricular Dilation and Increased Filling Pressure

Hemodynamic (Acute)

Dilation and increased end-diastolic pressure caused when increased venous return or decreased ejection increases end-diastolic volume. This form of dilation occurs when physiological (functional) signaling increases sarcomere length, which increases the heart's ability to perform work (Starling law of the heart)

Architectural (Chronic)

Dilation and increased filling pressures caused when hypertrophy increases cardiac myocyte length and alters passive muscle properties. By increasing wall stress, this growth response increases the energy demands of the heart and decreases cardiac efficiency, initiating a vicious circle that worsens heart failure. This form of dilation occurs when abnormal transcriptional (proliferative) signaling causes eccentric hypertrophy (systolic dysfunction), and it tends to progress (remodeling)

Adapted from Katz A: Ernest Henry Starling, his predecessors, and the "law of the heart." Circulation 106:2986, 2002.

Carroll JD and Hess OM. Ch 20, "Assessment of Normal and Abnormal Cardiac Function" Braunwald's Heart Disease, 7th ed. 2004.

TABLE 20–5 Normal Values of Parameters of Left Ventricular Diastolic Filling Measured by Doppler Echocardiography

Parameters	Adults <41 yr	Adults >55 yr
Peak mitral flow velocity (E) (cm/sec)	76 ± 13	63 ± 11
Peak mitral filling rate (A) (cm/sec)	38 ± 8	52 ± 9
Mitral E/A	2.1 ± 0.6	1.3 ± 0.3
Mitral E deceleration time	184 ± 24	—
Mitral E deceleration rate (m/sec^2)	5.6 ± 2.7	—
Isovolumetric relaxation time (msec)	74 ± 26	—
Peak pulmonary venous AR wave (cm/sec)	18 ± 3	25 ± 5
Peak pulmonary venous S wave (cm/sec)	41 ± 10	60 ± 10
Peak pulmonary venous D wave (cm/sec)	53 ± 10	38 ± 10

E/A = E wave/A wave ratio.

Data from Little WC. Downes TR: Clinical evaluation of left ventricular diastolic performance. Prog Cardiovasc Dis 32:273, 1990; and Rakowski H, et al: Canadian consensus recommendations for the measurements and reporting of diastolic dysfunction by echocardiography. J Am Soc Echocardiogr 9:745, 754, 1996.

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TABLE 20–6 Left Atrial and Ventricular Function Influences on the Pulmonary Venous Flow Velocity Profile

Pulmonary Venous Wave	Left Atrial Function	LV Function
First systolic wave	Atrial relaxation	
Second systolic wave	Reservoir function Atrial compliance	LV contraction RV contraction
Early diastolic wave	Conduit function	Ventricular relaxation Ventricular chamber stiffness
Atrial reversal wave	Booster pump function Atrial compliance	Ventricular chamber stiffness

LV = left ventricular; RV = right ventricular.

Adapted from Tabata T, Thomas JD, Klein AL: Pulmonary venous flow by Doppler echocardiography: Revisited 12 years later. J Am Coll Cardiol 41:1243-1250, 2003.

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TABLE 20–7 Echo/Doppler Assessment and MR Imaging of Right Ventricular Size, Shape, and Function

Parameter	Echo/Doppler	MR imaging
RV volume	Standard 2D views allow measurement of multiple dimensions (Fig. 20-15). The parasternal long-axis view shows the outflow tract diameter	Segmentation of individual slices provides chamber size. Adjacent areas are then summated to provide volume and shape measurements
Regional wall motion	Free RV wall and interventricular septum are imaged and paradoxical motion can easily be detected	Cine MR imaging provides contrast between the blood pool and the myocardial wall. RV wall motion is assessed using RVOT cines in the sagittal and short-axis cine images
RV mass	Approximated by wall thickness determinations along with chamber size measurements	Myocardium from the junction between the RV free wall and the interventricular septum can be traced on each slice from the base to the apex, including trabeculations. Myocardial volume computed from summated multiple slices is multiplied by 1.05 to give the mass in grams
RV wall composition	Not well studied in transthoracic images. Intracardiac ultrasound provides higher resolution data	MR imaging is potentially useful to distinguish fat from muscle
Regurgitant fraction	Doppler profiles provide semiquantitative approach	True regurgitant volumes can be measured from phase velocity maps in the main pulmonary artery and aortic root

RV = right ventricular; RVOT = RV outflow tract; 2D = two-dimensional.

