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Critical Care Medicine

The Essentials *and More*

John J. Marini
David J. Dries

Fifth Edition

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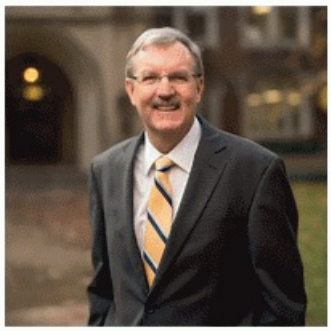
Dedication



This fifth edition of *Critical Care Medicine—The Essentials* is dedicated to my admired friend and coauthor of the initial four, Arthur P. Wheeler. Over the years, he was first my resident and fellow, then my collaborator and colleague. To those who knew him well, Art was an inspiring example of what is best in academic medical practice—a brilliant, incisively logical, well informed, straight shooting, innovative physician whose intellectual honesty and capability was matched by his empathy for his students, coworkers, and patients. With these qualities, Art contributed immensely to the Vanderbilt medical community and rose quickly to national prominence in our field of intensive care. Because he was practically minded, we could always count on him to drill to the core of the problem and then work to resolve it. Among many notable accomplishments, he shared leadership of the ARDS Network studies that helped set durable standards of care regarding safe ventilator settings, fluid management, and vascular catheter use. As an educator, Art had few peers and garnered numerous teaching awards, locally and at the national level. In his later years, he poured his energy and talents into the development of an outstanding advanced practice nursing program at Vanderbilt, years before the concept had taken hold in our field and gained its current enthusiastic attention. As was often the case, he saw the logic and need for such action well before the rest of us. As director of the Vanderbilt Medical ICU for more than two decades, he was recognized across disciplines by trainees, physicians, and nurses alike as a master intensivist gifted with rare bedside abilities. Devoted to his family and a man for all seasons, Art loved varied forms of music and became an instrumentrated airplane pilot as well as a hobby farmer. With high-level accomplishments coupled to his adventuresome spirit, engaging personality, ready humor, wisdom, and dedication to what's best in medicine, Art left a lingering example in science, education, and patient care for all to remember and emulate.

John J. Marini

Preface

Critical care is a high-stakes activity—from both outcome and cost perspectives. What should a young intensivist be taught and a seasoned practitioner ideally know? Our worlds of medical education and practice continue to change quickly. While electronic retrieval of patient records and information from scientific literature is of immeasurable help, electronically facilitated submission, peer review, and production methods have accelerated publication turnover. Pressures to shorten time in hospital and improve documentation tug the team toward the computer desk and away from the patient, placing strains on face-to-face communications among doctor, patient, family, and nurse. Because of mandated and pragmatic changes in practice, there has been a dramatic shift in care from a “one doctor-one patient” relationship to one in which there are frequent personnel changes. The chances for error or miscommunication in this evolving system are magnified. Simultaneously, older patients with chronic multisystem dysfunction and attendant complex problems account for a growing fraction of those admitted. While practicing on the cutting edge of intensive care medicine has always been challenging, there now seems more to know and too much to keep track of. At times, we do not seem to be keeping up.

Another worrisome trend seems clear. In this exciting age of molecular medicine, mastery of bedside examination and physiology has been deemphasized. Simultaneously, clinical research has shifted from exploration of everyday problems confronted at the bedside to large population-based interventional trials. When well done (and we are steadily getting better at them), these studies hold considerable value and often help decide initial “best practice” for many patients. Yet, clinical trials will never inform all decisions, and it is incumbent upon the practitioner to know when published clinical research does not apply to the patient at hand and to recognize when the course suggested by trial results should be ignored or highly modified. Physicians who apply “best practice” to the individual cannot rely only on protocols and the latest guidelines.

Recommendations come into and drop out of favor, but physiologic principles and fundamentals of critical care change very little. Because real-world problems are complex and treatment decisions interwoven, well-honed analytical skills are indispensable. To personalize critical care requires gathering and integration of a broad information stream, interpreted against a nuanced physiological background. Management must be guided by informed judgment, applying the best information presently known, and influenced by core physiological principles. Once made, the intervention must often be revised, guided by thoughtful observation of the patient's idiosyncratic response. Multidisciplinary cooperation among caregivers is essential to the success of these efforts.

Cardiorespiratory physiology forms the logical base for interpreting vital observations and delivering effective critical care. Committed to short-loop feedback and “midcourse” corrections, the intensivist should be aware of population-based studies of similar problems but not enslaved to their results. Likewise, it is important to realize that treatments that improve physiological end points do not always translate into improved patient outcomes and that failure of a patient to respond as expected to a given treatment does not invalidate that intervention for future patients. Add to these considerations the traits of cost consciousness, empathy, and effective communication, and you are well positioned to deliver cost-effective, quality care in our demanding practice environment.

Multiauthored books—even the best of them—have chapters of varying style and quality that are often lightly edited. We believe that a book intended for comprehension is best written with a single voice and consistent purpose. Therefore, every chapter in this book was written and revised by the two authors. After many years of working together in clinical practice, research, and education, we have felt free to comment freely, quibble, complain, and edit each other's work. Sadly, the coauthor of the first four editions, Art Wheeler—a brilliant physician, leader, and close friend, passed on prematurely 3 years ago. Fortunately, his place has been taken for this fifth edition by another, David Dries, whose expertise in surgery and trauma has added immeasurably to

the depth of this latest edition. Consistent with our

specialties, we practice in different dedicated ICUs of the same referral and community general hospital (Regions Hospital, St. Paul, MN). Yet, as investigators and professors of Medicine and Surgery of the University of Minnesota, our research and educational interests are well aligned. Close collaboration between medical and surgical professors in an educational effort of this type is quite unusual and may be unique. Whatever the truth of that, this diversity adds breadth and helps keep perspective on what is “essential”—or at least what's valuable and interesting to know in today's practice.

Since our last edition, major insights and changes in practice have enriched our evolving field. Among the most prominent of these are neurological critical care, bedside ultrasonography, and interventional radiology. There has been dawning awareness and prioritization of the need to be less invasive and to prevent the postintensive care syndrome. Although these now receive special emphasis, virtually every chapter has been thoroughly revised and updated. Trauma and surgical critical care material, as well as illustration content, have been markedly expanded and refined.

As before, we have tried to extract what seem to be those grounding bits of knowledge that have shaped and reshaped our own approaches to daily practice. We titled this book “*The Essentials*” when it was first written, but admit that in places it now goes into considerable depth and quite a bit beyond basic knowledge; hence, the slightly modified title. Our own tips and tricks—useful pearls that we think give insight to practice—have been sprinkled liberally throughout. This book was written to be read primarily for durable understanding; it is not intended for quick lookup on-the-fly. It is not a book of quick facts, bullet points, checklists, options, or directions. It would be difficult to find a white coat pocket big enough to carry it along on rounds. Depth of treatment has not been surrendered in our attempt to be clear and concise.

The field of critical care and the authors, both once young and inexperienced, have now matured. Fortunately, we remain committed to caring for the sickest patients, discovering new ways to understand and more effectively confront disease, and passing on what we know to the next generation. Many principles guiding surgery and medicine are now time-tested and more or less interchangeable. For the fifth edition, we have carefully examined and updated the content of each chapter, added and modified many illustrations, expanded content, and in a few cases, discarded what no longer fits. Mostly, however, we fine-tuned and built upon a solid core. This really is no surprise—physiologically based principles endure. It is gratifying that most of what was written four editions ago still seems accurate—and never more relevant.

John J. Marini

David J. Dries

Acknowledgments

Of all the paragraphs in this book, this one is among the most difficult to write. Perhaps it is because so many have helped me reach this point—some by their inspiring mentorship, some by spirited collaboration, some by invaluable support, and some by enduring friendship. I hope that those closest to me already know the depth of my gratitude. A special few have given me far more than I have yet given back. The debts I owe to Len Hudson, Bruce Culver, Luciano Gattinoni, and Elcee Conner cannot easily be repaid. By their clear examples, they have shown me how to combine love for applied physiology, scientific discovery, and education-never forgetting that the first priorities of medicine are to express compassion for and connection with others while advancing patient welfare.

“Each wave owes the essence of its line only to the withdrawal of the preceding one.” (Andre Gide)

John J. Marini

As word of my involvement in this book spread around our hospital, many colleagues offered advice and support ranging from images and algorithms to reality checks and encouragement. I would like to acknowledge the following individuals in this regard: Kim Cartie-Wandmacher, PharmD; Hollie Lawrence, PharmD; Jeffrey Evens, TSC; Jody Rood, RN; Carol Droegemueller, RN; Christine Johns, MD; Azhar Ali, MD; Don Wiese, MD; Andy Baadh, MD; Richard Aizpuru, MD; and Haitham Hussein, MD.

To Barbara and my family, please accept my thanks for prayers, guidance, and support. Our children and grandchildren have blessed and inspired us.

Finally, thanks to my colleagues on the faculty and staff at Regions Hospital for all they have taught me.

David J. Dries

Special Thanks

The authors gratefully acknowledge collaboration of the following contributors on this Fifth Edition:

Dr. Andrew Hartigan for help in the revision of Chapter 11; Kim Cartie-Wandmacher, PharmD, for the revision of Chapter 15; and Julie Jasken, RD, for the revision of Chapter 16. The expert, uplifting and tireless contributions of Sherry Willett at Regions Hospital, as well as those of the well-tuned production team of Keith Donnellan, Timothy Rinehart, and Jennifer Clements are sincerely appreciated.

John J. Marini

David J. Dries

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Chapter 1
Hemodynamics

• Key Points

1. Because of differences in wall thickness and ejection impedance, the two sides of the heart differ in structure and sensitivity to preload and afterload. The normal right ventricle is more sensitive to changes in its loading conditions than the left. When failing or decompensated, both ventricles are preload insensitive and afterload sensitive.
2. Right ventricular afterload is influenced by hypoxemia and acidosis, especially when the capillary bed is diminished and the vascular smooth musculature is hypertrophied, as in chronic lung disease. The ejection impedance of the left ventricle is conditioned primarily by peripheral vascular tone, wall thickness, and ventricular volume, except when there is an outflow tract narrowing or aortic valve dysfunction.
3. Regulating cardiac output to metabolic need requires appropriate values for average heart rate and stroke volume. *Either* or *both* may be the root cause of failing to do so.
4. Even when systolic function is well preserved, impaired ventricular distensibility and failure of the diseased ventricle to relax in diastole often produce pulmonary vascular congestion and predispose to "flash pulmonary edema." Echocardiographic diastolic dysfunction often precedes heart failure and commonly develops against the background of systemic hypertension, ischemia, or other diseases that reduce left ventricular compliance.
5. The relationship of cardiac output to filling pressure can be equally well described by the traditional Frank-Starling relationship or by the venous return curve. The driving pressure for venous return is the difference between mean systemic pressure (the average vascular pressure in the systemic circuit) and right atrial pressure. Venous resistance is conditioned by vascular tone and by anatomic factors influenced by lung expansion. At a given cardiac output, mean systemic pressure is determined by venous tone and degree of vascular filling.
6. Radiographic evidence of acute heart failure includes perivascular cuffing, a widening of the vascular pedicle, blurring of the hilar vasculature, and diffuse infiltrates that tend to spare the costophrenic angles. Lung ultrasound reveals characteristic signs. Radiographic infiltrates tend to lack air bronchograms and are seldom accompanied by an acute change in heart size. Chronic congestive heart failure is typified by Kerley B lines, dilated cardiac chambers, and increased cardiac dimensions.
7. The key directives in managing *cor pulmonale* are to maintain adequate right ventricle filling, to reverse hypoxemia and acidosis, to establish a coordinated cardiac rhythm, to reduce oxygen demand, to avoid both overdistention and derecruitment of lung tissue, and to treat the underlying illness.
8. Pericardial tamponade presents clinically with venous congestion, hypotension, narrow pulse pressure, distant heart sounds, and equalized pressures in the left and right atria. Diastolic pressures in both ventricles are similar to those of the atria.

CHARACTERISTICS OF NORMAL AND ABNORMAL CIRCULATION

Anatomy

Cardiac Anatomy

The circulatory and respiratory systems are tightly interdependent in their primary function of delivering appropriate quantities of oxygenated blood to metabolizing tissues. The physician's ability to deal with hemodynamic dysfunction requires a well-developed understanding of the anatomy and control of the circulation under normal and abnormal conditions. The bloodstream's interface with the airspace (the alveoli) together with cardiac check valves divide the circulatory path into two functionally distinct limbs—right, or pulmonary, and left, or systemic. Except during congestive failure, the atria serve primarily as reservoirs for blood collection, rather than as key pumping elements. The right ventricle (RV) is structured differently than its left-sided counterpart (Table 1-1). Because of the low resistance of the pulmonary vascular bed, the normal RV generates mean pressures only one seventh as great as those of the left side while driving the same output. Consequently, the free wall of the RV is normally thin, preload sensitive, and poorly adapted to an acute increase of afterload. The thicker left ventricle (LV) must generate sufficient pressure to drive flow through a much greater and widely fluctuating vascular resistance. Because the RV and LV share the interventricular septum, circumferential muscle fibers, and the pericardial space, their interdependence has important functional consequences. For example, when the RV swells in response to increased afterload, the LV becomes functionally less distensible, and left atrial pressure tends to increase. At the same time, the shared muscle fibers allow the LV to assist in generating the required rise in RV and pulmonary arterial pressures. Ventricular interdependence is enhanced by processes that crowd their shared pericardial fossa: high lung volumes, high heart volumes, and pericardial effusion.

Table 1-1. Right Versus Left Heart Properties

	Right Heart		Left Heart	
	Normal	**Failing**	**Normal**	**Failing**[a]
Preload sensitivity	+++	+	++	+
Afterload sensitivity	++	+++	+	+++
Contractility	++	+	+++	++
Effects of: Afterload (General)	±	+++	±	++
Pleural pressure	±	± to +	+	++
pH	++	+++	±	±
Hypoxemia	++	++++	±	±
Response to inotropic and vasoactive drugs	NA	++	NA	++++

[a]Not including aortic valve disease.

Coronary Circulation

The heart is nourished by the coronary arteries, and its venous outflow drains into the coronary sinus that opens into the right atrium. The right coronary artery emerges anteriorly from the aorta, distributing to the RV, to the sinus and atrioventricular (AV) nodes, and to the posterior and inferior surfaces of the LV. The left coronary system (circumflex and left anterior descending arteries) nourishes the interventricular septum, the conduction system below the AV node, and the anterior and lateral walls of the LV. If the heart were to relax completely, the difference between mean arterial pressure (MAP) and coronary sinus pressure would drive flow through the coronary circulation. However, because aortic pressure varies continuously and because the tension within the myocardium that surrounds the coronary vessels influences the *effective* downstream pressure, perfusion varies with the phases of the cardiac cycle. The LV is perfused most actively in early diastole—not when aortic pressure is at its maximum but when

myocardial tension is least. The LV myocardial pressure is highest close to the endocardium and lowest near the epicardium. Hence, under stress, the endocardium is more likely to experience ischemia.

Coronary blood flow normally parallels the metabolic activity of the myocardium. Because changes in heart rate are accomplished chiefly by shortening or lengthening diastole, tachycardia reduces the cumulative time available for diastolic perfusion while increasing the heart's need for oxygen. This potential reduction in mean coronary flow is normally overridden by vasodilatation. However, coronary disease prevents full expression of such compensation. During bradycardia, longer periods of time are available for diastolic perfusion and metabolic needs are less. However, diastolic myocardial fiber tension rises as the heart expands, and marked bradycardia may simultaneously lower both mean arterial and coronary perfusion pressures.

Vascular Anatomy

Left Side

Between heartbeats, the continuous flow of blood from the heart to the periphery is maintained by the recoil of elastic vessels that were distended during systole. Arterioles serve as the primary resistive elements, and by adjusting their caliber, these small vessels regulate tissue blood flow and aid in the control of arterial pressure. The true capacitance vessels forming the reservoir of the circulation are the venules and small veins. At any one time, only a minority of the total capacitance bed is recruited or distended and only a portion of the total blood volume actively circulates. The precise distribution of the circulating blood volume among various tissue beds is governed by metabolic or functional requirements and gated by arteriolar vasoconstriction. When under physiologic stress, the capacitance bed contracts or expands in support of the circulating volume (Fig. 1-1).

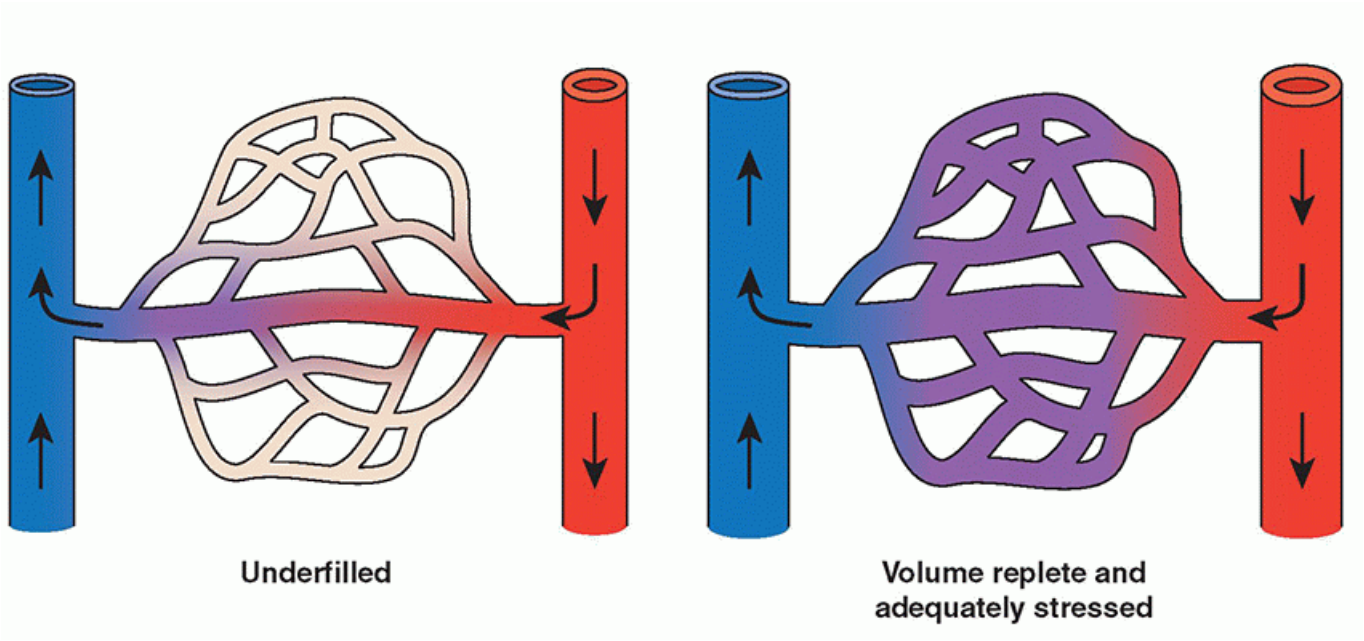

FIGURE 1-1. The underfilled or contracted peripheral vasculature **(left)** may not improve tissue perfusion and/or reverse shock physiology in response to vasopressor agents. The adequately filled and stressed vascular network **(right)** is better primed to increased blood pressure and perfusion of pressure dependent tissue beds when a vasopressor/inotrope is added.

Right Side

In the low-pressure pulmonary circuit, relatively few structural differences distinguish normal arteries from veins. The pulmonary capillary meshwork, however, is even more luxuriant and well filled than in the periphery. Apart from innate anatomy, blood flow distribution is influenced by gravity, alveolar pressure, regional pleural pressures, oxygen tension, pH, circulating mediators, and chemical stimuli (e.g., nitric oxide).

Circulatory Control

Determinants of Cardiac Output

When averaged over time, cardiac output (product of heart rate and stroke volume) must match the metabolic requirements. In a real sense, metabolic activity regulates the cardiac output of a healthy individual; insufficient cardiac output activates inefficient anaerobic metabolism that cannot be sustained indefinitely. Agitation, anxiety, pain, shivering, fever, and increased breathing workload intensify

systemic O_2 demands. In the critical care setting, matching output to demand is often achieved with the help of sedative, analgesic, antipyretic, inotropic, or vasoactive agents. It is important to remember that increasing or decreasing cardiac output can reflect shifting O_2 demands, rather than a change in ventricular loading conditions or response to therapeutic intervention.

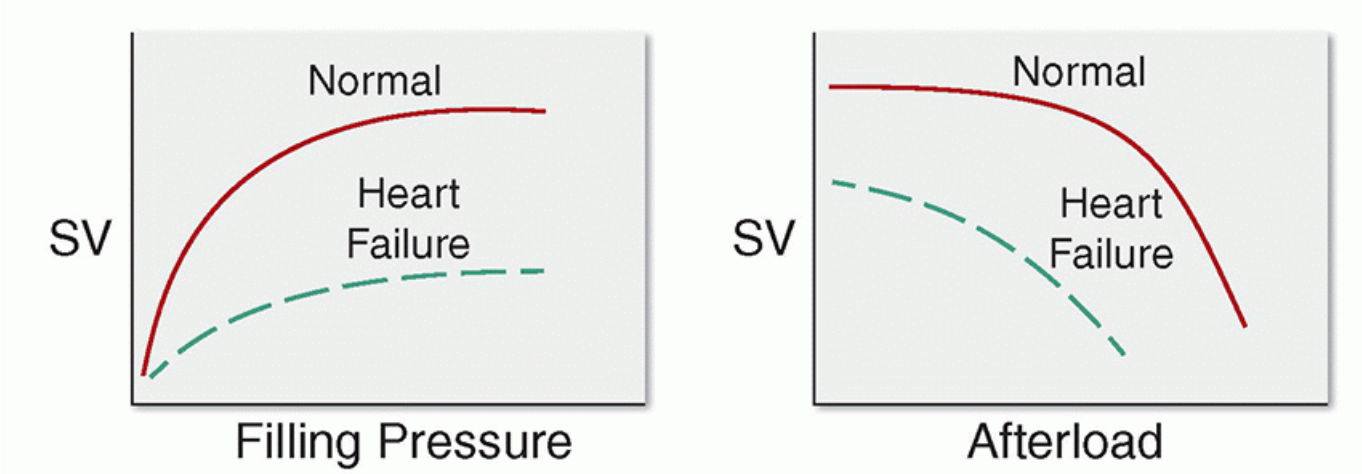

FIGURE 1-2. Stroke volume (SV) response of normal (NL) and failing heart to loading conditions. Impaired hearts are abnormally sensitive to afterload but show blunted responses to preload augmentation.

Although the precise mechanism that links output to metabolism remains uncertain, the primary determinants of stroke volume are well defined: precontractile fiber stretch in diastole (preload), the tension developed by the muscle fibers during systolic contraction (afterload), and the forcefulness of muscular contraction under constant loading conditions (contractility) (Fig. 1-2). Factors governing these determinants, as well as their normal values, differ for the two ventricles, even though over time the *average* stroke volume of both ventricles must be equivalent.

Determinants of Stroke Volume—General Concepts

Preload

According to the Frank-Starling principle, muscle fiber stretch at end diastole influences the extent of cardiac ejection. The tendency of ejected volume to increase as the transmural filling pressure rises normally constitutes an important adaptive mechanism that enables moment-by-moment adjustments to changing venous return. During heart failure, the Starling curve flattens, and the ventricle becomes preload insensitive—higher filling pressures become necessary to achieve a similar output. Although preload parallels end-diastolic ventricular volume, myocardial remodeling can gradually modify the relationship between absolute chamber volume and preload. Therefore, muscle fiber stretch within a *chronically* dilated heart may not differ significantly from normal. End-diastolic volume is determined by ventricular compliance and by the pressure distending the ventricle (the transmural pressure). Transmural pressure is the difference between the intracavitary and juxtacardiac pressures. In comparison to the LV, the normal RV operates with a comparatively steep relationship between transmural pressure and ventricular volume. A poorly compliant ventricle, or one surrounded by increased intrathoracic or pericardial pressure, requires a higher intracavitary pressure to achieve any specified end-diastolic volume and degree of precontractile fiber stretch (Fig. 1-3). The cost of higher filling pressure may be impaired myocardial perfusion or pulmonary edema. Functional ventricular stiffening can result from myocardial disease, pericardial tethering, or extrinsic compression of the heart (Table 1-2). The precise position of the ventricle on the Starling curve is difficult to determine. However, studies of animals and normal human subjects suggest that there is

little preload reserve in the supine position and that, once supine, further increases in cardiac output are met primarily by increases in heart rate and/or ejection fraction. Thus, the Frank-Starling mechanism may be of most importance during hypovolemia and in the upright position.

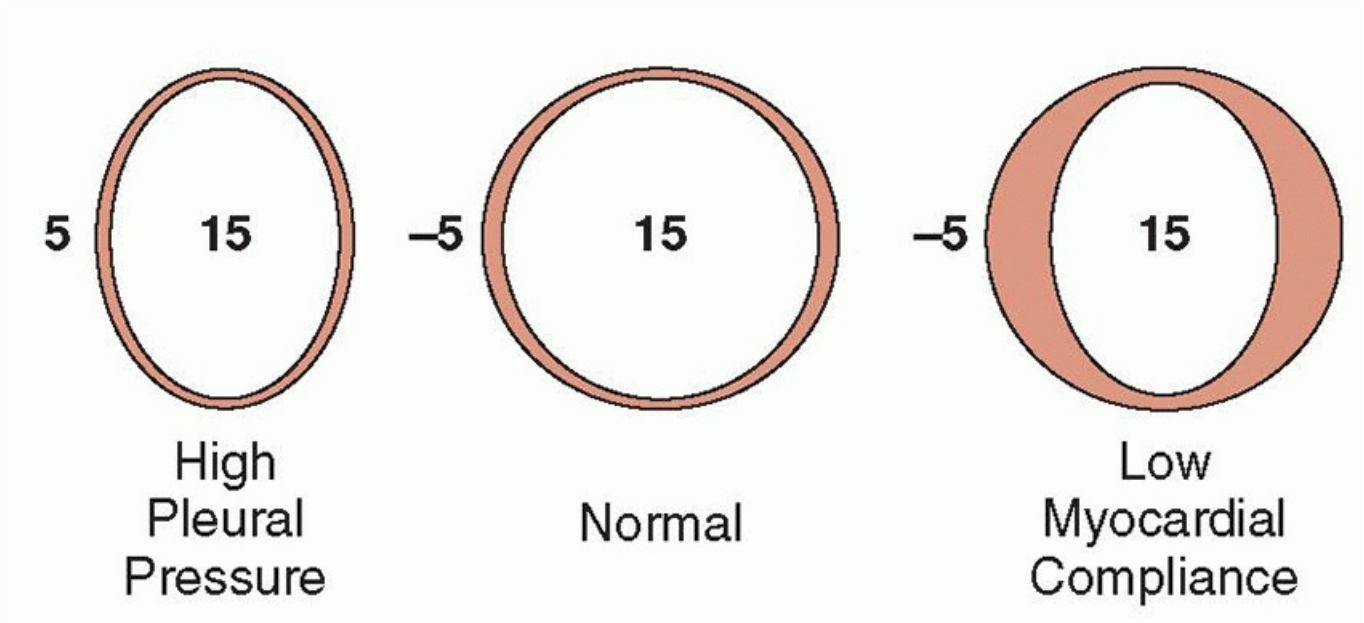

FIGURE 1-3. Concept of transmural pressure. The muscle fiber tensions that determine preload and afterload are developed by pressure differences across the ventricle. For example, in diastole, a measured intracavitary pressure of 15 mm Hg may correspond to a large or small chamber volume and myocardial fiber tension, depending on the compliance of the ventricle and its surrounding pressure.

Table 1-2. Reduced Diastolic Compliance

Myocardial Thickening or Dysfunction	Pericardial Disease	Extrinsic Compression
Ischemia/infarction	Tamponade	PEEP/hyperinflation
Hypertension	Constriction	Tension pneumothorax
Infiltration		RV dilation
Congenital defect		LV crowding
Valvular dysfunction		Impaired chest wall compliance

Diastolic Dysfunction

Diastole is usually considered a passive period in which transmural pressure distends elastic heart muscle. In normal individuals and many patients with heart disease, this approximation is more or less accurate. However, diastole is more properly considered an energy-dependent active process. (In fact, in some instances, more myocardial oxygen may be consumed in diastole than in systole.) Failure of the heart muscle to relax at a normal rate (secondary to ischemia, long-standing hypertension, or hypertrophic myopathy) can cause sufficient functional stiffening to produce pulmonary edema despite preserved systolic function. As defined by echocardiography, many apparently normally functioning elderly adults have abnormal patterns of cardiac relaxation. Perhaps one third or more of adult patients with congestive heart failure (CHF) develop symptoms on this basis, with the incidence increasing markedly with advancing age. Key echocardiographic features of diastolic dysfunction are described in Chapter 2. Diastolic dysfunction often precedes systolic dysfunction and should be considered an early warning sign of deterioration. Although diastolic and systolic impairments often coexist, the diastolic dysfunction syndrome is an especially likely explanation when signs of pulmonary

congestion predominate over those of systemic perfusion in the absence of mitral valve dysfunction. In all patients with diastolic dysfunction, the early rapid filling phase of ventricular diastole is slowed, and the extent of ventricular filling becomes more heavily influenced by terminal-phase atrial contraction. Sudden loss of the atrial "kick" often precipitates congestive symptoms. Flash pulmonary edema is often the consequence of sudden diastolic dysfunction resulting from ischemia, tachycardia, or atrial fibrillation. Diastolic dysfunction should be suspected when congestive symptoms develop despite normal systolic function in predisposed patients. Confirmation requires ancillary testing by echocardiography, radionuclide angiography, contrast ventriculography, or other imaging method. With all techniques, attention must be focused on diastole, particularly during the phase of rapid filling. In most institutions, echocardiography has become the method of choice for critically ill patients because of its convenience and reliability. Indicators of mitral valve function such as deceleration time, early diastolic (E) to late diastolic (A) wave velocity ratio, and isovolume relaxation time are helpful. Signals of the required clarity are often impossible to obtain, however, in the critically ill patient, particularly with transthoracic (as opposed to transesophageal) imaging. Regarding treatment, control of blood pressure, heart rate, and ischemia are the essential objectives. Diuretics are indicated to relieve congestive symptoms. Calcium channel blockers (e.g., verapamil, diltiazem, nifedipine) have been demonstrated to be useful in animal studies and in humans with hypertrophic cardiomyopathy. Selective β-blockers (e.g., metoprolol, carvedilol) can help reduce tachycardia, lower blood pressure, and promote long-term remodeling but must be chosen wisely and used with extreme caution when significant systolic dysfunction, conduction system disturbance, or bronchospasm coexist. Predictably, inotropes do not improve diastolic function.

Afterload

Although afterload is often equated with elevations of blood pressure or vascular resistance, it is better defined as the muscular tension that must be

developed during systole per unit of blood flow. As such, the systolic wall stress is affected by blood pressure, wall thickness, and ventricular volume. In the normal heart, moderate changes in afterload are usually countered by increases in contractility, preload, or heart rate, so that forward output is usually little affected. Heart size remains small, and filling pressures do not rise excessively. However, once preload reserves have been exhausted, raising afterload can profoundly depress cardiac output if contractile force and/or heart rate do not compensate. Just as the relationship between preload and stroke volume rises more steeply for the right than for the LV, so too is the normal RV more sensitive than the left to changes in afterload (Fig. 1-2). The dilated chambers of a *failing* heart—both right and left—are inherently afterload sensitive (Fig. 1-2). Cardiomegaly and mitral regurgitation are clinical findings that help identify potential candidates for afterload reduction. Quantitative assessment of ejection impedance can be made by determining pulmonary vascular resistance (PVR) and systemic vascular resistance (SVR). These indices, the quotients of driving pressure and cardiac output across their respective beds, are calculated as if the blood flow fulfilled the assumptions of Poiseuille law. Because cardiac output must be interpreted relative to body size, both indices have a wide range of normal values. Although SVR rising in response to adrenergic tone or drug treatment helps support the upstream arterial pressure that perfuses certain critical tissue beds (e.g., kidney) when cardiac output falls, elevating the vascular resistance may impair downstream capillary filling in others. Moreover, in aggregate, vascular impedance may rise sufficiently to compromise cardiac output. Judicious reduction of arterial vessel tone may then allow cardiac output to improve and vital organ perfusion to increase, while maintaining an acceptable blood pressure.