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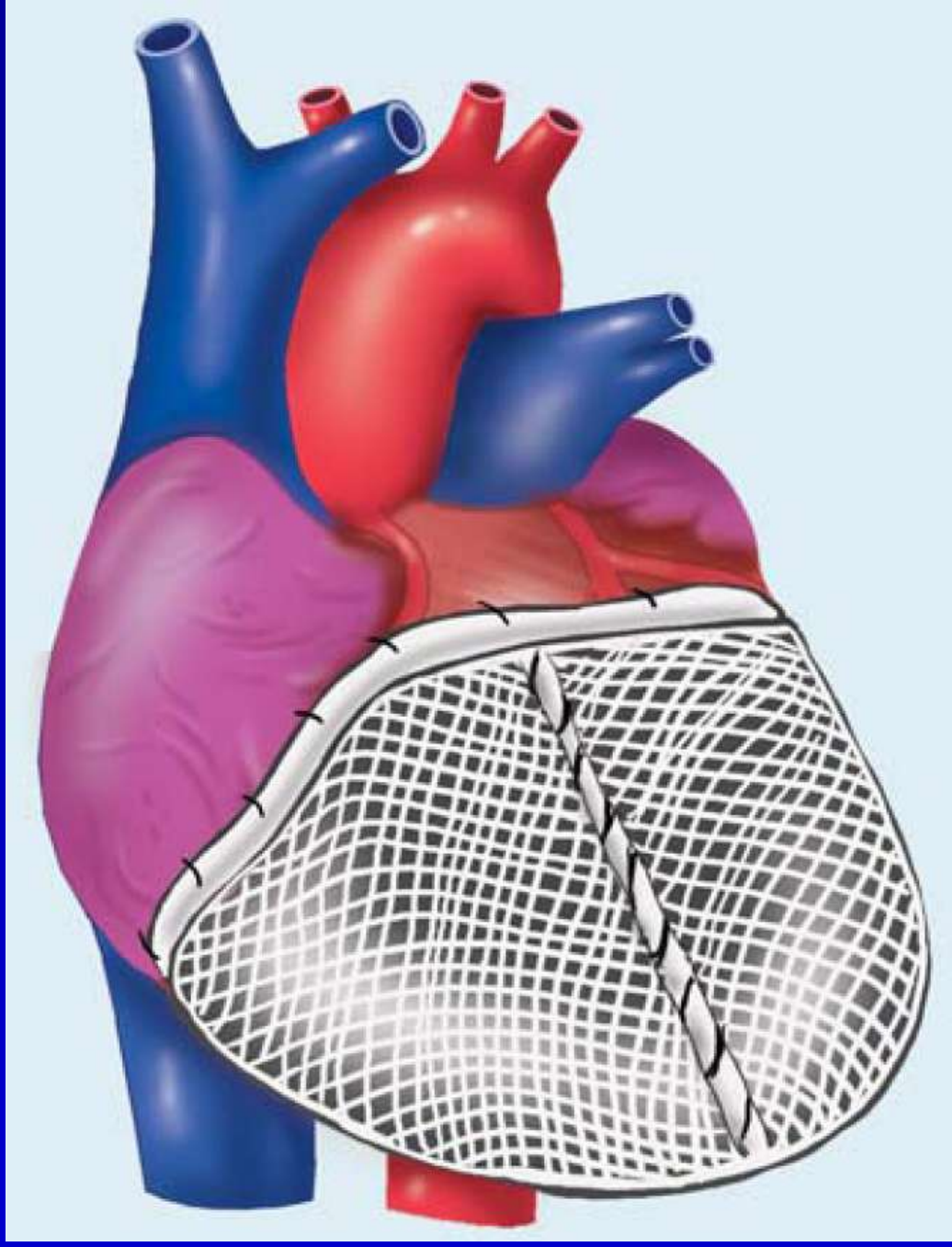