Chamber diameter also impacts afterload. In a dilated chamber, higher systolic fiber tension must be generated to produce a given intracavitary pressure, especially in fibers on the periphery. Thus, a diuretic or selective venodilator (nitroglycerine) may reduce afterload as well as preload. Apart from vessel length and diameter, blood viscosity is an important determinant of rheology and effective afterload. Blood viscosity rises nonlinearly

with hematocrit. With increasing hematocrit, crowded erythrocytes pass more sluggishly through tissues, and effective O_2 transport eventually reaches a maximum, the value of which depends on circulating blood volume relative to vascular capacity (Fig. 1-4). Individual tissue beds appear to have different tolerances to changes in hematocrit and different optimal values for oxygen extraction. Viscosity may also rise dramatically in the settings of hypothermia or hyperproteinemia.

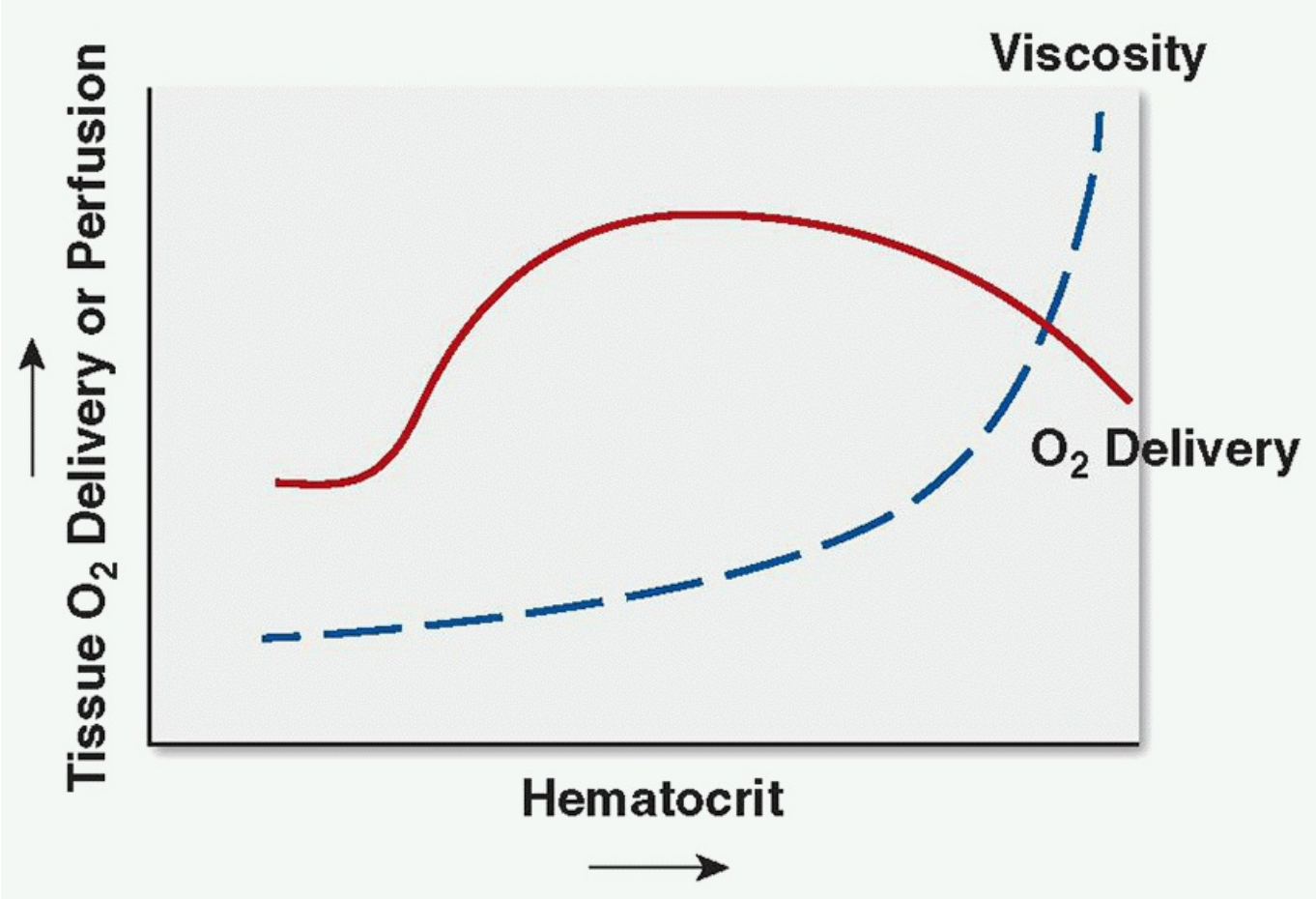

FIGURE 1-4. Increasing hematocrit helps open tissue beds and deliver O_2, when open. However, at very high values seldom encountered in the ICU, hematocrit increases viscosity, impairs perfusion, and reduces O_2 delivery.

Pleural Pressure and Afterload

Systolic pressure is a marker of the highest intracavitary pressure developed by contracting muscle fibers. The intracavitary pressure is a result of muscular forces and the regional pleural pressure that surrounds the heart. Variations in pleural pressure may significantly alter afterload and therefore, the function of the compromised LV. The paradoxical pulse observed during acute asthma results in part from inspiratory afterloading of the LV. When the pressure that surrounds the heart declines, greater muscle fiber tension must be developed during systole to generate intracavitary and systemic blood pressures. Such alterations of ventricular loading conditions help explain why vigorous breathing efforts impair the function of the ischemic or failing heart.

Right ventricular afterload tends to rise nonlinearly with increasing lung volume. The pulmonary vascular pressure-flow relationship may differ slightly for positive versus negative pressure breathing. However, the RV afterload corresponding to any given lung volume is not greatly influenced by changes of pleural pressure, because the vessel that accepts its outflow (the pulmonary artery) is subjected to similar variations in pressure.

Contractility

Many stimuli compete to influence the contractile state of the myocardium. Sympathetic impulses, circulating catecholamines, acid-base and electrolyte disturbances, ischemia, anoxia, and chemodepressants (e.g., drugs, mediators, toxins) or hormones (e.g., high dose insulin) may influence ventricular performance, independent of changes in preload or afterload (Fig. 1-5). Contractility is sometimes impaired transiently after blunt cardiac trauma, during intense adrenergic receptor stimulation (stress cardiomyopathy), or when ischemic myocardium is reperfused (e.g., after cardiopulmonary resuscitation, angioplasty, or lysis of coronary thrombosis). Such "stunned myocardium" may stage a complete recovery after several days of transient dysfunction. No physical sign reliably reflects altered contractility. An S_3 gallop, narrow pulse pressure, and poorly audible heart tones suggest impaired contractility, but these signs are difficult to quantify and are influenced by myocardial compliance, intravascular volume status, and vascular tone. Radionuclide ventriculograms and echocardiography provide excellent noninvasive means of determining ventricular size and basal contractile properties of the LV but are not well suited to continuous monitoring. The commonly used "ejection fraction" is influenced by the loading conditions of the heart. Two-dimensional echocardiographic images may misrepresent three-dimensional changes in chamber geometry.

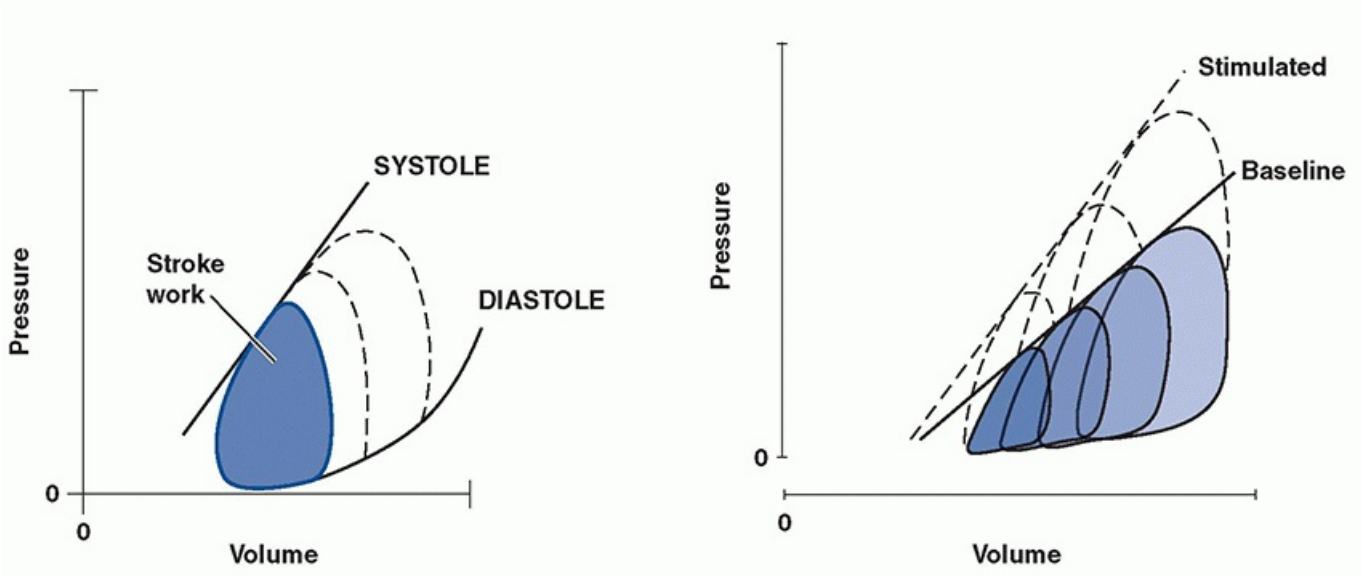

FIGURE 1-5. Transmural ventricular pressure volume loops. Left: Four complete cardiac cycles are represented for different states of ventricular filling. The end-diastolic pressure volume relationship defines the Frank-Starling curve. During each cycle, there are sequential stages of diastolic filling, isovolumic contraction, active systolic ejection, and isovolumic relaxation. The end-systolic pressure volume relationship (ESPVR) correlates well with contractility. **Right:** As the myocardium is stimulated by catecholamines, the slope of the ESPVR increases, resulting in a greater pressure and ejection fraction during systole for any degree of diastolic filling.

Heart Rate

Changes in the rate of the healthy heart result from the interplay between the two divisions of the autonomic nervous system. Ordinarily, parasympathetic tone predominates. (When both divisions of the autonomic nervous system are blocked, the intrinsic heart rate of young adults rises from approx. 70 to 105 beats/min.) The heart's ability to respond to an increased demand for output is largely determined by its capacity to raise the heart rate appropriately. Pathological bradycardias often depress cardiac output and O_2 delivery, especially when a diseased or failing ventricle is unable to call upon a preload reserve. Relative bradycardia is often observed in the clinical setting—a "normal" heart rate is not logically appropriate for a stressed patient with high O_2 demands or impaired myocardium. Because two key determinants of oxygen delivery are affected, bradycardia induced by

profound hypoxemia depresses O_2 delivery and may rapidly precipitate circulatory collapse. Marked increases in heart rate may also lead to circulatory depression when they cause myocardial ischemia, or when reduced diastolic filling time or loss of atrial contraction impair ventricular preload. (Good examples include mitral stenosis and diastolic dysfunction.) As a general rule, sinus heart rates exceeding (220 - age)/min reduce cardiac output and myocardial perfusion, even in the absence of ischemic disease or loss of atrial contraction.

(To illustrate, sinus-driven heart rate should not exceed 150 beats/min in a 70-year-old patient.)

Peripheral Circulation

Vascular tone is integral to cardiac output regulation—the heart cannot pump what it fails to receive in venous return, and vasoconstriction is a key determinant of afterload. In fact, control of cardiac output may be viewed strictly from a vascular perspective (Fig. 1-6). Under steady-state conditions, venous return is proportional to the quotient of venous driving pressure and resistance. Under most circumstances, the downstream pressure for venous return is right atrial pressure. The upstream pressure driving venous return, the mean systemic pressure (P_{MS}), is the volume-weighted average of pressures throughout the entire systemic vascular network. Because a much larger fraction of the total circulating volume is downstream from the resistance vessels, P_{MS} is much closer to the right atrial pressure (P_{RA}) than to MAP (Fig. 1-7). Were the P_{RA} to rise suddenly to equal the P_{MS}, all blood flow would stop. Indeed, in an experimental setting, P_{MS} can be determined by synchronously clamping the aorta and vena cava to stop flow and opening a wide-bore communication between them. Mean systemic pressure is influenced by the circulating blood volume and vascular capacitance, which in turn is a function of vascular tone. Thus, P_{MS} rises under conditions of hypervolemia, polycythemia, and right-sided CHF; it declines during abrupt vasodilation, sepsis, hemorrhage, and diuresis. Up to a certain point, lowering P_{RA} while preserving P_{MS} increases driving pressure and improves venous return. However, when P_{RA} is reduced below the surrounding tissue pressure, the thin-walled vena

cava collapses near the thoracic inlet. Effective downstream pressure for venous return then becomes the pressure just upstream to the point of collapse, rather than the P_{RA}.

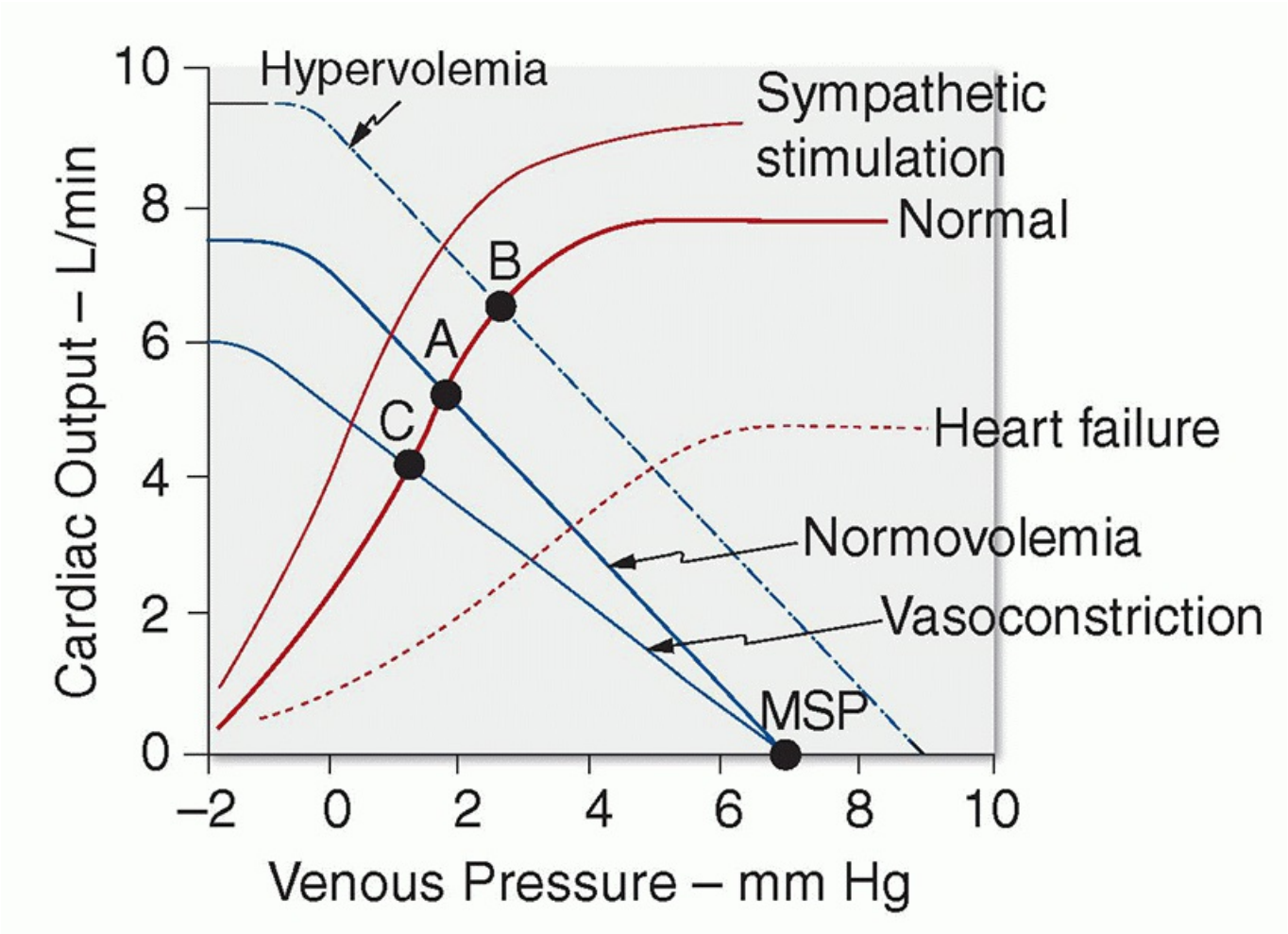

FIGURE 1-6. Interaction of Frank-Starling and venous return (VR) curves. With normal heart function, observed cardiac output is determined by such vascular factors as filling status (*A* → *B*) and vasoconstriction (*C*). Sympathetic stimulation and heart failure have opposing effects on the Starling curve and cardiac output. The upstream mean systemic pressure (MSP) that drives venous return is a hypothetical point determined by extrapolating the venous return curve to the venous pressure axis where all cardiac output ceases. Note that VR improves linearly as CVP falls—up to the point at which central vessels collapse.

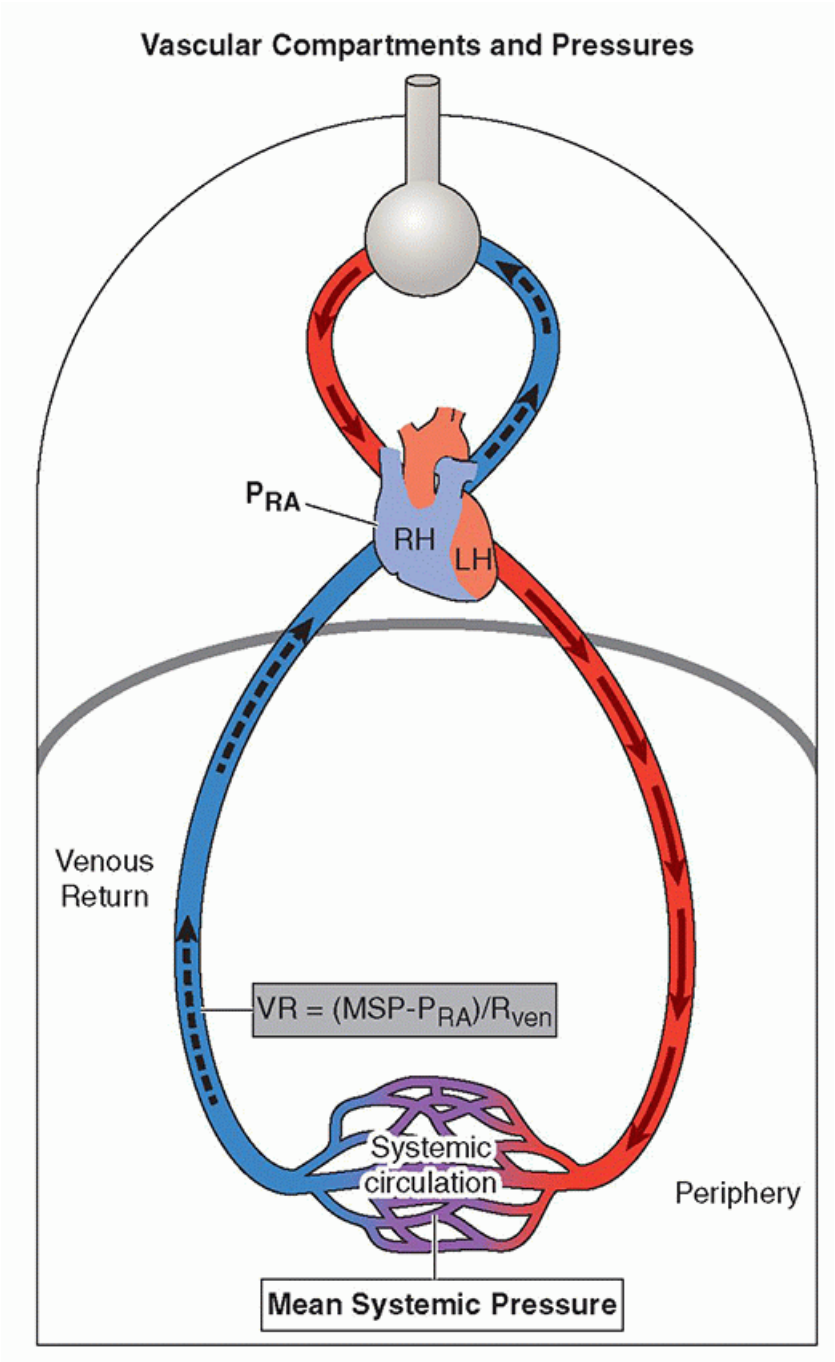

FIGURE 1-7. Forces driving the systemic circulation. The mean systemic circulatory pressure is the weighted average of arterial, capillary, and venous pressures and equals the blood pressure at any point with the circulation stopped. It is much closer to venous than to mean arterial pressure because of the large venous capacitance bed. MSP minus P_{RA} is the driving pressure for venous return.

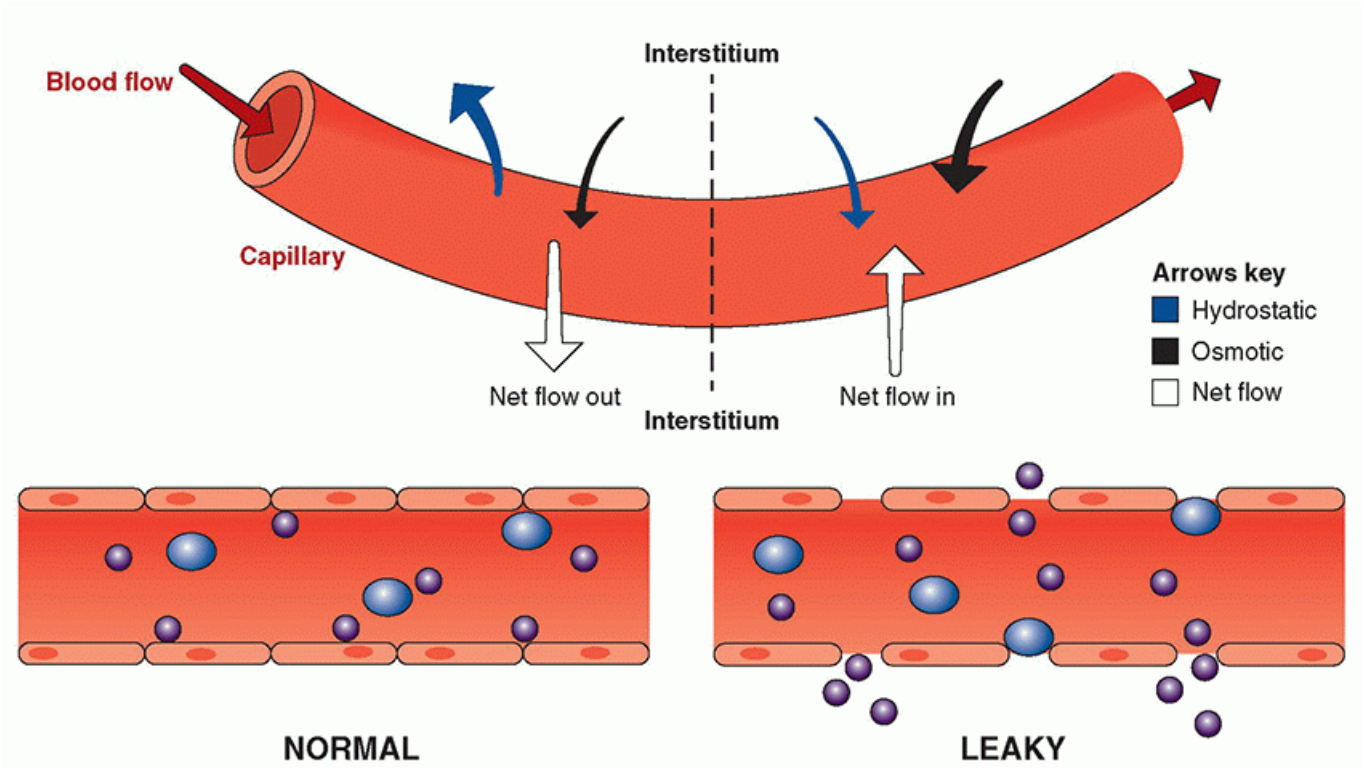

FIGURE 1-8. Microvascular fluid kinetics. Upper panel: Classic Starling kinetics of fluid exchange at the capillary level. On the upstream side, hydrostatic gradient between the lumen and the intercellular interstitium exceeds the osmotic drag tending to retain intravascular fluid. On the downstream side, the osmotic gradient prevails, allowing interstitial fluid to reenter the vessel. **Lower panel:** Normally, tight intercellular junctions prevent the escape of most large and small intravascular proteins, such as albumin. In the setting of inflammation, intercellular connections loosen and become leaky, allowing many small- and moderate-sized molecules to breech the vessel wall and leave the circulating bloodstream.

At any given moment, the cardiac output is determined by the intersection of the venous return curve and the Starling curve. In the analysis of a depressed cardiac output, both aspects of circulatory control must be considered. For example, when positive end-expiratory pressure (PEEP) is applied, P_{RA} rises, inhibiting the venous return. However, P_{MS} rises simultaneously, and compensatory vascular reflexes are called into action to reduce the venous capacitance and expand the circulating volume. Therefore, unlike patients with depressed vascular reflexes or hypovolemia, most healthy individuals do not experience a reduction of cardiac output under the influence of moderate PEEP. Although an increase in venous resistance can also reduce the venous return, it is uncommon for the venous resistance to increase without an offsetting change in P_{MS}. However, positional compression of the inferior vena cava by an intra-abdominal mass (e.g., during advanced pregnancy) may account for postural changes in cardiac output in such patients.

Capillary Fluid Filtration and Tendency for Tissue Edema

Classical concepts first developed by Starling and later modified to improve accuracy and clinical relevance indicate that fluid transport at the tissue level is normally determined by the hydrostatic and osmotic pressure differences between the capillary (P_{CAP}, Π_{CAP}) and interstitial (P_{IF}, Π_{IF}) compartments (Fig. 1-8, **left**). Rising hydrostatic pressure and depression of oncotic pressure favor edema formation, whereas the opposites favor its prevention or resolution. The capillary filtration coefficient (C_F), which increases with acute inflammation, characterizes the ease or difficulty with which any such differences cause a net shift between compartments. Expressed in equation form:

$$Q_F = C_F\left[\left(P_{CAP} - P_{IF}\right) - \left(\Pi_{CAP} - \Pi_{IF}\right)\right]$$

This relationship, though admittedly simplified, serves to indicate that increased interstitial fluid (edema) may form because of an increase in venous and capillary pressures, a fall in serum oncotic pressure, or increased number and leakiness of the capillary pores. All three are potential targets for clinical intervention (Fig. 1-8, **right**).

CHARACTERISTICS OF THE DISEASED CIRCULATION

Left Ventricular Insufficiency

Congestive Heart Failure

Diagnostics

The term "heart failure" (or CHF) is often loosely applied to conditions in which the filling pressures of the left heart are increased sufficiently to cause dyspnea or weakness at rest or mild exertion. Congestive symptoms can develop when systolic cardiac function is preserved (volume overload, renal insufficiency, diastolic dysfunction, RV encroachment, and pericardial effusion), as well as during myocardial failure itself. Unlike the normal LV, which is relatively sensitive to changes in its preload and insensitive to changes in its afterload, the failing LV has the opposite characteristics (see Fig. 1-2). Changes in afterload can therefore make a major difference in LV systolic performance, whereas preload manipulation usually elicits little benefit, unless it reduces afterload indirectly by shrinking chamber volume and wall tension. Wide QRS complexes characterize the ventricular asynchrony of bundle branch block, and in certain patients with such conduction delays, resynchronization by biventricular pacing may improve left ventricular (LV) filling time, reduce mitral regurgitation, and lessen dyskinesis. Together, these benefits often improve contractile efficiency impressively.

Radiographic evidence of acute heart failure includes perivascular cuffing, a widened vascular pedicle, blurring of the hilar vasculature, and diffuse infiltrates that tend to spare the costophrenic angles. Unlike pneumonia and acute respiratory distress syndrome (ARDS), these infiltrates tend to lack air bronchograms and are usually unaccompanied by an acute change in heart size. Chronic CHF is typified by Kerley B lines, dilated cardiac chambers, and increased cardiac dimensions.

The increased stretching of myocardial tissue in response to ventricular overload promotes the release of two endogenous natriuretic peptides: atrial natriuretic peptide (ANP) and B-type natriuretic peptide (BNP). Cardiac natriuretic peptides can lower excessive levels of angiotensin II, aldosterone, and endothelin I (another endogenous vasoconstrictive peptide) thus inducing a variety of beneficial effects—arterial and venous vasodilation, enhanced diuresis, and inhibition of sodium reabsorption.

ANP is stored within granules in the atria and ventricles, so even a minor amount of cardiac muscle stretch, such as that resulting from routine exercise, can cause an efflux of this peptide into the circulation. BNP, by contrast, is synthesized within the ventricles, and only minimal amounts are stored in granules. Instead, BNP is synthesized de novo, or as needed, in response to left ventricular wall elongation secondary to myocardial stress (e.g., volume overload). Thus, the BNP compensatory response to myocardial injury usually (but not invariably) indicates ventricular dysfunction or distention. BNP (and the closely related, less quickly degraded N-terminal BNP) levels consistently rise above their normal values in patients with CHF. The diuretic and vasodilating properties of BNP point to a potentially important role for this peptide, not only as a diagnostic tool in CHF but also as a treatment option for well-selected patients (e.g., nesiritide). To date, this therapeutic potential has not been fully realized (see below).

BNP measurements can provide useful information for excluding CHF, indicating its severity, tracking progress, and gauging likely outcome. Unfortunately, BNP is not selective for cardiac filling status, as it also increases in a variety of lung diseases, renal insufficiency, sepsis, and inflammatory states.

When faced with a patient who appears to have pulmonary venous congestion, a number of key questions should be asked in determining its etiology.

1. **Is forward output adequate to perfuse vital tissues?** When perfusion is severely impaired, consideration should be given to mechanical ventilation and invasive hemodynamic monitoring, especially in the setting of coexisting pulmonary venous congestion and lactic acidosis. Reducing tissue O_2 demand and correcting disturbances in oxygen content, serum pH, electrolyte balance, and ventricular loading conditions are of prime importance. Inotropic or vasopressor therapy may be indicated for hypotension, whereas hypertensive patients and those with a highly elevated SVR may benefit from vasodilators.
2. **Is there evidence of systolic dysfunction?** Adequate perfusion does not necessarily imply intact systolic function—forward output may be maintained at the cost of high preloading pressures and pulmonary vascular congestion. If perfusion is adequate and systolic function of cardiac valves and myocardium remains intact,

   the patient may simply be volume overloaded or manifesting diastolic dysfunction. Echocardiography helps greatly in this assessment.
3. **What is the LV size?** LV chamber dilation usually indicates a chronic process—most commonly long-standing ischemic heart disease, cardiomyopathy, or LV diastolic overload (aortic or mitral valvular insufficiency). Therapy in such cases should be directed at optimizing afterload (with systemic vasodilators) or at improving myocardial oxygen supply (coronary vasodilators). If there is excessive inspiratory effort, mechanical ventilation can reduce both O_2 demand and left ventricular afterload by raising inspiratory and mean pleural pressures. If left ventricular cavity size is normal, mitral stenosis, tamponade, constrictive pericarditis, acute myocardial infarction, hypertrophic cardiomyopathy, or diastolic dysfunction should be suspected. Left ventricular wall hypertrophy, myocardial infiltration, or interdependence with a swollen RV may limit stroke volume and cardiac output, despite normal contractility. A distended left atrium sometimes provides a clue in such cases.
4. **Does the LV show global or regional hypokinesis?** Regional hypokinesis/dyskinesis suggests localized disease (e.g., ischemia or infarction). Stress cardiomyopathy (Takotsubo) may temporarily show the signature findings of apical ballooning with preserved basilar contraction. Echocardiography and precordial electrocardiography (ECG) are instrumental in this assessment. Generalized hypokinesis of a heart with normal chamber size often reflects the stunned myocardium of trauma, diffuse ischemia, drug overdose, toxin ingestion, or post-tachycardia dysfunction.
5. **Is there evidence for valvular dysfunction?** Aortic stenosis may depress cardiac output by causing excessive afterload, myocardial ischemia, or hypertrophic impairment of ventricular filling. Mitral regurgitation impairs forward output and produces congestive symptoms by allowing partial retrograde venting of the ejected volume. Acute chamber enlargement (regardless of cause) may worsen congestive symptoms by producing transient mitral regurgitation because of papillary muscle dysfunction or mitral ring dilation.
6. **Is there evidence for increased pulmonary vascular permeability or hypoalbuminemia?** The tendency to form pulmonary edema relates not only to hydrostatic pressure but also to the plasma oncotic pressure and pulmonary capillary permeability. Hence, edema may form at a relatively low pulmonary venous pressure if oncotic pressure is reduced or the microvascular endothelium is leaky (ARDS). Conversely, the lungs may remain relatively dry despite high left heart filling pressures when enlarged lymphatic drainage channels with

greater capacity have had time to develop (e.g., mitral stenosis). Kerley lines are the radiographic signatures of lymphatic dilation.