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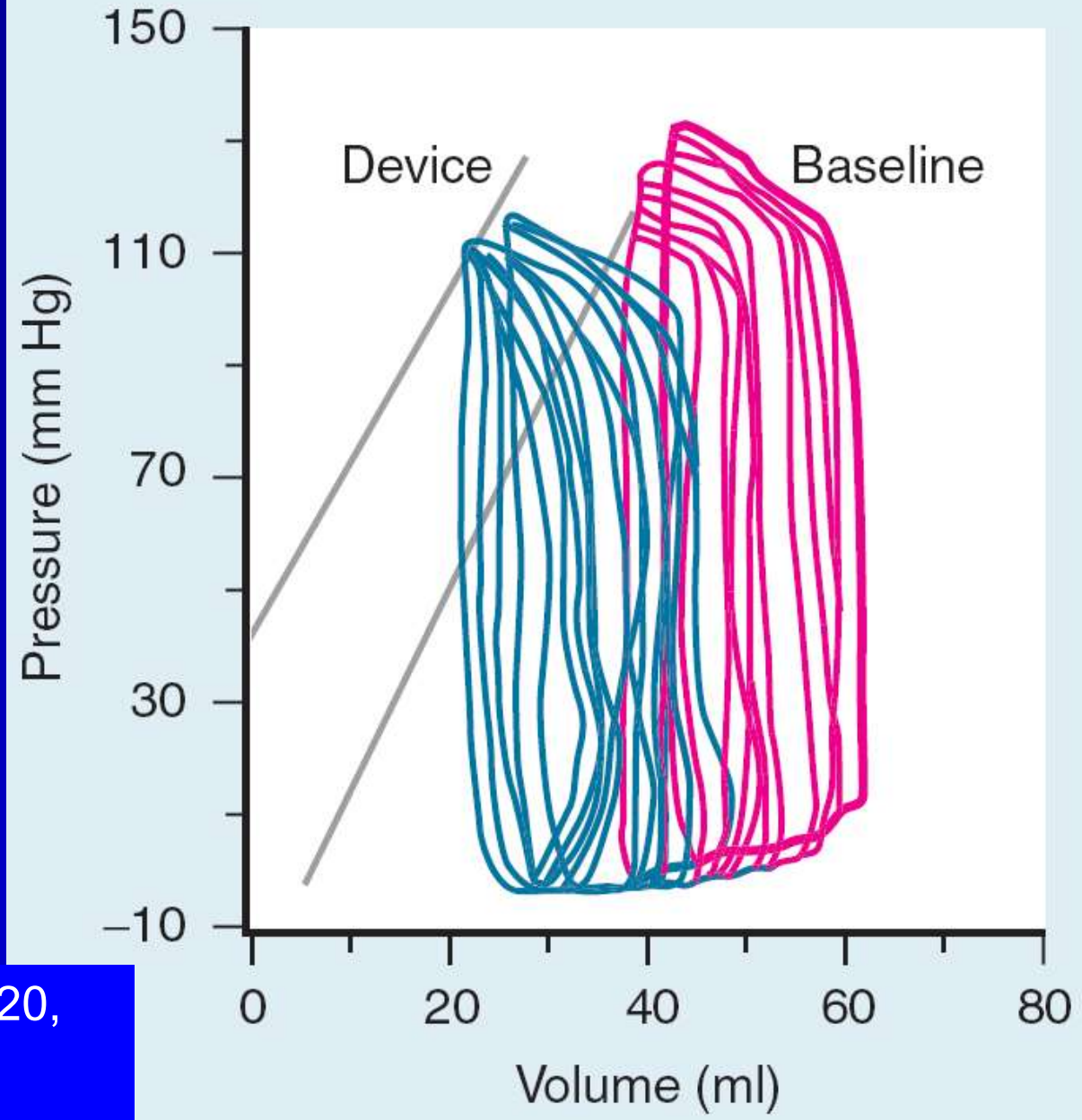