The physical examination should be directed toward the detection of hypoperfusion (reduced mental status, oliguria) and compensatory vasoconstriction (reduced skin temperature, prolonged capillary filling time, etc.). Rales (crackles) are often difficult to detect in bedridden patients who breathe shallowly and in those receiving mechanical ventilatory support. Auscultation of gravitationally dependent regions is mandatory. The chest X-ray (CXR) provides key information regarding heart size, vascular distribution, pulmonary infiltrates, and pleural effusions. Computed tomography using reconstructive imaging techniques is informative in questionable cases—as when the chest wall interferes with CXR interpretation. Echocardiography and radionuclide ventriculography provide important information regarding chamber size, contractility, diastolic filling, valvular function, P_{RA}, pericardial volume, and filling status of the central pulmonary veins. Although transesophageal echocardiography is not always feasible to perform, the detail it provides is generally superior to its transthoracic counterpart, especially in patients with obstructive lung disease or massive obesity.

Therapeutics

As a general rule, the therapy of CHF should be geared to document pathophysiology. Reversal of abrupt-onset tachycardias and arrhythmias is frequently the key to relieving congestion, especially in patients with valve dysfunction, or stiff or ischemic hearts. Whereas diuretics help in most cases, inotropic and vasoactive agents should be reserved for documented disorders of myocardial function refractory to adjustments of filling pressure, pH, and electrolytes. Angiotensin-converting enzyme (ACE) inhibitors (e.g., captopril, enalapril) and/or systemic vasodilators should be used when an elevated SVR and/or valvular insufficiency are documented in the setting of adequate preload and blood pressure. Nitrates may aid cardiac ischemia but can

precipitate hypotension in patients with borderline or inadequate filling pressures. New-onset atrial or ventricular arrhythmias or conduction disturbances (e.g., atrial fibrillation, atrial flutter, heart block) should be treated aggressively if they reduce forward output or cause pulmonary edema (see Chapter 4).

Although calcium channel blockers can benefit congestive failure by controlling hypertension, slowing tachycardia, or reversing coronary spasm, they should only be used in well-selected patients; these agents depress cardiac contractility and may impair conduction. In similar fashion, β-Blockers reduce myocardial oxygen consumption by decreasing the heart rate and contractility but have the potential to precipitate CHF, conduction system disturbances, or bronchospasm. β-Adrenergic blockade should be reserved for cases of documented ischemia or other firm indications (e.g., thyroid storm, delirium tremens, uncontrolled supraventricular tachycardia). They should not be considered first-line measures in other acute forms of CHF.

Nesiritide, hBNP, a 32-amino acid recombinant human BNP, represents a unique treatment for acutely decompensated CHF (ADHF) and was the first drug introduced in its class. hBNP has been approved for the IV treatment of patients with ADHF who have dyspnea at rest or with minimal exertion. hBNP has been shown to exert potent vasodilatory effects and to effect significant diuresis and natriuresis in patients with severe CHF. In patients with ADHF, hBNP also has been shown to significantly decrease plasma norepinephrine and aldosterone levels, as well as cardiac preload and vascular resistance, without stimulating the changes in heart rate seen with inotropic agents. When added to standard therapy in the treatment of ADHF, hBNP improves hemodynamic function to a significantly greater extent than nitroglycerin (see Chapter 3). Its use has become somewhat controversial, however, as it may cause profound hypotension, bradycardia, and renal dysfunction in some patients.

Another promising class of noncatecholamine-based agents is the calcium sensitizers. The initial representative of this category is levosimendan, a drug that is marketed but yet to be deployed on a wide scale (see Chapter 3).

It has distinct inotropic and vasodilating properties and must be used only with particular caution in patients who have severely impaired kidney or liver function and in those who are hypotensive and tachycardic.

Right Ventricular Dysfunction

Certain disease conditions account for the great majority of acute problems arising primarily from RV dysfunction: RV ischemia and infarction; cor pulmonale complicating parenchymal, vascular, or hypoventilatory hypoxemic lung diseases (e.g., sleep apnea); and ARDS.

Right Ventricular Infarction

The RV receives the majority of its blood supply from the right coronary artery. It is not surprising, therefore, that RV infarction complicates as many as 30% of inferior myocardial infarctions, as well as a smaller percentage of anterior infarctions. The diagnosis should be suspected when there are signs of systemic venous hypertension, an unimpressive or clear CXR, and evidence of ST segment elevation or Q waves over the right precordium (V_4R). A suggestive enzyme profile confirms the diagnosis. In the initial phase of management, RV infarctions typically demand aggressive administration of intravenous fluids to sustain optimal blood pressure and cardiac output. The LV may be required to take up the work of pumping blood through both the systemic circuit (directly) and the pulmonary circuit (indirectly), using ventricular interdependence. Dilatation of the RV and fluid loading tighten these linkages by crowding the two ventricles within the pericardial sac, stretching shared circumferential muscle fibers, and shifting the mobile interventricular septum. Recovery from, accommodation to, or compensation for RV infarction tends to occur over several days. If cardiac output can be supported during this interval, the outlook for patients without other cardiopulmonary diseases is generally good. Prognosis depends not only on the size of the infarction but also on the presence or absence of increased PVR.

Cor Pulmonale

Pathogenesis

In its purest form, *cor pulmonale* (see Chapter 21) is defined as hypertrophy, dilatation, or failure of the RV in response to excessive PVR. By definition, this term excludes cardiomyopathy or secondary changes in RV function resulting from pulmonary venous hypertension or LV failure. Three reinforcing causes of pulmonary hypertension are a restricted capillary bed, alveolar hypoxia, and acidosis. Although extensive obliteration, occlusion,

constriction, or compression of the capillary bed may be the underlying cause, increased cardiac output and superimposed hypoxemia or acidosis may dramatically elevate pulmonary arterial pressure (P_{PA}). The normal RV cannot sustain adequate forward output at mean pulmonary arterial pressures that exceed approximately 35 mm Hg. Given sufficient time, however, the RV wall can thicken sufficiently to generate pressures that rival those in the systemic circuit. Arterial smooth muscle also hypertrophies over time, intensifying the response to alveolar hypoxemia and pharmacologic vasoconstrictors. Most diffuse pulmonary insults can raise the PVR enough to decompensate an already compromised RV. Massive pulmonary embolism is the most common cause of acute cor pulmonale in a patient without prior cardiopulmonary abnormality. In mechanically ventilated patients, lung overdistention with attendant capillary compression may markedly accentuate RV loading.

Chronic cor pulmonale can result from severe lung disease of virtually any etiology (especially those that obliterate pulmonary capillaries and induce chronic hypoxemia). Acutely decompensated cor pulmonale occurs frequently in patients with chronic obstructive pulmonary disease (COPD). In such patients, RV afterload can fall dramatically with correction of bronchospasm, hypoxemia, and acidosis. Because about one half of the normal pulmonary capillary bed can be obstructed without raising the resting mean P_{PA} significantly above the normal

range, pulmonary hypertension in a normoxemic person at rest usually signifies an important reduction in the number of patent pulmonary capillaries. After the capillary reserve has been exhausted, P_{PA} varies markedly with cardiac output. Thus, in a predisposed patient, elevations of baseline pulmonary arterial pressure often signify variations in cardiac output, rather than worsening of lung pathology.

Diagnosis

The measurement of central venous pressure (CVP), pulmonary artery occlusion ("wedge") pressure (P_w), and the computation of PVR help separate right from left heart disease. Echocardiography is an invaluable diagnostic adjunct, often allowing estimation of pulmonary arterial pressure as well as providing detailed anatomical information regarding the dimensions and functions of the two ventricles. The physical findings of acute cor pulmonale are those of pulmonary hypertension: hypoperfusion, RV gallop, and a loud P_2. Pulsatile hepatomegaly, systemic venous congestion, a parasternal lift, and peripheral edema strongly implicate RV failure and severe pulmonary hypertension. Deep breathing may accentuate these right heart findings, as inspiratory increases of blood flow returning to the thorax raise P_{PA} and stress the compromised RV. Unfortunately, many of these signs are difficult to elicit in patients with hyperinflated or noisy lungs.

Ancillary Diagnostic Tests

Radiographic signs of pulmonary arterial hypertension include dilated, sharply tapering central pulmonary arteries with peripheral vascular " pruning." Although precise measurements are often difficult to make, a right lower lobar artery dimension greater than 18 mm diameter (on the standard PA film) or main pulmonary arteries greater than 25 mm in diameter (judged on lateral) strongly suggest subacute or chronic pulmonary hypertension. Overall heart size may appear normal until disease is advanced, especially in patients with hyperinflation. Encroachment of the RV on the retrosternal airspace in the lateral view is an early but nonspecific sign. When renal function allows, the contrast-enhanced computed tomography (CT) scan of the thorax confirms RV dilatation. Catheter-based techniques allow computation of RV volume and/or RV ejection fraction. Beat-by-beat analysis of the thermodilution temperature profile allows both to be assessed, whereas a double indicator (dye/thermodilution) method permits determination of these indices as well as central blood volume, stroke work, lung water, and others.

ECG criteria for RV hypertrophy are insensitive and nonspecific. In acute cor pulmonale, changes characteristic of hypertrophy are lacking. P pulmonale and a progressive decrease in the *R*/*S* ratio across the precordium are sensitive but nonspecific signs. Conversely, the S_1, Q_3, T_3 pattern, right axis deviation greater than 110 degrees, *R*/*S* ratio in V_5 or V_6 less than 1.0, and a QR pattern in V_1 are relatively specific but insensitive signs.

Radionuclide ventriculography and echocardiography more reliably document RV and LV functions noninvasively. In patients with true cor pulmonale, LV systolic function should remain unaffected.

Management of Acute Cor Pulmonale

The key directives in managing cor pulmonale are to maintain adequate RV filling and perfusion, to reverse hypoxemia and acidosis, to establish a

coordinated cardiac rhythm, reverse atelectasis, and treat the underlying illness. The majority of patients with decompensated COPD and cor pulmonale have a reversible hypoxemic component. Although oxygen must be administered cautiously, patients with baseline CO_2 retention should not be denied O_2 therapy. Acidosis accentuates the effect of hypoxemia on PVR, whereas hypercarbia without acidosis exerts less effect. This should be borne in mind when deciding the advisability of buffering pH in permissive hypercapnia.

Bronchospasm, infection, and retained secretions must be addressed. When extreme polycythemia complicates chronic hypoxemia, careful lowering of the hematocrit to approximately 55% may significantly reduce blood viscosity, decrease RV afterload, and improve myocardial perfusion. To improve blood viscosity, it helps to rewarm a profoundly hypothermic patient.

The effects of digitalis, inotropes, and diuretics in acute cor pulmonale are variable; these drugs should be employed cautiously. Gentle diuresis helps relieve symptomatic congestion of the lower extremities, gut, and portal circulation. Diuresis may reduce RV distention and myocardial tension, improving both its afterload and perfusion. Any depression of cardiac output resulting from diuresis may also cause a secondary reduction of P_{PA}. In patients requiring RV distention and ventricular interdependence to sustain adequate stroke volume, vigorous diuresis or phlebotomy (now seldom practiced) may have adverse consequences. Central vascular pressures, therefore, should be carefully monitored. The effects of cardiotonic agents in the treatment of acute cor pulmonale are also unpredictable. Digitalis has only a small inotropic effect on the performance of a nonhypertrophied RV but may be helpful in chronic cor pulmonale. Though slow to take effect, digoxin often proves useful in controlling rapid heart rate in atrial fibrillation without depressing myocardial function. Inotropes such as dopamine and dobutamine can improve left ventricular function and boost the perfusion pressure of the RV. Furthermore, because the ventricles share the septum and circumferential muscle fibers, it is likely that improved left ventricular contraction benefits the RV through systolic ventricular interdependence. Associated arrhythmias and conduction disturbances, however, may disrupt the AV coordination that is so vital to effective RV filling and performance.

For a minority of patients, calcium channel blockers (e.g., nifedipine, diltiazem, amlodipine) reduce PVR and boost cardiac output by decreasing RV afterload. This effect, however, is highly variable; these drugs may also depress myocardial function and/or reduce coronary perfusion pressure. Evaluation of response is best conducted cautiously during formal cardiac catheterization before they are prescribed. For patients with a clearly reversible component to the pulmonary hypertension, inhaled nitric oxide (or aerosolized prostacyclin [Flolan]) may prove to be a useful bridge to definitive therapy or physiologic adaptation. Unfortunately, tolerance to nitric oxide rapidly develops and in itself does not provide a long-term solution. For patients with severe ongoing pulmonary hypertension, anticoagulation is thought advisable. Several therapies recently released into clinical practice hold promise for chronic use in some patients with reactive pulmonary vasculature. These include epoprostenol, treprostinil, bosentan, and sildenafil and their derivatives.

Acute Respiratory Failure

Mechanisms of Circulatory Impairment in ARDS

Although cardiac output usually increases during the early stage of ARDS in response to the precipitating stress or in compensation for hypoxemia, this is less often true when the illness is far advanced. The performance of one or both ventricles may deteriorate as the lung disease worsens, compounding the problem of inadequate tissue O_2 delivery. The cardiac dysfunction that accompanies advanced respiratory failure is incompletely understood. Effective preload may be reduced by PEEP, third spacing, capillary leakage, and myocardial stiffening secondary to ischemia or catecholamine stimulation. Contractility of either ventricle may be impaired by hypotension, ischemia, electrolyte abnormalities, or cardiodepressant factors released during sepsis, injury, or other inflammatory condition. Compression, obliteration, and hypoxic vasoconstriction of the pulmonary vasculature impede ejection of the afterload-sensitive RV, a low pressure-high capacity pump. Increased wall tension also tends to diminish RV perfusion. Severe pulmonary hypertension is an ominous sign in the later stages of ARDS.

Assessing Perfusion Adequacy

The assessment of perfusion adequacy in ARDS is addressed in detail elsewhere (see “Oxygenation Failure,” Chapter 24). However, a few points deserve emphasis here. Individual organs vary widely with regard to O_2 demand, completeness of O_2 extraction, and adaptability to ischemia or hypoxia. Cerebral and cardiac tissues are especially

vulnerable to hypoxemia. In these organs, the O_2 requirement per gram of tissue is high, O_2 stores are minimal, and O_2 extraction is relatively complete—even under normal circumstances. Subtle changes in mental status may be the first indication of hypoxemia, but the multiplicity of potential causes (e.g., early sepsis, dehydration, anxiety, sleep deprivation, drug effects) renders disorientation and lethargy difficult to interpret. Although cool, moist skin often provides a valuable clue to inadequate vital organ perfusion, vasopressors, and disorders of vasoregulation common to the critically ill patient reduce the utility of this finding.