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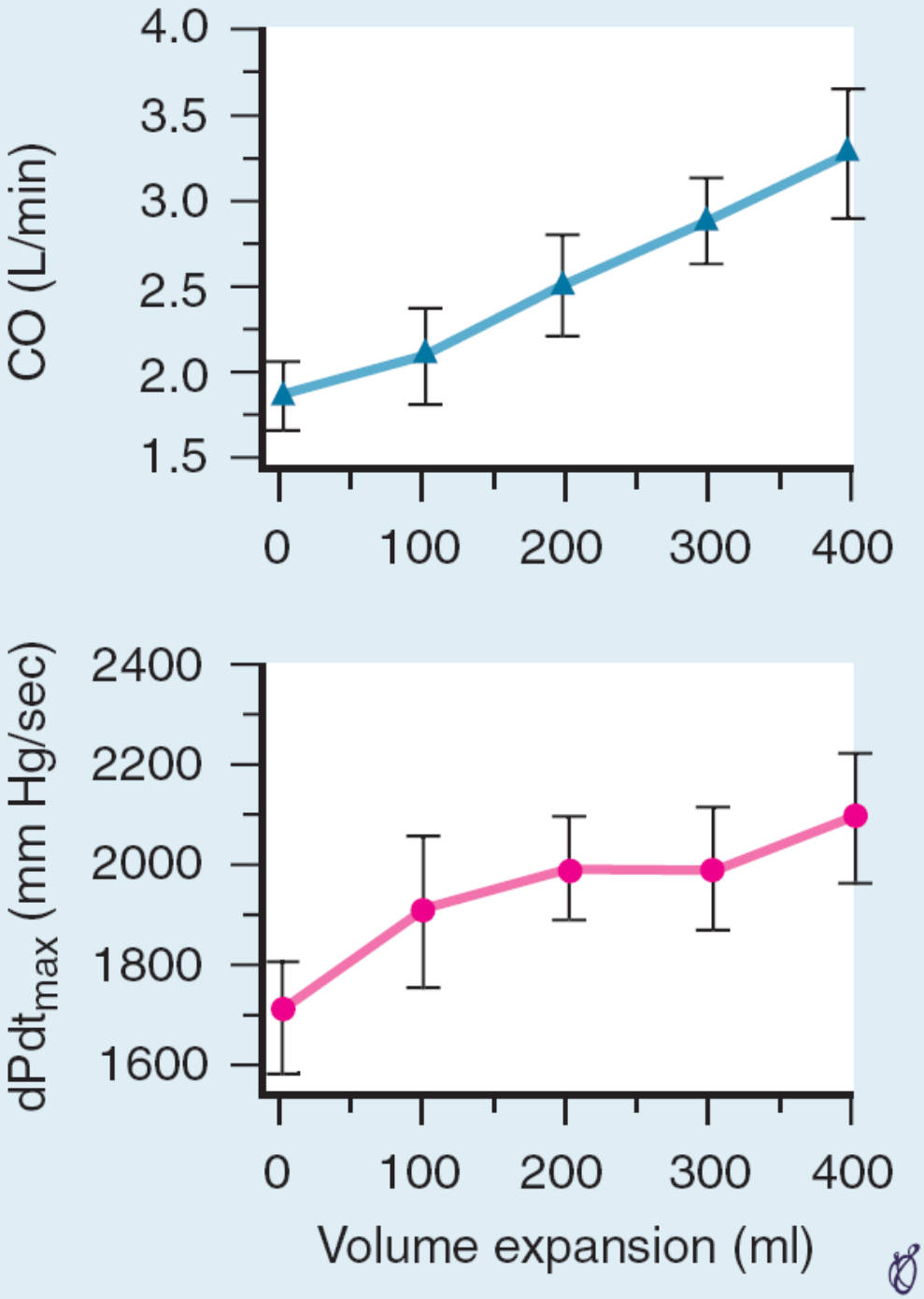

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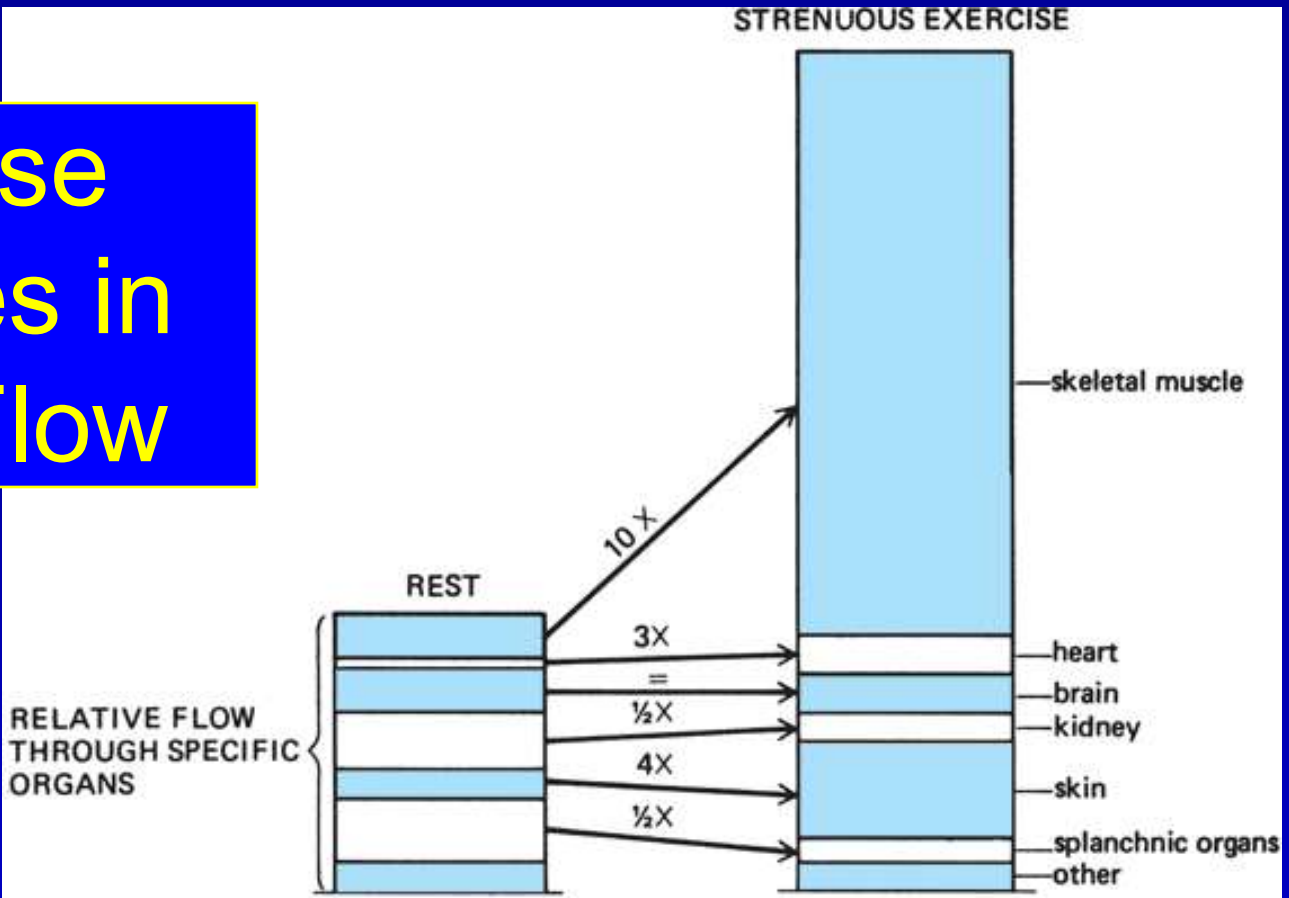
Exercise Changes in Blood Flow



cardiac output	6 L/min	18 L/min
heart rate	70 beats per minute	160 beats per minute
ejection fraction	60%	80%
arterial pressure	120/80 mmHg	150/80 mmHg
central venous pressure	2 mmHg	2 mmHg

Mohrman, DE et al. Cardiovascular Physiology. 1997. p. 185.