The kidney usually provides a window on the adequacy of vital organ perfusion through variation of its urine output, pH, and electrolyte composition. Adequate urine volume and sodium and bicarbonate excretion suggest sufficient renal blood flow when the kidneys are normally functioning. Unfortunately, rather than reflecting the adequacy of perfusion, variations in urine volume and alterations of urine composition are often due to drug effects, diurnal variations, and or glomerular or tubular dysfunction. As sustained hypoperfusion activates anaerobic metabolic pathways, arterial pH and bicarbonate concentrations decline and lactic acid levels rise, widening the anion gap. Although adequacy of cardiac output can seldom be determined unequivocally by any single calculated index, analysis of the O_2 contents of arterial and mixed venous blood is valuable when addressing questions of tissue O_2 supply and utilization. In recent years, near-infrared spectrophotometry, gastric mucosal pH, and sublingual PCO_2 have been investigated as markers of insufficient O_2 delivery to vital organs. Despite the potential value of such indices, inadequacy of systemic O_2 delivery is perhaps best judged from a battery of indicators, including the clinical examination of perfusion-sensitive organ systems (urine output and composition, mental status, ECG, etc.), the cardiac index, SVR, the presence or absence of anion gap acidosis, lactate levels and trends, the mixed venous oxygen saturation (SvO_2), and the calculated O_2 extraction.

Table 1-3. Causes of Pericarditis

Infections	Dissecting Aneurysm	Malignancy
Viral	Rheumatologic diseases	Trauma
TB	Dressler syndrome	Uremia
Bacterial	Anticoagulation	Radiation
Fungal	Myocardial infarction	Drugs

Improving Perfusion Adequacy in ARDS

Apart from efforts to improve cardiac output and arterial O_2 content (e.g., reversal of profound anemia, inotropic, or vasoactive drugs), tissue oxygenation and perfusion may be enhanced by reducing metabolic demand. Metabolic needs (and perfusion requirements) may be decreased impressively by controlling sepsis and fever,

alleviating anxiety and agitation, and providing assistance (O_2, bronchodilators, ventilatory support) to reduce the work of breathing. Therapy directed at improving cardiac output in the setting of ARDS should be guided by assessing the heart rate, contractility, and the loading conditions of each ventricle independently. Minor elevations of pulmonary venous pressure exacerbate edema, necessitating higher levels of PEEP, mean airway pressure, and supplemental O_2. Attempts should be made to reduce RV afterload by correcting hypoxemia and acidosis. Although a certain minimum level of PEEP must be maintained in the early phase of ARDS to avoid ventilator-induced lung damage, unnecessary elevations of mean airway pressure may overdistend patent lung units, thereby compressing alveolar capillaries and accentuating the impedance to RV ejection. Prone positioning may be a very helpful alternative.

Pericardial Constriction and Tamponade

The pericardium normally supports the heart, shields it from damage or infection, enhances diastolic ventricular coupling, and prevents excessive acute dilatation of the heart. In the intensive care unit (ICU), three types of pericardial disease are noteworthy: acute pericarditis, pericardial tamponade, and constrictive pericarditis.

Acute Pericarditis

Acute pericardial inflammation arises from diverse causes (Table 1-3). The characteristic complaint is chest pain, eased by sitting and leaning forward and aggravated by supine positioning, coughing, deep inspiration, or swallowing. Dyspnea, referred shoulder pain, and sensations of chest or abdominal

pressure are frequent. Unless muffled by effusion, pericarditis can usually be detected on physical examination by a single phase or multicomponent friction rub. The rub is often evanescent or recurrent, best heard with the patient leaning forward and easily confused with the crunch of pneumomediastinum, a pleural rub, coarse rhonchi, or an artifact of the stethoscope moving against the skin. Early ECG changes include ST segment elevation, which, unlike the pattern in acute myocardial infarction, is concave upward and typically present in all leads except AVR and V_1. The reciprocal depression pattern of regional infarction is absent. Initially, the T waves are upright in leads with ST segment elevation—another distinction from acute infarction. Depression of the PR segment occurs commonly early in acute pericarditis. The ST segments return to baseline within several days, and the T waves flatten. Troponins may be mildly elevated. Unlike acute myocardial infarction, ST segments usually normalize before the T waves invert. Eventually, T waves revert to normal, but this process may require weeks or months to complete. Management of uncomplicated pericarditis (without tamponade) includes careful monitoring, treatment of the underlying cause, and judicious use of nonsteroidal antiinflammatory agents for selected cases. Anticoagulation, though not absolutely contraindicated, should be recognized as posing some hazard. Occasionally, pericarditis is complicated by hydraulic cardiac compression (tamponade) or the development of a constricting pericardial sac.

Pericardial Tamponade

Although pericardial fluid tends to reduce pain and discomfort by buffering the friction between the heart and pericardium, the rapid accumulation of pericardial fluid may compress the heart, resulting in tamponade (see Chapter 3). At least 250 mL of fluid must collect before an obviously enlarged heart shadow is noted on the chest roentgenogram; a normal or unchanged chest film does not exclude the presence of a hemodynamically important effusion. Echocardiography is considerably more sensitive but not infallible. Effusions that cause tamponade can be circumferential, asymmetrical, or loculated. In the supine patient, small unloculated effusions pool posteriorly. Common settings include post-op from thoracic surgery, chest trauma, and catheterization or endovascular instrumentation (e.g., misplaced guidewires and/or central venous catheters).

Tamponade physiology classically results in a triad of low arterial pressure, elevated neck veins, and a quiet

precordium, and in its extreme form can produce pulseless electrical activity (PEA). Recumbency intensifies dyspnea, whereas sitting upright tends to relieve it. Although tamponade is properly considered a diagnosis founded on history and physical examination, massive obesity interferes with making a confident diagnosis from physical signs alone. Low QRS complex voltage and some degree of electrical variation are sometimes observed on the ECG tracing, but these classical findings are not reliable. (The ECG does help, however, in ruling out other diagnostic possibilities.) Arterial pressure tracings disclose exaggerated reductions of systolic pressure, a shared characteristic of the conditions that tend to mimic it. These include tension pneumothorax, severe gas trapping (auto-PEEP), massive pulmonary embolism, and cardiogenic shock. Echocardiography helps confirm the diagnosis of tamponade, serving as an invaluable bedside aid in distinguishing among these differential possibilities. Right atrial collapse in the face of distended central veins is a *sensitive* indicator, but RV collapse is more *specific*.

As fluid accumulates, nonspecific ECG findings include reduced QRS voltage and T wave flattening. In this setting, electrical alternans suggests the presence of massive effusion and tamponade. Although echocardiographic quantification of effusion size is imprecise, it is the most rapid and widely used technique. Large pericardial effusions (>350 mL) give rise to anterior echo-free spaces and exaggerated cardiac swinging motions. Diastolic collapse of the right heart chambers suggests a critical degree of fluid accumulation and tamponade. Alternative diagnostic techniques include the CT scan with intravenous contrast and the MRI scan (when feasible).

Physiology of Pericardial Tamponade

Acute pericardial tamponade is a hemodynamic crisis characterized by increased intracardiac pressures, limitation of ventricular filling throughout diastole, and reduction of stroke volume. Normally, intrapericardial pressure is similar to intrapleural pressure, but less than either right or left ventricular diastolic pressures. Rapid accumulation of pericardial fluid causes sufficient pressure within the sac to compress and equalize right and left atrial pressures, reducing maximal diastolic dimensions and stroke volume. Reflex increases in heart rate and adrenergic tone initially maintain cardiac output. In this setting, any process that quickly reduces venous return or causes bradycardia (e.g., hypoxemia, β-blockade) can precipitate shock.

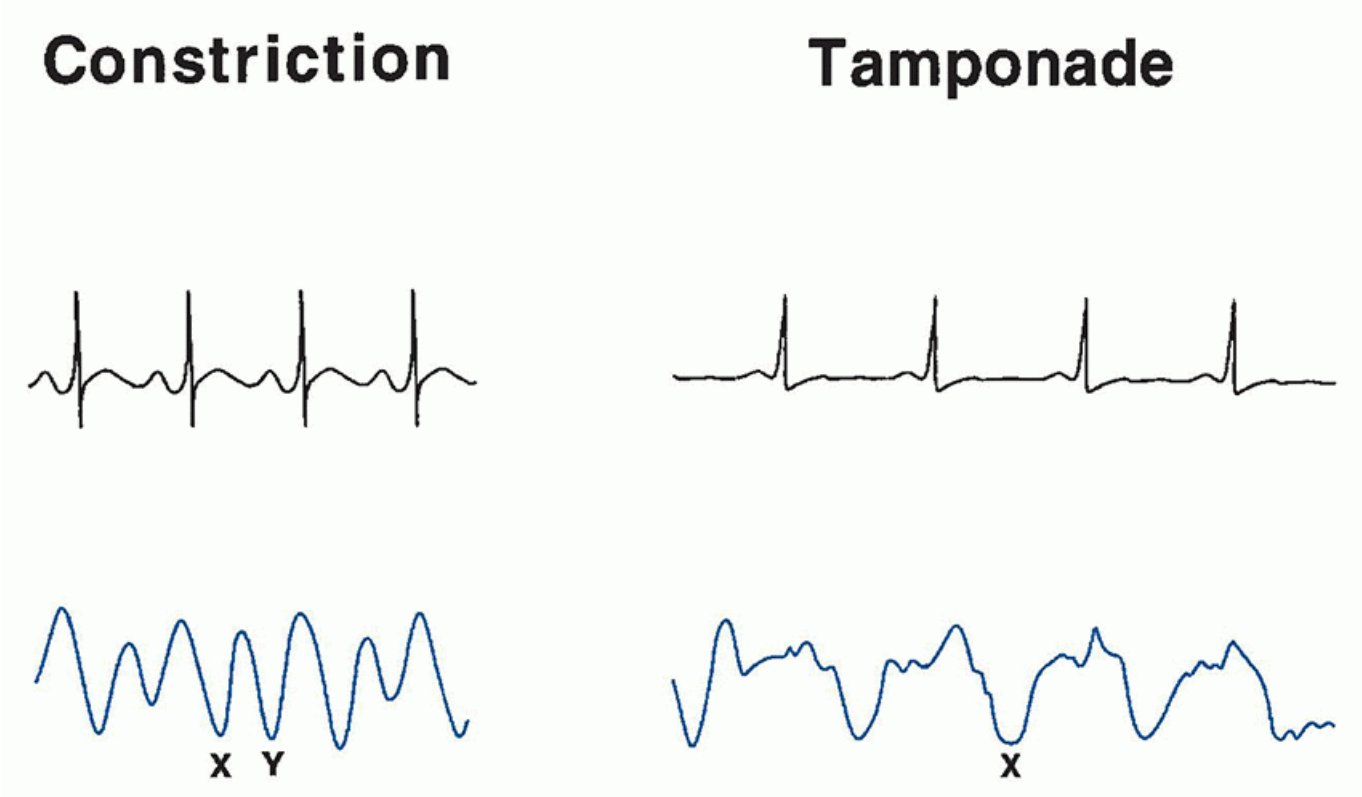

FIGURE 1-9. Contrast of pericardial constriction and tamponade as reflected in CVP tracings (lower panels). Unlike the venous pressure tracing of constriction, the "Y descent" is attenuated in tamponade because early diastolic filling is impaired. The systolic "X descent" is well preserved in both conditions.

Tamponade alters the dynamics of systemic venous return and cardiac filling (Fig. 1-9). As cardiac volume transiently decreases during ejection, pericardial pressure falls, resulting in a prominent X descent on the venous pressure tracing. Tamponade attenuates the normal early diastolic surge of ventricular filling and abolishes the Y descent (its representation on the venous pressure tracing). Pulsus paradoxus, a result of exaggerated normal physiology, may develop simultaneously. Inspiration is normally accompanied by an increase in the diastolic dimensions of the RV and a small decrease in LV volume. These changes reduce LV ejection volume and systolic pressure (<10 mm Hg) during early inspiration. Pericardial tamponade accentuates this normal fluctuation to produce pulsus paradoxus. With an arterial line in place, paradoxical pulse is easily quantified by noting the respiratory variation of systolic pressure during the end-inspiratory and end-expiratory phases of the ventilatory cycle. Paradoxical pulse can also be detected in traditional fashion by lowering the cuff pressure of a sphygmomanometer slowly from a point 20 mm Hg above systolic pressure until the Korotkoff sounds are heard equally well throughout both inspiration and expiration. The "paradox" is the difference between the pressure at which systolic sound is first audible and the point at which the systolic sound is heard consistently throughout the respiratory cycle. Pulsus paradoxus and certain other hemodynamic manifestations of pericardial tamponade depend on inspiratory augmentation of systemic venous return; as the RV swells, it restricts left ventricular chamber volume. Paradox may be absent in pericardial tamponade if underlying heart disease markedly elevates left ventricular diastolic pressure or if the LV fills by a mechanism independent of respiratory variation (e.g., aortic regurgitation). It may be hard to detect in the presence of tachycardia or arrhythmia.

Clinical Manifestations of Pericardial Tamponade

Reduced systemic arterial pressure and pulse volume, systemic venous congestion, and a small, quiet heart comprise the classic presentation of pericardial tamponade. However, other disorders, including obstructive pulmonary disease, restrictive cardiomyopathy, RV infarction, massive pulmonary embolism, and constrictive pericarditis, may also present with systemic venous distention, pulsus paradoxus, and clear lungs. Hyperactivity

of the adrenergic nervous system is evidenced by tachycardia and cold, clammy extremities. The most common physical findings are jugular venous distention and pulsus paradoxus. However, tachypnea may render these signs difficult to elicit. Orthopnea that is not explained by neuromuscular weakness, obstructive lung disease, or pulmonary edema warrants strong consideration of tamponade.

Laboratory Evaluation

No feature of the CXR is diagnostic of pericardial tamponade. Electrical (QRS) alternans on the ECG in a patient with a known pericardial effusion is suggestive, but not definitive evidence. Electrical alternans may also occur with constrictive pericarditis, tension pneumothorax, severe myocardial dysfunction, and after myocardial infarction. Adjunctive studies are needed to confirm tamponade physiology. Apart from demonstrating pericardial fluid, the echocardiogram can provide additional clues. These

include reduction of the "E to F" slope, brisk posterior motion of the intraventricular septum during inspiration, RV diastolic collapse, prominent "swinging" of the heart, and exaggerated inspiratory increases and expiratory decreases in RV size. Yet, however suggestive they may be, the findings of a single echocardiographic study cannot predict the presence or severity of pericardial tamponade. Cardiac catheterization confirms the diagnosis, quantifies the magnitude of hemodynamic compromise, and uncovers coexisting hemodynamic problems. Catheterization typically demonstrates an elevated P_{RA} with a prominent systolic X descent and diminutive or absent Y descent (Fig. 1-9). There is elevation and diastolic equilibration of intrapericardial, RV, and left ventricular pressures ("equalization"). RV diastolic pressures lack the "dip and plateau" configuration characteristic of constrictive pericarditis.

Management

In pericardial tamponade, it is essential to maintain adequate filling pressure and heart rate. Peripheral vascular tone must be maintained with pressors, if needed. Volume depletion (e.g., excessive diuresis), hypoxemia, and β-blockade (and other causes of bradycardia) can be life-threatening. As a general rule, fluids should be "wide open" and sinus tachycardia—a compensatory response—left untreated. Intubation of the airway must not be performed unnecessarily and when delay is not prudent, performed only with extreme caution. Positive pressure can further reduce cardiac filling, and vasodilation may drop the central pressures needed for compensation. Because the pressure-volume curve of the distended and liquid-filled pericardial sac is very steep, aspirating 50 to 100 mL of fluid usually leads to a striking reduction in intrapericardial pressure and improvements of systemic arterial pressure and cardiac output. Pericardiocentesis lowers the diastolic pressures in the pericardium, right atrium, RV, and LV and reestablishes normal pressure gradients.

Pericardial fluid can be evacuated by one of three methods: needle pericardiocentesis, pericardiotomy via a subxiphoid window (often under local anesthesia), or pericardiectomy. During pericardiocentesis, the probability of success and the safety of the procedure relate directly to the size of the pericardial effusion. Whereas partial drainage of a massive pericardial effusion may be lifesaving, aspiration of a small pericardial effusion (<200 mL) that is freely mobile within the pericardial sac may be only marginally helpful. A significant hemodynamic effect is also unusual in the absence of a documented anterior effusion, or when loculated clot or fibrin inhibits the free withdrawal of fluid. Pericardiocentesis must not be undertaken by inexperienced personnel or in an inappropriate environment. Needle aspiration should be conducted whenever possible in the cardiac catheterization suite by an experienced cardiologist, using fluoroscopic and needle electrode ECG guidance. Complications include coronary laceration, pneumothorax, myocardial injury, and life-threatening arrhythmias.