Milnor – Hemodynamics, 2nd ed., 1989, Chapter 10, "Cardiac Dynamics"

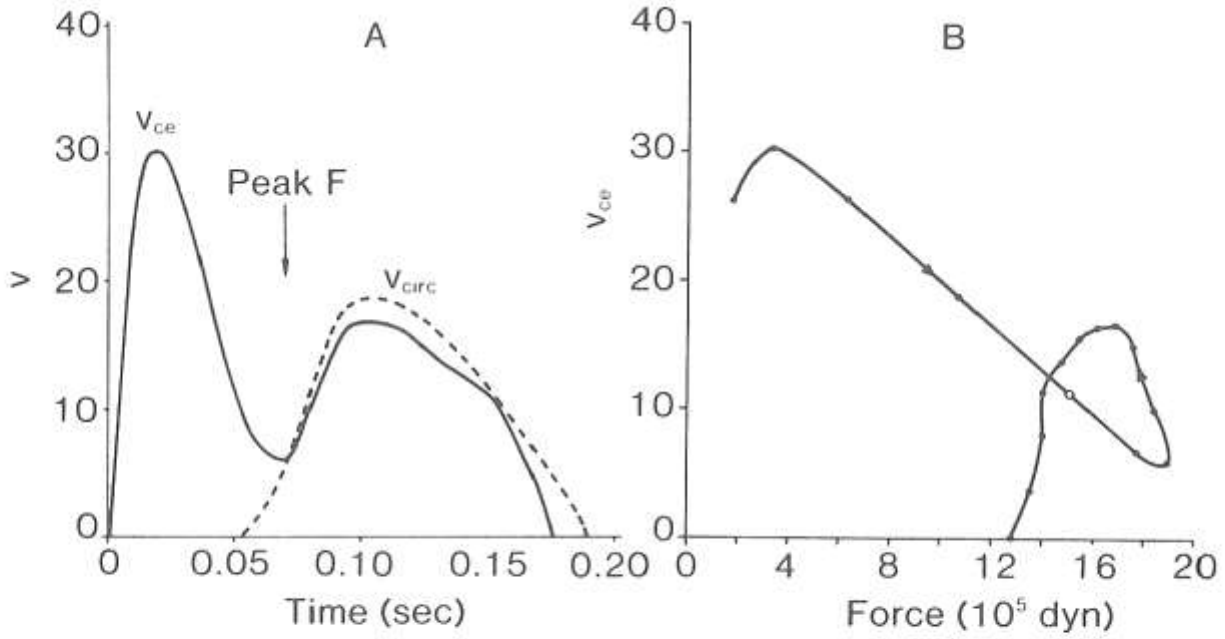


Fig. 10.7. Nichols, Walker, and Milnor, unpublished data. Force, velocity, and time relationships in the left ventricle of an anesthetized, open chest dog. *Ordinates,* velocities of contractile component (v_{ce}) and muscle fibers (v_{circ}), in cm/sec. *Left,* time course of v_{ce} (*continuous line*) and v_{circ} (*dashed line*); *arrow* indicates time of peak force. *Right,* force versus v_{ce}; points at intervals of 0.01 sec; *open circle,* beginning of ejection.

Milnor – Hemodynamics, 2nd ed., 1989, Chapter 10, "Cardiac Dynamics"

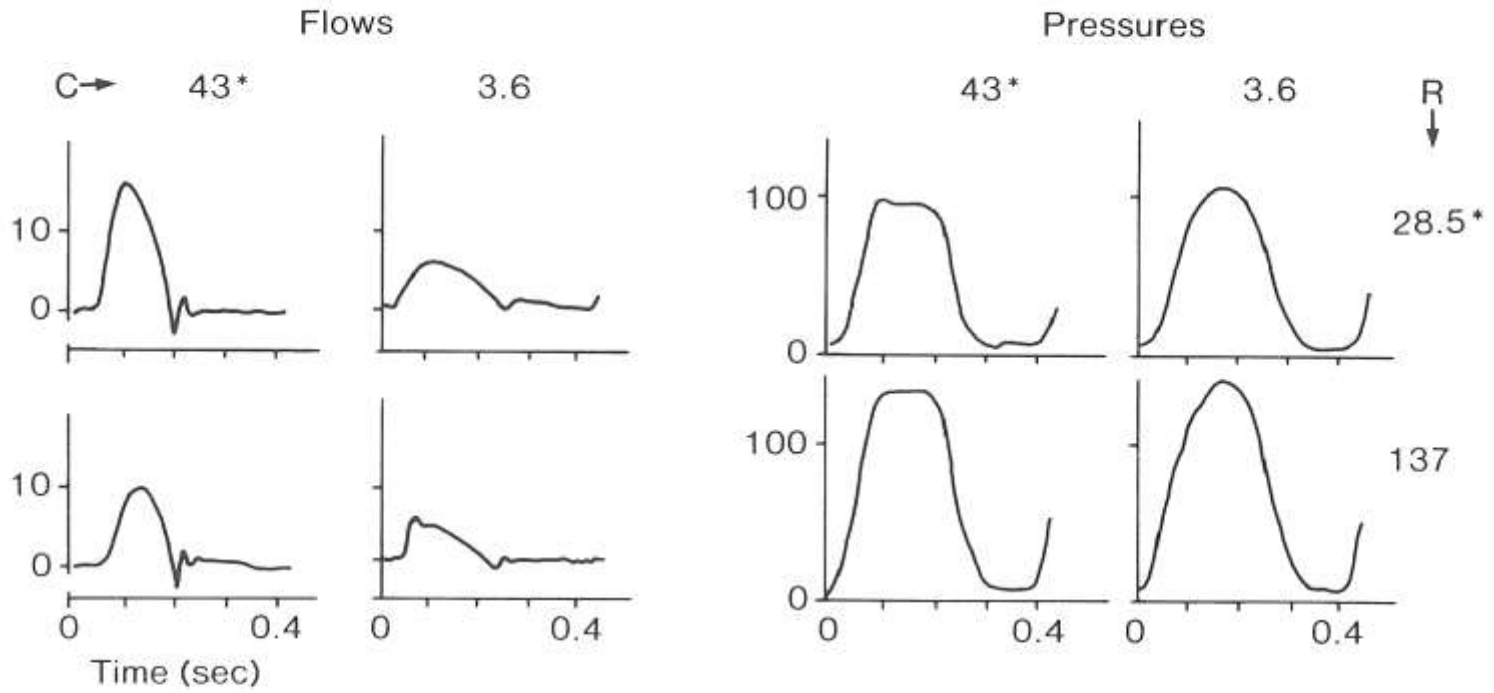
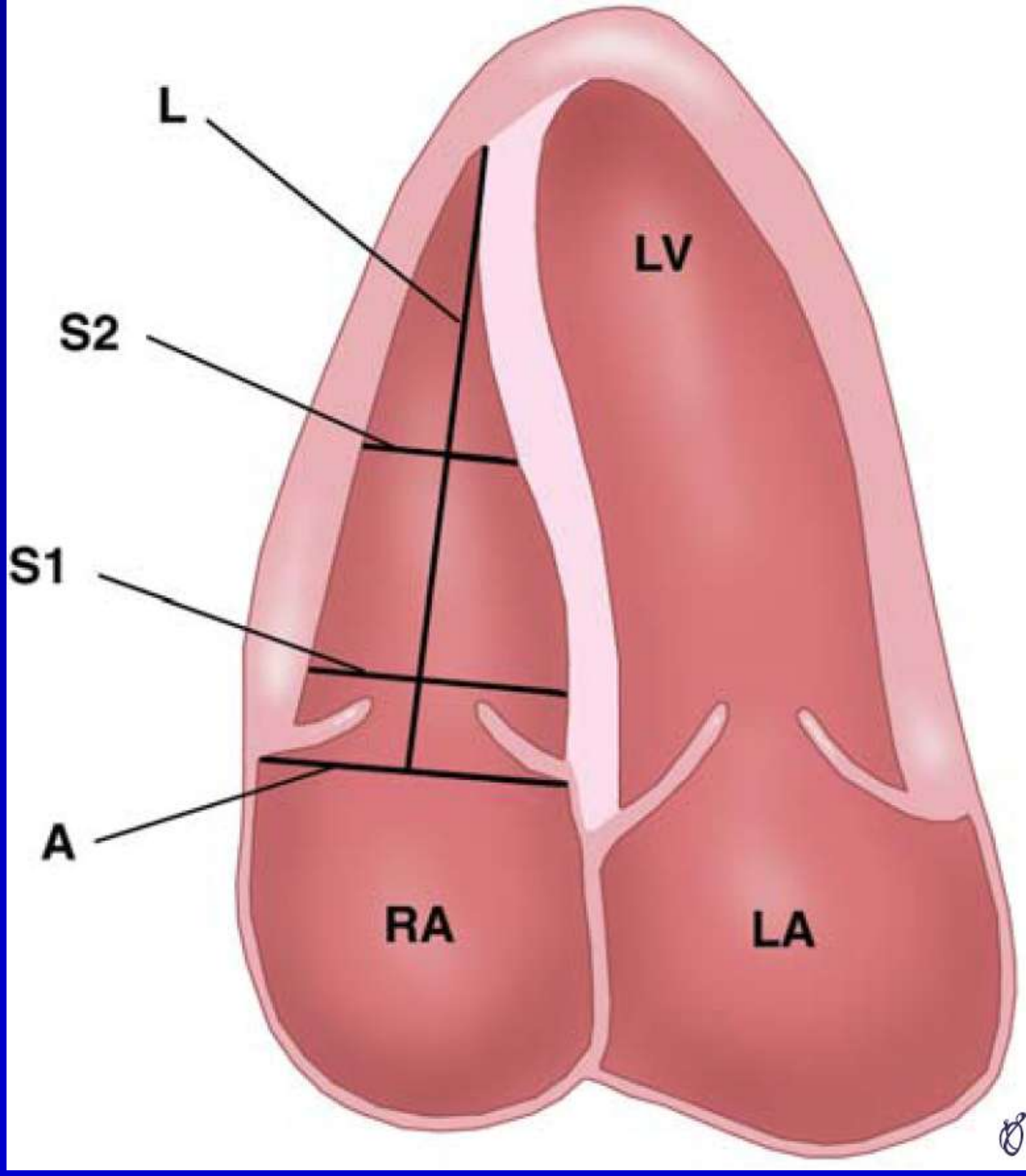


Fig. 10.9. Modified from Elzinga and Westerhof, 1973. Responses of left ventricle of isolated cat heart to alterations of the resistance and capacitance of a hydraulic model that replaced the aorta and arterial tree. *Left*, ventricular outflow; *right*, intraventricular pressure. Numbers above the curves indicate capacitance of the model. (C, in 10^{-6} cm^{4}sec^2/g (mass)). Numbers on the *right* represent model resistance (R, in 10^3 g (mass) cm^4/sec). *Asterisks* indicate approximate normal values *in vivo*. Capacitance of 43×10^{-6} cm^{4}sec^2/g (mass) is equivalent to volume distensibility of about 0.06 cm^3/mm Hg.



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