Subxiphoid pericardiotomy can be performed safely under local anesthesia in certain critically ill patients. Regardless of drainage method, successful relief of tamponade is documented by the fall of intrapericardial pressure to normal, the reduction of elevated P_{RA}, separation of right from left heart filling pressures,

augmentation of cardiac output, and disappearance of pulsus paradoxus. After drainage, the majority of patients should be closely monitored for at least 24 hours in the ICU for evidence of recurrent tamponade. Persistent elevation and equilibration of right and left ventricular diastolic pressures after pericardiocentesis or subxiphoid pericardiotomy suggests a component of pericardial constriction. Pericardiectomy may be required in patients with a component of constriction and in those who experience recurrent tamponade despite repeated needle or subxiphoid drainage.

Constrictive Pericarditis

Constrictive pericarditis results from a confining pericardial shell that prevents adequate chamber filling. Although both constriction and tamponade are characterized by elevation and equilibration of right and left ventricular diastolic pressures, they can be differentiated by several key hemodynamic features (Table 1-4). Constrictive pericarditis limits filling primarily in late diastole, whereas tamponade affects filling throughout. Whereas constrictive pericarditis may sometimes demonstrate atrial pressure changes reminiscent of tamponade, the RV pressure contour usually shows a prominent dip and plateau ("square root") configuration. Pericardial constriction can be mimicked by restrictive or ischemic cardiomyopathy: in both conditions, RV and left ventricular diastolic pressures are elevated, SV and cardiac output are depressed, left ventricular end-diastolic volume is normal or decreased, and end-diastolic filling is impaired. Common ECG findings include low QRS voltage, generalized T wave flattening or inversion,

and an atrial abnormality suggestive of P mitrale. Because constrictive pericarditis tends to progress inexorably, surgical intervention is eventually required if the patient is an otherwise appropriate candidate. Hemodynamic and symptomatic improvement is evident in some patients immediately after operation; in others, however, improvement may be delayed for weeks or months.

Table 1-4. Tamponade Versus Constriction

Feature	Pericardial Tamponade	Constrictive Pericarditis
Radiographic heart "shadow"	↑ or ↑ ↑	↔ to ↑ ↑
Kussmaul sign	Usually absent	Usually present
Pulsus paradoxus	Very prominent	May be absent
RV tracing	Prominent X descent	Dip and plateau
RA tracing	Negligible Y descent	M or W contour
		Prominent Y descent
Pericardial fluid	Always present	May be present
ECG	Often reduced amplitude Alternans possible	Low QRS T wave depression

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Chapter 2
Hemodynamic Monitoring

• Key Points

1. As a general principle, therapeutic decisions are usually best guided by dynamic variables and evaluation of integrated patient responses as opposed to static vital signs and vascular pressures interpreted in relation to fixed targets. Such "functional" monitoring has a better chance to gauge fluid responsiveness and adequacy of cardiac output.
2. The complete hemodynamic profile includes ultrasonic, blood gas, lactate, and data from invasive catheterization. Although now used less frequently, the pulmonary artery catheter often provides data of value that cannot otherwise be collected or monitored.
3. Arterial blood pressure monitoring and waveform analysis are an invaluable aid to the management of patients with shock, hemodynamic instability, respiratory compromise, or brain injury and should be strongly considered in those who are in need of frequent BP or arterial blood gas assessment.
4. Before using hemodynamic information derived from catheter measurements, the transducer system must be accurately zeroed and calibrated, usually an automated function. The dynamic pressure response of the catheter-transducer system should be checked by the rapid flush technique ("snap test").
5. All vascular pressures of interest are influenced to varying degrees by variations in pleural pressure. Respiratory fluctuations of pleural pressure are conditioned by the alveolar pressure transmission fraction: $C_l/(C_l + C_w)$.
6. It is always hazardous to infer the status of a dynamic system from a single number. The monitored "challenge" is a key maneuver in determining hemodynamic reserves. This may involve reversible noninvasive maneuvers (e.g., a change of measurement of respiratory pulse pressure variation during passive breathing, leg lifting) or rapid fluid bolusing. A notable improvement in key target variables (cardiac output, systemic blood pressure) without the development of symptoms or excessive cardiac filling pressures encourages an increase in the rate of fluid administration.
7. A comprehensive hemodynamic profile includes sampling of mixed or central venous blood for O_2 saturation, a comparison of central venous and pulmonary artery wedge pressures, and calculations of systemic vascular resistance and pulmonary vascular resistance. Without such information, adequacy of cardiac output and mechanisms of hemodynamic impairment are often difficult to determine.
8. Echocardiogram and ultrasound provide vital data that complement catheterization and physical examination. Wall motion abnormalities, ventricular contractility, chamber dimensions, dynamics of the central veins, diastolic properties, and valve functioning are well evaluated by this noninvasive method. The pulmonary artery (Swan-Ganz) catheter remains an excellent option for well-selected patients whose clinicians understand the physiologic data stream it provides.

CONDITIONAL IMPORTANCE OF MONITORING HEMODYNAMICS AND FLUID STATUS

Restoring normal perfusion to the vital organs is an undeniable objective of resuscitation and management. However, determining the adequacy and functional status of the cardiovascular system that powers the circuit and distributes nutritive blood flow requires evaluation of its multiple components and of tissue responses to fluid

and drug challenges so that culprit variables can be logically addressed. A panel of observations is required, as no simple indicator exists that characterizes vascular filling

status, cardiac functioning, and tissue response. Before an overt shock state is established in sepsis, for example, compensatory changes in vascular tone, cardiac contractility, venous capacitance, and heart rate may support mean blood pressure (BP) and mask the need for volume resuscitation.

As a general principle, therapeutic decisions are usually best guided by dynamic variables and evaluation of integrated patient responses as opposed to static vital signs and vascular pressures interpreted in relation to fixed targets. For example, an abnormally low mean systemic BP of 60 mm Hg may appropriately signal inadequate perfusion and the requirement for fluid resuscitation if observed in conjunction with rapid tachycardia, whereas the same pressure with normal heart rate does not necessarily carry the same significance. The primary therapeutic tools at hand for addressing hemodynamic imbalances are vascular volume expansion, inotropes, pressor agents, and reduction of metabolic demand (as with ventilator support). Excesses of any of these interventions, however, have deleterious consequences.

Unguided and indiscriminate administration of fluid has the potential to harm. Sufficient fluid must be provided to fully prime the system; but it should be kept in mind that restoring arterial pressure does not assure appropriate vital organ perfusion. Mean arterial pressure (MAP) may be normalized by modest fluid and vasopressors despite inadequate vascular filling, insufficient regional flows, and ongoing tissue ischemia. The converse is also true; hypotension does not always respond to aggressive fluid administration alone. In fact, indiscriminate fluid loading in hypotensive patients with sepsis increases cardiac output (CO) only half the time. Early catecholamine support of BP is often required to optimize perfusion during fluid resuscitation. Such nuances of requirements and response emphasize that unguided practices regarding fluid management are concerning, as any surplus not eliminated by the kidneys will appear as pulmonary or systemic organ edema. Recent work indicates that significant cumulative excesses of administered fluid are associated with adverse outcomes.

Even appropriate and careful attention to hemodynamics does not guarantee that the targeted tissues will always benefit. Although acute deficiencies of perfusion promote anaerobic metabolism and must be reversed, tissues may eventually conform to continued oxygen privation over time. Moreover, pushing CO and oxygen delivery does not necessarily mean that the mitochondria will be able to take advantage of this increased O_2 supply. Impaired hemodynamics is *not* always the primary problem in shock states. Perhaps for this reason, reaching normal or even supranormal targets for O_2 delivery does not assure better outcome—perhaps in some cases, quite the opposite. Making judgments regarding interventions must be guided by objective and quantifiable data.

Nutritive blood flow is delivered with energy supplied by the heart, and fundamental principles of physics indicate that the energy per minute expended is the product of flow and pressure. It is logical, then that the important global indicators of performance are either flow based (CO, stroke volume) or pressure based (systolic, diastolic, mean, and pulse pressures [PPs]). Because vascular resistance changes little over brief periods, variation of the PP may be considered a crude flow indicator, even though the coupling between PP and stroke volume is imprecise. If hydrostatic gradients are taken into account, the arteriovenous differences in pressure across all vascular beds are similar; flows are not because the local resistances differ. Therefore, whether a given pressure and flow profile measured at the macro level is appropriate must be monitored by metabolic responses such as anion gap and lactate (see below). But these, too, are macro-level variables. Although tissue O_2 responses to ischemia-reperfusion challenges (e.g., BP cuff inflation) can be performed at the periphery with the aid of advanced tissue oxygen sensing technologies, what we currently lack at the bedside is micro level are indicators of perfusion adequacy at the levels of the specific vital organs.

Vascular volume expansion, inotropes, vasoactive drugs, and cardiac rhythm control are the interventions

available to augment the performance of the heart. Therefore, when hemodynamics are clearly in need of support, the questions the physician must answer at the bedside are (1) Is there sufficient circulating volume to optimize preload?; (2) Will intervention-enhanced contractility or reduction of afterload boost cardiac performance? (3) Is vasomotor tone increased, normal, or decreased? (4) Are the cardiac rate and rhythm appropriate for output? To make wise decisions, reliable indicators of fluid adequacy, contractility responsiveness, and vascular tone are required. Lacking these, the answers must often be empirically determined. Nonetheless, static measures (such as arterial pressures, venous pressures, heart rate, CO, and vena caval dimensions) as well

as the dynamic responses of such “static” measures to physiologic and physician-imposed challenges (“functional monitoring”) can both provide indispensible guidance, particularly with regard to prediction of fluid responsiveness. When linked to echocardiography, venous oxygen saturation, serum lactate, and urinary output measurements, these form the logical core of today's hemodynamic evaluation.

STATIC VERSUS DYNAMIC ASSESSMENTS

Certain physical signs clearly help in the hemodynamic assessment. For a patient not on vasopressors, skin temperature, capillary refill time, and urine flow give indications of output adequacy. Heart rate and pulse volume are nonspecific but qualitatively helpful in assessing performance and adrenergic response. All of these observations from physical examination become somewhat less reliable in the patient already receiving catecholamines in high doses.

Central venous pressure (CVP), wedge pressure, and vena caval diameter by ultrasonography have long been used as indicators of preload status. These static measurements are all helpful when very high or very low, but each is influenced by intrathoracic pressure and loses specificity over the broad mid-ranges that are so frequently encountered in practice. For example, CVP is influenced by right ventricular afterload, compliance, and pleural pressure. An absolute value for CVP that is less than 8 mm Hg when receiving passive mechanical ventilation does suggest that preload reserve is barely adequate, whereas a value greater than 16 mm Hg is reassuring. However, midrange CVP values hold little information in that regard and neither accurately predicts response to a fluid challenge. This same indecisiveness applies to absolute IVC dimensions assessed by ultrasound; a diameter less than 12 mm suggests cardiac underfilling, whereas a dimension greater than 20 mm indicates adequacy. Values in between are not reliably predictive. During spontaneous breathing, the numbers will change, but the same principle holds: extremes of static values are informative, but the usually encountered midrange values are not.

Value of Dynamic Functional Monitoring

Although single (static) values of central vascular pressure have limited utility, dynamic changes in these same indicators during passive inflation are useful in predicting fluid volume responsiveness. Arterial pulse pressure, CVP, and IVC dimensions undergo phasic changes with passive positive pressure ventilation to degrees that depend upon the upstream mean systemic venous pressure to compensate. Wide tidal swings of these indicators strongly suggest fluid volume responsiveness unless there are violations of the underlying assumption that intrabreath variations of pleural pressure and preload account entirely for the observed fluctuation. Utility therefore depends on a large enough tidal swing of pleural pressure, the absence of spontaneous breathing effort, right ventricular failure, cardiac arrhythmia (variable diastolic filling), and intra-abdominal hypertension. During arrhythmia and/or spontaneous breathing, functional monitoring can still be usefully undertaken with an appropriately performed leg lift maneuver (see below).

ARTERIAL BLOOD PRESSURE MONITORING

Noninvasive Arterial Pressure Monitoring

Sphygmomanometer pressures are notoriously inaccurate when cuff width is less than two thirds of arm circumference. Spurious elevations of BP occur when measurements are made with an inappropriately narrow cuff and when arteriosclerosis prevents the brachial artery from collapsing under pressure. Conversely, because tight proximal occlusions can artifactually lower the BP, BP should initially be checked in both arms. It is always wise to compare readings obtained from an arterial line with a cuff pressure periodically and whenever the monitored number disagrees with the clinical impression. In many hypotensive patients with low CO, the "muffle" and disappearance points of diastolic pressure are poorly audible. In profound shock, all Korotkoff sounds may be lost. In this setting, Doppler ultrasonography may detect systolic pressures below the audible range.

Arterial Pressure Waveform

Normally, MAP is similar in all large arterial vessels of a supine subject; there is only a slight pressure gradient between aortic and radial vessels. Posture-related hydrostatic increases of pressure are shared equally between arteries and veins, so that perfusion pressure is little affected. Although MAP is

largely the same throughout the arterial tree, waveform contours differ with the caliber of the arterial vessel in question. Peak systolic pressure actually rises in the periphery because of wave reflection. When a vessel is totally occluded by a monitoring catheter, wave reflection may amplify pressure fluctuations to produce sharp spikes of systolic arterial pressure, usually easy to suspect from tracing distortion (Fig. 2-1). The ability of any specific gradient between arterial and venous pressures to perfuse tissue depends directly on the resistance of the vascular bed. An MAP of 65 mm Hg may produce relatively luxuriant flow through dilated vascular beds, whereas an MAP of 100 mm Hg may be inadequate during accelerated hypertension.

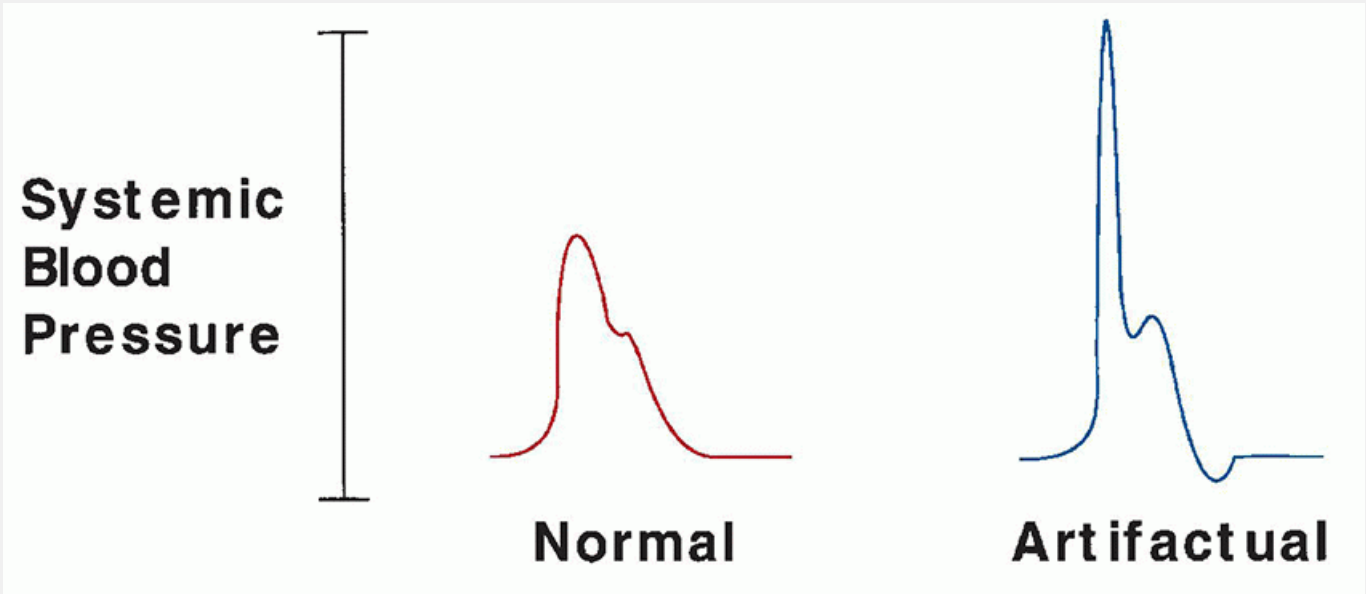

FIGURE 2-1. Artifactual elevation of systolic arterial pressure. An underdamped arterial pressure tracing amplified by reflection within an occluded artery may exaggerate the systolic pressure as well as any mean pressure computed from the raw "systolic" and diastolic pressure values.

Depending on the shape of the arterial pressure waveform, the peak systolic (P_S) and nadir diastolic (P_D)

pressures contribute to varying degrees to MAP. At normal heart rates (60 to 100 beats/min), MAP ≈ P_D + 1/3 (P_S - P_D). Because its duration is generally longer, the diastolic pressure is the most important contributor to MAP. During tachycardia, P_S contributes relatively more, and during bradycardia, P_S contributes relatively less. The arterial pressure waveform changes its contour as well as its precise systolic, diastolic, and (to a lesser extent) mean values, depending on where the arterial system is accessed (Fig. 2-2).

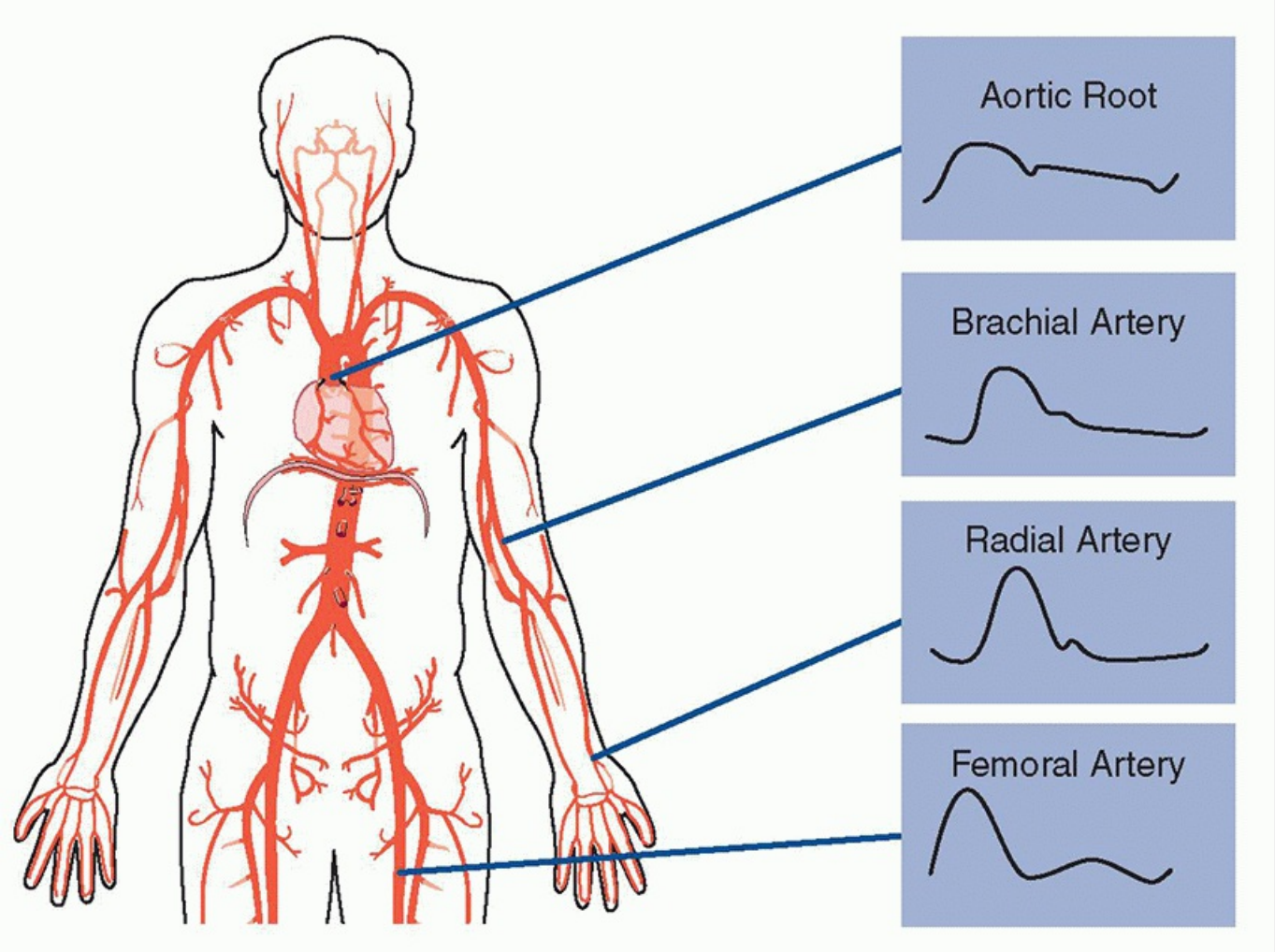

FIGURE 2-2. Site-specific contours of the arterial pressure waveform. Note that mean arterial pressure is highest at the aortic root.

Arterial Waveform Analysis for Cardiac Output Estimation

It is important to remember that pressure imperfectly indexes flow: unlike pressure, flow is approximately continuous—not pulsatile—and depends on vascular resistance. However, though not appropriate for patients with irregular rhythms and shock states, monitoring devices that analyze the shape of the arterial pressure waveform do a creditable job during sinus rhythm of tracking and trending the CO. Their value is seriously compromised by atrial

fibrillation and other chaotic arrhythmias. Although imperfect, analytics of the pressure tracing can yield important information regarding variations in arterial flow as well as the pressure driving it through the circulation. Moreover, it affords an opportunity to evaluate stroke volume variation (SVV), a parameter that may be used in conjunction with pulse pressure variation (PPV) to indicate tone in the large arteries: pulse pressure variation (%) = 100 × [PPmax - PPmin]/[(PPmax + PPmin)/2]. A similar equation defines SVV: SV variation (%) = 100 × [SVmax - SVmin]/[(SVmax + SVmin)/2]. PPV/SVV changes in proportion to vascular

elastance.

Simplified Functional Hemodynamic Monitoring

Useful classification of hemodynamic compromise can be attempted using a few simple bedside observations that determine MAP and reflect stroke volume. The arterial pressure waveform is central to such an analysis, in that, it provides the MAP and the SVV during passive respiration that reflects intravascular volume (Fig. 2-3). A greater than 12% change of PP with passive respiration suggests the need for additional preload. PPV (%) = 100 × [PPmax - PPmin]/[PPmax + PPmin/2]. It must be borne in mind, however, that arrhythmias, active breathing, and small tidal volume excursions negate the value of PPV. With this proviso, combining an evaluation of MAP and variation of PP can yield an insight into the type of therapy indicated. A low MAP combined with a low stroke volume (as indicated by wide PPV) strongly suggests hypovolemia, hemorrhage, heart failure, or tamponade. A low MAP combined with negligible PPV is more compatible with sepsis. The responses of these indices to a reversible volume challenge intervention (such as lifting the legs with the upper torso horizontal) can also help to identify the appropriate therapeutic approach (see Passive Leg Raising, below).

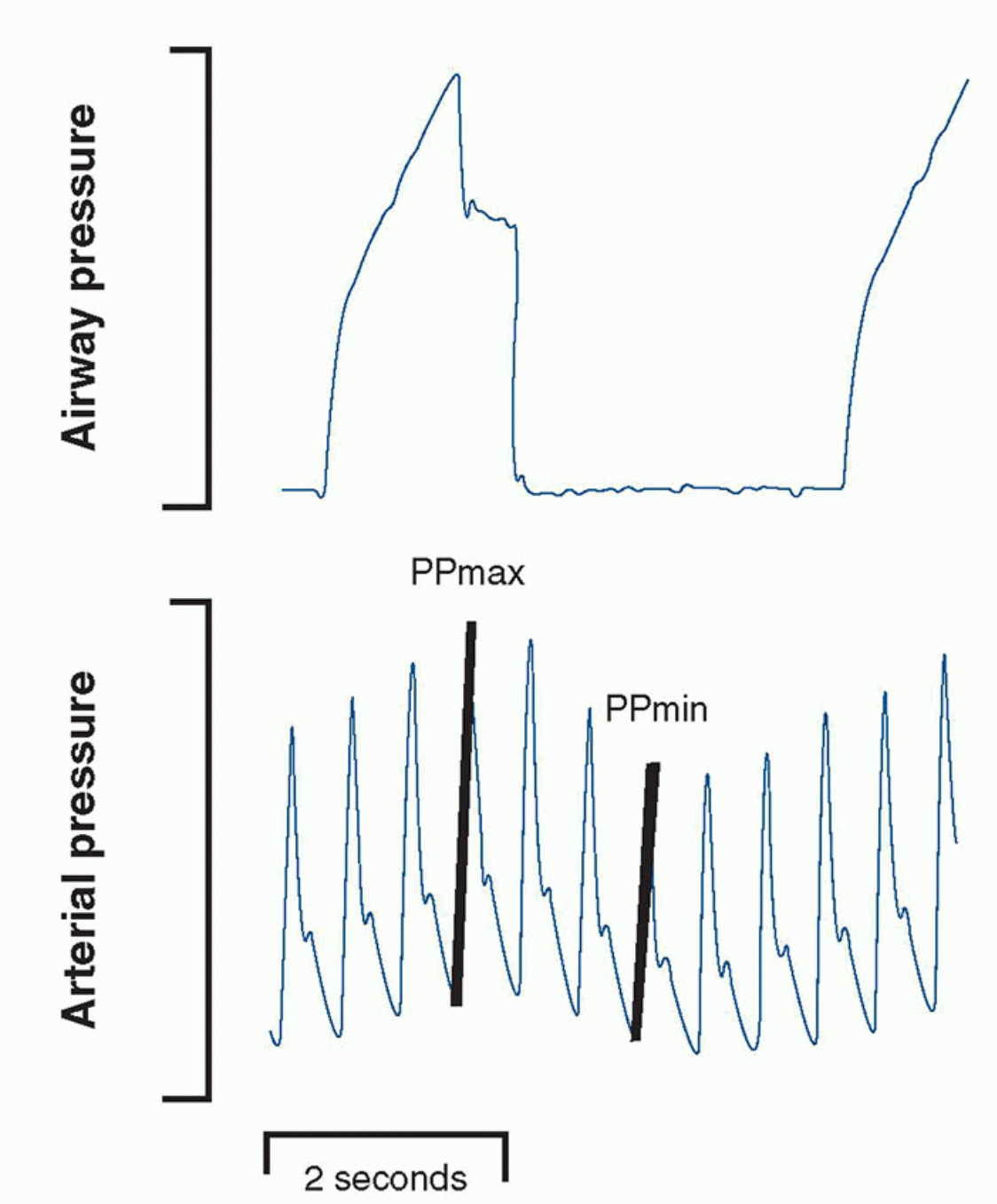

FIGURE 2-3. Changes in pulse pressure variation with respiration in a passively ventilated subject. The relatively large difference in pulse pressure during different phases of the ventilation cycle suggests relative underfilling of the vasculature.

Invasive Arterial Pressure Monitoring

Indications

The decision to initiate invasive arterial monitoring must be undertaken cautiously. Many critically ill patients can be adequately monitored by intermittent sphygmomanometry (manual or automated) in combination with the physical examination. However, patients with hemodynamic instability or shock, malignant hypertension, or failure to oxygenate are most likely to benefit from arterial cannulation. A well-adjusted catheter system provides accurate pressure information necessary for hemodynamic monitoring and facilitates blood sampling.

Although convenient and usually reliable, indwelling arterial catheters occasionally give misleading information—especially when the radial artery has been cannulated for an extended time. Errors are most likely to arise in patients who are elderly, are hypotensive, or have underlying vascular disease. Attempts should be made at least once daily to confirm the line pressure by sphygmomanometry. This is especially important in patients receiving vasoactive drugs regulated by radial line pressures. Consideration should be given to measuring femoral pressure when the cuff-derived value and clinical impression disagree seriously with the recorded value.

Complications

Serious complications can arise because of local hemorrhage, infection, and thrombosis. For this reason, the radial artery of the nondominant arm

should be used whenever possible. Although common, regional thrombosis of the radial artery seldom results in tissue-damaging ischemia; digital embolization is the greater hazard. Large catheter size, low CO, preexisting arteriopathy, absence of collateral ulnar perfusion, vasopressors, and small wrist circumference increase the risk. (Normal artery caliber tends to parallel the wrist size.)

The Allen test is performed by raising the wrist well above the heart level and compressing the radial and ulnar arteries simultaneously for 10 seconds, blanching the capillary bed. When the ulnar artery is then released, flushing should occur within a few seconds. Not all patients in shock can be tested in this fashion, as sluggish flow may falsely suggest a high risk when none exists. Conversely, although a positive Allen test is reassuring, it does not preclude the development of ischemic damage following radial artery thrombosis. A 20-gauge Teflon catheter is preferred for arterial measurements and sampling because it facilitates insertion, minimizes the risk of thrombosis, and promotes adequate dynamic frequency response. Larger catheters occlude the vessel, creating standing waves, whereas smaller-gauge catheters tend to kink or clot off. Rarely, the arterial catheter may erode the vessel wall to cause aneurysm, localized hematoma, compressive neuropathy, or arteriovenous fistula. Although local colonization is very common, serious soft tissue infections are rare during percutaneous cannulation if the puncture site is kept

sterile, the catheter is used for only a few days, and precautions are taken during blood sampling to preserve sterility. Femoral catheters and “cutdowns” are more likely to become infected. The radial artery is not an appropriate site for injection of any drug. Intra-arterial injections of certain drugs, particularly calcium channel blockers and vasopressors, can cause ischemic necrosis of the hand, a functionally devastating injury. Prolonged, high-pressure flushing can potentially drive clot or gas bubbles retrograde, with risk of (rarely) producing cerebral embolism.

DATA FROM VASCULAR CATHETERS

Concern for the performance or stability of the cardiorespiratory system helps define the need for intensive care. Reliable data relevant to the heart and vasculature are instrumental in diagnosing problems, in selecting and regulating therapy, and in timing interventions. Yet, interpreting the complex relationships among vascular pressures and flows is often complicated by spontaneous fluctuations in metabolism and by variations of the respiratory pressures that influence them. Relatively few clinicians become expert in data interpretation. Balloon flotation pulmonary artery (PA) catheters have been relegated to a secondary status with the recognition that echocardiography (ECHO), noninvasive CO monitoring (e.g., arterial waveform analyzers), and information from CVP catheters—conventional and specially modified—suffice for most purposes. Yet, the PA catheter provides data of clinical value that cannot be obtained otherwise (e.g., pulmonary venous [wedge] pressure and true mixed venous oxygen saturation). Moreover, because the PA catheter incorporates the CVP and requires similar insertion principles, it serves as an appropriate focal point for discussion.

Inserting the Balloon Flotation Catheter

Although detailed descriptions and video demonstrations of insertion technique for the balloon flotation catheter are available elsewhere, a few points are worth emphasizing here. In patients with bleeding disorders, the physician should select a site conducive to applying direct pressure. As opposed to the subclavian and femoral sites, the internal jugular approach tends to be the simplest and least fraught with complications. The right side provides more direct and reliable access to the superior vena cava (SVC) than the left, but either approach can be used effectively. For puncture of the internal jugular or subclavian veins, insertion must be accomplished with the patient supine or even in the Trendelenburg position to ensure vessel distention and minimize the risk of air embolism. In a dyspneic patient with orthopnea, this may require prior sedation and endotracheal intubation. If intubation is not an option and noninvasive ventilation is ineffective in relieving orthopnea, the femoral or brachial approach should be considered.

Difficult Insertion and Placement

Problems that occur during placement are generally of two types: (1) difficulty entering the central veins of the thorax and (2) difficulty directing the catheter tip into the PA. Both types of problem can be mastered only by gaining sufficient direct experience. With regard to central vein entry, placement of the

introducer/sheath assembly is the crucial step. The internal jugular vein lies superficial and lateral to the carotid artery. Ultrasonic imaging with a purpose-designed instrument is a valuable aid in locating the vein, monitoring the puncture, and avoiding complications. Ultrasound can also be used to quickly scan the lungs after puncture attempts to assure the absence of pneumothorax. The stab incision made to facilitate the puncture must be sufficient to allow relatively easy passage of the vein dilator. Although catheter insertion must be gentle and never forced, dilator insertion may require traction of loose skin and subcutaneous tissues, especially in obese